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TRANSITION METAL- AND ORGANO-CATALYZED CYCLOREDUCTIONS, CYCLOADDITIONS AND CYCLOISOMERIZATIONS

COMMITTEE:

Supervisor Michael J. Krische

Eric V. Anslyn

John C. Gilbert

David A. Vandenbout

Kevin N. Dalby

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by

Ana Liza Luis, B.S.; M. A.

Dissertation

Presented to the Faculty of the Graduate School
of The University of Texas at Austin
in Partial Fullfillment
of the Requirements
for the Degree of

Doctor of Philosophy

The University of Texas at Austin
December, 2005

Dedication

To my parents, Hipolito Luis Pena and Carolina Trevino de Luis, whose love and encouragement have made this possible.

TRANSITION METAL- AND ORGANO-CATALYZED CYCLOREDUCTIONS, CYCLOADDITIONS AND CYCLOISOMERIZATIONS

Publication No. _____

Ana Liza Luis, PhD
The University of Texas at Austin, 2005

Supervisor: Michael J. Krische

The catalytic activation of enones in C-C bond forming processes represents a promising alternative to the prefabrication of chemically labile enols and enolates. Through the use of a (diketonato)cobalt/silane catalyst system, we have devised highly diastereoselective aldol and Michael cycloreductions (J. Am. Chem. Soc. 2001, 123, 5112). Modulation of the catalyst system has enabled the first intramolecular metal-catalyzed alkene [2+2]cycloaddition (J. Am. Chem. Soc. 2001, 123, 6716). Finally, the concept of catalytic nucleophilic enone activation embodied by the Morita-Baylis-Hillman and Rauhut Currier reactions has been utilized to develop an organic catalyst system for the cycloisomerization of bis-enones, i.e. an intramolecular Rauhut Currier reaction (J. Am. Chem. Soc. 2002, 124, 2402). Notably, this protocol allowed for the selective "crossed" cyclization of unsymmetrical bis-enone substrates.

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Chapter 1. Enones as Latent Enolates in Catalysis: Catalytic Enolate Generation and Subsequent Trapping in Formal Aldol and Michael Reactions

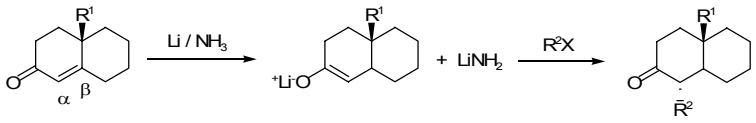
Enolates are among the most broadly utilized reactive intermediates employed in C-C bond formation. As versatile intermediates for the formation of α-substituted carbonyl compounds, they are frequently utilized for the synthesis of complex molecules. Their generation plays a crucial role in numerous classical transformations, including the aldol and Michael reactions.[1,2] Because of their importance in synthetic organic chemistry, it is essential to fully address the issues of selectivity posed by the generation and employment of enolate nucleophiles.

Catalytic processes employing enolate intermediates should use unmodified reactants (carbonyl compounds) and yield products exemplifying control of both relative and absolute stereochemistry. As a requisite for this ideal, reactants having more than one set of acidic hydrogens should be subject to chemo- and regioselective deprotonation. In recent years, there have been considerable advances in the direct catalytic asymmetric aldol[3] and Michael[4] condensation of unmodified ketone and aldehyde partners. Still, these attempts fail to address the issue of regioselective enolate formation and therefore require symmetric ketone partners, ketones possessing a single acidic site or the use of hydroxy-directing groups.[4,3f] It is through the use of enol derivatives that the diastereo- and enantioselectivity issues of catalytic aldol and Michael reactions are more adequately addressed.[1,2] However, improved selectivities come at the expense of preforming the often chemically labile enol derivatives, and regioselectivity is again an issue when preparing enol derivatives from unsymmetrical ketone precursors.

In 1961, Stork established the use of enones as a promising alternative to the prefabrication of chemically labile enols and enolates.[5] This was demonstrated via tandem dissolving metal reduction-enolate alkylation of α,β-unsaturated ketones (Scheme 1.1).

Regiospecific enolate formation was achieved for an unsymmetrical ketone due to the position of the olefin determining the site of enolate formation.

Scheme 1.1



These studies revealed nucleophilic activation of enones via conjugate reduction to be an effective means of controlling regiochemistry in enolate-mediated C-C bond formations. However, the development of selective catalytic systems for nucleophilic activation of enones, which are suited for a diverse group of electrophilic partners, lingers as an unresolved challenge.

Catalytic methods for the regiospecific generation of enolate nucleophiles may be grouped into three categories: nucleophilic activation of enones *via* conjugate reduction, i.e. catalytic hydrometalation, nucleophilic activation *via* conjugate addition, i.e. catalytic carbometalation, and nucleophilic activation *via* reversible conjugate addition, i.e. nucleophilic organocatalysis. Subsequent trapping of the newly formed enolate intermediates leads to the formation of a new α C-C bond. The goal of Chapter I is to review catalytic reactions which involve *i*. the nucleophilic activation of α,β-unsaturated carbonyl compounds via hydrometalation, carbometalation and/or organocatalysis, and *ii*. the capture of enolate intermediates with aldehydes or ketones in aldol reactions and activated olefins in Michael reactions.

Part 1. Nucleophilic Activation of Enones *via* Hydrometalation

Catalytic 1,4-hydrometalation of enones provides a reliable and efficient method for regioselective formation of metalloenolates. Many catalytic systems involving enone conjugate reductions to afford enol derivatives have been described.[6,7,8,9] These include Rh(I)-, Pt(0)-, Ni(II)-, and Cu(I)-catalyst systems. The catalytic reduction of enones by these systems has been achieved using silanes, stannanes and alanes as terminal reductants. Much attention has been given to the development of catalytic systems effecting both enolate formation and subsequent reaction with carbon electrophiles (couplings).[10] Although α,β-unsaturated carbonyl compounds have been somewhat explored as electrophiles, almost all enone conjugate reduction-electrophilic trapping sequences involve the use of aldehydes and ketones as electrophiles. Chapter 1. Part 1. is organized *i*. with respect to the electrophilic partner and *ii*. with respect to the terminal reductant.

I. Reductive Aldol Reaction

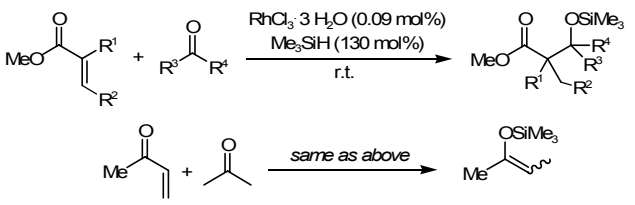
Catalytic transformations involving enone-aldehyde coupling, or "reductive aldol" reactions, have been extensively studied. Several transition metal complexes serve as effective catalysts for this tandem process and have employed silanes and elemental hydrogen as terminal reductants.

A. Organosilanes as Terminal Reductants

Based on precedented 1,4-hydrosilylations catalyzed by rhodium and palladium, the earliest transition metal catalyzed reductive aldol reactions also involve complexes of these metals. It was in 1987 that the first reductive aldol reaction, which employed a Rh(III) precatalyst, was reported by Revis and Hilty (Scheme 1-1.1).[11] The coupling of methyl methacrylate, acetone and trimethylsilane carried out with a catalytic amount of $RhCl_3 \cdot 3H_2O$ gave the expected aldol product in 95% yield. Both ketones and aldehydes proved viable electrophilic partners for this transformation. The reductive aldol condensation of methyl

crotonate and acetone proceeded smoothly, whereas methyl acrylate resulted in a diminished yield of aldol product. In the case of methyl vinyl ketone, the major product was the silyl enol ether, not the expected reductive aldol adduct.

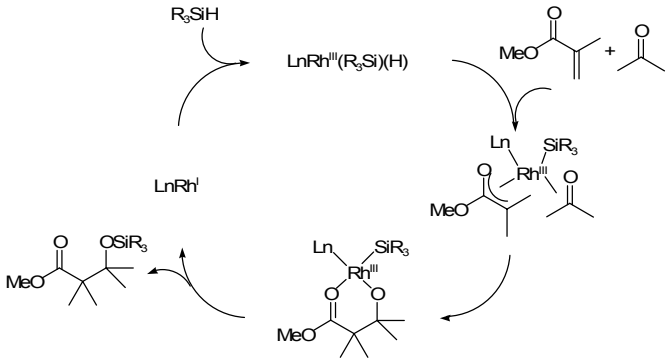
Scheme 1-1.1



Entry	R^1	R^2	R^3	R^4	Yield (%)
1	Me	H	Me	Me	95
2	Me	H	Me	Et	91
3	Me	H	Me	H	78
4	Me	H	Me	OEt	0
1	H	Me	Me	Me	89
2	H	H	Me	Me	24

Although highly speculative, the catalytic cycle is presumed to start with the oxidative addition of the silane to give a hydrido-rhodium species (Scheme 1-1.2). Hydrometalation of the enone affords a Rh^{III}-enolate intermediate, which complexes and undergoes addition to the carbonyl compound giving a Rh^{III}-alkoxide. Oxygen-silicon reductive elimination affords the aldol product in the form of the silyl ether and regenerates the rhodium(I) active catalyst. A possible mechanistic alternative involves oxygen-silicon reductive elimination at the stage of the Rh^{III}-enolate followed by aldol condensation of the resulting silyl enol ether.

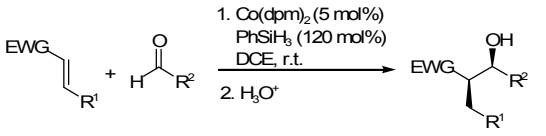
Scheme 1-1.2



A $Co(dpm)_2$-phenylsilane catalyst system was also found to successfully promote the intermolecular reductive aldol reaction (Scheme 1-1.3).[12] α,β-Unsaturated amides coupled with aromatic and aliphatic aldehydes giving the desired β-hydroxy amides in good to excellent yields with moderate diastereoselectivities. However, reactions of α,β-unsaturated

esters and nitriles afforded the corresponding aldol adducts as equimolar mixtures of *syn*/*anti* isomers.

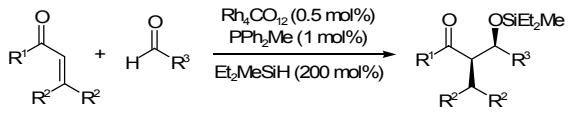
Scheme 1-1.3



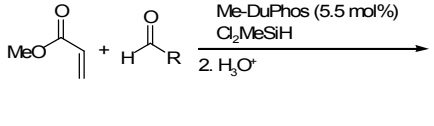
Entry	EWG	R_1	R_2	Yield (%)	*syn*:*anti*
1	$CONMe_2$	H	Ph	95	80:20
2	$CONMe_2$	H	$(CH_2)_2Ph$	90	70:30
3	$CONMe_2$	Me	Ph	72	70:30
4	COOMe	H	CH=CHPh	80	50:50
5	CN	H	Ph	93	50:50

Subsequently, work by the groups of Matsuda and Morken improved on the diastereoselectivity of this rhodium-catalyzed reductive aldol reaction (Scheme 1-1.4).[13] Reactions of enones with aromatic and aliphatic aldehydes utilizing a $Rh_4CO_{12}/PPh_2Me/Et_2PhSiH$ catalyst system gave aldol products as silyl enol ethers in good yields and diastereoselectivities. In all cases, the *syn* isomer was favored. The reaction catalyzed by $[Rh(COD)Cl_2]_2$/Me-DuPhos/Cl_2MeSiH was also highly *syn*-selective but provided diminished yields of aldol adducts.

Scheme 1-1.4



Entry	R^1	R^2	R^3	Yield (%)	*syn*:*anti*
1	Me	H	Ph	99	83:17
2	Me	H	Hex	80	68:32
3	Et	H	Ph	100	84:16
4	Et	H	Hex	45	74:26
5	Me	Me	Ph	86	80:20

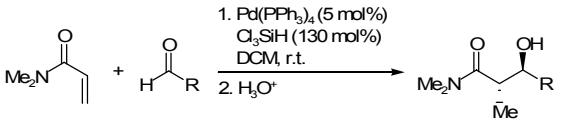


Entry	R	Yield (%)	*syn*:*anti*
1	Ph	69	23:1
2	*t*-Bu	38	21:1
3	*i*-Pr	15	15:1
4	CH=CHPh	41	>20:1

In 1998, Kiyooka et al. reported a palladium-catalyzed reductive coupling of *N*,*N*-dimethylacrylamide with a variety of aromatic aldehydes (Scheme 1-1.5).[14] Interestingly, *anti*-selectivity was observed for the reaction. The coupling of acrylic esters with aromatic aldehydes under the same reaction conditions resulted in low yields of product with normal *syn*-selectivity. On the basis of the *anti*-selectivity observed, the authors suggest the mechanism differs from that most likely operating in the Rh-catalyzed reductive aldol

reaction. They speculate that after hydrometalation of the enone, Pd-enolates may undergo reductive elimination to give trichlorosilyl enol intermediates, which undergo aldol reaction.

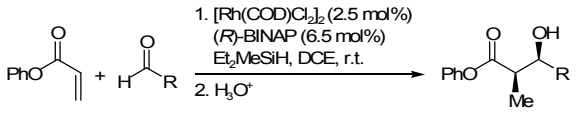
Scheme 1-1.5



Entry	R	Yield (%)	*syn*:*anti*
1	Ph	87	32:68
2	1-Nap	78	24:76
3	2-Nap	93	30:70
4	*p*-MePh	72	31:69
5	*p*-NO_2Ph	68	28:72
6	*p*-ClPh	75	36:64

The successful development of diastereoselective reductive couplings led to advances in the asymmetric variant of the reductive aldol reaction. Morken et al. reported the first diastereoselective and enantioselective catalytic reductive coupling reaction in 2000 (Scheme 1-1.6).[15] Good to excellent levels of enantioselectivity were achieved for couplings of acrylate esters, aromatic or aliphatic aldehydes and diethylmethylsilane using a complex derived from $[Rh(COD)Cl]_2$ and (*R*)-BINAP. A decrease in both diastereomeric and *syn*-enantiomeric ratios was observed with an increase in substrate size.

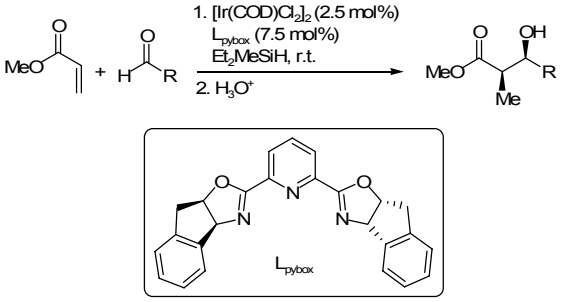
Scheme 1-1.6



Entry	R	Yield (%)	*syn*:*anti*	*ee syn* (*anti*)
1	Ph	72	3.4:1	87 (34)
2	Et	59	5.1:1	88 (7)
3	*c*-Hex	54	3.9:1	84 (48)
4	*t*-Bu	48	1.8:1	45 (>99)
5	1-Nap	82	3.8:1	80 (13)

A subsequent publication reported remarkable enantioselectivity by the use of $[Ir(COD)Cl]_2$, an aminoindanol-derived indanepybox ligand (L_{pybox}) and Et_2MeSiH, albeit with limited substrate scope (Scheme 1-1.7).[16] The reaction proceeded smoothly with aromatic aldehydes. However, aliphatic aldehydes required oxygenation at the α-position to participate in the reaction. A detailed discussion concerning the mechanism was not given. However, the authors did suggest that oxidative addition of silane followed by reductive elimination of Si-Cl may generate an iridium hydride active catalyst, based on the observation that many iridium salts exhibit similar reactivity.[17]

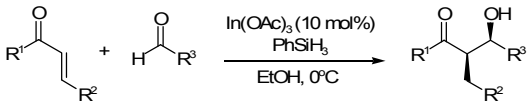
Scheme 1-1.7



Entry	R	Yield (%)	*syn*:*anti*	*er* (*syn*)
1	Ph	68	6.6:1	97:3
2	CH_2OBn	49	9.9:1	98:2
3	CH_2OTBS	47	8.2:1	98:2
4	Et	<5	-	-
5	$(CH_2)_2OBn$	65	2.7:1	91:9

Recently in 2004, an $In(OAc)_3$-catalyzed coupling reaction of α,β-unsaturated compounds, aldehydes and $PhSiH_3$ was reported by Hosomi and co-workers (Scheme 1-1.8).[18] The reductive aldol reaction of phenyl enones and aromatic aldehydes proceeded in high yield and *syn*-diastereoselectivity. The use of aliphatic aldehydes resulted in diminished yields and *syn*-selectivities. Aliphatic enones also participated in the reductive coupling to give the desired aldol products in moderate yields. With respect to the mechanism, Hosomi speculates that transmetalation between $In(OAc)_3$ and $PhSiH_3$ forms the indium hydride species which hydrometalates the enone.

Scheme 1-1.8

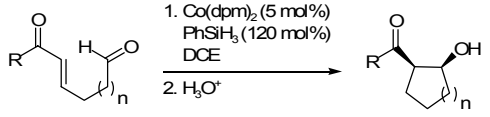


Entry	R^1	R^2	R^3	Yield (%)	*syn*:*anti*
1	Ph	Me	1-Np	83	92:8
2	Ph	Me	*n*-C_7H_{15}	66	77:23
3	Ph	Me	*c*-Hex	37	72:28
4	Ph	H	1-Np	92	92:8
5	Me	H	1-Np	47	88:12

Transition metal catalyzed intramolecular reductive aldol reactions, or aldol cycloreductions, were unknown until recently. Predicated on the work of Mukaiyama[12], our research group developed the first aldol cycloreduction in 2002 (Scheme 1-1.9).[19] Synthesis of both five- and six-membered aldol cycloadducts was possible utilizing the $Co(dpm)_2/PhSiH_3$ catalyst system. Whereas diastereoselectivity is problematic for the intermolecular Co-catalyzed process, exceptionally high *syn*-selectivity (>95:5) was observed for this intramolecular variant. Aromatic enone-aldehyde substrates underwent cyclization

much more efficiently than aliphatic enone-aldehydes. A seven-membered aldol cycloadduct was also formed, albeit in low yield.

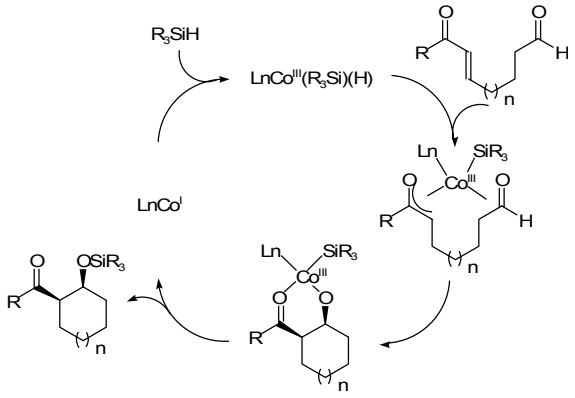
Scheme 1-1.9



Entry	n	R	Yield (%)	*syn:anti*
1	1	Ph	70	>95:5
2	2	Ph	87	>95:5
3	2	Me	38	>95:5
4	3	Ph	35	>95:5

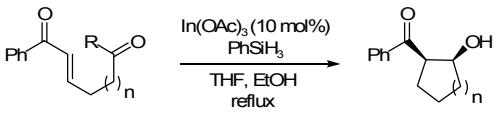
A Co(I)-Co(III) catalytic cycle is envisioned for this transformation (Scheme 1-1.10). Oxidative addition of silane to LnCo(I) followed by hydrometalation of the enone affords a Co(III)-enolate. Addition to the appendant aldehyde provides a Co(III)-alkoxide, which undergoes oxygen-silicon reductive elimination to give the aldol product as a silyl ether and regenerate LnCo(I). The proposed mechanism is similar to that commonly accepted for alkene hydrosilylation, the Chalk-Harrod process.[20]

Scheme 1-1.10



In the same report describing the In-catalyzed intermolecular reductive aldol reaction[19], Hosomi et al. disclosed that $In(OAc)_3$ also efficiently catalyzes the cyclization of aromatic enone-aldehyde and enone-ketone substrates (Scheme 1-1.11). Excellent levels of diastereoselectivity were obtained for six-membered ring products while only moderate diastereoselectivity was observed in the case of five-membered adducts.

Scheme 1-1.11



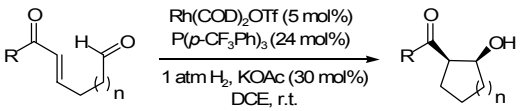
Entry	n	R	Yield (%)	*cis*:*trans*
1	2	H	77	>99:1
2	1	Me	85	62:38
3	2	Me	90	>99:1

B. Elemental Hydrogen as Terminal Reductant

Although the 1,4-reduction of enones under hydrogenative conditions is well known,[21] the hydrogen-mediated reductive generation of enolates is not. Additionally, reductive C-C bond formations under hydrogenative conditions have only been achieved for processes involving migratory insertion of carbon monoxide, such as alkene hydroformylation[22] and the Fischer-Tropsch reaction[23]. The advantage of using hydrogen gas as a terminal reductant for the generation of transition metal enolates is apparent. Such reactions would represent a mild and atom economical means of enolate generation, avoiding the formation of stoichiometric byproducts.

Recently, our research group reported a rhodium-catalyzed enone conjugate reduction protocol using elemental hydrogen as the terminal reductant.[24] The rhodium-enolates generated were trapped by aldehydes inter- and intramolecularly in reductive aldol and aldol cycloreduction reactions, respectively. Cationic $Rh(COD)_2OTf$ was used in conjunction with substoichiometric quantities of potassium acetate (mild base) for both processes. For the aldol cycloreduction, aromatic, heteroaromatic and aliphatic enone-aldehyde substrates afforded five- and six-membered ring aldol products in moderate to good yields with negligible quantities of conjugate reduction adducts (Scheme 1-1.12). *Syn*-diastereoselectivities were observed for this intramolecular process except in the case of an aliphatic enone-aldehyde substrate (entry 6).

Scheme 1-1.12

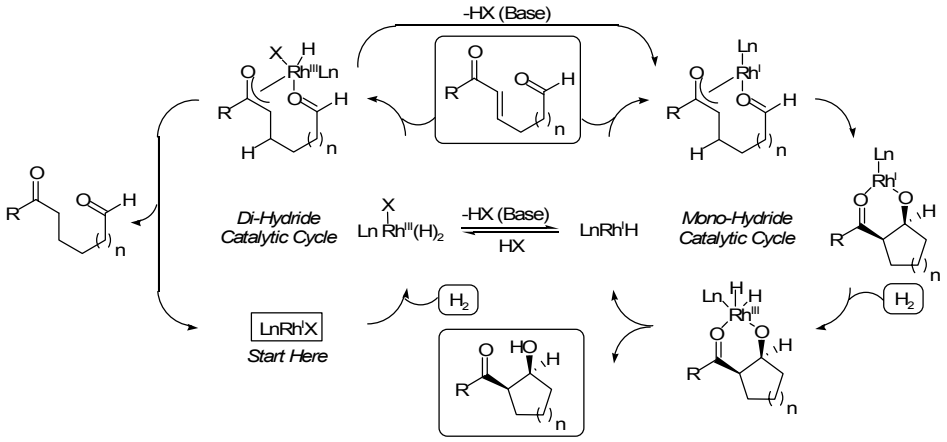


Entry	n	R	Yield (%)	*syn*:*anti*
1[a]	2	Ph	57	14:1
2	2	Ph	89	10:1
3	1	Ph	71	24:1
4	2	2-furyl	70	6:1
5	2	*p*-MeOPh	74	5:1
6	2	Me	65	1:5

[a] Reaction ran without any basic additive. A 22% yield of 1,4-reduction product was also formed.

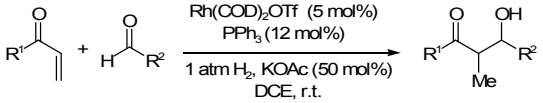
For this transformation, at least two distinct mechanistic pathways potentially operate (Scheme 1-1.13). Whereas neutral rhodium(I)-complexes such as Wilkinson's catalyst induce homolytic hydrogen activation,[25] the use of cationic rhodium(I)-complexes in conjunction with basic additives is thought to promote heterolytic activation pathways.[26] Monohydride mediated hydrometalation generates a Rh^{I}-enolate that does not contain hydride ligands. In this way, direct enolate-hydrogen reductive elimination leading to undesired 1,4-reduction products is disabled and capture of the Rh^{I}-enolate by the appendant aldehyde is facilitated giving a Rh^{I}-enolate species. Hydrogen oxidative addition followed by oxygen-hydrogen reductive elimination affords the aldol product and regenerates the cationic Rh(I) catalyst.

Scheme 1-1.13



In principle, Rh^{I}-enolates may *i*. engage in aldolization or *ii*. hydrogenolytically cleave via oxidative addition of hydrogen followed by reductive elimination. Intermolecular capture of this Rh^{I}-enolate should suffer due to competitive conventional hydrogenation. In practice, only a modest excess of enone was needed to compensate for such 1,4-reduction manifolds (Scheme 1-1.14). Phenyl vinyl ketone reacted with aromatic and heteroaromatic aldehydes giving good yields of the aldol product, albeit with poor diastereoselectivity. The use of aliphatic aldehydes resulted in diminished yields. Methyl vinyl ketone was also a viable nucleophilic partner in the reductive aldol reaction, whereas ethyl acrylate exclusively provided products of 1,4-reduction.

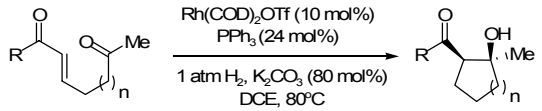
Scheme 1-1.14



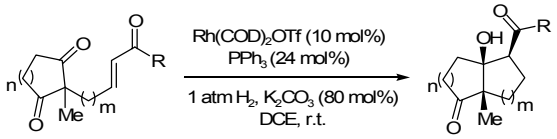
Entry	R^1	R^2	Yield (%)	*syn*:*anti*
1	Ph	*p*-NO_2Ph	92	1.8:1
2	Ph	*p*-MeOPh	75	1.7:1
3	Ph	2-furyl	88	2.5:1
4	Ph	*n*-C_3H_7	44	2:1
5	Me	*p*-NO_2Ph	70	2:1
6	OEt	*p*-NO_2Ph	0	-

A subsequent publication involved a challenging variation, the use of ketones as electrophilic partners in aldol cycloreductions (Scheme 1-1.15).[27] Exposure of aromatic enone-ketone substrates to catalytic hydrogenation resulted in formation of five- and six-membered ring aldol products in good yield with excellent *syn*-diastereoselectivity. The formation of cycloreduction products was accompanied by significant quantities of the corresponding conjugate reduction adducts (8-24%). It was reasoned that conjugate reduction pathways should be suppressed for reactions utilizing more reactive ketone electrophiles. As expected, catalytic hydrogenation of enone-1,3-dione substrates gave the corresponding bicyclic aldol adducts in >95:5 *de*. With the exception of a substrate which formed a strained *cis*-decalone ring system (entry 6), conjugate reduction products were not formed. Diones are more reactive electrophilic partners due to inductive effects and relief of dipole-dipole interactions.

Scheme 1-1.15



Entry	n	R	Aldol (%)	1,4-reduction (%)
1	1	Ph	75	8
2	2	Ph	72	20
3	1	2-furyl	70	24
4	2	2-furyl	83	8
5	1	3-indole	74	8
6	2	3-indole	72	17



Entry	n	m	R	Yield (%)
1	1	1	Ph	84
2	1	1	Me	88
3	1	2	Ph	86
4	2	1	Ph	81
5	2	1	Me	73
6	2	2	Ph	65 (15)[a]

[a] Yield of conjugate reduction adduct.

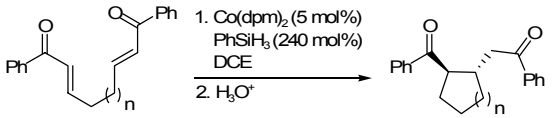
II. Reductive Michael Reaction

Despite the vast research conducted on aldol and Michael reactions, catalytic reductive Michael reactions, whether inter- or intramolecular, were unknown until recently.

A. Organosilanes as Terminal Reductants

In 2002, the first reductive Michael condensation was developed by our research group (Scheme 1-1.16).[19] The reaction is catalyzed by a $Co(dpm)_2$-phenylsilane catalyst system and may be viewed as a reductive diene cyclization. This methodology is applicable to the synthesis of both five- and six-membered ring products and exhibits exceptionally high *anti*-diastereoselectivity. A catalytic cycle analogous to the proposed aldol cycloreduction mechanism is believed to be in effect.

Scheme 1-1.16

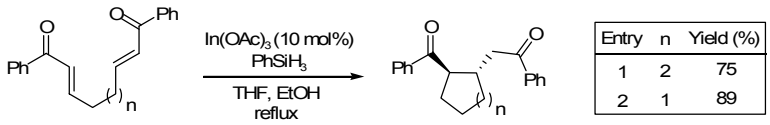


Entry	n	Yield (%)	*anti*:*syn*
1	2	73	>95:5
2	1	62	>95:5

Subsequently, Hosomi et al. disclosed that $In(OAc)_3$ is also an efficient catalyst for the Michael cycloreduction of aromatic bis-enone substrates (Scheme 1-1.17).[18] Good yields of both five- and six-membered ring products with complete *trans*-selectivity were obtained.

With regards to the mechanism, as previously mentioned, Hosomi merely comments on a possible transmetalation between $In(OAc)_3$ and $PhSiH_3$ to form the indium hydride species responsible for hydrometalation of the enone.

Scheme 1-1.17



Entry	n	Yield (%)
1	2	75
2	1	89

III. Conclusion

Catalytic 1,4-hydrometalation of enones provides an efficient means for regioselective formation of metal enolates. Tandem conjugate reduction-enolate trapping with aldehydes/ketones and α,β-unsaturated carbonyl compounds gives rise to reductive aldol and Michael reactions, respectively. A significant advantage of such reductive processes lies in that stoichiometric preformation of metal enolates or silyl enol ethers is circumvented. Despite their unquestionable efficacy, investigations aimed at the development of such reactions have not been many.

Reports on reductive aldol reactions employing organosilanes are scarce, yet it is apparent that a variety of late transition metals may be used. While high yields are often realized for the intermolecular variant, diastereo- and enantioselection remain challenging for most catalyst systems and mechanistic details are not clear. The highly enantioselective protocol using an iridium-pybox catalyst system exhibits only moderate diastereoselectivity and a highly limited substrate scope. Exceptionally high diastereoselection is observed for both aldol and Michael cycloreductions originally developed by our group, but no efforts have been made toward an asymmetric variant.

Only recently was the regioselective catalytic generation of enolates under hydrogenation conditions described by our research group, leading to completely atom economical catalytic reductive aldol processes. Intermolecular couplings result in low

diastereoselection, while high yields and diastereoselectivities are observed for the catalytic aldol cycloreduction. Enantioselective variants and analogous Michael processes have yet to be developed.

Part 2. Nucleophilic Activation *via* Carbometalation

Conjugate addition reactions of carbon nucleophiles to α,β-unsaturated compounds are among the most widely used methods for C-C bond formation in organic synthesis.[28] Catalytic enone 1,4-carbometalation provides a reliable and efficient method for regioselective formation of metalloenolates embodying a new β carbon-carbon bond. Electrophilic capture of these enolate intermediates installs a new α carbon-carbon bond resulting in an overall vicinal difunctionalization of enones. The functionalization of α,β-unsaturated carbonyls by conjugate addition-aldol/Michael sequences is a central transformation in organic synthesis. Systems effecting these transformations include Cu(I)-, Rh(I)-, and Ni(II)-catalyst systems. Catalytic enone conjugate additions by these systems have been achieved using grignard, organozirconium, organozinc, organoboronic acid, organoboronate and organotitanium pronucleophiles. As the key steps in the synthesis of many biologically active compounds including steroids, prostaglandins and terpenes, the development of efficient catalytic enantioselective variants has been an important challenge. Due to the large number of reactions in this field, the following review will cover select examples for each metal-organometallic reagent system focusing on recent developments. Chapter 1. Part 2. is organized *i*. with respect to the electrophilic partner, *ii*. with respect to the metal catalyst and *iii*. with respect to the pronucleophilic organometallic reagent employed.

I. Tandem Conjugate Addition-Aldol Reaction

A. Copper Catalysis

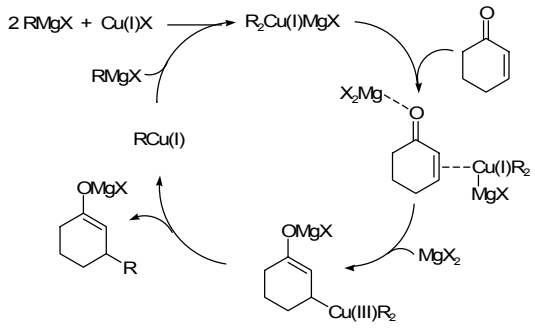
More than half a century after Kharasch and Tawney's initial discovery,[29] organocopper reagents are still one of the most useful synthetic reagents among transition metal organometallics.[30] Copper-catalyzed conjugate addition chemistry was dominated by magnesium-based systems until the mid 1980s, but now routinely utilizes much milder

organometallic reagents such as organozinc and zirconium reagents as well. Organocopper-generated enolates can be trapped by a variety of aldehydes in a directed-aldol fashion to give β-hydroxylated products. This process appears to be one of the most reliable of the conjugate addition-enolate trapping reactions: a range of organocopper reagents can be employed, only *C*-enolate trapping is observed and good yields are obtained.

1. Grignard Pronucleophiles

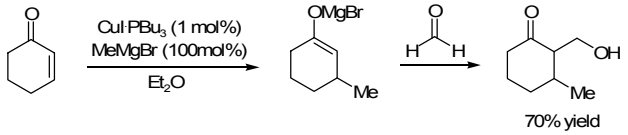
The first copper-catalyzed conjugate addition was reported by Kharash in 1941 and employed Grignard reagents. Conjugate addition by these reagents was once suggested to take place through direct 1,2-addition of R-Cu across the C-C double bond.[31] Theoretical studies on related Gilman alkylations have shown that the 1,2-addition occurs through a "trap-and-bite" mechanism. A simplified catalytic cycle is depicted in Scheme 1-2.1. π-Complexation of the enone followed by oxidative addition affords a β-cuprio(III) enolate intermediate. Reductive elimination installs a new C-C bond at the β-position of the enone substrate and regenerates the alkylcopper(I) species.

Scheme 1-2.1



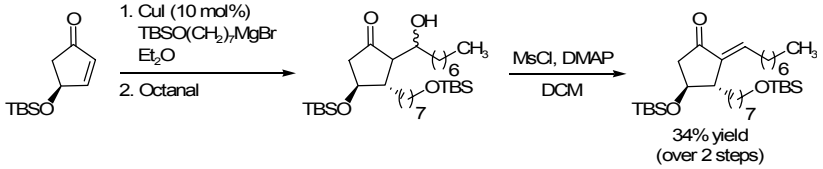
The first example of a catalytic tandem conjugate reduction-aldol sequence was reported in 1974 (Scheme 1-2.2).[32] Employing Grignard reagents and a copper(I) catalyst, the enolate generated from cyclohexenone was trapped with formaldehyde giving 2-hydroxymethyl-3-methylcyclohexanone in 70% yield as a mixture of stereoisomers.

Scheme 1-2.2



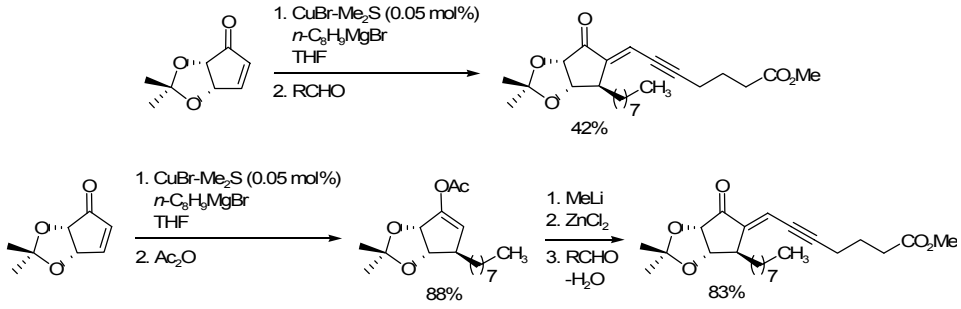
Noyori's three component coupling protocol has emerged as the most efficient synthesis of cyclopentenone prostanoids.[33] Conjugate addition-aldol sequences have developed in parallel with three-component coupling synthesis of prostaglandins. Employing this approach by means of a Grignard and copper(I) iodide, Evans successfully trapped the resulting magnesium enolate intermediate directly with octanal (Scheme 1-2.3).[34]

Scheme 1-2.3



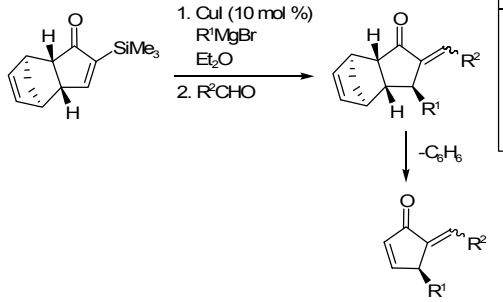
Indirect approaches involving enol acetates, though not as practical, are sometimes more effective. In a report targeting the synthesis of prostanoid intermediates, Johnson demonstrated this by comparing a direct conjugate addition-aldol sequence with one involving the generation of enol acetate intermediates (Scheme 1-2.4).[35] The most promising procedure was found to be that involving trapping of the initial enolates as enol acetates and regeneration of enolates with methyllithium, followed by aldol and dehydration reactions.

Scheme 1-2.4



Evans employed a variation of the three-component coupling protocol for the construction of cross conjugated cyclopentenones (Scheme 1-2.5).[36] The synthesis was achieved in two steps via a one-pot conjugate addition-Peterson olefination sequence using *exo*-2-trimethylsilyl-3a,4,7,7a-tetrahydro-4,7-methanoinden-1-one, followed by a *retro*-Diels Alder. The 1,4-addition of a variety of alkyl organometallics, including sterically hindered *iso*-propylmagnesium chloride and vinylmagnesium bromide, proceeded smoothly and the corresponding magnesium enolates reacted efficiently with aromatic as well as aliphatic aldehydes. The conjugate addition was highly diastereoselective with addition occurring from the less hindered face of the enone.

Scheme 1-2.5



Entry	R^1	R^2	Yield (%)	*E*:*Z*
1	*i*-Pr	Ph	81	58:42
2	vinyl	Ph	94	93:7
3	vinyl	*i*-Pr	88	52:48
4	Me	*i*-Pr	83	30:70
5	*n*-Oct	$CO_2Me(CH_2)_5$	57	35:65

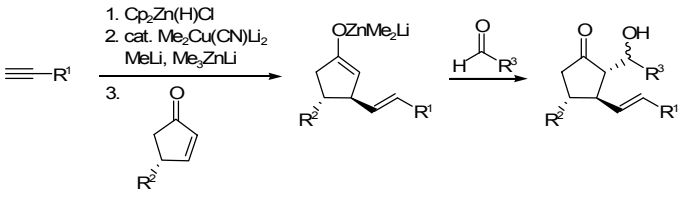
2. Organozirconium Pronucleophiles

Alkenes and alkynes are easily hydrometalated with Schwartz' reagent ($Cp_2Zr(H)Cl$).[37] The resulting alkyl- and alkenylzirconocenes readily participate in copper-catalyzed conjugate additions. Considerable steric crowding around zirconium decreases the nucleophilicity of zirconocenes. Transmetalation to more reactive copper derivatives has greatly facilitated the use of these reagents as carbanion equivalents.[38]

In 1994, Lipshutz designed a one-pot three-component coupling for the synthesis of prostanoids involving conjugate addition of *E*-vinylic zirconocenes, derived from hydrozirconation of alkynes *in situ*, to cyclopentenones followed by enolate trapping with

aldehydes (Scheme 1-2.6).[39] A variety of alkynes readily participate, including heavily oxygenated ones. Good yields are obtained, albeit with poor diastereoselectivity.

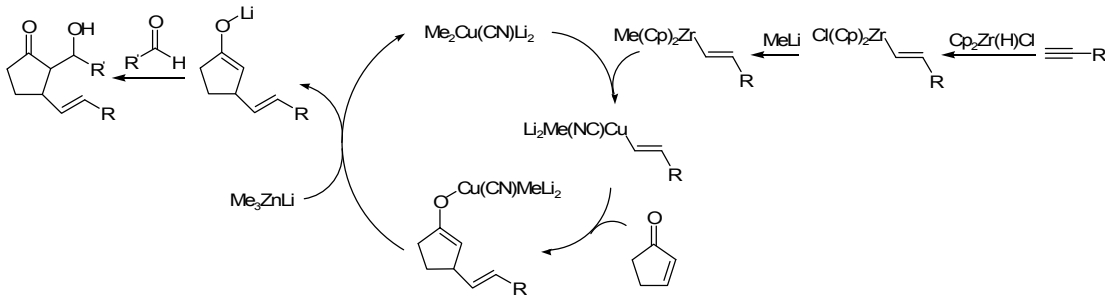
Scheme 1-2.6



Entry	Alkyne	Enone	Aldehyde	Yield (%)
1	OTIPS	O	O, H	80
2	OTIPS	"	O, H, CO_2Me	74
3	n-C_5H_{11}, BnO	"	"	75
4	n-C_4H_9, OTMS, Me	O, TBSO	O, H, 5, CO_2Me	79
5	n-C_5H_{11}, MEMO	"	"	83

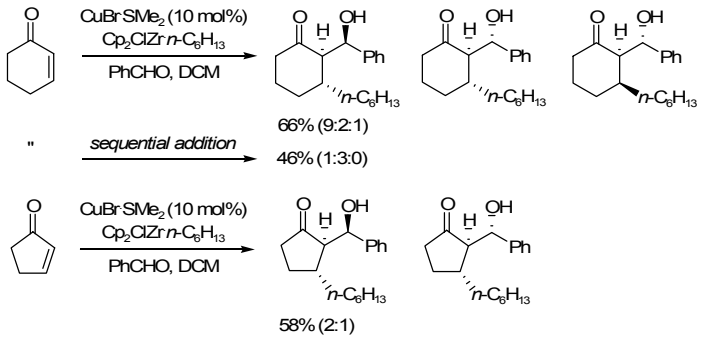
The mechanism involves a transmetalation–1,4-addition–transmetalation–aldol sequence (Scheme 1-2.7). Hydrozirconation of the alkyne with Schwartz' reagent,[40] followed by reaction with MeLi produces the methyl *E*-vinylzirconium reagent. Subsequent transmetalation with the higher-order cuprate $Me_2Cu(CN)Li_2$ and conjugate addition to cyclopentanone gives a copper enolate intermediate. Me_3ZnLi regenerates the higher-order cuprate catalyst, by donating a methyl group to copper, and affords a lithium enolate intermediate. Finally, addition of this enolate to an aldehyde yields the aldol product.

Scheme 1-2.7



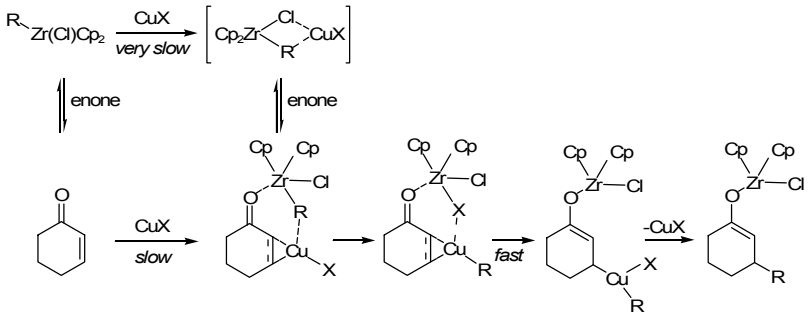
In the same year, Wipf et al. utilized alkylzirconocenes to effect copper-catalyzed tandem conjugate addition-enolate trapping reactions with aldehydes (Scheme 1-2.8).[41] The one-pot coupling of cyclohexenone, *n*-hexylzirconocene and benzaldehyde at 22ºC proceeded smoothly with an overall *syn* selectivity of 3:1, a ratio consistent with observations of Yamamoto[42] and Panek[43] on zirconium-mediated aldol reactions. For the coupling reaction in which benzaldehyde was added at -78ºC following conjugate addition, the selectivity inverts to favor the *anti* aldol product in a 3:1 ratio. Lower yield and selectivity was observed for the vicinal difunctionalization of cyclopentenone.

Scheme 1-2.8



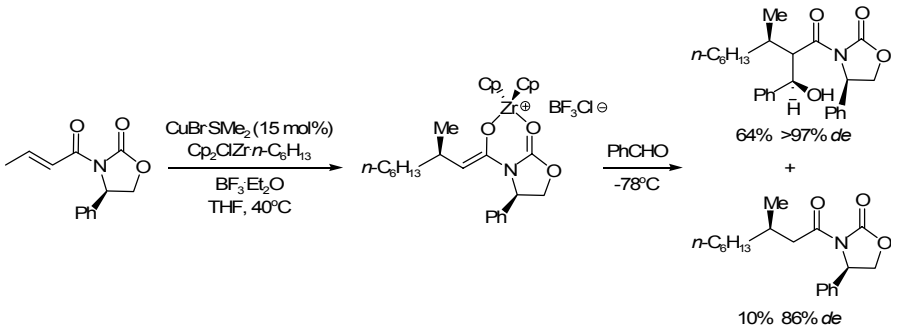
An NMR analysis of the reaction of $CuBr{\cdot}SMe_2$ with *n*-hexylzirconocene did not detect evidence for the intermediate formation of an alkylcopper species. Having discarded a zirconium-copper transmetalation, Wipf proposed the following mechanism for the copper-catalyzed conjugate addition mediated by alkylzirconium (Scheme 1-2.9). Complexation of the enone carbonyl group to zirconium facilitates complexation to copper(I) and transmetalation of the alkyl substituent. The resulting copper(III) intermediate undergoes reductive elimination regenerating the copper(I) catalyst to give the zirconium enolate intermediate. It is unclear if transmetalation precedes or follows the formation of the copper(III) species.

Scheme 1-2.9



In a subsequent report, Wipf disclosed the first enantioselective copper-catalyzed 1,4-addition of alkylzirconocenes to α,β-unsaturated *N*-acyl oxazolidinones (Scheme 1-2.10).[44] The phenylglycine-derived oxazolidinone chiral auxiliary provides the highest diastereoselectivities. Conjugate addition-enolate trapping with benzaldehyde installs three consecutive chiral centers in very high (>97%) diastereoselectivity. The use of the hard Lewis acid $BF_3{\cdot}Et_2O$ is needed to attain good yields.

Scheme 1-2.10

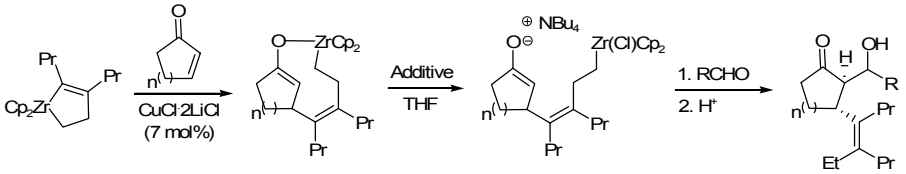


3. Zirconocyclopentene Pronucleophiles

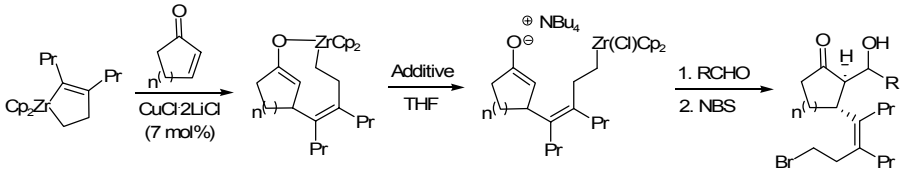
Zirconocyclopentenes are bifunctional species that may be viewed as organometallic reagents possessing vinyl and alkyl nucleophilic substituents, making electrophilic trapping at each carbon-zirconium bond possible. These reagents can be easily prepared by the reaction of diethylzirconocene, generated *in situ* by treatment of Cp_2ZrCl_2 with ethylmagnesium halide or ethyllithium, with the desired alkyne.[45] As an alternative to the preparation of $Cp_2Zr(H)Cl$ for hydrozirconation of alkynes[46], Lipshutz reported the use of

zirconocyclopentenes in one-pot copper-catalyzed conjugate addition-aldol and conjugate addition-aldol-halogenation sequences (Scheme 1-2.11).[47] The zirconocyclopentene reagent effects β-vinylation of the enone substrate. The resulting enolate species reacts chemoselectively at the α-carbon upon aldehyde addition; the aldol reaction occurs without affecting the C_{sp^3}-$ZrCp_2Cl$ bond. This last nucleophilic site is *i*. quenched with a proton during aqueous workup (Eq. 1) and *ii*. trapped with a halide (Eq. 2). Note that converting the zirconium enolate in Eq. 1 to the "naked" enolate via addition of *n*-Bu_4NCl greatly accelerates the rate of aldehyde addition.

Scheme 1-2.11



Entry	n	Additive	R	Time (h)	Yield (%)
1	2	none	Ph	17	63
2	2	*n*-Bu_4NCl	Ph	1.5	78
2	1	*n*-Bu_4NCl	Ph	2	77
2	1	*n*-Bu_4NCl	*n*-C_5H_{11}	3	84

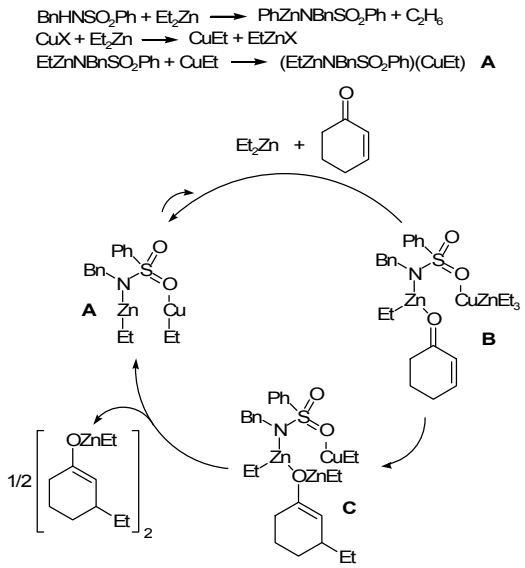


4. Organozinc Pronucleophiles

Organozinc reagents are inert to a wide variety of functional groups, including α,β-unsaturated ketones. Transmetalation to a more reactive copper species has made organozinc-mediated conjugate additions possible. The mechanism of this transformation is still arguable and the nature of the transition state for the conjugate addition step is unclear. In order to gain insight into the catalytic cycle, Noyori and Kitamura conducted kinetic and NMR studies on the reaction of Et_2Zn and cyclohexenone catalyzed by a mixture of CuCN and *N*-benzylsulfonamide.[48] Studies revealed first-order kinetics in enone, Et_2Zn and

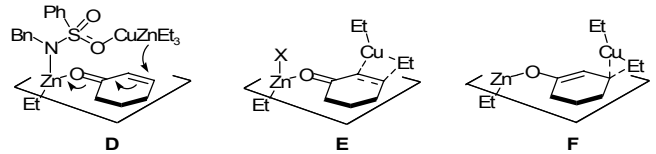
catalytic complex **A**. NMR and molecular weight measurement analysis determined the product to be a dimeric *O*-bound zinc enolate. However, no useful information was obtained of the structures corresponding to the true catalyst and reactive intermediates. A mechanism based on experimental observations is illustrated in Scheme 1-2.12. Intermediates **A**-**C** represent only the chemical essentials of the actual species that would constitute more complex structures.

Scheme 1-2.12



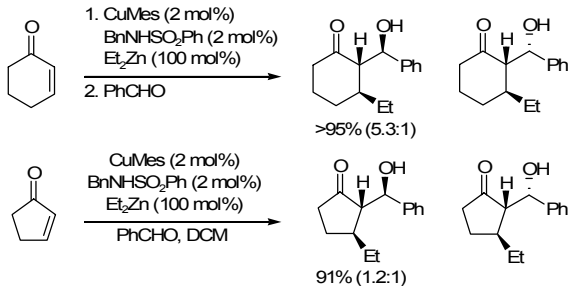
In a subsequent report, Kitamura presented evidence which indicates the ethyl transfer onto the β-carbon occurs in a concerted manner via transition state **D**, not via carbocupration (**E**) nor reductive elimination (**F**) (Scheme 1-2.13). Observed $^{12}C/^{13}C$ isotope effects at all three enone sp^2 carbons are in agreement with the concerted mechanism via **D**, although the transferring atom could is not identified.

Scheme 1-2.13



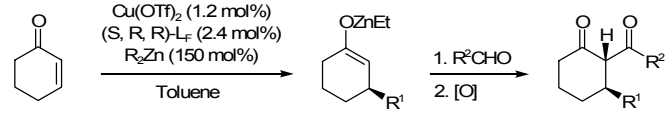
In 1996, Noyori published the first copper-catalyzed conjugate-addition aldol sequence employing diorganozinc reagents (Scheme 1-2.14).[49] The zinc enolate generated from cyclohexenone and Et_2Zn in the presence of a catalytic mixture of CuMes and *N*-benzylbenzenesulfonamide readily undergoes aldol reaction upon addition of benzaldehyde. The cyclopentenone enolate behaves differently. Under the same reaction conditions a low 28% yield of the aldol adduct is obtained due to homo-condensation of the enolate. Vicinal difunctionalization is only successful when benzaldehyde is added at the start of the reaction. Additionally, *anti*-selectivity is much lower than for the cyclohexanone reaction.

Scheme 1-2.14

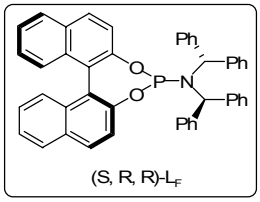


Enantioselective conjugate addition has become truly useful through the use of dialkyl zinc, a cationic copper catalyst and a chiral ligand.[50] Phosphorus(III) ligands are considered to be among the best soft ligands for copper(I) and a large number of complexes have been described.[51] The catalytic enantioselective conjugate additions using phosphoramidites as chiral ligands represent a great advancement.[52] The first highly enantioselective catalytic 1,4-additions of R_2Zn reagents using copper complexes based on these novel chiral ligands were reported in 1997 (Scheme 1-2.15).[50a] The zinc enolate generated from conjugate addition to cyclohexenone was trapped by aromatic, vinylic and aliphatic aldehydes in subsequent aldol reactions (in the presence or absence of Lewis acids). The aldol products obtained were oxidized to a single isomer of the corresponding diketones with *ee*'s exceeding 90%.

Scheme 1-2.15

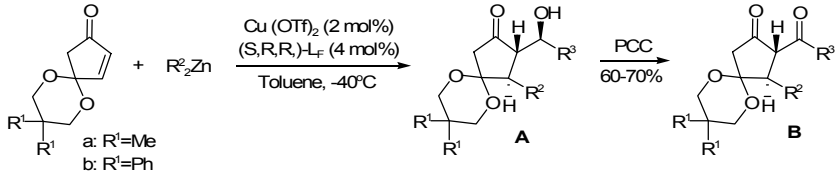


Entry	Lewis acid	R^1	R^2	Yield (%)	*ee* (%)
1	-	Et	Ph	88	95
2	-	Et	*m*-BrPh	85	93
3	BF_3Et_2O	Et	*m*-BrPh	78	92
4	$ZnCl_2Et_2O$	Et	Et	88	91
5	-	Et	vinyl	92	95
6	$ZnCl_2Et_2O$	Me	Ph	64	91
7	-	Me	Ph	67	91
8	$ZnCl_2Et_2O$	Me	Et	81	97



In 2000, Feringa reported an enantioselective tandem conjugate addition-aldol reaction of dialkylzinc reagents to cyclopentene-3,5-dione monoacetals (Scheme 1-2.16).[53] The conjugate addition was highly enantioselective and great stereocontrol was observed for the subsequent aldol reaction with >95:5 diastereomeric ratios. This tandem reaction served as the key step in the total synthesis of (-)-PGE_1 methyl ester.

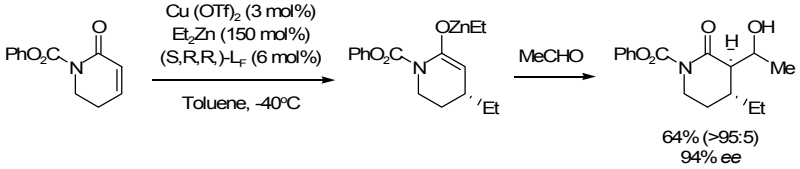
Scheme 1-2.16



Entry	enone	R^2	R^3	Yield **A** (%)	*ee* **B** (%)
1	a	Et	Ph	67	87
2	a	*n*-Bu	Ph	64	87
3	b	Et	Ph	76	94
4	b	*n*-Bu	Ph	69	94
5	b	Et	*p*-BrPh	69	96
6	b	*n*-Bu	*p*-BrPh	64	97
7	b	$(CH_2)_4CO_2Me$	$SiMe_2Ph$	64	

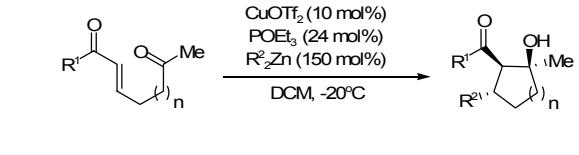
Next, Feringa extended the scope of this enantioselective catalytic conjugate addition-aldol reaction to include α,β-unsaturated lactams as Michael acceptors (Scheme 1-2.17).[54] The intermediate zinc enolate was trapped with acetaldehyde giving a mixture of aldol products with 94% *ee*.

Scheme 1-2.17

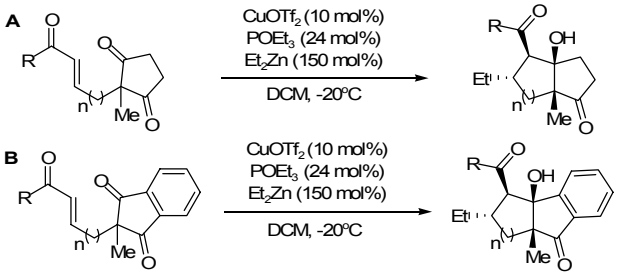


In 2004, our research group reported the first use of ketones as electrophilic traps in copper-catalyzed 1,4-addition of diorganozinc reagents (Scheme 1-2.18).[55] The conjugate addition-aldol cyclizations proceeded with a variety of dialkylzincs. In general, enone-ketone and enone-diketone substrates exhibited *syn*-selectivity, with phenyl enone substrates yielding *syn* aldol adducts exclusively and methyl enone substrates leading to a diastereomeric ratio of products.

Scheme 1-2.18



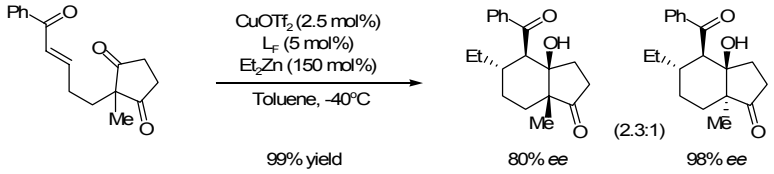
Entry	n	R^1	R^2	Yield (%)	*dr*
1	1	Ph	Me	83	>95:5
2	1	Ph	Et	81	>95:5
3	1	Ph	*n*-Bu	91	>95:5
4	1	Me	Et	77	3:1
5	2	Ph	Et	98	>95:5
6	2	Me	Et	96	2.2:1



Entry	n	R	Yield (%)	*dr*
1**A**	1	Ph	99	>95:5
2**A**	1	Me	96	2:1
3**A**	2	Ph	99	10:1
4**B**	1	Ph	84	8:1
5**B**	2	Me	78	3:1
6**B**	2	Ph	94	>95:5

Although diastereoselectivity was low, the tandem reaction of a ketone-1,3-dione substrate in the presence of Feringa's ligand L_F proceeded with excellent yield and good to excellent enantioselectivity (Scheme 1-2.19).

Scheme 1-2.19

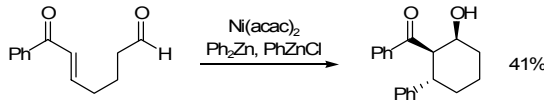


B. Nickel Catalysis

1. Organozinc Pronucleophiles

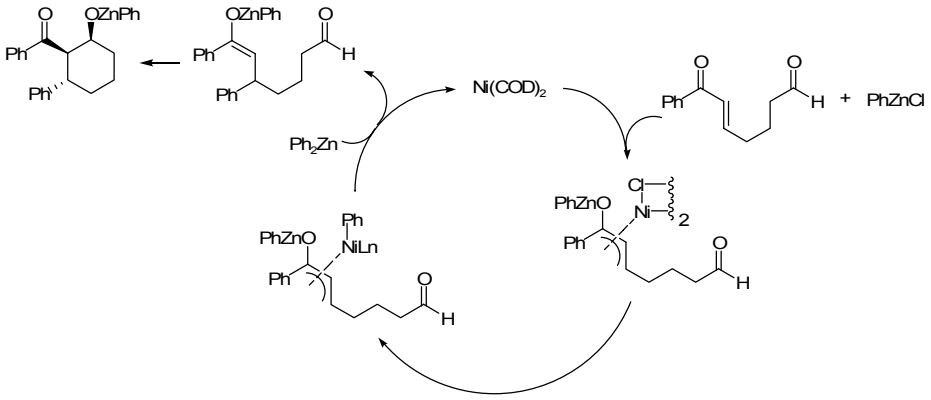
In 1997, Montgomery reported that sp^2-hybridized organozincs such as diphenylzinc undergo conjugate addition to enones with tethered unsaturation (Scheme 1-2.20).[56] Tandem conjugate addition-aldol cyclization of an enone-aldehyde substrate occurred upon exposure to $Ni(COD)_2$, Ph_2Zn and PhZnCl. The use of sp^3-hybridized organozincs led to products derived from reductive cyclizations.

Scheme 1-2.20



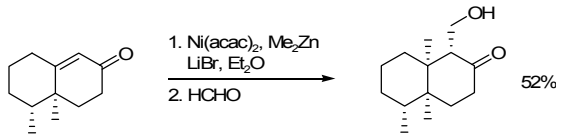
While recognizing that the mechanistic issues associated with these transformations are highly speculative, the author proposed the following mechanism based on experimental observations (Scheme 1-2.21). Oxidative addition of the low-valent nickel catalyst to the organozinc-activated enone affords a nickel π-allyl complex. Ni-Zn transmetalation followed by reductive elimination regenerates the Ni(0) catalyst and affords a zinc enolate, which cyclizes to the aldol product.

Scheme 1-2.21



Recently, this tandem vicinal difunctionalization procedure was employed in an intramolecular sense toward the synthesis of (-)-nakamurol A, an enantiomer of the marine sponge diterpenoid nakumurol-A (Scheme 1-2.22).[57] The process was completely stereoselective giving a single diastereomer of the desired aldol adduct.

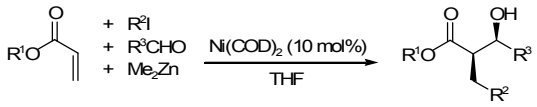
Scheme 1-2.22



2. Aryl Iodide Pronucleophiles

Recently, Montgomery disclosed a novel nickel-catalyzed process allowing the coupling of aryl iodides, acrylates and aldehydes mediated by dimethylzinc (Scheme 1-2.23).[58] This method involves the direct introduction of a haloaromatic, avoiding the requirement of preparing sensitive, metalated organometallic nucleophiles. The scope was broad with respect to aryl iodide and aldehyde, and included acetone as an electrophilic trap. Good yields and diastereoselectivities were observed in all cases, with the exception of suppressed diastereoselectivity in the case of a tertiary aldehyde (*t*-BuCHO).

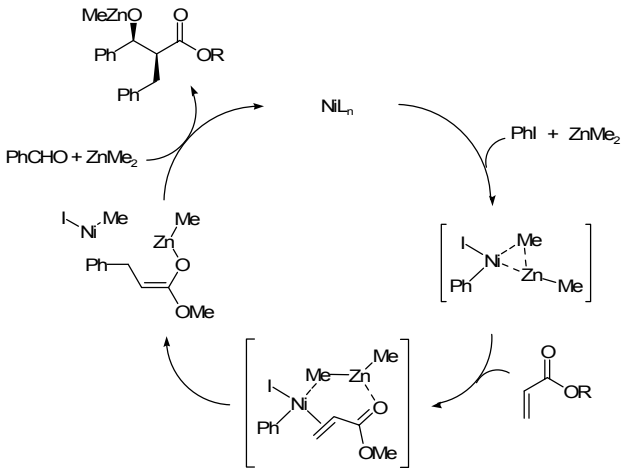
Scheme 1-2.23



Entry	R^1	R^2	R^3	Yield (%)	*dr*
1	*t*-Bu	Ph	Ph	88	86:14
2	Me	Ph	Ph	76	89:11
3	*t*-Bu	Ph	*p*-OMePh	73	82:18
4	*t*-Bu	Ph	2-furyl	76	84:16
5	*t*-Bu	Ph	Et	75	85:15
6	*t*-Bu	Ph	*i*-Pr	78	88:12
7	*t*-Bu	Ph	*t*-Bu	71	66:34
8	*t*-Bu	Ph	acetone	54	-
8	*t*-Bu	1-Naphthyl	Ph	71	87:13
9	*t*-Bu	*p*-MePh	Ph	79	88:12
10	*t*-Bu	*m*-CO_2EtPh	Ph	54	87:13
11	*t*-Bu	3-(CH_2OTBS)Ph	Ph	73	88:12

Montgomery concluded that arylzincs are not reactive intermediates produced in the reaction of dimethylzinc and aryliodides under nickel catalysis (Scheme 1-2.24). He proposed a catalytic cycle in which the organozinc's function is to activate the catalyst and enone through a Lewis acid/base interaction and reduce the Ni(II) species back to the Ni(0) active catalyst.

Scheme 1-2.24

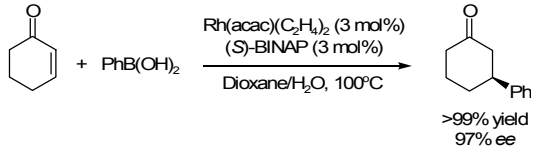


C. Rhodium Catalysis

1. Organoboronic Acid and Organoborane Pronucleophiles

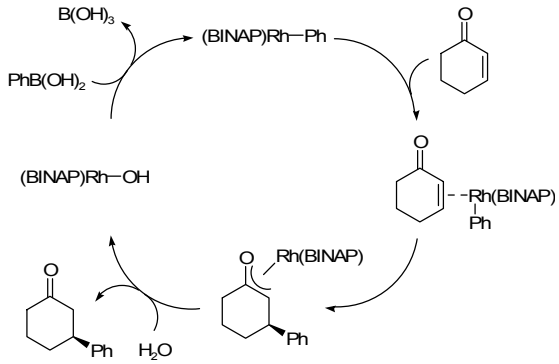
The first Rh(I)-catalyzed conjugate addition of readily available 1-aryl- or 1-alkenylboronic acids to enones was reported by Miyaura in 1997.[59] An asymmetric variant to this methodology reported by Hayashi proceeded with high enantioselectivity in the presence of a chiral BINAP-rhodium catalyst (Scheme 1-2.25).[60] The combination of $Rh(acac)(C_2H_4)_2$ and (*S*)-BINAP was identified as highly effective for the enantioselective conjugate addition of aryl- and alkenylboronic acids to enones.

Scheme 1-2.25



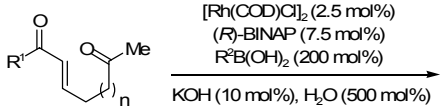
All intermediates and transformations pertaining to the Rh-catalyzed asymmetric 1,4-addition reaction were observed through NMR studies of the actual catalyst system.[61] The catalytic cycle clearly involves *i*. transmetalation of the phenyl group from boron to rhodium giving a phenyl-rhodium complex, *ii*. insertion of the enone into the phenyl-rhodium bond forming a oxa-π-allylrhodium intermediate, and *iii*. hydrolysis of the oxa-π-allylrhodium species with water giving the conjugate addition product and regenerating the hydroxorhodium catalyst (Scheme 1-2.26).

Scheme 1-2.26



One major drawback of this catalyst system is that the newly formed Rh-enolates are hydrolyzed under the reaction conditions, precluding their use in further transformations. The realization of conjugate addition-enolate trapping sequences requires that capture of rhodium-enolates by the chosen electrophile be much faster than enolate protonation. In 2003, our research group successfully trapped these rhodium-enolates generated via conjugate addition of arylboronic acids (Scheme 1-2.27).[62] This was accomplished in the context of conjugate addition-aldol cyclizations by conducting reactions with a minimal amount of water (5 equivalents with respect to substrate). Five- and six-membered ring products from aromatic and aliphatic enone-ketone substrates were formed in good yields with high levels of relative and absolute stereochemical control. Highest yields were achieved when reactions were performed using KOH as an additive.

Scheme 1-2.27

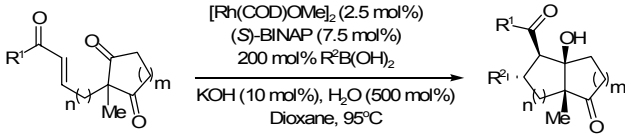


Entry	n	R^1	R^2	Yield (%)	*ee* (%)
1	1	Ph	Ph	78	77
2	1	Ph	Ph	88	88
3	1	Me	Ph	88	94
4	2	Me	Ph	69	95
5[a]	2	Ph	Nap	40	-
6[a]	2	Me	Nap	70	-

[a] Reaction using racemic dppb ligand (7.5 mol%).

Next, symmetrical 1,3-diones were employed as electrophilic traps in the rhodium-catalyzed asymmetric conjugate addition-aldol cyclization (Scheme 1-2.28).[63] The rhodium enolates generated from enone-dione substrates successfully differentiated between the four diastereotopic π-faces of tethered diones. Products embodying four contiguous stereocenters, including two adjacent quaternary centers, were formed with quantitative diastereoselection and high enantioselectivities. In order to achieve good yields, the methoxy-bridged rhodium dimer $[Rh(COD)(OMe)]_2$ was used.

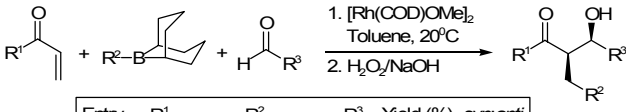
Scheme 1-2.28



Entry	n	m	R	R^2	Yield (%)	*dr*	*ee* (%)
1	1	1	Me	*p*-OMePh	83	>99:1	90
2	1	1	Me	Ph	87	>99:1	90
3	1	1	Ph	Ph	94	>99:1	87
4	1	1	Me	Br	88	>99:1	94
5	1	2	Me	*p*-OMePh	97	>99:1	90
6	1	2	Me	Ph	87	>99:1	91
7	1	2	Ph	Ph	86	>99:1	85
8	1	2	Me	*p*-BrPh	77	>99:1	92
9	2	1	Me	Ph	82	>99:1	85
10	2	1	Me	*p*-OMePh	80	>99:1	88
11	2	1	Me	*p*-BrPh	85	>99:1	86
12	2	2	Me	Ph	65	>99:1	88

Another means of achieving rhodium-catalyzed conjugate addition-enolate trapping sequences involves the use of nonaqueous reaction conditions. Using this approach, Hayashi developed highly selective tandem conjugate addition-aldol reactions using *B*-aryl- and *B*-alkenyl-9BBN reagents and $[Rh(OMe)(COD)]_2$ (Scheme 1-2.29).[64] High yields and *syn* selectivities are observed for a variety of aliphatic and aromatic enones and aldehydes.

Scheme 1-2.29

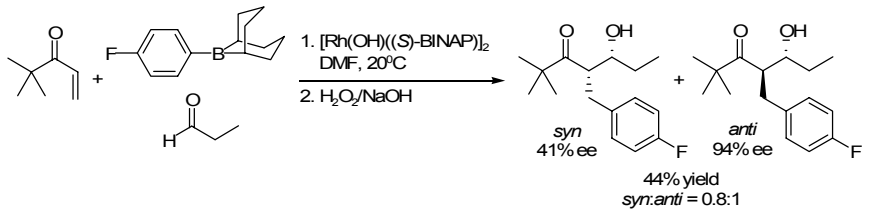


Entry	R^1	R^2	R^3	Yield (%)	*syn*:*anti*
1	*t*-Bu	*p*-FPh	Ph	96	9.6:1
2	*t*-Bu	Ph	Ph	97	10.7:1
3	*t*-Bu	*p*-OMePh	Ph	99	8.9:1
4	*t*-Bu	$CH_3(CH_2)_4CH{=}CH$	Ph	85	21.4:1
5	*t*-Bu	*p*-FPh	Et	72	12.4:1
6	Ph	*p*-FPh	Ph	88	9:1
7	Ph	*p*-FPh	*i*-Pr	93	9:1
8	Me	*p*-FPh	Ph	99	5.7:1

The use of the chiral catalyst [Rh(OH)-((*S*)-BINAP)]$_2$ resulted in enantiomerically enriched aldol products (Scheme 1-2.30). This result rules out the intermediacy of a boron enolate in the catalytic cycle, meaning that both of the C-C bond-forming steps are promoted sequentially by a rhodium complex. NMR experiments, which revealed that conjugate

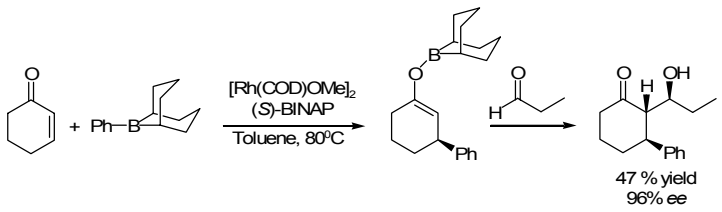
addition does not proceed in the absence of aldehyde, also suggested that the conjugate addition and aldol steps are both catalyzed by a rhodium complex, possibly via a termolecular aggregate.

Scheme 1-2.30



In contrast, exposure of cyclohexenone to *B*-Ph-9BBN and [Rh(COD)OMe]$_2$/(*S*)-BINAP at high temperature led to the highly enantioselective catalytic formation of the corresponding boron enolate (Scheme 1-2.31).[65] Subsequent reaction with propanal afforded the *anti* aldol product as a single diastereomer. Cyclopentenone was also a viable substrate for this asymmetric transformation, whereas cyclopentenone and acyclic enones failed to undergo reaction under identical reaction conditions.

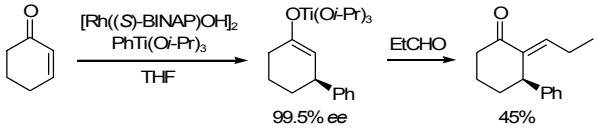
Scheme 1-2.31



2. Organotitanium Pronucleophiles

In 2003, Hayashi reported that enantiomerically enriched titanium enolates can be generated by the rhodium-catalyzed addition of aryltitanium triisopropoxide (ArTi(OPr-*i*)$_3$) to enones (Scheme 1-2.32). Treatment of the chiral Ti-enolate derived from cyclohexenone with propanal gives the corresponding (*E*)-enone product *via* sequential aldol addition and elimination.

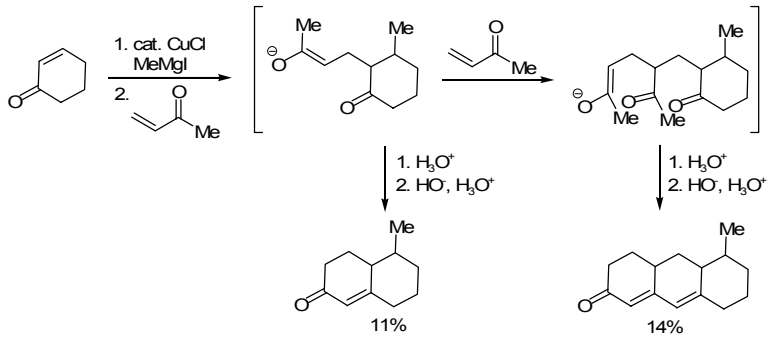
Scheme 1-2.32



II. Tandem Conjugate Addition-Michael Reaction

Enolates generated via conjugate addition have also been trapped with Michael acceptors. The first examples, reported in 1972, involved the copper-catalyzed addition of methylmagnesium iodide to cyclohexenone and trapping with methyl vinyl ketone, ethyl vinyl ketone and ethyl acrylate.[66] The products of these reactions were cyclized under basic conditions. For the reaction with MVK, the expected enone adduct was obtained in 11% yield along with a dienone adduct formed by a double addition of methyl vinyl ketone in 14% yield (Scheme 1-2.33). The corresponding monoadducts were also obtained in very low yield in the case of ethyl vinyl ketone and ethyl acrylate. Later work confirmed the formation of bis-adducts as a problematic side-reaction for this transformation.[67]

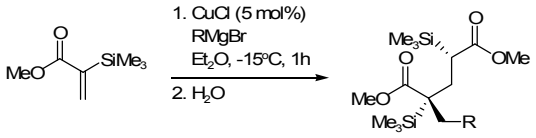
Scheme 1-2.33



This has been a huge obstacle for the development of catalytic direct tandem conjugate addition-Michael reactions. Most successful reports involve trapping of the metal enolate as silyl enol ethers[68] followed by addition to the Michael acceptor in a separate step or employ stoichiometric cuprate reagents.[69]

Catalytic tandem conjugate addition-Michael reactions have been realized through the use of α-silylated vinyl ketones though (Scheme 1-2.34).[70] Enolates generated via copper-mediated conjugate addition of Grignard reagents to methyl 2-(trimethylsilyl)propenoate have been found to undergo Michael addition to another molecule of 2-(trimethylsilyl)propenoate. The trimethylsilyl group stabilizes the intermediate enolate and suppresses multiple condensations. All products were obtained as single diastereomers.

Scheme 1-2.34



Entry	R	Yield (%)
1	Me	71
2	Et	73
3	*n*-Pr	67
4	*n*-Bu	65
5	*i*-Pr	19
6	*i*-Bu	62

III. Conclusion

The vicinal difunctionalization of α,β-unsaturated carbonyls by tandem conjugate addition/aldol reaction is a central transformation in organic synthesis, enabling the formation of multiple C-C bonds. Efficient metal-catalyzed sequences involving Grignard, organozirconium, organoborane, organoboronic acid and organozinc reagents have been developed.

Strategies catalyzed by copper are the most widely used. The kinds of activated olefins which have been employed are fairly limited though. Aside from the intramolecular copper-mediated reactions developed by our research group, most of the work involving copper catalysis has been limited to cyclic alkenones. Highly enantioselective conjugate addition/aldol sequences have been achieved using dialkylzinc reagents and Feringa's phosphoramidite ligand under copper catalysis. Although a great advancement, this asymmetric protocol has only been applied to cyclic alkenones, limiting its utility.

Development of broadly applicable catalytic methods as well as asymmetric variants remains a challenge.

Nickel and rhodium systems that enable conjugate addition to acyclic substrates followed by inter- and intramolecular aldol reaction have recently been reported. Still in their infancy, many more reports on these promising reactions are expected. Expansion of the scope as well as better understanding of the role of both the metal and the organometallic reagent in these metal-catalyzed processes is needed.

Reports on catalytic tandem conjugate addition-Michael reactions are scarce. Not much growth has occurred since its discovery. The identification of efficient protocols capable of overcoming the biggest hurdle, double addition of the Michael acceptor, is crucial for future progress.

Part 3. Nucleophilic Activation *via* Organocatalysis

Perhaps the mildest and most operationally simple method for regiospecific enolate generation involves nucleophilic catalysis *via* conjugate addition of tertiary organic nucleophiles, usually amines or phosphines. The newly formed enolates can be trapped with aldehydes/ketones (Morita-Baylis-Hillman) and activated alkenes (Rauhut Currier). The utilization of organocatalysts represents a highly attractive alternative to the use of transition metals in C-C bond forming reactions. Such reactions are attracting attention as environmentally benign protocols, avoiding the use of stoichiometric reagents and formation of stoichiometric byproducts (atom economical).[71] Chapter 1. Part 3. is organized *i*. with respect to the electrophilic partner, *ii*. with respect to the organocatalyst and *iii*. with respect to the molecularity of the reaction.

I. Morita-Baylis-Hillman Reaction

The Morita-Baylis-Hillman reaction (MBH) is among the most economical and useful C-C bond forming reactions in organic synthesis. It is the base-catalyzed condensation of α,β-unsaturated carbonyl compounds with aldehydes or ketones to give α-methylene-β-hydroxycarbonyl products. Therefore, this reaction can be regarded as equivalent to the addition of a vinyl carbanion to an aldehyde under mild conditions. To date, the Morita-Baylis-Hillman reaction corresponds to the most advanced body of work dealing with organocatalytic nucleophilic activation of enones. Though discovered in 1972, it was not until the early 1980s that organic chemists truly started exploring various aspects of this transformation. The exponential growth and the importance of this reaction are evidenced by the publication of four major reviews.[72] Due to the vast body of literature pertaining to the amine-catalyzed intermolecular Morita-Baylis-Hillman reaction, this section (Chapter1. Part3. I.A.1.) will be structured differently than the others. It will be organized into a. background (1972-1997), b. mechanistic studies, c. recent developments (1998-present) and d.

asymmetric variant. Sub-sections a. background and d. asymmetric variant will be broken down further for clarification purposes.

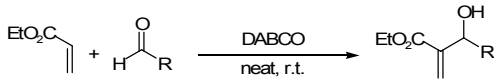
A. Tertiary Amine Catalysis

1. Intermolecular Process

a. Background

Organocatalytic condensation of α,β-unsaturated carbonyl compounds with aldehydes was first reported by Morita in 1968 using a tertiary phosphine catalyst.[73] However, phosphines were soon replaced by tertiary amines as catalysts. Baylis and Hillman utilized 1,4-diazabicyclo[2.2.2]octane (DABCO) to catalyze the reaction of acrylonitrile and ethyl acrylate with various aldehydes in 1972 (Scheme 1-3.1).[74] This transformation represents the first amine-catalyzed MBH reaction.

Scheme 1-3.1



Many more reports on the amine-catalyzed variant of this transformation appeared in the 1980s. Although DABCO was more commonly used, tertiary amine catalysts such as quinuclidine, 3-hydroxyquinuclidine, 3-quinuclidone, triethylamine and diethylmethylamine were also employed.[72] Activated alkenes other than acrylonitrile and acrylic esters that participate in this reaction include vinyl ketones,[75] acrylamides,[76] vinyl sulfones,[77] vinyl sulfonates,[78] vinyl sulfoxides[77d] and vinyl phosphonates[79]. Variation of the electrophilic partner is less diverse and is generally limited to aldehydes[72] and α-keto esters[80], although ketones have been used.[81] The MBH reaction has traditionally suffered from low conversions, low yields and limited substrate scope. This reaction is slow having typical reaction times of days or even weeks at room temperature. At elevated temperatures, polymerization of the activated olefin is a problematic side-reaction. Attempts to accelerate the reaction include the use of excess catalyst,[72] reactive activated alkenes[71,72,82] reactive

electrophiles,[72,80c] microwave irradiation,[76] hydrogen bonding,[83] aqueous medium,[76,84] and high pressure[81a,85]. For example, the reaction of β-substituted activated alkenes with aldehydes is extremely sluggish. Successful examples of the Morita-Baylis-Hillman reaction using β-substituted activated alkenes such as crotononitrile[81a] or crotonic acid esters[81a,86] were only achieved under high pressure or by microwave irradiation. Unactivated ketones require high pressure as well to participate as electrophiles in this reaction.[81a]

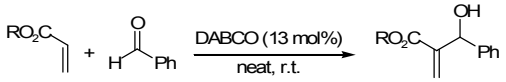
i. The Activated Olefin

The reactivity of activated alkenes generally decreases in the order phenyl vinylsulfonate > α,β-unsaturated ketones > acrylonitrile > acrylic esters = ethyl vinylphosphonate > phenyl vinylsulfone > phenyl vinylsulfoxide = acrylamides. With the unusual exception of phenyl vinylsulfonate, reactivity increases with increasing electronegativity of the olefin activating group.

Acrylates

Although not the most reactive, acrylates have been the most frequently used activated olefins in the MBH reaction. Reaction times of one week are common, and some reactions have been reported to take more than one month to complete. In the DABCO-catalyzed coupling of alkyl acrylates with benzaldehyde,[81a] reaction time increases with increasing steric bulk of the acrylate (4-62 days) (Scheme 1-3.2). With the exception of the bulky adamantyl acrylate, yields of product are moderate to good. Acrylates bearing electron-withdrawing alkyl groups react much faster (2-4 days) under identical conditions.

Scheme 1-3.2

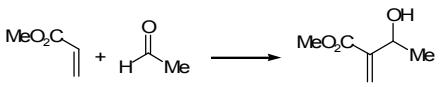


Entry	R	Time (d)	Yield (%)
1	Me	6	89
2	Et	7	79
3	*n*-Bu	4	85
4	*i*-Bu	16	85
5	*t*-Bu	28	65
6	*n*-C_6H_{13}	9	82
7	*n*-C_8H_{17}	12	78
8	*n*-$C_{10}H_{21}$	14	75
7[a]	2-Adamantyl	62	40

[a] Reaction was carried out in dioxane

Aliphatic aldehydes also undergo MBH reaction with acrylates in good yield in the presence of DABCO. But, as is the case with aromatic aldehydes, lengthy reactions times are common. Remarkably, lowering the temperature for the reaction of methyl acrylate with acetaldehyde is reported to increase the rate of reaction and consequently reduce reaction time from days to hours (Scheme 1-3.3).[87]

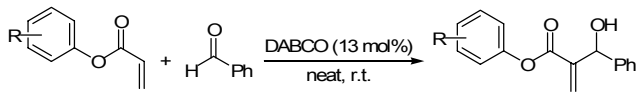
Scheme 1-3.3



Entry	Conditions	Yield (%)
1	DABCO (11mol%), neat, rt, 7d	88
2	DABCO (9mol%), dioxane, 0°C, 8h	74

The coupling of aryl acrylates with benzaldehyde proceeds at significantly greater rates than that for alkyl acrylates, but these faster rates are generally accompanied by lower product yields (Scheme 1-3.4).[81a] No correlation of substituent σ values with rate was observed. Acrylates bearing 4-trifluoromethylphenol (σ=0.53), 4-cyanophenol (σ=0.70) and 4-nitrophenol (σ=0.81) substituents fail to undergo the reaction altogether.

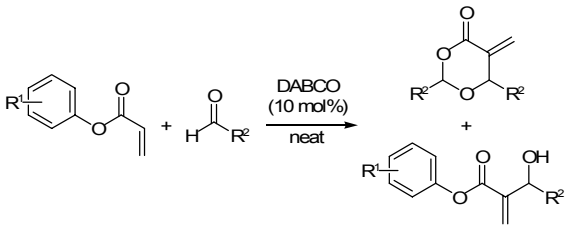
Scheme 1-3.4



Entry	R	s	Time (h)	Yield (%)
1	*p*-Me_2N	-0.63	84	62
2	*p*-MeO	-0.28	8	54
3	*p*-Me	-0.14	36	55
4	*m*-Me_2N	-0.10	20	61
5	H	0	5	55
6	*m*-MeO	0.10	24	43
7	*p*-F	0.15	72	39
8	*m*-F	0.34	5	43
9	*m*-CF_3	0.46	24	22

The reaction of aromatic acrylates with aliphatic aldehydes results in the formation of 5-methylene-1,3-dioxan-4-one adducts exclusively or accompanied by normal MBH products (Scheme 1-3.5).[81b]

Scheme 1-3.5

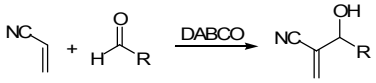


Entry	R^1	R^2	Conditions	Yield (%) dioxanone	Yield (%) MBH
1	H	Me	rt, 2h	57	0
2	*p*-MeO	Me	rt, 8h	69	0
3	H	*i*-Pr	rt, 14h	25	25
4	2,4,6-Me_3	Me	rt, 14h	5	43

Acrylonitrile

Acrylonitrile appears to be slightly more reactive that alkyl acrylates. The DABCO-catalyzed reaction with an aliphatic aldehyde affords the corresponding MBH adduct in 84% yield (Scheme 1-3.6). A lower yield is obtained with aromatic aldehydes under identical reaction conditions. However, microwave irradiation of the reaction greatly accelerates the rate and produces the α-hydroxyalkylation product in excellent yield.[76]

Scheme 1-3.6



Entry	R	Cat. (mol%)	Conditions	Yield (%)
1	*n*-C_9H_{19}	30	rt, 7d	84
2	*m*-NO_2Ph	30	rt, 1d	22
2	*p*-NO_2Ph	50	rt, 3d	45
3	*p*-NO_2Ph	50	microwave (650W) 10 min	95

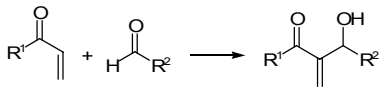
The use of water as solvent also speeds up the DABCO-catalyzed reaction between acrylonitrile and benzaldehyde (Scheme 1-3.7). The reaction time is only 2-3 hours and the product is obtained in 93% yield. This rate-enhancing effect is attributed to the protonation of the zwitterionic intermediate proposed for the mechanism of the MBH reaction (see mechanism section).

Scheme 1-3.7

α,β-Unsaturated Ketones

α,β-Unsaturated ketones constitute the most reactive group of activated olefins employed in the MBH reaction. The coupling of alkyl vinyl ketones with aldehydes proceeds well with tertiary amine catalysts (Scheme 1-3.8).[75b,83b] α-Branching in the vinyl ketone retards the rate of the DABCO-catalyzed MBH reaction and results in diminished product yields.[88]

Scheme 1-3.8

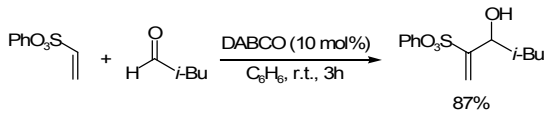


Entry	R^1	R^2	Conditions	Yield (%)
1	Me	Et	DABCO (11mol%), rt, 24h	84
2	Me	Et	3-HQ (5mol%), rt, 15h	85
3	*i*-Pr	Et	DABCO (20mol%), rt, 6d	22
4	*i*-Pr	*i*-Pr	DABCO (20mol%), rt, 6d	20

Vinyl Sulfonate, Vinyl Sulfone and Vinyl Sulfoxide

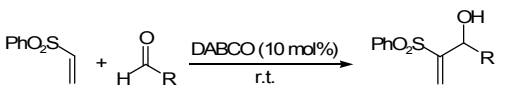
In the single known example of a MBH reaction involving a vinyl sulfonate, phenyl vinylsulfonate exhibits high reactivity under DABCO catalysis resulting in a good yield of product (Scheme 1-3.9).[78]

Scheme 1-3.9



The addition of aldehydes to phenyl vinylsulfone also proceeds at ambient temperature and pressure, but the reaction is much slower resulting in reaction times of days or weeks with varying yields (Scheme 1-3.10).[77b,c]

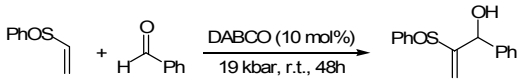
Scheme 1-3.10



Entry	R	Time	Yield (%)
1	3-pyridyl	1 d	46
2	Me	2 wk	84
3	Ph	3 wk	57
4	*t*-Bu	21 wk	10

On the other hand, the reaction of phenyl vinylsulfoxide with benzaldehyde fails under ambient conditions.[77b] Under 19 kbar pressure, a "satisfactory" yield of the desired MBH adduct is obtained as a 1:1 mixture of diastereomers (Scheme 1-3.11).[77d]

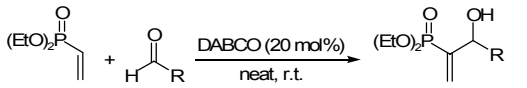
Scheme 1-3.11



Vinylphosphonates

Diethyl vinylphosphonate can be coupled with aldehydes in the presence of DABCO to give good yields of the corresponding α-hydroxyalkyl phosphonates (Scheme 1-3.12).[79] The reactivity of diethyl vinylphosphonate, the only reported example in its class, has been compared to that of alkyl acrylates.

Scheme 1-3.12



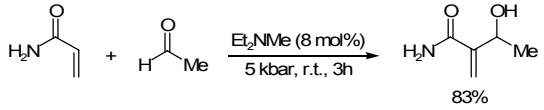
Entry	R	Time (d)	Yield (%)
1	Me	7	83
2	*n*-Pr	10	73
3	*i*-Pr	14	74
4[a]	*n*-Bu	21	68

[a] Reaction ran using 30 mol% DABCO

Acrylamides

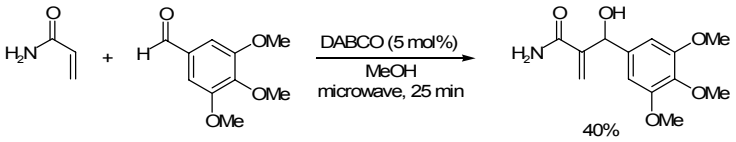
Not surprisingly, the MBH reaction of acrylamides with aldehydes does not proceed under ambient conditions. Even the highly reactive 2-pyridinecarboxaldehyde fails to react with acrylamide or *N*,*N*-dimethylacrylamide.[89] Under 5-kbar pressure, though, the diethylmethylamine-catalyzed reaction of acetaldehyde with acrylamide produces the MBH adduct in 83% yield (Scheme 1-3.13).[81c]

Scheme 1-3.13



The DABCO-catalyzed addition of acrylamide with 3,4,5-trimethoxybenzaldehyde has been reported to proceed in methanol under microwave irradiation (Scheme 1-3.14).[76] No experimental details or structural evidences were provided.

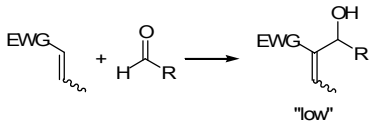
Scheme 1-3.14



β-Substituted Olefins

Additions of aldehydes to β-substituted olefins under ambient conditions are also unknown. DABCO-catalyzed couplings of methyl crotonate and crotononitrile under high pressure have been reported however (Scheme 1-3.15). Only a "low" yield of the corresponding MBH adduct is obtained from the reaction of methyl crotonate with acetaldehyde under 10 kbar pressure.[81a] The same is described for the coupling of crotononitrile with acetaldehyde[81a] and benzaldehyde[86] under similar reaction conditions.

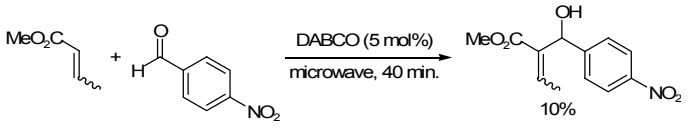
Scheme 1-3.15



Entry	EWG	R	Conditions
1	CO_2Me	Et	DABCO (8mol%), 10 kbar, 55°C, 20h
2	CN	Et	DABCO (8mol%), 10 kbar, 55°C, 20h
3	CN	Ph	DABCO (10mol%), 8 kbar, $CHCl_3$, 17h

Microwave irradiation is also reported to promote the reaction of methyl crotonate with *p*-nitrobenzaldehyde, although no structural proof has been provided (Scheme 1-3.16).[76]

Scheme 1-3.16

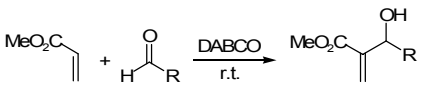


ii. The Electrophile

Aldehydes

Aldehydes are by far the most popular electrophiles for the MBH reaction. Catalyzed by DABCO, aliphatic aldehydes with chains of about 6 carbons or less react much faster with methyl acrylate than those containing longer chains or α-branching (Scheme 1-3.17).[90] Aldehydes bearing electron-withdrawing substituents on the α-carbon, though, are highly reactive.[91]

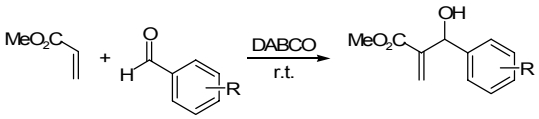
Scheme 1-3.17



Entry	R	Time	Yield (%)
1	Me	7 d	88
2	*n*-$C_{14}H_{29}$	9 d	72
3	*i*-Pr	13 wk	68
4	CCl_3	20 h	>55
5	CO_2Me	48 h	74

Aryl aldehydes, especially those with electron-withdrawing substituents on the aromatic ring, add to activated olefins in high yield (Scheme 1-3.18).[92] Heteroaromatic aldehydes are also excellent electrophiles because of their increased eletrophilicity.[92a]

Scheme 1-3.18

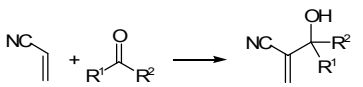


Entry	R	Time	Yield (%)
1	H	2 d	92
2	*o*-Cl	4 d	90
3	*p*-NO_2	18 h	95
4	*p*-MeO	20 d	90

Ketones

Ketones are much less reactive electrophiles for the MBH reaction than aldehydes. Unactivated ketones fail to react all together under ambient conditions. Under high pressure, acetone, methyl ethyl ketone and cyclohexenone couple with acrylonitrile, but not with methyl acrylate (Scheme 1-3.19).[81]

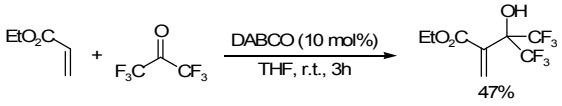
Scheme 1-3.19



Entry	R^1	R^2	Conditions	Yield (%)
1	Me	Me	Et_2NMe (8mol%), THF, 12 kbar, rt, 1h	92
2	Me	Et	DABCO (6mol%), 10 kbar, 26°C, 20h	14
3	$-(CH_2)_5-$		DABCO (10mol%), 9 kbar, 26°C, 1h	42

Hindered ketones, such as diisopropyl ketone and aryl alkyl ketones, fail to undergo MBH reaction even under high pressure.[81a] Conversely, the MBH reactions of halogenated ketones, even hindered ones, with acrylonitrile and ethyl acrylate are known to proceed readily under ambient pressure and temperature (Scheme 1-3.20).[90]

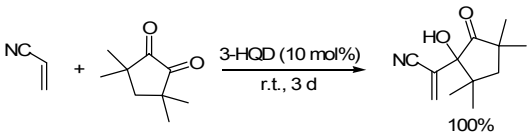
Scheme 1-3.20



α-Diketones

Nonenolizable α-diketone such as 3,3,5,5-tetramethyl-1,2-cyclopentanedione can be coupled with acrylonitrile, but not methyl acrylate, in high yield (Scheme 1-3.21).[93] 2,3-Bornanedione and 2,3-norbornanedione are also viable electrophiles, whereas 3,3,6,6-tetramethylcyclohexane-1,2-dione fails to undergo MBH reaction.

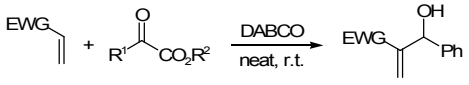
Scheme 1-3.21



α-Keto Esters and α-Keto Lactones

Activated ketones such as α-keto esters and α-keto lactones are highly reactive electrophiles for the MBH reaction. A variety of α-keto esters couple with acrylates, acrylonitrile and α,β-unsaturated ketones in moderate to good yields (Scheme 1-3.22).[94,80c]

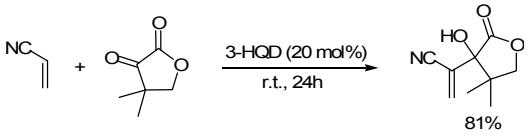
Scheme 1-3.22



Entry	EWG	R^1	R^2	Yield (%)
1	CN	Me	Me	38
2	CO_2Me	Me	Me	78
3	COMe	CO_2Et	Et	74
4	CO_2Me	CO_2Et	Et	77
5	CN	Ph	Et	65
6	CO_2Me	Ph	Et	49
7	CN	CF_3	Me	30
8	CO_2Et	CF_3	Me	72
9	COMe	CF_3	Me	80

α-Keto lactones are somewhat less reactive and do not couple with methyl acrylate, probably for steric reasons, but do with acrylonitrile (Scheme 1-3.23).[80b]

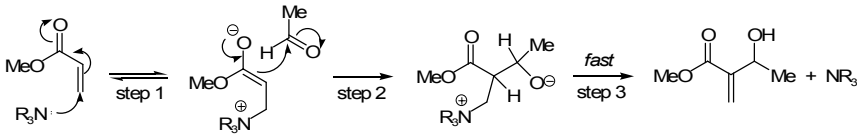
Scheme 1-3.23



b. Mechanistic Studies

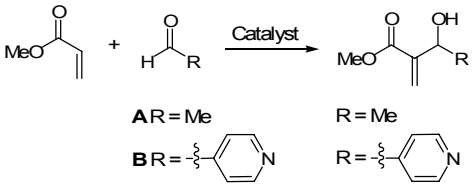
In the mid 1980's, no mechanistic work had been published for the MBH reaction. At the time, the most likely route for this reaction was thought to involve an addition elimination sequence. The mechanism is illustrated for the reaction between methyl acrylate and acetaldehyde (Scheme 1-3.24). Step 1 consists of the Michael addition of the tertiary amine catalyst to methyl acrylate, which generates the zwitterionic enolate intermediate. Step 2, assumed to be the rate determining step, involves the addition of the enolate species to acetaldehyde giving an aldol-type zwitterionic intermediate. In step 3, an intramolecular prototropic shift followed by elimination of the catalyst yields the allylic alcohol product.

Scheme 1-3.24



This early assumption concerning the nature of the rate determining step led Kaye and co-workers to explore the effects of using highly electrophilic aldehydes and hydroxylated species as general acid catalysts (Scheme 1-3.25).[81a] For the reaction of methyl acrylate with various aldehydes, the reaction half-lives ($t_{1/2}$)[10] were reduced by the addition of methanol, increasing catalyst loading, using 3-HQD instead of DABCO and utilizing electrophilic aldehydes. The results of this study were consistent with the proposed rate determining step.

Scheme 1-3.25



Entry	RCHO	Catalyst	Reactant Ratio [M] [1:2:catalyst:MeOH]	$t_{1/2}$ x 10^{-3} (min.)[a]	Yield
1	**A**	DABCO	1:0.7:0.03	3[b]	90
2	**A**	DABCO/MeOH	1:0.6:0.03:0.1	2	-
3	**A**	DABCO/MeOH	1:0.7:0.1:0.1	1	-
4	**A**	3-HQD	1:0.6:0.03	< 0.9	-
5	**A**	3-HQD	1:0.7:0.07	0.2	-
6	**B**	DABCO	1:1.1:0.05	0.01	83
7	**B**	3-HQD	1:1.1:0.05	< 0.005	-

[a] Estimated from ^{1}H NMR integral data for neat reactants in NMR tube at ambient temperature on a Varian T60 NMR spectrometer. [b] Integral data collected on a Varian FT80A NMR spectrometer using a kinetic data collection program.

In 1990, Hill and Isaacs published a study aimed at deducing the mechanism of the MBH reaction between acrylonitrile and acetaldehyde catalyzed by DABCO.[95] Evidence based on kinetics, volumes of activation of reaction and kinetic isotope effects indeed led them to a mechanism in which the amine catalyst first undergoes conjugate addition, the resulting enolate adds to the aldehyde in a rate-determining step and finally the catalyst is eliminated by an E_2 mechanism.

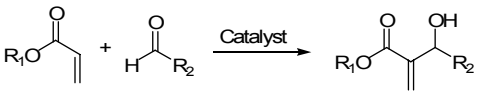
First, the reaction was followed by gas-liquid chromatography and relative rate constants were obtained while varying the concentrations of acrylonitrile, acetaldehyde and DABCO separately. In each case, the rate had a linear first order dependence on each concentration or third-order kinetics overall, confirming the empirical rate expression:

$$\text{rate} = k_3 \text{ [MeCHO] [ACN] [DABCO]}$$

Therefore, the transition state corresponding to the rate determining step must contain all three species (acrylonitrile, acetaldehyde and DABCO). This data points to step 2 (Scheme 3) being the rate determining step. Next, the rate of reaction of α-[^{2}H]-acrylonitrile was compared to that of its ^{1}H analogue. The kinetic isotope effect was calculated at k_H / k_D = 1.03 ± 0.1. This result corroborates that abstraction of the α-H does not occur in the rate determining step. Finally, the volume profile also confirms the inference above. Rates of reaction were measured by a sampling technique at pressures up to 740 bar. A large pressure effect was observed. The volume of activation which was calculated at -79 ± 5 cm^3 mol^{-1} corresponds to a 15-fold increase at only 1000 bar. The large magnitude of this value cannot be accounted for by simple bond formation. It is reasonable that such a large value be the result of a process involving two successive bond formations accompanied by the creation of full charges, as proposed in Scheme 3 steps 1-2. It must be assumed that step 1 is reversible in order for step 2 to be rate determining.

The following year, Bode and Kaye published a kinetic and mechanistic study on the MBH reaction.[96] The reactions of acrylate esters with pyridinecarboxaldehydes were followed by ^{1}H NMR spectroscopy while varying the amine catalyst, the substrate substituents R_1 and R_2, and the component concentrations separately (Scheme 1-3.26). For given concentrations of catalyst, the reactions exhibited linear second order plots. The experimental data acquired was consistent with overall third-order kinetics for this reaction (eq. 1) or pseudo second-order kinetics if the amine concentration was held constant (eq. 2). The third-order rate constants (k_{obs}) are given in the table (Scheme 5). The proposed mechanism was consistent with the experimentally determined rate equations. The rate of formation of the zwitterionic intermediate formed in Scheme 1-3.24, Step 2 is expressed in terms of equation 3. This step is deemed to be rate-determining as equation 3 is identical to the experimentally determined equation 1 for $k_{obs} = k_2K_1$.

Scheme 1-3.26



Rate = k_{obs}[1][2][catalyst] (eq. 1)

Rate = k_a[1][2] (eq. 2)
where $k_a = k_{obs}$[catalyst]

Rate = k_2K_1[1][2][catalyst] (eq. 3)

Entry	R_1	R_2	Catalyst	[M] (mol kg^{-1}) 1:2:catalyst	k_{obs}[a] ($mol^{-2}kg^2s^{-1}$)
1	Me	pyr-4	3-HQD	1.82:1.82:0.10	(1.42 ± 0.04) x 10^{-3}
2	Et	pyr-4	3-HQD	1.82:1.82:0.10	(9.03 ± 0.01) x 10^{-4}
3	^{i}Pr	pyr-4	3-HQD	1.82:1.82:0.10	(4.60 ± 0.14) x 10^{-4}
4	Me	pyr-4	3-HQD	1.82:3.63:0.10	(1.32 ± 0.02) x 10^{-3}
5	Me	pyr-4	3-HQD	1.82:1.82:0.19	(1.42 ± 0.06) x 10^{-3}
6	Me	pyr-4	3-HQD	3.63:1.82:0.10	(9.77 ± 0.10) x 10^{-4}
7	Me	pyr-4	D-3-HQD	1.82:1.82:0.10	(1.09 ± 0.06) x 10^{-3}
8	Me	pyr-4	DABCO	3.63:3.63:0.18	(1.51 ± 0.02) x 10^{-4}
9	Me	pyr-4	3-HQD	3.63:3.63:0.19	(1.11 ± 0.09) x 10^{-3}
10	Me	pyr-2	3-HQD	1.82:1.82:0.10	(2.89 ± 0.04) x 10^{-4}

Mechanistic studies of the MBH reaction up to this point supported the mechanism illustrated in Scheme 1-3.24. This mechanism was thought to initiate with the conjugate addition of the tertiary amine catalyst to the activated olefin, but the resulting zwitterionic intermediate had never been isolated. In 1993, Drewes et al discovered that a white crystalline material had precipitated out of the reaction between methyl acrylate and 2-hydroxybenzaldehyde in the presence of DABCO (Scheme 1-3.27). The crystalline compound was identified as the coumarin salt shown below by X-ray analysis. Isolation of this compound confirmed that the elusive Michael adduct, postulated as an intermediate in the generally accepted mechanism, did exist. The authors reasoned that the formation of this intermediate, instead of the usual elimination of the catalyst, probably resulted due to the stability of the end product in this case.

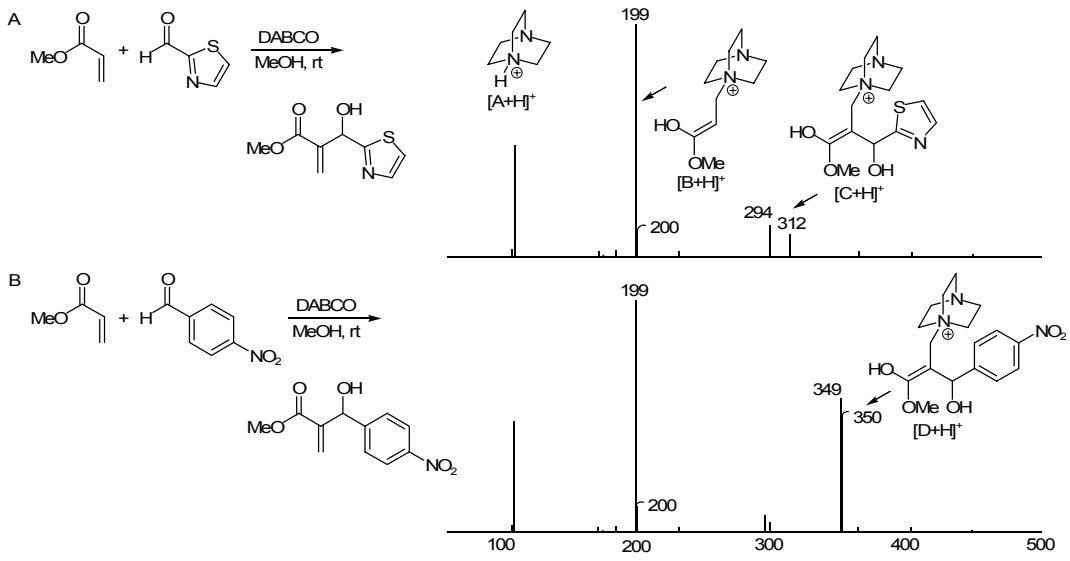
Scheme 1-3.27

81%

In 2004, Eberlin and co-workers published a study aimed at detecting and structurally characterizing several proposed intermediates of the MBH reaction using electrospray ionization (ESI) and tandem mass spectrometry (MS).[97] This work began with the ESI-MS monitoring of the reaction of methyl acrylate with two aldehydes catalyzed by DABCO in

methanol (Scheme 1-3.28). The neutral zwitterionic intermediates formed during the MBH reaction are expected to be in equilibrium with their protonated forms in methanolic solution. ESI is an "ion-fishing" technique that gently transfers preformed ions directly from solution to the gas phase for their MS interception, mass analysis and MS/MS structural characterization. Within a few minutes, three covalently bonded cationic species directly related to the proposed MBH catalytic cycle were detected as major ions for each reaction. This data is strong evidence confirming the mechanistic proposals regarding the MBH reaction initially made by Isaacs and Hill and later refined by others.

Scheme 1-3.28



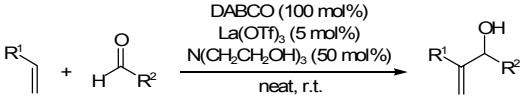
c. Recent Developments

Aside from advancements involving asymmetric MBH reactions, which will be covered in the next section, recent efforts have mainly focused on improving the notoriously slow rates of this reaction and limited substrate scope. Alkyl acrylates are especially slow to react, while acrylamides and β-substituted olefins fail to react all together under ambient conditions. Early attempts to overcome this significant drawback generally involved physical methods such as microwave irradiation and high pressure. More recently, however, highly

basic amines, hydrogen bonding solvents, salts and Lewis-acid catalysts have also been untilized to accelerate the reaction.

Aggarwal et al. examined the use of metals and ligands in the MBH reactions of acrylates and acrylonitrile and benzaldehyde (Scheme 1-3.29).[98] It was discovered that scandium triflate and lanthanide triflate catalyze the reactions with significant rate acceleration when using a stoichiometric amount of DABCO and that further increase in rate can be achieved when catalytic amounts of oxygen-rich donor ligands such as (+)-BINOL, L-diethyltartrate and triethanolamine are employed. The best protocol determined as 5 mol% $La(OTf)_3$, 50 mol% triethanolamine and 100 mol% DABCO resulted in up to a 40-fold rate increase for acrylates and approximately 5-fold for acrylonitrile giving good yields of MBH adducts. The siginificant rate increase can be clearly appreciated with the reaction of *t*-butyl acrylate with benzaldehyde. This reaction, which normally takes 28 days using 10 mol% DABCO, is now complete in 6 days. This system was also effective for the coupling of methyl acrylate with aldehydes both more and less reactive than benzaldehyde.

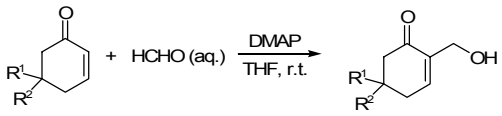
Scheme 1-3.29



Entry	R^1	R^2	Time	Yield (%)
1	CO_2Me	Ph	12 h	83
2	CO_2Et	Ph	12 h	84
3	$CO_2{}^tBu$	Ph	72 h	74
4	CN	Ph	1.5 h	92
5	CO_2Me	*p*-NO_2Ph	3 h	90
6	CO_2Me	*p*-MeOPh	2 d	65

Rezgui and El Gaied reported the first use of DMAP as catalyst for the coupling of cyclohexenone derivatives with formaldehyde in an aqueous medium (Scheme 1-3.30).[99] β-Substituted cyclohexenones did not undergo MBH reaction. Additionally, the reaction of cyclohexenone with formaldehyde failed under traditional conditions (DABCO).

Scheme 1-3.30

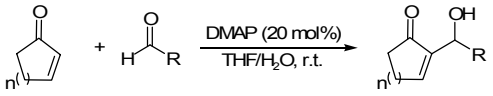


Entry	R^1	R^2	Cat. (mol%)	Time	Yield (%)
1	H	H	10	15 h	82
2	H	Me	15	3 d	76
3[a]	Me	Me	20	5 d	68
4	H	Ph	20	6 d	71

[a] Reaction was carried out at 60°C

Subsequently, Kim et al. also utilized DMAP for the MBH reaction of cyclopentenone and cyclohexenone with various aldehydes (Scheme 1-3.31).[100] A catalytic amount of DMAP in aqueous THF gave good yields for both aromatic and aliphatic aldehydes.

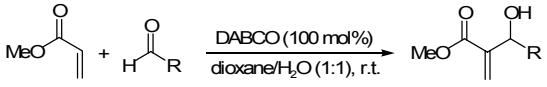
Scheme 1-3.31



Entry	n	R	Time (h)	Yield (%)
1	1	Ph	24	54
2	1	*p*-NO_2Ph	18	63
3	1	*n*-Pent	12	56
4	2	Ph	72	55
5	2	*m*-OMePh	96	63
6	2	*o*-NO_2Ph	72	56

Hu and co-workers demonstrated that the MBH reaction of methyl acrylate could be accelerated by conducting the reaction in aqueous dioxane solution (Scheme 1-3.32).[101] Both aliphatic and aromatic aldehydes were converted to their corresponding MBH products in 41-100% yield in short reaction times.

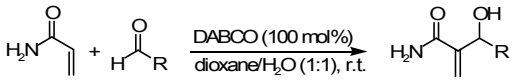
Scheme 1-3.32



Entry	R	Time (h)	Yield (%)
1	Me	10	86
2	Et	14	83
3	*p*-NO_2Ph	3	83
4	*p*-ClPh	36	53
5	2-furyl	20	85
6	2-pyridyl	1	100

A subsequent report revealed that acrylamide, the most unreactive activated olefin employed in the MBH reaction, couples to highly activated aldehydes in good yield under identical reaction conditions (Scheme 1-3.33).[102]

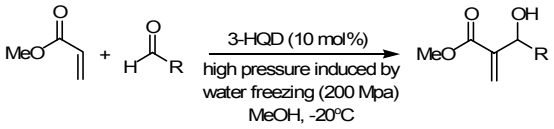
Scheme 1-3.33



Entry	R	Time (h)	Yield (%)
1	o-NO_2Ph	24	85
2	m-NO_2Ph	24	73
3	p-NO_2Ph	24	95
4	2-pyridyl	24	89
5	5-(hydroxymethyl)-2-furyl	48	61

Hayashi et al. observed rate acceleration in the 3-HQD-catalyzed MBH reaction of methyl acrylate under the high pressure produced by water freezing in a sealed autoclave (Scheme 1-3.34).[103] The reaction of electron-deficient as well as electron-rich aromatic aldehydes proceeded smoothly under 200 Mpa pressure to give higher yields than those obtained under ambient pressure. Rate enhancement was not observed for aliphatic aldehydes. Other activated olefins such as *t*-butyl acrylate and MVK also underwent MBH reaction under these conditions with faster rates and higher yields.

Scheme 1-3.34

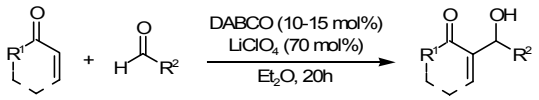


Entry	R	Time (h)	Yield (%)	Yield (%)[a]
1	Ph	24	78	40
2	*o*-ClPh	24	72	49
3	*p*-FPh	24	84	28
4	*p*-OMePh	104	62	8
5	2-furyl	20	89	62
6	*n*-Bu	20	7	16

[a] Reactions conducted under ambient temperature and pressure for comparison

Kawamura and Kobayashi showed that the use of lithium perchlorate in conjunction with a catalytic amount of DABCO in ether can lead to increased rates (Scheme 1-3.35).[104] α,β-Unsaturated ketones, esters and nitriles reacted smoothly with aliphatic and aromatic aldehydes in good yields. Note that the otherwise slow reaction of *t*-butyl acrylate with benzaldehyde gave the corresponding MBH adduct in 50% yield (48 h) under these conditions.

Scheme 1-3.35

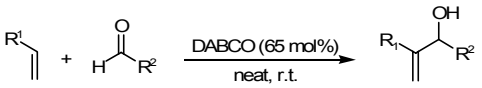


Entry	R^1	R^2	Temp (°C)	Yield (%)
1[a]	OCH_2Ph	Et	-25	79
2	OEt	Ph	0	81
3	O^{t}Bu	Ph	0 - rt	35 (50)[b]
4[a]	Me	Et	-20 - 0	82
5	Me	Ph	-20 - 0	75
6	$CH_2CH_2CH_2$	Ph	0	56
5	CN	Ph	rt	85

[a] Reaction conducted using 10 mol% $LiClO_4$. [b] Reaction time 48 h

Coelho et al. systematically investigated the effect of ultrasound in the MBH reaction of methyl acrylate, MVK and acrylonitrile with both aromatic and aliphatic aldehydes.[105] In all cases the use of DABCO and ultrasound augmented the reaction rate and the chemical yields. Representative examples are illustrated in Scheme 1-3.36.

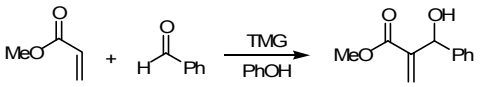
Scheme 1-3.36



Entry	R^1	R^2	without ultrasound Time (h)	without ultrasound Yield (%)	with ultrasound Time (h)	with ultrasound Yield (%)
1	CO_2Me	Ph	144	25	96	74
2	CO_2Me	*p*-NO_2Ph	72	45	16	88
3	CO_2Me	*m*-OH-*p*-OMePh	480	0	96	51
4	CO_2Me	*o*-BrPh	102	12	26	73
5	CO_2Me	*p*-MePh	196	15	72	79
6	CO_2Me	Et	120	71	72	72
7	COMe	*p*-NO_2Ph	50	54	24	73
8	COMe	*o*-pyridyl	24	81	0.75	91
9	COMe	Et	24	84	5	82
10	CN	*o*-pyridyl	24	92	0.75	98
11	CN	Et	40	81	8	80

Leadbeater and co-workers reported the first use of tetramethylguanidine (TMG) as a catalyst for the MBH reaction.[106] The use of phenol as co-catalyst at 48°C led to significant rate acceleration for the coupling of methyl acrylate with benzaldehyde (Scheme 1-3.37). Good yields of product were obtained with other aromatic aldehydes, whereas aliphatic aldehydes failed to react under these conditions.

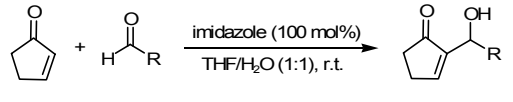
Scheme 1-3.37



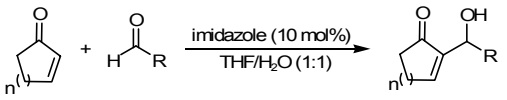
Entry	Ratio of acrylate: PHCHO:TMG:PhOH	Time (h)	Temp. (°C)	Yield (%)
1	1 : 1 : 0.1 : 0	6	25	58
2	1 : 2 : 0.1 : 0.1	6	25	61
3	1 : 2 : 0.2 : 0.15	3	25	67
4	1 : 2 : 0.2 : 0.15	1	48	75

Cheng et al.[107] and Gatri and El Gaied[108] independently examined the coupling of cycloalkenones with aldehydes in aqueous media mediated by imidazole in stoichiometric and catalytic quantities, respectively (Scheme 1-3.38). Stoichiometric reactions of aromatic aldehydes proceeded with fast rates and good yields. Catalytic reactions took much longer, however, heating to 50°C led to further increase in rate resulting in acceptable reaction times for reactions using a catalytic amount of imidazole.

Scheme 1-3.38



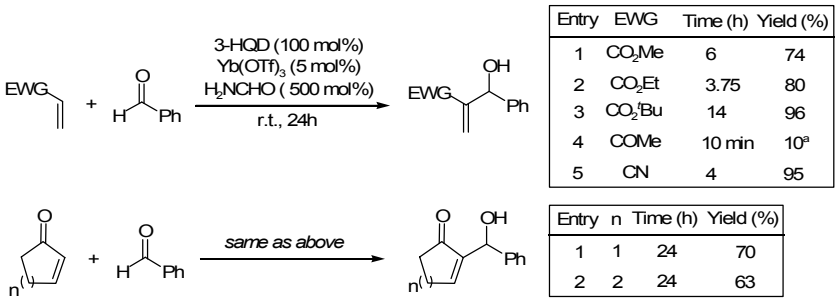
Entry	R	Time (h)	Yield (%)
1	Ph	96	74
2	*m*-NO_2Ph	40	91
3	*p*-ClPh	60	88
4	*p*-MePh	144	42
5	*i*-Bu	96	27



Entry	n	R	Temp (°C)	Time (d)	Yield (%)
1	2	Ph	rt	65	69
2	2	Ph	50	20	61
3	2	*p*-NO_2Ph	rt	10	65
4	2	Me	50	15	70
5	1	Ph	50	2	35
6	1	*p*-NO_2Ph	rt	6	62
7	1	Me	50	3	51

Aggarwal and co-workers investigated the effect of protic solvents (water, formamide) on the 3-HQD-catalyzed MBH reaction (Scheme 1-3.39).[109] Substantial rate accelerations were observed with a range of activated olefins and benzaldehyde in the presence of small amounts of formamide and $Yb(OTf)_3$. Rate enhancements of up to 120-fold were observed in the coupling of ethyl acrylate with benzaldehyde over the standard DABCO-catalyzed reaction. Various hindered and deactivated aldehydes coupled efficiently with ethyl acrylate.

Scheme 1-3.39

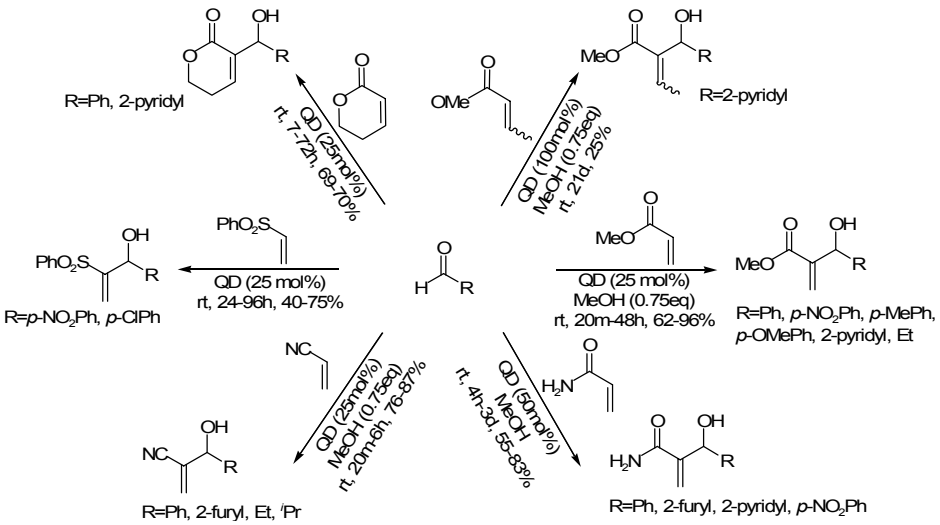


Entry	EWG	Time (h)	Yield (%)
1	CO_2Me	6	74
2	CO_2Et	3.75	80
3	$CO_2{}^tBu$	14	96
4	COMe	10 min	10[a]
5	CN	4	95

Entry	n	Time (h)	Yield (%)
1	1	24	70
2	2	24	63

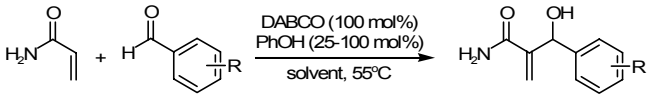
In a subsequent publication, the reactivity of a variety of quinuclidine-based catalysts was studied (Scheme 1-3.40).[110] A correlation between the basicity of the base and reactivity was established. In contrast to previous reports stating the contrary, quinuclidine, which has the highest pK_a, was found to be the most active catalyst. The combination of quinuclidine and methanol was determined the most effective system for MBH reactions and found to be general for a broad range of substrates. Methyl acrylate, acrylonitrile and vinyl sulfones coupled with a variety of aldehydes in higher yield and shorter reaction times than with any previous catalytic systems. Using this system, previously unreactive partners (acrylamide and benzaldehyde) coupled and new activated olefins (α,β-unsaturated δ-lactones and crotonates) were employed.

Scheme 1-3.40



Connon et al. reported an acceleration of the DABCO-catalyzed MBH reaction of acrylamides by the use of elevated temperature, phenol as a co-catalyst and alcoholic/aqueous medium (Scheme 1-3.41).[111] These new conditionds enabled expansion of the acrylamide MBH reaction scope to include deactivated aromatic aldehydes.

Scheme 1-3.41



Entry	R	Solvent	Time (d)	Yield (%)
1	Ph	^{t}BuOH/H_2O	5	70
2	*o*-NO_2Ph	^{t}BuOH/H_2O	0.75	91
3	*o*-ClPh	^{t}BuOH/H_2O	3.2	67
4	Nap	neat	6	50
5	*p*-MePh	neat	11	72
6	*o*-MePh	neat	7	37
7	*o*-MePh	neat	5	74
8	*p*-MeOPh	neat	11	21

d. Asymmetric Variant

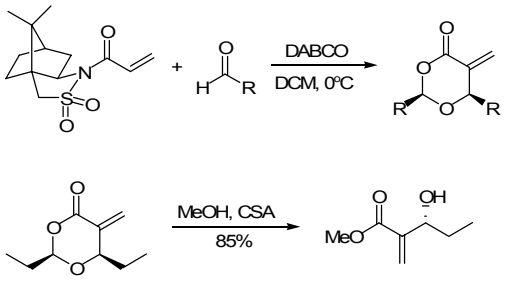
Development of an asymmetric MBH reaction has focused mainly on the amine-catalyzed variant, and some progress has been made towards the development of a suitably general catalytic asymmetric MBH reaction. Two stereocenters are formed during the MBH reaction, one of which remains in the product. Asymmetric induction in the product may be controlled by using the activated alkene, the electrophile or the catalyst as a chiral source. What follows is a highlight of the most successful methods for the amine-catalyzed asymmetric MBH reaction, categorized by the chiral source employed.

i. Diastereoselective Reaction of Chiral Activated Alkenes

In 1997, Leahy and co-workers demonstrated that the camphor-derived Oppolzer's sultam can be employed as a highly efficient chiral auxiliary in the MBH reaction.[112] The reaction using the sultam-functionalized acrylamide proceeded smoothly with a variety of aldehydes providing products in moderate to excellent yields with >99% ee (Scheme 1-3.42). One drawback was the requirement for 15 equivalents of aldehyde. It is noteworthy that addition of a second equivalent of aldehyde resulted in the cleavage of the chiral auxiliary under the reaction conditions. Additionally, the resulting 1,3-dioxan-4-one products were

easily converted into α-methylene-β-hydroxyesters by methanolysis in good yield. Aldehyde substrates with branching at the α-position were problematic giving low yields, if the reaction proceeded at all (entry 8).

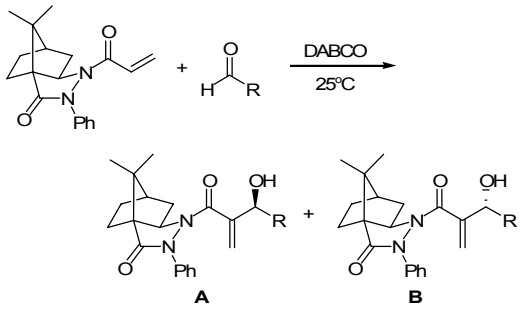
Scheme 1-3.42



Entry	R	Yield (%)	*ee* (%)	$[a]_D$
1	Me	85	>99	+ 73.4°
2	Et	98	>99	+ 70.2°
3	Pr	70	>99	+ 87.2°
4	^{i}Pr	33	>99	+ 42.7°
5	CH_2CH_2Ph	68	>99	+ 47.2°
6	CH_2OAc	68	>99	+ 80.0°
7	$CH_2CH(CH_3)_2$	67	>99	+ 59.8°
8	Ph	0	-	-

A few years later, Chen et al. reported the synthesis and use of a highly effective chiral auxiliary, structurally related to Oppolzer's camphor sultam, for the asymmetric induction of the MBH reaction (Scheme 1-3.43). However, instead of providing lactone products, reaction of the chiral acryloylhydrazide with aldehydes in the presence of DABCO afforded β-hydroxy-α-methylene carbonyl derivatives **A** and **B** in up to 98% de. Additionally, either diastereomer of **A** and **B** could be obtained with high optical purity from the same chiral auxiliary by changing the solvent. Using the aprotic solvent DMSO favored the formation of **A**, while having a THF/H_2O (5/1) solvent system gave preference to the formation of **B**. Aliphatic aldehydes participated in the reaction giving good yields and high diastereoselectivities. The reaction with an aromatic aldehyde proceeded smoothly with DMSO as solvent, but not with the THF/H_2O solvent system (entries 6 & 10). α-Branched aliphatic aldehydes gave rise to many unidentified products, one which was assigned to be a dimerized compound.

Scheme 1-3.43

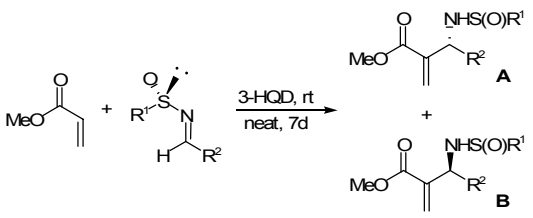


Entry	R	Solvent	Time (d)	Ratio **A:B**	Yield (%)
1	Me	neat	1/3	75:25	92
2	Me	THF	1/2	58:42	82
3	Me	DMSO	2	97:3	88
4	Et	DMSO	4	99:1	85
5	$CH_2CH(CH_3)_2$	DMSO	2	97:3	75
6	Ph	DMSO	7	99:1	80
7	Me	THF/H_2O	4	3:97	73
8	Et	THF/H_2O	3	1:99	85
9	$CH_2CH(CH_3)_2$	THF/H_2O	3	1:99	81
10	Ph	THF/H_2O	21	-	0

ii. Diastereoselective Reactions of Chiral Electrophiles

Highly efficient diastereoselective MBH reactions utilizing chiral electrophiles have not been reported in the case of aldehydes. Even though reactions employing imines as electrophiles have been excluded from this discussion, an example will be included below to illustrate the concept of chiral electrophiles. In 2002, Aggarwal et al. looked at enantiomerically pure *N*-*p*-toluenesulfinimines as electrophiles in the MBH reaction of methyl acrylate with and without Lewis acids (Scheme 1-3.44). It was reasoned that placing the chiral controller on the nitrogen of the imine would be more useful as both aromatic and aliphatic imines could then be used. Screening bases and Lewis acids revealed that 3-HQD was the optimum base and $In(OTf)_3$ was the optimum Lewis acid providing 89% yield of the desired product **B** with good diastereoselectivity. A *p*-nitrophenyl imine derivative reacted faster than the parent phenyl derivative, giving high diastereoselectivity in moderate yield. An aliphatic imine also reacted in moderate yield and good diastereoselectivity. The less electrophilic *p*-methoxyphenyl derivative was unreactive. Hoping to attain higher levels of diastereocontrol, an *N*-*p*-butanesulfinimine was tested. Higher diastereoselectivities were observed in the presence of Lewis acids but the yields were very poor.

Scheme 1-3.44



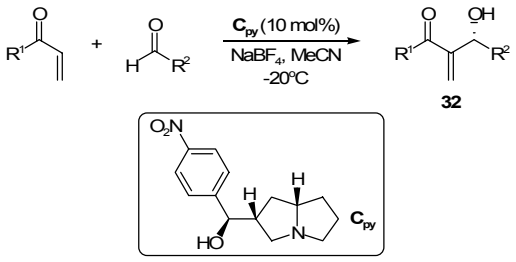
Entry	R^1	R^2	Ratio **A**:**B** (Yield (%))[b] $Sc(OTf)_3$	$Yb(OTf)_3$	$In(OTf)_3$
1	*p*Tol	Ph	23:77 (78)	20:80 (74)	18:82 (89)
2[a]	*p*Tol	*p*NO_2Ph	9:91 (50)	6:94 (52)	14:86 (48)
3	*p*Tol	*p*MeOPh	-	-	-
4	*p*Tol	*n*Pr	14:86 (46)	15:85 (45)	13:87 (47)
5	$C(CH_3)_3$	Ph	8:92 (10)	9:91 (10)	18:82 (17)

[a] Reaction time was 2 days. [b] Yield of isolated major diastereomer **B**.

iii. Enantioselective Reactions of Chiral Catalysts

In 1998, the utility of the chiral hydroxypyrrolizidine catalyst $\mathbf{C_{py}}$ in the asymmetric MBH reaction was examined by Barrett and co-workers (Scheme 1-3.45).[113] Optimization efforts revealed that although yields were optimal at -40ºC, superior enantioselectivities were obtained at the higher temperature -20ºC. Therefore, the reactions of ethyl and methyl vinyl ketone with a variety of aldehydes were run at -20ºC to secure maximum ee's and with a sodium additive to increase the yields. Modest yields and enantioselectivities were obtained with a number of *ortho*-substituted aromatic aldehydes using chiral catalyst $\mathbf{C_{py}}$. The absolute configuration of the α-methylene-β-hydroxyketone (R^1=Me, R^2=*o*-NO_2Ph) was assigned *R*. Aldehydes having *meta*- and *para*-substituents afforded the corresponding MBH products in very low optical purity.

Scheme 1-3.45

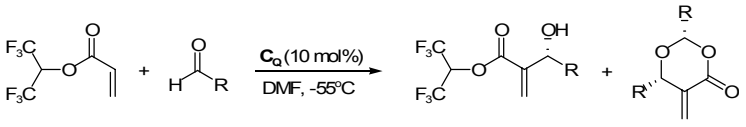


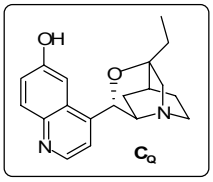
Entry	R^1	R^2	t (h)	Yield (%)	*ee* (%)
1	Et	*o*-NO_2Ph	18	71	67
2	Me	*o*-NO_2Ph	18	71	53
3	Me	*o*-FPh	48	31	63
4	Me	*o*-ClPh	14	58	72
5	Me	*o*-BrPh	72	63	71
6	Me	*m*-NO_2Ph	18	51	37
7	Me	*p*-NO_2Ph	48	17	39

Hatakeyama et al. examined various tertiary amines derived from cinchona alkaloids as catalysts for an asymmetric version of the MBH reaction (Scheme 1-3.46).[114] Tertiary amine catalyst $\mathbf{C_Q}$ derived from quinidine was found to be the best catalyst for the reaction of the highly reactive 1,1,1,3,3,3-hexafluoroisopropyl acrylate with various aldehydes. The

catalyst was more nucleophilic than quinidine due to the free hydroxy group, and so it increased the rate of reaction. The MBH products were obtained with very high enantioselectivities (up to 99% ee (*R*)), albeit in low yields due to the competitive formation of dioxanone adducts. Dioxanone adducts showed the opposite chirality (*S*) and irregular *ee* values. The highest yields of MBH adducts were obtained with aromatic aldehydes. This reaction was also applicable to aliphatic aldehydes, but yields diminished with increasing steric bulk. Still, the yields obtained for aldehydes branched at the α-position were an advantage over other reaction methods, such as one using Oppolzer's chiral auxiliary (Scheme 1-3.42).

Scheme 1-3.46





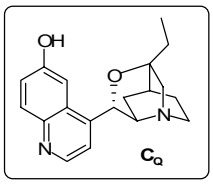
Entry	R	t (h)	% Yield (% *ee*) MBH	dioxanone
1	*p*-NO_2Ph	1	58 (91)	11 (4)
2	Ph	48	57 (95)	-
3	(E)-PhCH=CH	72	50 (92)	-
4	Et	4	40 (97)	22 (27)
5	$(CH_3)_2CHCH_2$	4	51 (99)	18 (85)
6	*i*-Pr	16	36 (99)	25 (70)

Shi and Xu employed chiral tertiary amine $\mathbf{C_Q}$, previously used by Hatakeyama, as catalyst in an asymmetric aza-MBH reaction (Scheme 1-3.47).[115] Reactions of methyl acrylate or MVK with aromatic aldehydes were sluggish or failed all together. Therefore, expecting a tosylated amino group to be more reactive, *N*-arylidene-4-methylbenzenesulfonamides were used instead. Initial investigations with MVK uncovered that the best conditions for attaining both high ee's and yields were MeCN/DMF (1:1) at -30ºC. Under these conditions, MVK reacted with a variety of aromatic *N*-tosylated imines giving aza-MBH adducts with high *ee* values and moderate to good yields. Imines having strongly electron-deficient aromatic substituents afforded only moderate yields and enantioselectivities (entries 6,7). Efforts with aliphatic imines only resulted in numerous

unidentified products. Reactions of methyl acrylate with aromatic *N*-tosylated imines proceeded smoothly in dichloromethane at 0ºC giving the corresponding MBH adducts in good yields and *ee*'s. Yields and selectivities were lower than those obtained with MVK. The high enantioselectivities reported here are unparalleled for MBH reactions involving MVK or methyl acrylate as acceptor.

Scheme 1-3.47

Entry	Ar	Yield (%)	*ee* (%)
1	Ph	80	97
2	*p*-MePh	76	96
3	*p*-EtPh	74	96
4	*p*-MeOPh	64	99
5	*m*-FPh	55	90
6	*p*-NO_2Ph	60	74
7	2-furyl	58	73

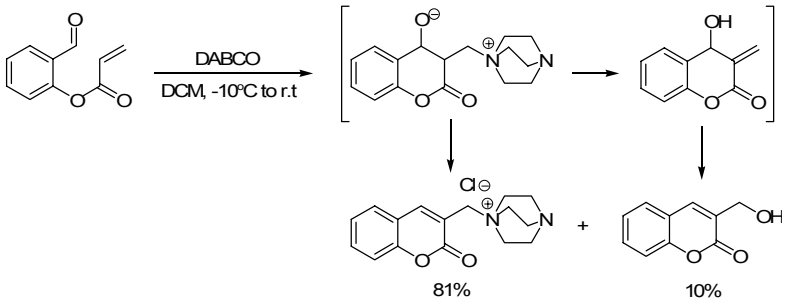


Entry	Ar	Yield (%)	*ee* (%)
1	Ph	62	83
2	*p*-MePh	67	80
3	*p*-EtPh	62	82
4	*p*-MeOPh	64	70
5	*m*-FPh	87	83
6	*p*-NO_2Ph	58	72
7	*p*-ClPh	60	83

2. Intramolecular Process

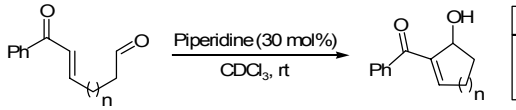
Although the amine-catalyzed MBH reaction is well documented in the literature, its intramolecular version has not been studied in depth. As mentioned in the mechanism section **b.**, Drewes et al discovered that a white crystalline material had precipitated out of the reaction between methyl acrylate and 2-hydroxybenzaldehyde in the presence of DABCO in 1993 (Scheme 1-3.48). Along with the coumarin salt, the major product, was produced 10% of an isomerized MBH adduct. This reaction is considered the first amine-catalyzed intramolecular MBH reaction.

Scheme 1-3.48



In 1997, Murphy et al. reported that treatment of phenyl enone-aldehydes with a catalytic amount of piperidine gave five- and six-membered aldol adducts (Scheme 1-3.49).[116] The five-membered ring cyclization was faster and a higher yield was obtained. A subsequent publication in 2001 reiterated these results and reported that enoate-aldehyde and thioenoate-aldehyde substrates decomposed under identical reaction conditions.[117]

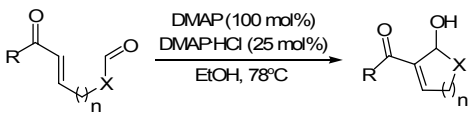
Scheme 1-3.49



Entry	n	Time (d)	Yield (%)
1	1	7	55
2	2	14	24

Kech and Welch were the first to successfully cyclize thioenoate-aldehyde substrates (Scheme 1-3.50).[118] Although not catalytic, the reaction proceeded to give five-membered products in good yield when exposed to a mixture of DMAP and DMAP·HCl. A six-membered cyclization was slow resulting in a low yield of the corresponding cyclohexenol adduct. The same was observed for the formation of a cyclopentenol adduct from an enoate-aldehyde substrate.

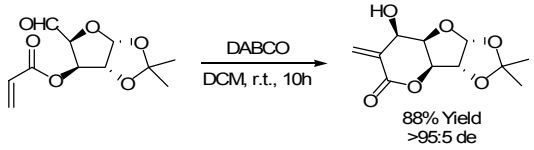
Scheme 1-3.50



Entry	R	n	X	Yield (%)
1	SEt	1	CH_2	87
2	SEt	2	CH_2	29
3	SEt	1	$C(CH_3)_2$	88
4	OEt	1	CH_2	40

Recently in 2004, Krishna and co-workers described the first diastereoselective intramolecular MBH reaction of chiral substrates (Scheme 1-3.51).[119] A sugar-derived chiral enoate-aldehyde was cyclized in the presence of DABCO to give the corresponding α-methylene-β-hydroxylactone in good yield as a single isomer.

Scheme 1-3.51

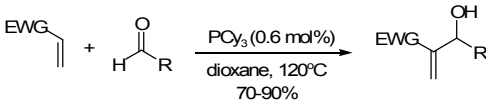


B. Tertiary Phosphine Catalysis

1. Intermolecular Process

Phosphines are the original catalysts for the MBH reaction. In 1968, Morita reported that coupling of acrylonitrile and methyl acrylate to various aldehydes catalyzed by tricyclohexylphosphine gave products in 70-90% yields (Scheme 1-3.52).[120] However, the conversion of this reaction remained below 25%.

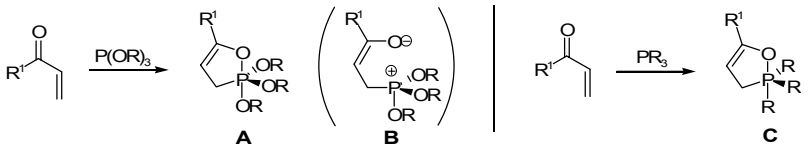
Scheme 1-3.52



EWG = CO_2Me, CN
R= Me, Et, *i*-Pr, *n*-Pr, Ph, *p*-Cl-C_6H_4, *p*-Me-C_6H_4

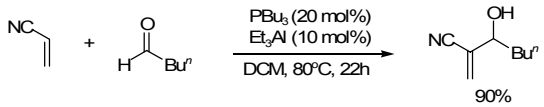
A It is known that 1,4-addition of trialkylphosphite to enones affords 1,2-λ^5-oxaphospholenes 1 (Scheme 1-3.53).[121] These 1,2-λ^5-oxaphospholenes can be regarded as phosphoenol ethers. While their reactivities are of the 'open' enolate/phosphonium species **B**, they clearly exist as the cyclic pentacovalent species **A** as evidenced by ^{31}P NMR spectroscopy. Likewise, the zwitterionic intermediates resulting from the conjugate addition of phosphines to enones are thought to exist as cyclic structures **C**.

Scheme 1-3.53



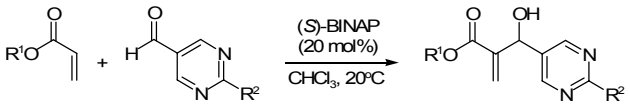
As mentioned previously, after the initial report by Morita in 1968, phosphines were replaced by tertiary amines as catalysts in the MBH reaction. In the last few years, however, phosphines emerged again as catalysts and were used sporadically. Phosphines are generally less basic and more nucleophilic than their amine counterparts. As a result, they are now used more and more in cases where a more reactive catalyst is needed and have become popular nucleophilic catalysts in the last few years. Tertiary phosphines, in general, gave higher yields in shorter reaction times when compared to their amine counterparts. In 1984, Kawanisi et al. reported the reaction of acrylonitrile with aliphatic aldehydes by the use of an acid-base complex catalyst (tributylphosphine and triethylaluminum) (Scheme 1-3.54).[122] The improved yields for this reaction were 70-90% with 100% conversion. Acrylonitrile reacted with *n*-butanal giving the desired MBH product in 90% yield. The Lewis acid is believed to activate the aldehydes by coordination to the carbonyl oxygen. The reaction with benzaldehyde resulted in a low 27% yield of product under identical conditions, limiting the aldehyde partners to saturated aliphatic ones. Subsequently, Leahy observed faster rates and better yields for the coupling of methyl acrylate and various aldehydes at lower temperature (0ºC).[87] At this temperature, both aliphatic and aromatic aldehydes were viable substrates. Yields and conditions were given for amine-catalyzed reactions. However, the authors stated phosphine catalysts were equally effective.

Scheme 1-3.54



In 1998, Soai et al. reported the first enantioselective phosphine-catalyzed intermolecular MBH reaction (Scheme 1-3.55).[123] In reactions between various acrylates and pyrimidine carboxaldehydes, products in 9-44% enantiomeric purities were obtained when (*S*)-BINAP was used. The yield and *ee* were dependent on the size of the acrylate; the less bulky acrylate gave the higher yield and *ee*.

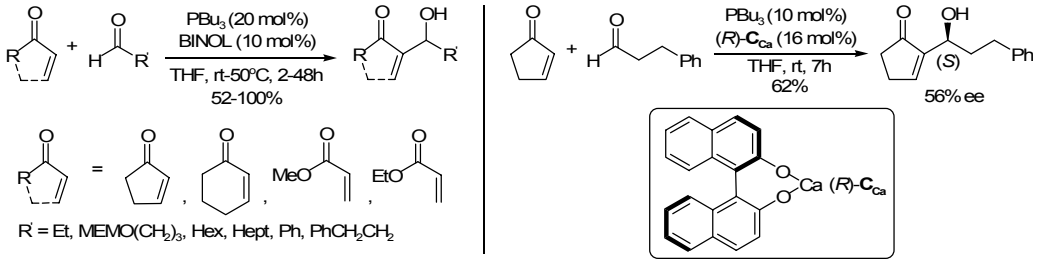
Scheme 1-3.55



Entry	R^1	R^2	t/h	Yield (%)	*ee* (%)
1	Pr^i	H	95	8	9
2	Et	H	62	12	25
3	Me	H	85	24	44
4	Me	Me	329	18	37
5	Me	Me	62	26	30

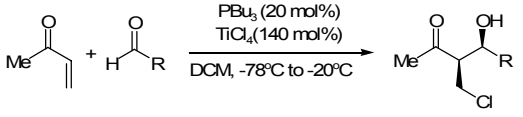
Later Ikegami and co-workers found that the cooperative catalysts of tributylphosphine and (±)-1,1´-bi-2-naphthol (BINOL) are effective for MBH reactions between activated alkenes and aldehydes to give α-methylene-β-hydroxyalkanones in high yield (Scheme 1-3.56).[124] Both cyclic and acyclic activated alkenes and aliphatic and aromatic aldehydes were successfully utilized. Reactions using (*R*)-BINOL failed to give any significant enantioselectivities (<10%). However, employing an optically active calcium catalyst (*R*)-**C_{Ca}** as a chiral Lewis acid with tributylphosphine as an achiral Lewis base in the reactions of cyclopentenone and 3-phenylpropanal afforded the desired MBH adduct with 56% *ee* in 62% yield.

Scheme 1-3.56



Subsequently, Shi et al. examined the tributylphosphine-promoted reaction between MVK and aldehydes in the presence of several Lewis acids ($TiCl_4$, $ZrCl_4$ and BCl_3) (Scheme 1-3.57).[125] The activities of Lewis acids for this reaction were $TiCl_4$ > $ZrCl_4$ > BCl_3. Good yields of the α-chloro aldol adducts were obtained using $TiCl_4$ as the Lewis acid in the case of aromatic aldehydes. Aliphatic aldehydes gave much lower yields (entry 7). Poor enantioselectivity was observed when the chiral phosphine (*R*)-BINAP was employed.

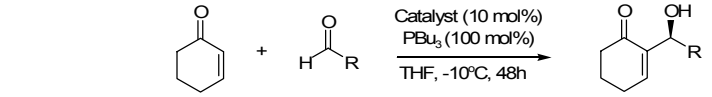
Scheme 1-3.57

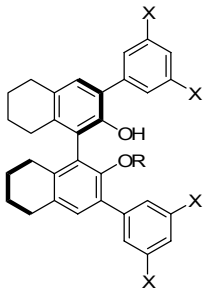


Entry	R	T (°C)	t/h	Yield (%)
1	*p*-NO_2Ph	-78	12	80
2	*m*-NO_2Ph	-78	12	80
3	*p*-CF_3Ph	-78	48	81
4	*p*-EtPh	-20	72	51
5	*p*-ClPh	-20	72	52
6	Ph	-20	72	57
7	$CH_3(CH_2)_3$	-20	72	40

Recently in 2003, Schaus and co-workers reported a highly enantioselective asymmetric coupling of cyclohexenone with aldehydes using a chiral Brønsted acid as the catalyst and triethylphosphine as the nucleophilic promoter (Scheme 1-3.58).[126] Several BINOL-derived Brønsted acids were examined; optimal results were obtained with catalysts $\mathbf{C_{B3}}$ and $\mathbf{C_{B4}}$. High yields and enantioselectivities were observed with aliphatic aldehydes. Aromatic or conjugated aldehydes gave much lower yields and enantioselectivities. Two structural features of the catalyst found to be important for achieving high enantioselectivity were saturation of the BINOL derivative and substitution at the 3,3´-positions. BINOL-derived catalysts lacking substitution at the 3,3´-positions, such as catalyst $\mathbf{C_{B1}}$, or having only one Brønsted acid equivalent, such as catalyst $\mathbf{C_{B2}}$, exhibited diminished catalytic activity and selectivity. This finding supports the idea that the Brønsted acid promotes the conjugate addition step, and then remains hydrogen-bonded to the resulting enolate in the enantioselectivity-determining aldehyde addition step.

Scheme 1-3.58



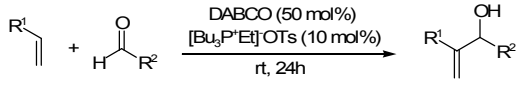


C_{B1}: R = H , X = H
C_{B2}: R = CH_3 , X = H
C_{B3}: R = H , X = CH_3
C_{B4}: R = H , X = CF_3

Entry	R	Catalyst	Yield (%)	*ee* (%)
1	CH_2CH_2Ph	C_{B1}	73	48
2	CH_2CH_2Ph	C_{B2}	43	3
3	CH_2CH_2Ph	C_{B4}	88	90
4	CH_2CH_2OBn	C_{B4}	74	82
5	$CH_2CH_2CH{=}CHCH_2CH_3$	C_{B3}	72	96
6	Cy	C_{B3}	71	96
7	$CH(CH_3)_2$	C_{B3}	82	95
8	Ph	C_{B4}	40	67
9	CH=CHPh	C_{B4}	39	81

The following year Karodia et al. examined the application of phosphonium salts and DABCO as co-catalysts for the MBH reaction (Scheme 1-3.59).[127] Lengthy reaction times are normally required in the traditional MBH reaction using acrylates. For example, the reaction of ethyl acrylate and benzaldehyde requires seven days to achieve a reasonable yield of product.[128] In this study, excellent yields were obtained for the reaction of acrylate esters and acrylonitrile with benzaldehyde in 24 hours, while only a low 35% yield was obtained with methyl vinyl ketone (entries 1-3). Other aromatic as well as aliphatic aldehydes gave good results in the reaction with methyl acrylate with yields ranging from 97% to 99%. An aldehyde bearing an electron-donating group, *p*-methylbenzaldehyde, resulted in a diminished yield of product. Karodia's method utilizes readily available, stable and inexpensive co-catalysts for the MBH reaction.

Scheme 1-3.59

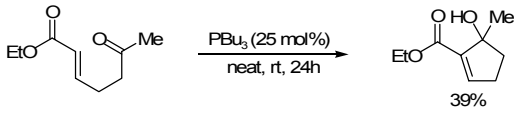


Entry	R^1	R^2	Yield (%)
1	CO_2Me	Ph	92
2	CN	Ph	100
3	COMe	Ph	35
4	CO_2Me	*p*-MePh	56
5	CO_2Me	*o*-ClPh	99
6	CO_2Me	*m*-FPh	99
7	CO_2Me	*p*-NO_2Ph	96
8	CO_2Me	^{n}Pr	97

2. Intramolecular Process

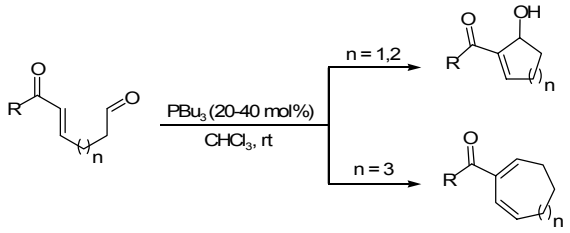
Intramolecular reactions have dramatically increased rates and selectivities when compared to their intermolecular counterparts. The first report of an intramolecular variant of the MBH reaction was made by Frater and co-workers in 1992 (Scheme 1-3.60).[129] The cyclization is not particularly efficient, but it has to be kept in mind that the corresponding intermolecular reaction, addition of acetone to methyl crotonate, fails even under high pressure.

Scheme 1-3.60



Murphy et al. investigated the cyclization of an α,β-unsaturated alkene onto an aldehyde using amines, phosphines and thiols as catalysts.[130] The phosphine-mediated cyclizations work best for six- and seven-membered enones and for six-membered enoates to give MBH adducts (Scheme 1-3.61). Less success was observed with five-membered enone and enoate substrates, while thioenoates decomposed under the reaction conditions. Eliminated cycloheptadiene products are obtained with seven-membered enones and enoates instead of the normal MBH adducts.

Scheme 1-3.61

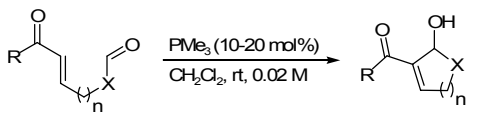


Entry	R	n	Cat. (mol%)	t/h	Yield (%)
1	Ph	1	20	17	20
2	Ph	2	20	2	75
3	OEt	1	40	672	40
4	OEt	2	20	24	50
5	Ph	3	20	48	77
6	OEt	3	20	144	10

Kech and Welch were the first to successfully cyclize a thioenoate onto an appendant aldehyde using trimethylphosphine (Scheme 1-3.62).[131] The reaction proceeded to give both five- and six-membered products in good yield when conducted at a low substrate

concentration (entries 1-3). Cyclization of an enoate onto an appendant aldehyde was slow and resulted in a low yield of the corresponding cyclopentenol adduct (entry 4).

Scheme 1-3.62



Entry	R	n	X	Yield (%)
1	SEt	1	CH_2	82
2	SEt	2	CH_2	75
3	SEt	1	$C(CH_3)_2$	83
4	OEt	1	CH_2	33

II. Rauhut Currier Reaction

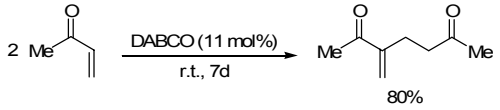
Head-to-tail dimers are formed when the activated olefin also acts as the electrophile under MBH conditions. Predating Morita's 1972 publication on organocatalytic condensation of α,β-unsaturated carbonyl compounds with aldehydes, Rauhut and Currier disclosed a patent on the dimerization of ethyl acrylate catalyzed by tributylphosphine.[132] This process is referred to as the Rauhut Currier reaction or sometimes as the vinylogous Morita-Baylis-Hillman reaction. Though discovered a decade before the MBH reaction, a small number of reports on the Rauhut Currier reaction have been published in comparison. Polymerization is a problematic side reaction; under the reaction conditions, the dimeric products are susceptible to further reaction. Therefore, trimeric adducts tend to be the major product in many cases. Many studies attempt to suppress polymerization through modulation of the catalyst, solvent and temperature.[133] Initial work investigated the use of phosphine and amine catalysts. Most if not all recent publications involve tertiary phosphine catalysts, as they proved to be more effective for this transformation.

A. Tertiary Amine Catalysis

1. Intermolecular Process

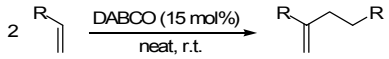
It was Amri and Villieras who first established that the tertiary amine, DABCO, could effect the dimerization of MVK in 1986 (1-3.63).[134] A slow Michael-type addition (7 days) provides 3-methylene hepta-2,6-dione in 80% yield.

Scheme 1-3.63



The following year Basavaiah et al. extended this DABCO-induced Michael-type dimerization to include a range of α,β-unsaturated ketones and nitriles (Scheme 1-3.64).[135] Reaction times varied between 15 minutes (phenyl vinyl ketone) and 10 days (acrylonitrile) having yields from 40-60%.

Scheme 1-3.64

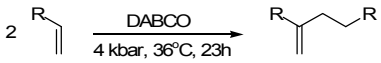


Entry	R	Time	Yield (%)
1	*p*-MePhCO	1 h	49
2	PhCO	15 min	62
3	EtCO	40 h	60
4[a]	MeCO	4 d	59
5[b]	CN	10 d	40

[a] Reaction carried out in THF. [b] Reaction carried out with 50 mol% DABCO

It was noticed that methyl and ethyl acrylate do not dimerize at room temperature even with equimolar amounts of DABCO and that the dimerization of acrylonitrile is very slow resulting in a low yield of product.[81a,136] Hill and Issacs showed that DABCO-catalyzed couplings of methyl and ethyl acrylate under 4 kbar pressure were possible, albeit in low yields (Scheme 1-3.65).[119a,b] High pressure also increased the rate of reaction for acrylonitrile and consequently the yield of dimer.

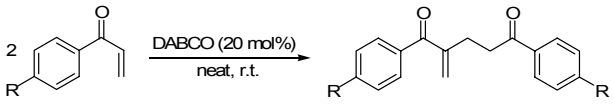
Scheme 1-3.65



Entry	R	Cat. (mol%)	Yield (%)
1	CO_2Me	5	25
2	CO_2Et	2	9
3	CN	1	65

In 1990, Drewes and co-workers described the dimerization of a variety of aromatic acrylates in the presence of 20 mol% DABCO (Scheme 1-3.66). The reaction proceeded with excellent yields under ambient pressure and temperature.

Scheme 1-3.66

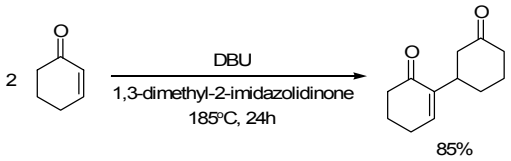


Entry	R	Time (h)	Yield (%)
1	H	15	98
2	*p*-Me	15	98
3[a]	*p*-NO_2	9	99

[a] Reaction carried out in THF

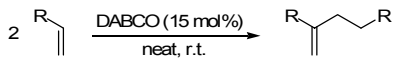
The first account involving the dimerization of cyclic enones appeared in 1992 (Scheme 1-3.67).[137] Exposure of cyclohexenone to DBU at 185ºC provided the corresponding dimer in 85% yield.

Scheme 1-3.67



A decade passed without mention of the amine-catalyzed intermolecular Rauhut Currier reaction. Recently in 2002, Kaye et al. reported a DABCO-catalyzed dimerization of a variety of activated olefins (Scheme 1-3.68).[138] Aliphatic and aromatic α,β-unsaturated ketones and phenyl vinyl sulfonate gave moderate yields of the dimerization adducts. Reactions of acrylonitrile, aliphatic acrylates and phenyl vinyl sulfone were low yielding.

Scheme 1-3.68



Entry	R	Yield (%)	Entry	R	Yield (%)
1	COPh	65	5[a]	CO_2Et	5
2	COMe	59	6	SO_2Ph	20
3	COEt	55	7	SO_3Ph	60
4[a]	CO_2Me	10	8	CN	12

[a] Reaction carried out with DBU as catalyst

2. Intramolecular Process

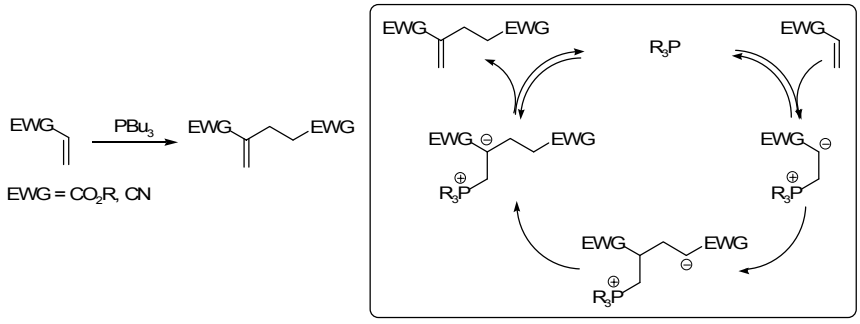
To the best of my knowledge, there are no reports of intramolecular Rauhut Currier reaction catalyzed by tertiary amines.

B. Tertiary Phosphine Catalysis

1. Intermolecular Process

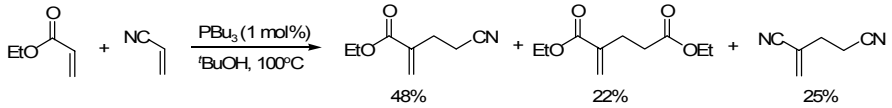
Predating the MBH reaction, Rauhut and Currier disclosed a patent on the tributylphosphine-catalyzed dimerization of ethyl acrylate in 1963.[139] Later, McClure and Baizer and Anderson independently examined the dimerization of acrylonitrile employing triarylphosphines (Scheme 1-3.69).[140] Like for the MBH reaction, the mechanism of this transformation is believed to start with the conjugate addition of phosphine to the activated alkene resulting in the formation of a zwitterionic intermediate. Michael addition onto a second activated alkene followed by a prototropic shift and finally β-elimination of phosphine yields the dimeric product and completes the catalytic cycle.

Scheme 1-3.69



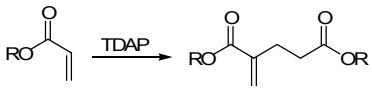
In 1970, McClure described the first cross-coupling reaction (Scheme 1-3.70).[141] Reaction of equimolar amounts of ethyl acrylate and acrylonitrile gave rise to a single product, 2-ethoxycarbonyl-4-cyano-1-butene, in 48% yield. The low yield was a result of dimerization products of both reactants being formed.

Scheme 1-3.70



There was little mention of the phosphine-catalyzed Rauhut-Currier reaction for many years. Then in 1989, Villieras et al. reported the dimerization of ethyl and *tert*-butyl acrylates using trisdimethylaminophosphine (TDAP) as catalyst (Scheme 1-3.71). The corresponding dimeric products were produced in good yields.

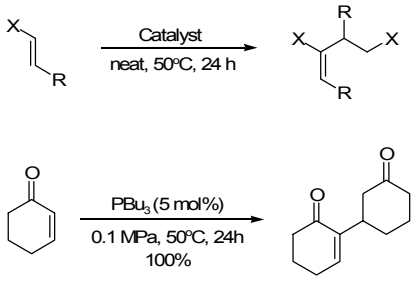
Scheme 1-3.71



Entry	R	Cat. (mol %)	T (°C)	t/h	Yield (%)
1	Et	20	60	2	61
2	^{t}Bu	10	20	16	72

Later, in the year 2000, Jenner studied the dimerization of acrylic nitriles, esters and ketones.[142] Several phosphines and tertiary amines were screened. Traditional MBH catalysts, DABCO and quinuclidinol, were virtually inactive even at high pressures. Phosphines and complex cyclic amines were more efficient, the best catalysts being $P[N(CH_3)_2]_3$ and PBu_3. Whereas unhindered activated alkenes underwent phosphine-catalyzed dimerization at ambient pressure to give the corresponding adducts, β-substituted activated alkenes usually required high pressures (Scheme 1-3.72). Cyclohexenone was an exception, giving the dimeric product in quantitative yield under atmospheric pressure. Several reports on the amine-catalyzed variant of the Rauhut-Currier reaction were also published. However, polymerization of starting materials and poor selectivity in the cross-coupling process remained a problem.[143]

Scheme 1-3.72

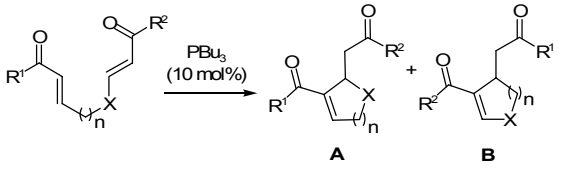


Entry	X	R	Catalyst (mol%)	Yield (%) 0.1MPa	300 MPa
1	CN	H	$P(C_4H_9)_3$ (5)	98	-
2	"	Me	$P[N(CH_3)_2]$ (5)	87	-
3	"	Et	$P(C_4H_9)_3$ (5)	0	86
4	"	"	$P[N(CH_3)_2]$ (5)	8	96
5	CO_2CH_3	H	$P(C_4H_9)_3$ (5)	59	-
6	"	Me	$P(C_4H_9)_3$ (10)	0	0
7	"	"	$P[N(CH_3)_2]$ (10)	0	38
8	"	"	$P[N(CH_3)_2]$ (30)	0	88

2. Intramolecular Process (Michael Cycloisomerization)

While the intramolecular Morita-Baylis-Hillman reaction is known, related catalytic Michael condensations were unknown until recently. In 2001, an intramolecular variant of the Rauhut-Currier reaction was simultaneously developed by our research group and Roush.[144] Trialkylphosphines turned out to be far better catalysts than triarylphosphines and amines for this intramolecular variant. In studies done by our lab, symmetric bis-enones gave five- and six-membered ring products in high yield over short reaction times using 10 mol% PBu_3 (representative example shown in Scheme 1-3.73, entry 1). The kinetic bias in favor of intramolecular addition suppresses polymerization, a common problem in the intermolecular process. Another advantage of the intramolecular variant was the ability to carry out selective crossed cycloisomerizations. An aromatic-aliphatic bis-enone provided cyclopentene products as a 1:1 mixture of isomers (**A**:**B**), while the homologous substrate provided the corresponding cyclohexenes in a 7:1 ratio (entries 2 & 3). This suggested that the initial formation of phosphine adducts was indiscriminate and in the case of five-membered ring formation, the kinetic phosphine adducts were trapped via cyclization. The slower cyclization rate of six-membered rings allowed for a pre-equilibrium of phosphine adducts to be established and cyclization now became the product and rate-determining step. Enone-enoate substrates cyclized with high chemoselectivity to the product derived from initial conjugate addition of phosphine to the more electrophilic enone partner (entry 4). Remote *para* substituents also directed the formation of a single isomeric cycloisomerization product (entry 5). In the absence of a strong electronic bias, steric factors directed selectivity (entry 6). These studies also revealed a dramatic increase in reaction rate with increasing solvent polarity.

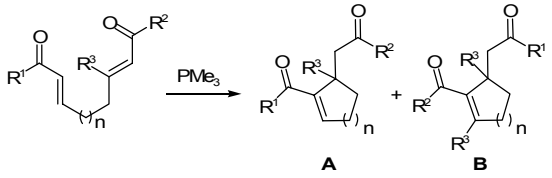
Scheme 1-3.73



Entry	n	R^1	R^2	X	Yield (%)	**A:B**
1	1	Ph	Ph	CH_2	86	-
2	1	Ph	Me	CH_2	79	1 : 1
3	2	Ph	Me	CH_2	77	7 : 1
4	1	Me	OEt	CH_2	87	> 95 : 5
5	2	*p*-NO_2Ph	*p*-OMePh	CH_2	75	> 95 : 5
6	1	Me	Ph	$C(CH_3)_2$	81	> 95 : 5

In studies by Roush the smaller trialkylphosphine, PMe_3, proved to be superior. Employing 10 mol% PMe_3, an enone-enoate substrate (entry 1) gave 95% of a single isomeric cycloisomerization product (Scheme 1-3.74). This is an improvement to Krische's 87% yield obtained with PBu_3. Conducting the reactions in more dilute conditions, enal-enone and enal-enoate substrates also underwent cycloisomerization smoothly to form five- and six-membered ring products in good to excellent yields using 20-100 mol% PMe_3 (entries 2-5). The reactions favored the product isomer **A** derived from initial conjugate addition of the catalyst to the more electrophilic enone or enal partner. A β-substituted enone substrate also participated in the reaction to give the product derived from initial conjugate addition of PMe_3 to the sterically less-hindered and more electron-deficient enone partner (entry 6). However, this reaction was not catalytic, requiring 200 mol% of PMe_3 .

Scheme 1-3.74

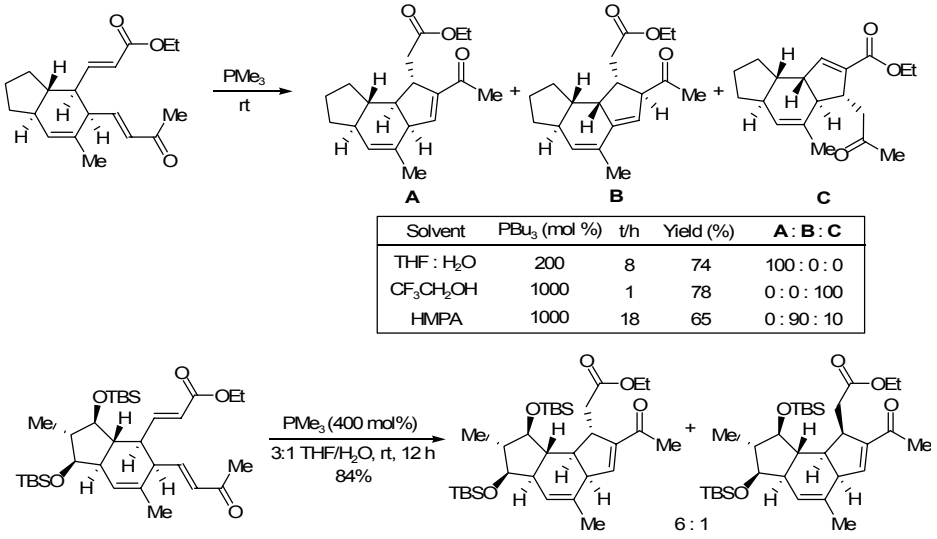


Entry	n	R^1	R^2	R^3	PMe_3 (mol%)	Yield (%)	**A:B**
1	1	Me	OEt	-	10	95	97:3
2	1	H	Me	-	20	79	93:7
3	2	H	Me	-	50	55	89:11
4	1	H	OEt	-	20	90	9:1
5	2	H	OEt	-	100	67	97:3
6	1	Me	OMe	Me	200	60	only

In 2003, Roush utilized the intramolecular Rauhut-Currier reaction in the synthesis of the *as*-indacene substructure of FR182877, an antimitotic agent (Scheme 1-3.75).[145] The Michael cycloisomerization of the enone-enoate model system was highly solvent-dependent. Performing the cyclization using 200 mol% PMe_3 in 3:1 THF:H_2O provided the desired product **A** in 74% yield. The opposite mode of cyclization was observed in CF_3CH_2OH while

using HMPA as solvent caused olefin migration giving **B** as the major product. The model system with the substitution pattern present in FR182877 underwent the Michael cycloisomerization to the desired product in good yield in all three solvent systems with between 4:1 and 6:1 diastereoselectivity.

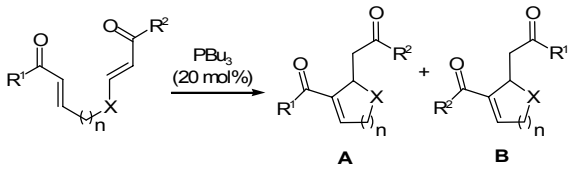
Scheme 1-3.75



Solvent	PBu_3 (mol %)	t/h	Yield (%)	**A** : **B** : **C**
THF : H_2O	200	8	74	100 : 0 : 0
CF_3CH_2OH	1000	1	78	0 : 0 : 100
HMPA	1000	18	65	0 : 90 : 10

Our research group applied the intramolecular Rauhut-Currier reaction toward the synthesis of the furanosesquiterpene lactone ricciocarpin A (Scheme 1-3.76).[146] A highly chemoselective crossed cycloisomerization of thioenoates with appendant enone and enoate partners was described. Motivation for these studies arose from the failure encountered in the Michael cycloisomerization of bis-enoates. Cyclization of mono-thioenoate and bis-thioenoate substrates proceeded smoothly to provide good yields of the corresponding cyclopentene or cyclohexene products (entries 2-5). For unsymmetrical substrates, the favored regioisomer **A** arose from 1,4-addition of the catalyst to the more electrophilic partner. A lower yield was obtained in the Michael cycloisomerization of an enone-enal substrate (entry 6). The key cycloisomerization reaction performed using a furyl-substituted enone-ethyl thioenoate substrate afforded product **A** exclusively in 81% yield (entry 7).

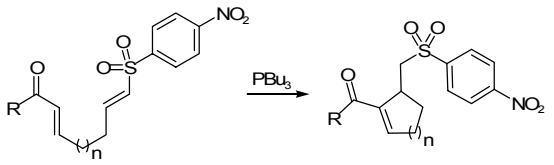
Scheme 1-3.76



Entry	n	R^1	R^2	X	Yield (%)	A:B
1	1	OEt	OEt	CH_2	0	-
2	1	SEt	SEt	CH_2	96	-
3	2	SEt	SEt	CH_2	87	-
4	1	SEt	OEt	CH_2	89	98:2
5	2	SEt	OEt	CH_2	82	99:1
6	2	H	Furyl	$C(CH_3)_2$	51	100:0
7	2	SEt	Furyl	$C(CH_3)_2$	81	100:0

Recently, our research lab published studies aimed at expanding the types of reacting partners that participate in the crossed Michael cycloisomerization reaction.[147] Inspired by the versatility of the sulfone moiety in organic synthesis,[148] *p*-nitrophenyl substituted vinyl sulfones were examined and found to be highly effective reacting partners for this reaction (Scheme 1-3.77). Good to excellent yields of 5- and 6-membered ring products were obtained for enones and enoates with appendant vinyl sulfone partners in the presence of PBu_3. As previously observed, the ideal choice of temperature and reaction solvent was highly substrate dependent. In each case, the vinyl sulfone moiety serves as the Michael acceptor and a single isomeric cycloisomerization product is formed.

Scheme 1-3.77



Entry	n	R	Cat. (mol%)	Solvent	T (°C)	Yield (%)
1	1	EtS	10	^{t}AmylOH	50	89
2	2	EtS	10	MeCN	rt	86
3	1	Ph	10	EtOAc	50	97
4	2	Ph	10	Acetone	rt	74
5	1	Me	20	^{t}BuOH	82	84
6	2	Me	20	^{t}AmylOH	60	80

III. Conclusion

The Morita-Baylis-Hillman has become one of the most useful and popular C-C bond forming reactions with enormous synthetic utility, promise and potential. However, the reaction has traditionally suffered from low reaction rates and limited substrate scope. A number of physical and chemical methods have been developed to accelerate the notoriously

slow Baylis-Hillman reaction. Apart from significantly increased rates, these methods have made possible the coupling of previously unreactive partners. Still there is considerable room for scope expansion of the MBH reaction.

The Rauhut Currier reaction has been investigated to a much lesser extent. The intermolecular process suffers from polymerization of the starting materials and poor selectivity in the cross-coupling process. Alkyl acrylates provide low chemical yields while acrylamides are completely unreactive. Significant improvements in both chemical yields and substrate scope are essential to the utility of this reaction. For the intramolecular process, high yields are attained for a variety of activated olefins. Additionally, the cyclizations exhibit exceptionally high chemoselectivity.

Continuing sophistication in synthetic organic chemistry requires and even demands the continuous evolution of synthetic methods that meet the requirements of atom economy and very high levels of selectivity. The MBH and Rauhut Currier reactions are totally atom-efficient processes since all the carbon atoms from the reagents are incorporated in the end product. However, the chiral catalysts performing MBH reactions with a high degree of enantioselectivity are applicable only to selected activated olefins and electrophiles. Therefore, there remains a need for developing effective chiral bases that are universally applicable to a broad range of reactants. Enantioselective protocols for the Rauhut Currier reaction are yet to be developed.

Solving these problems is essential for the better application of the MBH and Rauhut Currier reactions in various aspects of organic synthesis and, therefore, this remains a challenge for organic chemists. Low rates, chemical yields, substrate scope and stereoselectivity remain important issues to be carefully addressed in all future studies.

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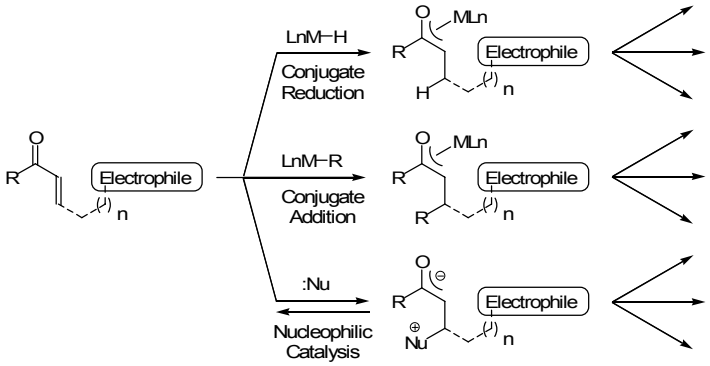
Chapter 2. Catalytic Reaction Development

Part 1. Research Objective

The Stork established the use of enones as latent enolates as an efficient means of controlling regiochemistry in enolate-mediated C-C bond formations for stoichiometric processes. However, selective catalytic systems for the nucleophilic activation of enones, which are suited for a range of electrophilic partners, remain undeveloped. As part of a program focused on catalytic reaction development, the use of enone precursors in catalytic enolate generation-electrophilic trapping sequences is currently under investigation in the Krische lab. Specifically, hydrometalation (1,4-reduction),[1] carbometalation (1,4-addition),[2] and nucleophilic organocatalysis (reversible 1,4-addition)[3] have been applied to the regiospecific generation of enolate nucleophiles, setting the stage for addition to a variety of appendant electrophilic partners. Indeed, by varying the method of enolate generation and the electrophile employed, a family of catalytic transformations has been developed (Scheme 2-1.1). Enolates generated by these catalytic processes have been found to engage in subsequent additions to aldehydes,[1a-c] ketones,[1d,1e,2] esters,[2c] nitriles,[2c] activated alkenes,[1a,1b,3a,3b,3e,4] Pd(II)-π-allyls[3c] and triarylbismuth(V) reagents.[3d]

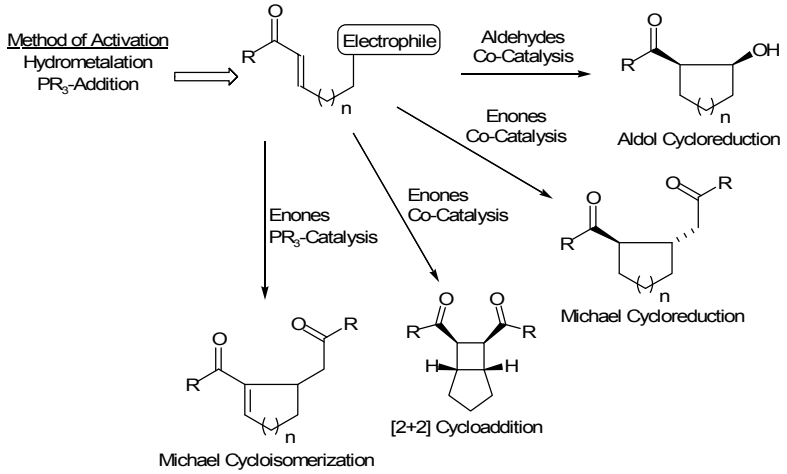
Scheme 2-1.1



The author's research focused on the development of catalytic C-C bond forming reactions arising from *i*. the nucleophilic activation of enones *via* hydrometalation and nucleophilic organocatalysis and *ii*. capture of the resulting enolates with aldehydes and

activated olefins in formal aldol and Michael reactions, respectively. These studies led to the development of the aldol cycloreduction[1a], Michael cycloreduction[1a], [2+2] cycloaddition[4] and Michael cycloisomerization[3a] methodologies. The means of enone activation and the electrophile used for each transformation are illustrated in Scheme 2-1.2.

Scheme 2-1.2



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Chapter 3. Tandem Catalytic Reactions Enabled by the Nucleophilic Activation of Enones via Hydrometalation

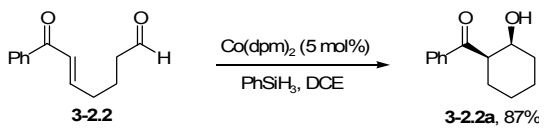
Part 1. Respective Contributions

Development of the cobalt-catalyzed aldol and Michael cycloreduction and [2+2] cycloaddition reactions was a collaborative effort between Dr. Tae-gon Baik, Dr. Long-Cheng Wang and the author. Studies on the mechanism of the aldol and Michael cycloreductions and [2+2] cycloadditions were conducted by Dr. Long-Cheng Wang, Dr. Hye-Young Jang, Dr. Yeonsuk Roh, Dr. Vincent Lynch, Dr. Arthur J. Schultz and Xiaoping Wang.

Part 2. Cobalt-Catalyzed Aldol Cycloreduction[1]

Given the lack of development in the area of intramolecular reductive aldol reactions, a catalytic approach to this transformation was sought. The $Co(dpm)_2$ (dpm=dipivaloylmethane)-phenyl silane catalyst system employed in the intermolecular reductive aldol reaction reported in 1989 by Mukaiyama,[12f] was used in initial exploratory studies. Whereas the intermolecular process exhibits poor diastereoselectivity, the geometrical requirements for the intramolecular reaction are more stringent and, hence, high diastereoselectivities were anticipated. Initial efforts focused on enone-aldehyde **3-2.2**. Gratifyingly, exposure of **3-2.2** to a preformed solution containing 5 mol% $Co(dpm)_2$ and 120 mol% phenylsilane in dichloroethane at 25°C provided cycloreduction product **3-2.2a** in 87% isolated yield with a *syn:anti* ratio of >99:1 as determined by HPLC analysis (Scheme 3-2.1). The structure of compound **3-2.2a** was evidenced by the resonances at δ 4.23 (m, 1H) and δ 3.32 (ddd, J = 3.1, 3.2, 11.2 Hz, 1H) in the ^{1}H NMR corresponding to methine protons α to the hydroxy and carbonyl groups, respectively. The regio- and stereochemical assignment was corroborated by single-crystal X-ray analysis.

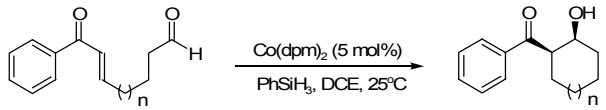
Scheme 3-2.1



3-2.2 **3-2.2a**, 87%

Encouraged by this result, a variety of enone-aldehyde substrates were prepared. The viability of five-, six- and seven-membered ring formation was probed using substrates **3-2.1**, **3-2.2** and **3-2.8** (Scheme 3-2.2). A low yield of the seven-membered ring adduct **3-2.8a** was obtained, but both five- and six-membered ring formations proceeded in good yield under standard conditions.

Scheme 3-2.2

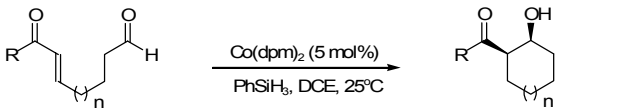


3-2.1, n=0
3-2.2, n=1
3-2.8, n=2

3-2.1a, 70%
3-2.2a, 87%
3-2.8a, 35%

Having established the viability of five- and six-membered cyclizations, the tolerance of various acyl residues was examined. Aromatic substrates, (*p*-trifluoromethyl)-phenyl- and 2-naphthyl-substituted enone-aldehydes underwent cycloreduction smoothly (Scheme 3-2.3).

Scheme 3-2.3

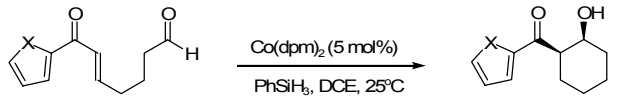


3-2.3, R=F_3CPh
3-2.4, R=2-Nap

3-2.3a, R= F_3CPh, 70%
3-2.4a, R=2-Nap, 87%

Heteroaromatic substrates **3-2.6** and **3-2.7** also afforded the corresponding cycloreduction adducts in good yield (Scheme 3-2.4). The presence of the sulfur-containing residue in substrate **3-2.7** did not diminish the efficiency of the catalyst.

Scheme 3-2.4



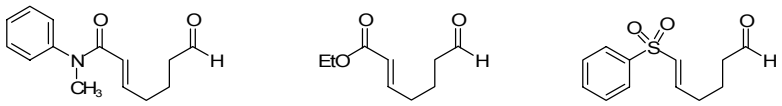
3-2.6, X=O
3-2.7, X=S

3-2.6a, X=O, 75%
3-2.7a, X=S, 73 %

Subsequent investigations attempted to broaden the scope of this methodology. Several enone-aldehyde substrates were prepared to assess the electronic requirements for the pronucleophilic partner. Substrates containing less electrophilic enone partners such as

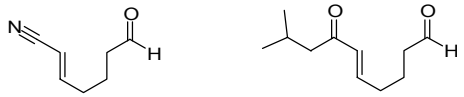
α,β-unsaturated amides, α,β-unsaturated esters or vinyl sulfones were completely unreactive under standard conditions. Numerous experiments varying the catalyst loading, temperature and concentration only resulted in recovered starting materials.

Figure 3-2.1



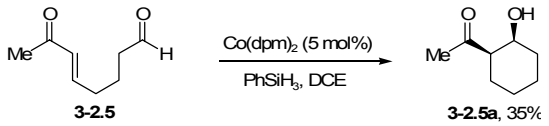
An α,β-unsaturated nitrile-aldehyde substrate and an isovaleryl enone-aldehyde also failed to undergo aldol cycloreduction (Figure 3-2.2). Increasing the catalyst loading or temperature resulted in significant amounts of unidentified byproducts without a trace of the desired cycloreduction product.

Figure 3-2.2



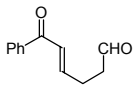
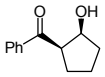
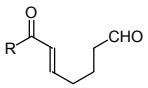
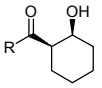
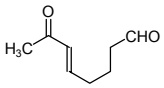
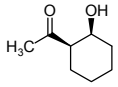
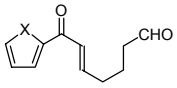
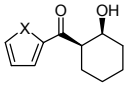
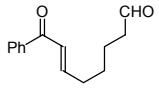
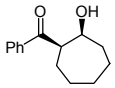
A methyl enone-aldehyde **3-2.5** did undergo aldol cycloreduction. However, a reduced yield was obtained when exposed to standard reaction conditions (Scheme 3-2.5). In all cases, irrespective of yield, only the *syn*-diastereomers of cycloreduction products were obtained. Results for viable substrates are summarized in Table 3-2.1.

Scheme 3-2.5



3-2.5 **3-2.5a**, 35%

Table 3-2.1. Cobalt-catalyzed aldol cycloreductions

Entry	Substrate	Product	Temperature	$PhSiH_3$ (eq.)	Yield (%)
1					
	3-2.1	**3-2.1a**	**25°C**	**1.2**	**70**
2					
	3-2.2, R = Ph	**3-2.2a, R = Ph**	**25°C**	**1.2**	**87**
	3-2.3, R = *p*-CF_3Ph	**3-2.3a, R = *p*-CF_3Ph**	**25°C**	**1.2**	**72**
	3-2.4, R = 2-naphthyl	**3-2.4a, R = 2-naphthyl**	**25°C**	**1.2**	**68**
3					
	3-2.5	**3-2.5a**	**25°C**	**1.2**	**38**
4					
	3-2.6, X = O	**3-2.6a, X = O**	**25°C**	**1.2**	**75**
	3-2.7, X = S	**3-2.7a, X = S**	**25°C**	**1.2**	**73**
5					
	3-2.8	**3-2.8a**	**35°C**	**1.2**	**35**

Part 3. Cobalt-Catalyzed Michael Cycloreduction[1]

Cobalt enolates generated *via* enone hydrometalation should be subject to capture by a variety of π-unsaturated electrophilic partners. For example, conjugate addition to an appendant enone would provide formal Michael addition products. The development of a catalytic Michael cycloreduction would not only illustrate the generality of this methodology, but would more importantly represent the first catalytic system for reductive Michael condensation.

Submitting the symmetrical bis-enone **3-3.2** to conditions employed for the catalytic aldol cycloreduction afforded the expected Michael cycloreduction adduct in 41% yield. The yield was improved to 73% by increasing the stoichiometry of phenylsilane to 240 mol% (Scheme 3-3.1). The structure of **3-3.2a** was evidenced by the occurrence of two resonances in the ^{1}HNMR at δ 3.34 (ddd, *J* = 3.2, 10.4, 12.8 Hz, 1H) and δ 3.14 (dd, *J* = 2.4, 12.8 Hz, 1H) corresponding to methine protons α and β to the carbonyl group, respectively.

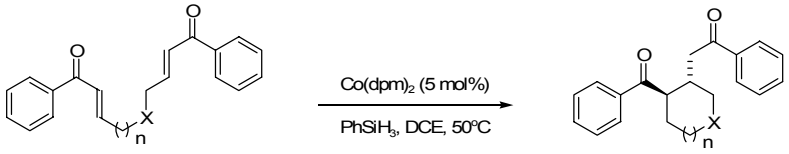
Scheme 3-3.1

3-3.2 **3-3.2a**

Substrate	$Co(dpm)_2$ (equiv.)	Silane (equiv.)	Yield (%)
3-3.2	0.05	1.2	41
3-3.2	0.05	2.4	**73**

Five- and six-membered rings may be formed in good yields under these conditions (Scheme 3-3.2). As evidenced by the ether-linked substrate **3-3.3**, heteroatoms are tolerated in the tether connecting the enones.

Scheme 3-3.2

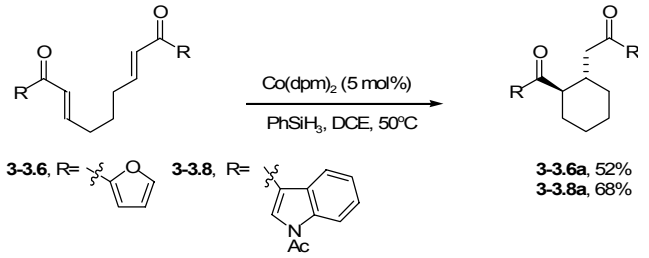


3-3.1, n=0, X=CH_2
3-3.2, n=1, X=CH_2
3-3.3, n=1, X=O

3-3.1a, 62%
3-3.2a, 73%
3-3.3a, 63%

Numerous substrates containing different acyl moieties were surveyed next. Symmetrical heteroaromatic enones afforded good yields of Michael cycloreduction products, as illustrated by the reductive cyclization of 2-furoyl substituted bis-enone **3-3.6** and the 3-indoloyl substituted bis-enone **3-3.8** (Scheme 3-3.3).

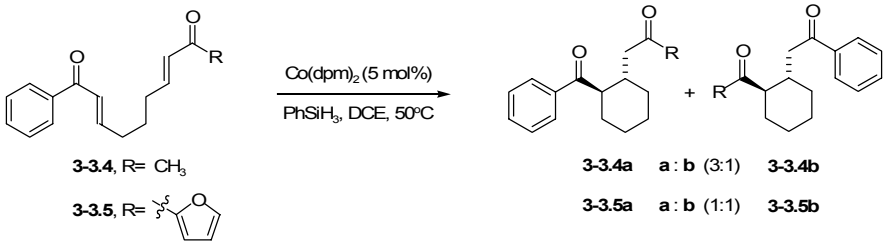
Scheme 3-3.3



3-3.6a, 52%
3-3.8a, 68%

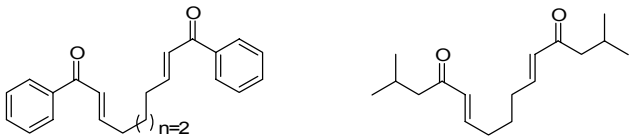
The chemoselectivity of the Michael cycloreduction is exemplified by the reaction of the mixed bis-enones **3-3.4** and **3-3.5** (Scheme 3-3.4). The unsymmetrical bis-enone **3-3.5** containing phenyl- and furyl-substituted enone partners yields a mixture of isomeric products **3-3.5a** and **3-3.5b**. In contrast, mixed enone **3-3.4**, containing phenyl- and methyl-substituents, exhibits a preference for hydrometalation of the phenyl-substituted enone. Isomeric products **3-3.4a** and **3-3.4b** were formed in a 3:1 ratio. These results suggest that the level of chemoselectivity increases as the electronic bias between enone partners increases.

Scheme 3-3.4



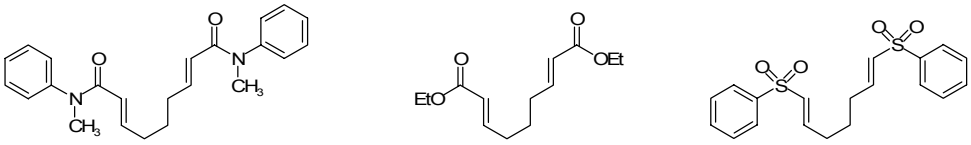
Attempts at the seven-membered ring formation of a phenyl bis-enone led to complex mixtures of oligomeric materials (Figure 3-3.1). The reaction of isovaleryl-substituted bis-enone also gave rise to significant amounts of undesired side-products.

Figure 3-3.1



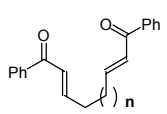
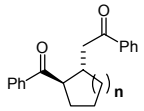
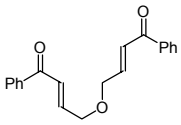
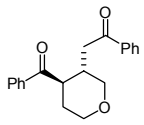
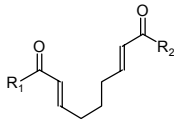
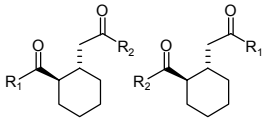
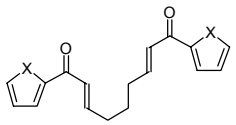
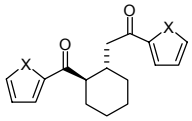
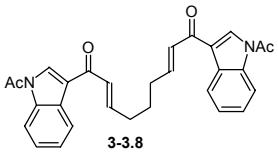
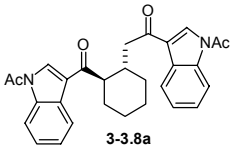
As in the aldol cycloreduction, substrates containing less electrophilic enone partners did not undergo Michael cycloreduction (Figure 3-3.2). Bis (α,β-unsaturated amides), bis α,β-unsaturated esters) and bis (vinyl sulfones) failed to provide the corresponding products.

Figure 3-3.2



Michael cycloreduction adducts **3-3.1a** – **3-3.8a** (Table 3-3.1) were obtained as single diastereomers as determined by HPLC analysis. Whereas the aldol cycloreduction exhibited high levels of *syn*-diastereoselectivity, *anti*-stereochemistry was observed exclusively for products of reductive Michael cyclization.

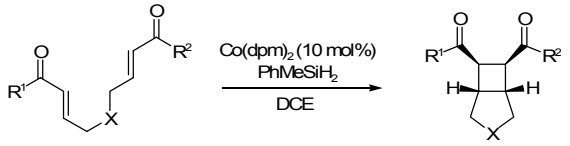
Table 3-3.1. Cobalt-catalyzed Michael cycloreductions

Entry	Substrate	Product	T(°C)	$PhSiH_3$ (eq.)	Yield (%)
3					
	3-3.1, n = 1	3-3.1a	50°C	2.4	62
	3-3.2, n = 2	3-3.2a	50°C	2.4	70
4					
	3-3.3	3-3.3a	50°C	2.4	63
5					
	3-3.4, R_1 = Ph, R_2 = CH_3	3-3.4a 3-3.4b	70°C	2.4	62
	3-3.5, R_1 = Ph, R = 2-furyl	3-3.5a 3-3.5b	50°C	2.4	54
		Ratio 3-3.4a:3-3.4b (3:1)			
		Ratio 3-3.5a:3-3.5b (1:1)			
6					
	3-3.6, X = O	3-3.6a	50°C	2.4	53
	3-3.7, X = NMe	3-3.7a	50°C	2.4	54
7					
	3-3.8	3-3.8a	50°C	2.4	68

Part 4. Cobalt-Catalyzed [2+2] Cycloaddition

Metal catalyzed intramolecular [2+2] cycloadditions were unknown until recently.[2,3] In 2002, the first transition metal catalyzed intramolecular [2+2] cycloaddition was reported by our group (Scheme 3-4.1).[4] This methodology allows for the construction of substituted bicyclo[3.2.0] ring systems in diastereomerically pure form.

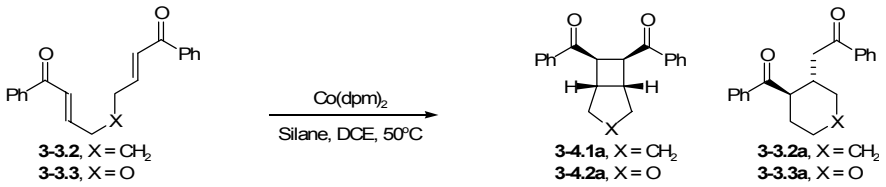
Scheme 3-4.1



In the course of optimizing the Michael cycloreduction of **3-3.2** and **3-3.3**, the following observations were made. Reactions conducted using 1.2 equivalents of phenylsilane gave roughly equal proportions of α- and β-coupled products. Here, β-coupling corresponds to [2+2] cycloadducts **3-4.1a** and **3-4.2a**. Attempts to optimize the [2+2] cycloaddition reaction revealed that Michael cycloreduction and [2+2] cycloaddition manifolds could be partitioned *via* modulation of the silane source.[31] When 2.4 equivalents of phenylsilane are employed, Michael cycloreduction occurred exclusively forming α-coupled products **3-3.2a** and **3-3.3a**. Decreasing the amount of phenylsilane below 1.2 equivalents only resulted in decreased yields for both products. In the absence of silane, no reaction was observed. Alternative silane sources were screened and excess phenylmethylsilane was found to favor β-coupling products. Using this silane source, catalyst loading and temperature were varied to optimize the reaction (Table 3-4.1). The best yields of the [2+2] cycloadducts **3-4.1a** and **3-4.2a**, 72% and 69% respectively, were obtained with 4.0 equivalents of phenylmethylsilane in the presence of 10 mol% $Co(dpm)_2$ at 50˚C. The Michael cycloaddition pathway was not suppressed, but was greatly inhibited. Like the aldol and Michael cycloreductions, the substituted bicyclo[3.2.0] products of the [2+2] cycloaddition reaction were obtained as single diastereomers. The obtention of **3-4.1a** was verified by the

resonances at δ 3.90 (d, *J* = 4.2 Hz, 2H) and δ 3.22 (m, 2H) in the ^{1}HNMR corresponding to methine protons α and β to the carbonyl groups, respectively. The structural assignment of **3-4.1a** was further corroborated *via* X-ray diffraction analysis of a single crystal.

Table 3-4.1



3-3.2, X = CH_2
3-3.3, X = O

3-4.1a, X = CH_2
3-4.2a, X = O

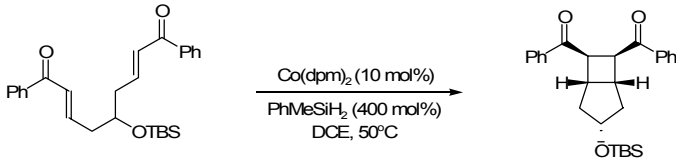
3-3.2a, X = CH_2
3-3.3a, X = O

Substrate	$Co(dpm)_2$ (equiv.)	Silane (equiv.)	Yield (%) [2+2]	Yield (%) Michael
3-3.2	0.05	$PhSiH_3$ (1.2)	38	41
3-3.2	0.05	$PhSiH_3$ (2.4)	--	**73**
3-3.2	0.10	$PhMeSiH_2$ (4.0)	**72**	11
3-3.3	0.05	$PhSiH_3$ (1.2)	16	31
3-3.3	0.05	$PhSiH_3$ (2.4)	--	**63**
3-3.3	0.10	$PhMeSiH_2$ (4.0)	**69**	9

A variety of bis-enones were submitted to the optimized reaction conditions (Table 3-4.2). First, the tolerance of this catalyst to functionality in the tether connecting bis-enones was assessed. Substrates containing heteroatoms in the tether, as in oxygen- and nitrogen-linked bis-enones **3-3.3** and **3-4.3**, did not affect the efficiency of the catalyst system (Table 4, entry 1). Substrate **3-4.4** also participated in the reaction, unfortunately, geminal substitution in the tether gave increased amounts of cycloreduction.

Substrate-directed diastereoselectivity was examined using the siloxy-substituted bis-enone **3-4.5** (Scheme 3-4.2). The [2+2] cycloadduct **3-4.5a** was obtained as a single stereoisomer with the siloxy substituent residing on the concave face of the bicyclo[2.3.0] ring system.

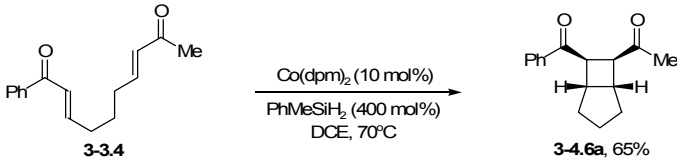
Scheme 3-4.2



3-4.5 **3-4.5a**, 65%

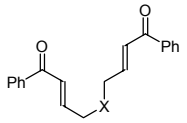
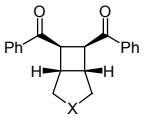
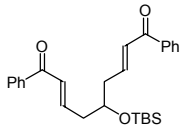
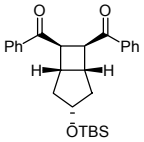
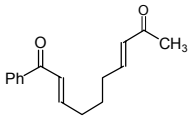
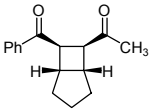
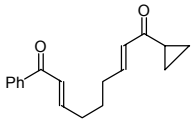
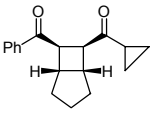
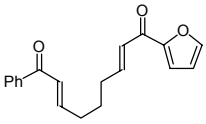
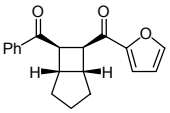
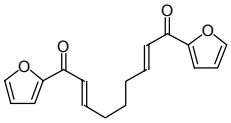
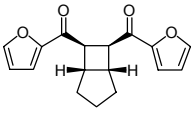
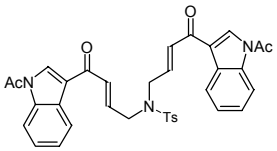
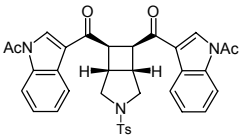
Mixed bis-enones bearing aliphatic and aromatic enone moieties also undergo cycloaddition. Example **3-3.4**, containing phenyl- and methyl-substituted bis-enone partners, affords the [2+2] cycloadduct **3-4.6a** in moderate yield (Scheme 3-4.3). The presence of the aliphatic enone residue required a higher reaction temperature for the cycloaddition to occur. Aliphatic bis-enones do not participate in the cycloaddition suggesting that at least one aromatic enone partner is required. Heteroaromatic bis-enones **3-3.6** and **3-4.10** also readily undergo [2+2] cycloaddition (Table 3-4.2, entries 6 and 7).

Scheme 3-4.3



3-3.4 **3-4.6a**, 65%

Table 3-4.2. Cobalt-catalyzed [2+2] cycloadditions

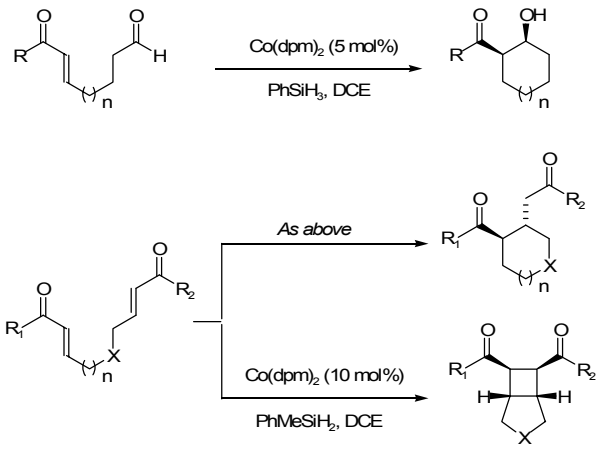
Entry	Substrate	Product	T(°C)	Yield (%) [2+2]	Yield (%) Michael
1					
	3-3.2, X = CH_2	**3-4.1a, X = CH_2**	**50°C**	**72**	**11**
	3-3.3, X = O	**3-4.2a, X = O**	**50°C**	**63**	**10**
	3-4.3, X = NTs	**3-4.3a, X = NTs**	**50°C**	**72**	**--**
	3-4.4, X = $C(CO_2Et)_2$	**3-4.4a, X = $C(CO_2Et)_2$**	**50°C**	**50**	**23**
2					
	3-4.5	**3-4.5a**	**50°C**	**65**	**--**
3					
	3-3.4	**3-4.6a**	**70°C**	**65**	**5**
4					
	3-4.7	**3-4.7a**	**70°C**	**42b**	**---**
5					
	3-3.5	**3-4.8a**	**50°C**	**48**	**18 (1:1)**
6					
	3-3.6	**3-4.9a**	**50°C**	**65**	**2**
7					
	3-4.10	**3-4.10a**	**70°C**	**51**	**15**

Part 5. **Mechanistic Details for Cobalt-Catalyzed Cycloreduction and Cycloaddition Reactions**

I. Diastereoselective Aldol and Michael Cycloreductions

A highly diastereoselective catalytic method for aldol and Michael cycloreductions was developed by our research group. In the process of optimizing the Michael cycloreduction, a related metal catalyzed [2+2] cycloaddition was discovered whereby bis-enones are converted to diastereomerically pure bicyclo[3.2.0] ring systems (Scheme 3-5.1). Mechanistic studies were conducted to reveal the mechanism and partitioning of these catalytic cycloreductions and cycloadditions.[5]

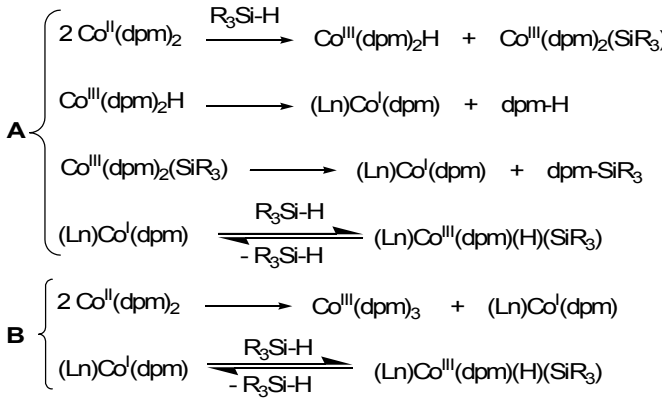
Scheme 3-5.1 Cobalt-Catalyzed Cycloreduction and Cycloaddition Reactions



The interaction of silane with the (diketonato)cobalt precatalyst is a key feature of the cycloreduction mechanism. Tetrahedral d^7-metal complexes such as $Co(dpm)_2$ undergo single electron oxidative addition with elemental hydrogen and a variety of organic alkyl halides through a free radical mechanism.[6] Disproportionation of Co(II) is well-known.[7] Thus, formation of the hydrido-metal intermediates required for initiation of the catalytic cycle *via* enone hydrometalation may arise through (**A**) single electron oxidative addition of silane, with subsequent reductive elimination to produce Co(I), followed by two-electron oxidative addition to silane or (**B**) disproportionation followed by two-electron oxidative addition of silane to Co(I) (Scheme 3-5.2). The latter pathway is supported by HRMS analysis of

$Co(dpm)_2$ in the presence and absence of $PhMeSiH_2$. An intense signal consistent with the mass of $Co(dpm)_3$ is only seen in the presence of $PhMeSiH_2$. Direct oxidative addition of silane to $Co(dpm)_2$ would result in the formation of a Co(IV) intermediate. Having cobalt in this unstable oxidation state makes the direct oxidative addition very unlikely.

Scheme 3-5.2

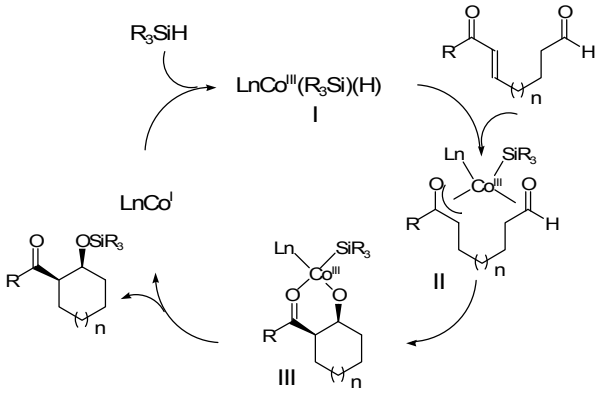


In principle, hydrido-metal intermediates may arise from σ-bond metathesis of silane to $Co(dpm)_2$. The Ti-catalyzed reductive cyclization of 1,5-enones and 1,5-enals employs silane and is thought to proceed through a σ-bond metathesis mechanism.[15,16] This mechanistic pathway is well recognized for catalytic reactions involving early transition metals, actinides and lanthanides.[8] Additionally, mechanisms involving σ-bond metathesis have been proposed for catalytic reactions of late transition metals with silanes and boranes.[9]

A mechanism predicated on a Co(I)-Co(III) catalytic cycle is depicted in Scheme 3-5.3 and is proposed as a working model. Generally, alkenes undergo hydrosilylation in the presence a transition metal catalyst and silane. The most commonly accepted mechanism for hydrosilylation is the Chalk-Harrod process.[10] According to this mechanism, oxidative addition of silane to the metal is followed by hydride-olefin insertion and then alkyl-silicon reductive elimination to afford the product. Our proposed catalytic cycle is similar. Oxidative addition of silane to LnCo(I) affords hydrido-cobalt species **I**. Hydrometalation of the enone provides cobalt enolate **II**, which undergoes carbonyl addition to the appendant aldehyde to

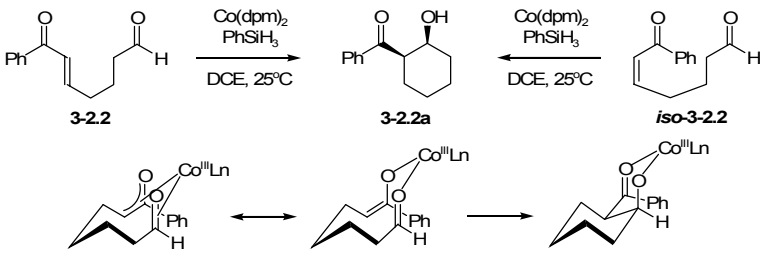
provide cobalt-alkoxide **III**. Oxygen-silicon reductive elimination liberates the aldol product in the form of the silyl ether and regenerates LnCo(I) to complete the catalytic cycle.

Scheme 3-5.3



An analogous catalytic cycle is envisioned for the related Michael cycloreduction. Elemental hydrogen is evolved throughout the course of these cycloreductions suggesting the active catalyst also participates in the competitive dehydrogenative coupling of silane.[11] Consistent with the mechanism depicted above, the *syn*-selectivity observed for the aldol cycloreduction is unaffected by alkene geometry (Scheme 3-5.4). A *cis*-configured enone-aldehyde substrate affords product **3-2.2a**, identical to that obtained with *trans*-configured phenyl enone **3-2.2**, with a *syn*:*anti* ratio of >99:1 as determined by HPLC analysis. A model accounting for the observed diastereoselectivity in both aldol and Michael cycloreductions is shown below. The formation of the *Z*-enolates is preferred on the basis of sterics, i.e. allylic 1,2 strain.[12]

Scheme 3-5.4



Deuterium labeling studies further support the proposed mechanism. Exposure of **3-2.2** to aldol cycloreduction conditions using d^3-phenylsilane affords the mono-deuterated adduct deuterio-**3-2.2a** as a 1:1 mixture of stereoisomers (Figure 3-5.1). The stereochemical assignment of deuterio-**3-2.2a** was corroborated by ^{1}H NMR analysis and single crystal neutron diffraction analysis. The latter also gave an assessment of the stereoisomeric ratio and ^{1}H:^{2}H ratio at the β-position (Table 8).

Figure 3-5.1. Structure of deuterio-**3-2.2a** determined by neutron diffraction. Atoms are drawn at their 50% probability level. Left: syn,syn epimer Right: syn,anti epimers

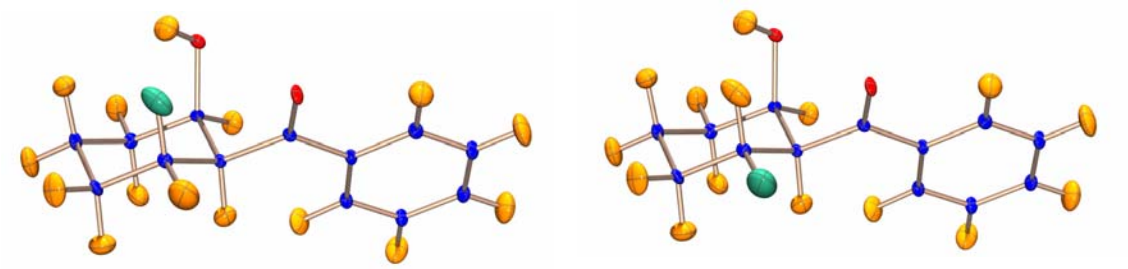
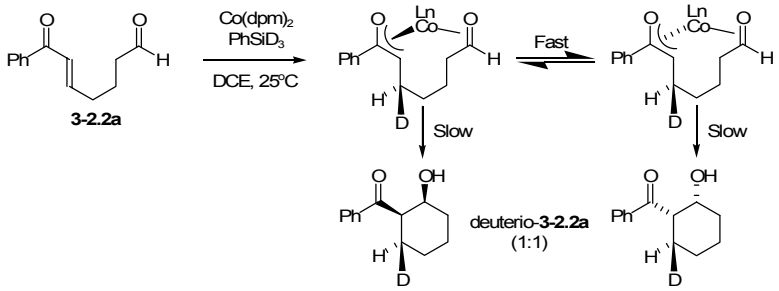


Table 3-5.1. Site occupancies of H and D atoms at the β-position as determined by neutron diffraction for deuterio-**3-2.2a**

Atom	Occupancy	Total Occupancy	Total H/D Ratio	Site H/D Ratio	Syn/AntiRatio
H-syn	0.476(6)	0.988(9)	0.976(9)	0.908(9)	0.518(syn)
H-anti	0.512(6)				
D-syn	0.524(6)	1.012(9)		1.049(9)	0.482
D-anti	0.488(6)				

The formation of deuterio-**3-2.2a** as a 1:1 mixture of stereoisomers suggests that π-facial interconversion of the metallo-enolate is faster than aldehyde addition (Scheme 3-5.5). Isomerization and aldehyde addition are both likely to occur through the η^1-haptomer of the enolate, as supported by related studies of Ni(II)-enolates.[13]

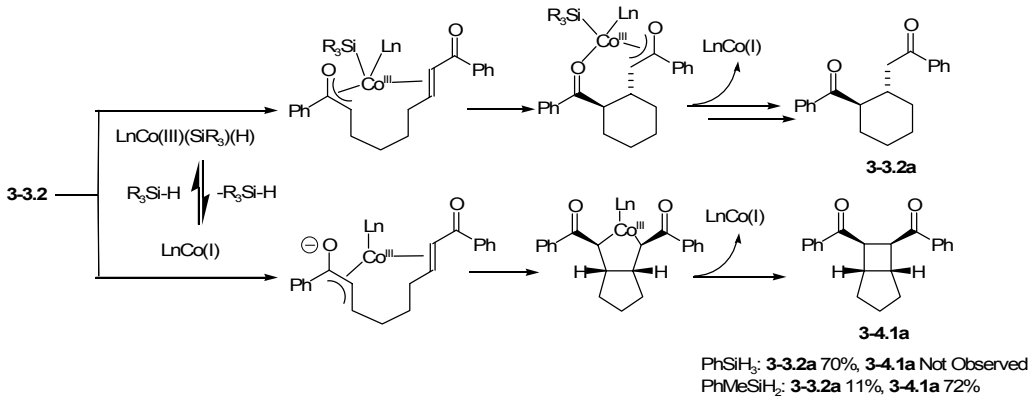
Scheme 3-5.5



II. Competitive α- and β-Coupling Manifolds

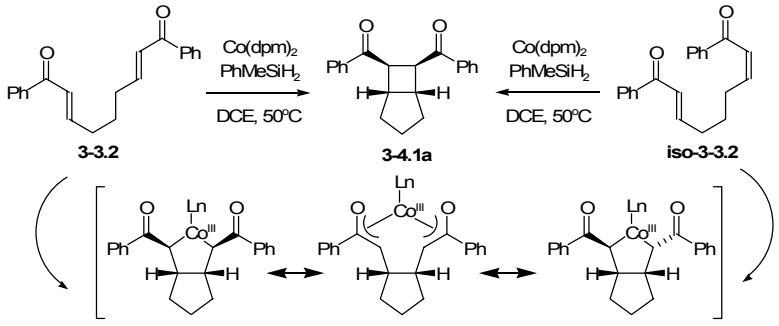
Exposure of bis-enone **3-3.2** to the $Co(dpm)_2$-phenylsilane catalyst system affords both Michael cycloreduction and [2+2] cycloaddition adducts, **3-3.2a** and **3-4.1a**, respectively. As previously discussed, these competitive reaction manifolds can be partitioned *via* modulation of the silane source. Phenylsilane promotes Michael cycloreduction while methylphenylsilane promotes the [2+2] cycloaddition pathway (Scheme 3-5.6). Competitive formation of [2+2] cycloaddition and Michael cycloreduction products and the partitioning of these reaction manifolds as a function of silane is consistent with the proposed Co(I)-Co(III) catalytic cycle. Whereas Co(III) hydride is responsible for initiating the Michael cycloreduction *via* enone hydrometalation, LnCo(I) initiates the [2+2] cycloaddition pathway. Therefore, partitioning of these reaction manifolds relates to the respective abilities of phenylsilane *vs* phenylmethylsilane to undergo oxidative addition to LnCo(I). In the presence of phenylsilane, facile oxidative addition promotes the hydrometallative pathway. Conversely, in the presence of methylphenylsilane, oxidative addition to the secondary silicon center is hindered due to crowding of the incipient adduct, stabilizing LnCo(I) and promoting the [2+2] cycloaddition *via* the intermediacy of a Co(III)-oxy-π-allyl.

Scheme 3-5.6



As with the aldol cycloreduction, the stereochemical outcome of the [2+2] cycloaddition is independent of alkene geometry (Scheme 3-5.7). The convergent stereochemical outcome for the cycloaddition of **3-3.2** and iso-**3-3.2** supports the mechanism invoking the intermediacy of a bis-(Co(III)-enolate). Rapid π-facial interconversion of Co-enolates was demonstrated through deuterium labeling studies performed on **3-3.2**. Equilibration of the intermediate bis-(Co-enolate) should favor the haptomer in which the benzoyl substituents reside on the convex face of the metallobicyclo ring system. Reductive elimination then results in the *syn*-cycloaddition product **3-4.1a**.

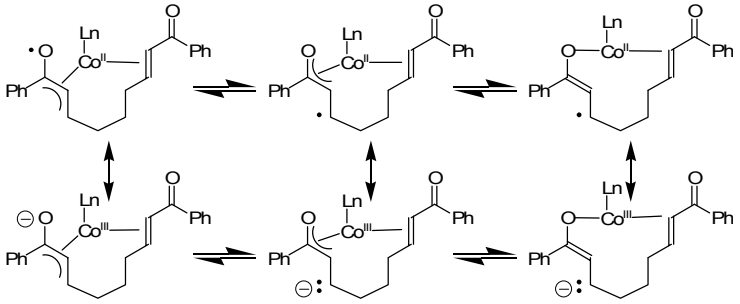
Scheme 3-5.7



Co(II)-complexed anion radicals are formed from one-electron reduction of the bis-enone precursor. They can be viewed as mesomeric forms of Co(III)-oxy-π-allyls, which result from two-electron reduction of the precursor. In collaboration with Dr. Nathan Bauld, it

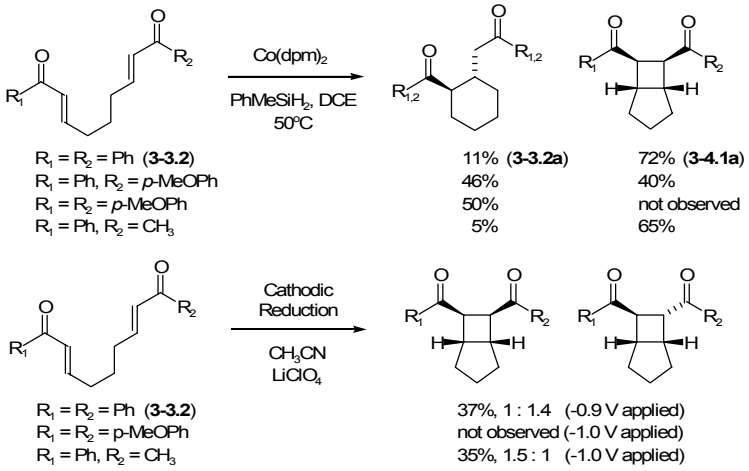
was demonstrated that cathodic reduction of substrate **3-3.2** yielded the same [2+2] adduct obtained with our $Co(dpm)_2$-silane catalyst system.[1] These electrochemical studies render the existence of Co(II)-complexed anion radicals as reactive intermediates a possibility (Scheme 3-5.8).

Scheme 3-5.8



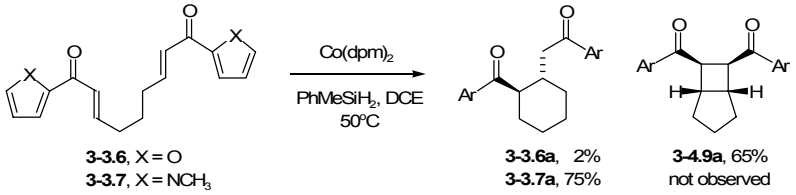
To further evaluate the plausibility of reactive intermediates embodying anion radical character, the electrochemically promoted cycloadditions of several bis-enones were performed[14] and compared to Co-catalyzed reactions (Scheme 3-5.9). Equivalent outcomes for the electrochemically promoted and the Co-catalyzed cycloadditions would support a mechanism involving intermediates possessing radical anion character. For the metal catalyzed process, the following observations were made. The [2+2] cycloaddition pathway clearly predominates for the bis-benzoyl **3-3.2**. The benzoyl- and anisoyl-containing derivative gave comparable amounts of cycloreduction and cycloaddition adducts. Michael cycloreduction was exclusively observed for the bis-anisoyl substrate. These results tell us electron-rich enones do not easily undergo cycloaddition because of their decreased electrophilicities. The trends observed for the electrochemically promoted and metal catalyzed transformations have significant similarities. Under both cobalt catalysis and cathodic reduction, bis-benzoyl substrate **3-3.2** affords [2+2] cycloadducts, while the bis-anisoyl substrate does not. Results for the aliphatic- and benzoyl-containing derivative demonstrates that only one aroyl moiety is required for both electrochemically promoted and Co-catalyzed reactions.

Scheme 3-5.9



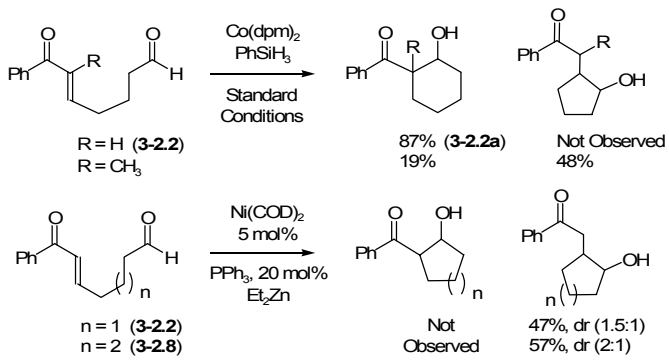
As such, for reactions performed under Co-catalysis, the requirement of aroyl-substituted enones and the observed effects of enone electronics on partitioning of the reaction manifolds likely relates to the susceptibility of a given enone moiety to reduction by LnCo(I). Electron-deficient bis-enones undergo facile reduction and, therefore, cycloaddition pathways predominate. Electron-transfer-mediated reduction is disfavored for more electron-rich substrates, i.e. substrates bearing electron-donating groups, enabling competitive hydrometallative pathways. Results obtained for heteroaromatic bis-enones **3-3.6** and **3-3.7** support the observation that the cycloaddition manifold is disfavored for electron-rich enones (Scheme 3-5.10). Cycloaddition predominates for 2-furyl substituted bis-enone **3-3.6**, while cycloreduction represents the exclusive pathway for the more electron-rich 2-(*N*-methylpyrrolyl) substituted bis-enone **3-3.7**.

Scheme 3-5.10



Competitive reduction pathways are also evident for the Co-catalyzed aldol cycloreductions. While the hydrometalative pathway predominates for enones mono-substituted at the α-position, α-disubstituted enones afford mixtures of α- and β-coupling products. Under Co-catalysis, substrate **3-2.2** yields the product of α-coupling exclusively. Exposure of an α-disubstituted enone-aldehyde to reductive aldol reaction conditions affords 19% of cycloreduction product and 48% of "homo-aldol" cycloreduction product (Scheme 3-5.11). For α-disubstituted substrates, it is likely that the rate of hydrometalation is suppressed due to crowding of the incipient Co-enolate, enabling the [2+2] cycloaddition pathway *via* enone conjugate reduction. Under Ni-catalysis, homo-aldol cycloreduction products are observed even for enones that are not α-disubstituted.[15]

Scheme 3-5.11



The homo-aldol cycloreduction products obtained with this low valent nickel catalyst may derive from transition metal-complexed anion radical intermediates. Mesomerically related Ni(II)-trimethylsilyloxy-π-allyls, obtained via enal reduction in the presence of chlorotrimethylsilane, have been isolated and characterized *via* single-crystal x-ray diffraction (Scheme 3-5.12).[16] Anion radical pathways are further supported by reports of electrochemically induced homo-aldol cycloreductions.[17] The reactive intermediates in the Co-catalyzed [2+2] cycloaddition are probably best described as oxy-π-allyls with anion radical character.

Scheme 3-5.12

Part 6. Conclusion

The development of highly diastereoselective aldol and Michael cycloreductions illustrates the utility of the hydrometalative activation of enones as enolate nucleophiles. The $Co(dpm)_2$-$PhSiH_3$ catalyst system overcomes several limitations: *i*. the absence of intramolecular transition metal catalyzed aldol processes and *ii*. the absence of transition metal catalyzed reductive Michael processes. The transformations are viable for both five- and six-membered ring formations in high yield and competitive alkene and aldehyde hydrosilylation are not observed. One drawback to these transformations is the requirement of at least one aroyl-moiety for viable substrates, which limits substrate scope.

A significant aspect of these studies is competitive enone reduction manifolds. Whereas enone hydrometalation enables catalytic aldol and Michael cycloreduction, electron transfer results in the formation of homo-aldol products and [2+2] cycloadducts. The exact nature of the reactive intermediate responsible for the conception of β-coupling products remains uncertain. The formation of identical [2+2] and homo-aldol adducts for the electrochemically promoted and the Co-catalyzed cycloadditions lends credence to the viability of anion radical pathways. Thus, any mechanistic hypotheses should consider the intermediacy of transition metal anion radicals in addition to metal-complexed oxy-π-allyls. None the less, via modulation of the catalyst system, the first metal-catalyzed [2+2] cycloaddition of tethered enones that affords diastereomerically pure substituted bicyclo[3.2.0] ring systems was developed.

Part 7. References

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[10] "Homogeneous Catalysis. II. The Mechanism of the Hydrosilation of Olefins Catalyzed by Group VIII Metal Complexes," Chalk, A. J.; Harrod, J. F. *J. Am. Chem. Soc.* **1965**, *87,* 16.

[11] "Catalytic Dehydrogenative Coupling of Secondary Silanes Using Wilkinson's Catalyst," Rosenberg, L.; Davis, C. W.; Yao, J. *J. Am. Chem. Soc.* **2001**, *123*, 5120 and references therein.

[12] Hofmann, R. W. *Chem. Rev.* **1989**, *89* 1841 and references therein.

[13] "Structure of a η^1-Nickel O-Enolate: Mechanistic Implications in Catalytic Enyne Cyclizations," Amarasinghe, K. K. D.; Chowdhury, S. K.; Heeg, M. J.; Montgomery, J. *Organometallics* **2001**, *20*, 370.

[14] "Anion Radical Chain Cycloaddition of Tethered Enones: Intramolecular Cyclobutanation and Diels-Alder Cycloaddition," Roh, Y.-S.; Jang, H.-Y.; Lynch, V.; Bauld, N. L.; Krische, M. J. *Org. Lett.* **2002**, *4*, 611.

[15] "Nickel-Catalyzed Organozinc-Promoted Carbocyclizations of Electron-Deficient Alkenes with Tethered Unsaturation," Montgomery, J.; Oblinger, E.; Savchenko, A. V. *J. Am. Chem. Soc.* **1997**, *119*, 4911.

[16] (a) "A practical reversed-polarity alternative to organocuprate conjugate addition chemistry. Halocarbon coupling reactions of enal- and enone-derived allylnickel reagents," Johnson, J. R.; Tully, P. S.; Mackenzie, P. B.; Sabat, M. *J. Am. Chem. Soc.* **1991**, *113*, 6172. (b) "Nickel-catalyzed, chlorotrialkylsilane-assisted conjugate addition of alkenyltributyltin reagents to α,β.-unsaturated aldehydes. Evidence for a [1-[(trialkylsilyl)oxy]allyl]nickel(II) mechanism," Grisso, B. A.; Johnson, J. R.; Mackenzie, P. B. *J. Am. Chem. Soc.* **1992**, *114*, 5160.

[17] "Electroreductive Cyclization. Ketones and Aldehydes Tethered to α,β-Unsaturated Esters (Nitriles). Fundamental Investigations," Little, R. D.; Fox, D. P.; Van Hijfte, L.; Dannecker, R.; Sowell, G.; Wolin, R. L.; Moens, L.; Baizer, M. M. *J. Org. Chem.* **1988**, *53*, 2287.

Part 8. Experimentals

I. General Procedures

All reactions were run under an atmosphere of argon, unless otherwise indicated. Anhydrous solvents were transferred by an oven-dried syringe. Flasks were flame-dried and cooled under a stream of nitrogen. Dichloromethane and dichloroethane were distilled from calcium hydride. Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone ketyl.

Analytical thin-layer chromatography (TLC) was carried out using 0.2-mm commercial silica gel plates (DC-Fertigplatten Krieselgel 60 F_{254}). Preparative column chromatography employing silica gel was performed according to the method of Still.[1] Solvents for chromatography are listed as volume/volume ratios. Melting points were determined on a Thomas-Hoover melting point apparatus in open capillaries and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 1420 spectrometer. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported as m/e (relative intensity). Accurate masses are reported for the molecular ion (M+1) or a suitable fragment ion.

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with a Varian Gemini (300 MHz) spectrometer. Chemical shifts are reported in delta (δ) units, parts per million (ppm) downfield from trimethylsilane. Coupling constants are reported in Hertz (Hz). Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded with a Varian Gemini 300 (75 MHz) spectrometer. Chemical shifts are reported in delta (δ) units, parts per million (ppm) relative to the center of the triplet at 77.00 ppm for deuteriochloroform. ^{13}C NMR spectra were routinely run with broadbrand decoupling.

General Procedure A for the Preparation of Substrates 3-2.1 – 3-2.8, 3-3.1, 3-3.2, 3-3.4 – 3-3.8 and 3-4.7. To a solution of aldehyde (100 mol%) in dichloromethane (0.3 M) at room

([1]) Still, W. C.; Kahn, M; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

temperature, was added Wittig reagent (20-30 mol% of Wittig reagent was used for the preparation of enone-aldehydes and 300-400 mol% of Wittig reagent was used for the preparation of bis-enones) followed by stirring for 12-24 h at room temperature. The volatiles were removed under reduced pressure by rotary evaporation and the residue was purified via flash chromatography on silica. Charaterization data for substrate **3-2.1**,[2] **3-2.2**,[3] **3-2.5**,[4] **3-2.8**,[5] **3-3.1**,[6] **3-3.2**[7] was consistent with that reported in the literature. Succinaldehyde was generated from 2,5-dimethoxyfuran.[7]

General Procedure B for the Preparation of Substrates 3-3.3, 3-4.1 – 3-4.5 and 3-4.10. In accord with general procedure A with following modifications, a solution of cyclic alkene (100 mol%) in dry dichloromethane (0.5M) was treated with ozone at –78°C. Triphenylphosphine (100 mol%) and Wittig reagent (300 mol%) were added into the reaction mixture followed by stirring for 12-24 h at room temperature.

General Procedure C Aldol Cycloreduction. To a solution of $Co(dpm)_2$ (5 mol%) in dichloroethane (0.45 M with respect to substrate) at room temperature was added $PhSiH_3$ (120 mol%). The reaction mixture was allowed to stir for 30 min., at which point a solution of enone (100 mol%) in dichloroethane (0.45 M) was added via syringe. The reaction progress was monitored by TLC. Upon complete consumption of starting materials, the reaction mixture was quenched with methanol/10% $HCl_{(aq)}$ and allowed to stir at room temperature for 30 minutes. The reaction mixture was partitioned between ethyl acetate and $NH_4Cl_{(aq)}$. The aqueous layer was extracted and the combined organic extracts were dried (Na_2SO_4), filtered

(2) Black, G.P.; Dinon, F.; Fratucello, S.; Murphy, P.J.; Nielsen, M.; Williams, H. L. *Tetrahedron Lett*. **1997**, *38*, 8561.
(3) Montgomery, J. Savchenko, A. V.; Zhao, Y. *J. Org. Chem*. **1995**, *60*, 5699.
(4) Kovalev, B. G.; Dormidontova, N. P.; Shamshurin, A. S. *J. Org. Chem. USSR* **1969**, *5*, 1722.
(5) Montgomery, J.; Oblinger, E.; Savchenko, A. V. *J. Am. Chem. Soc.* **1997**, *119*, 4911.
(6) Black, G. P.; Murphy, P. J.; Walshe, N. D. A. *Tetrahedron* **1998**, *54*, 9481.
(7) Fakstorp, J.; Raleigh, D.; Schniepp, L. E. *J. Am. Chem. Soc.* **1950**, *72*, 869.

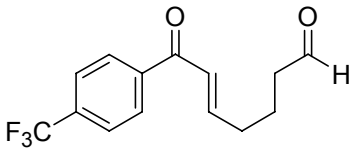
and evaporated. Chromatographic purification of the residue on silica gel provided aldol cycloreduction products **3-2.1a** – **3-2.8a**.

General Procedure D Michael Cycloreduction. To a solution of $Co(dpm)_2$ (5 mol%) in dichloroethane (0.45 M) at room temperature was added $PhSiH_3$ (240 mol%). The reaction mixture was allowed to stir for 30 min., at which point a dichloroethane solution of bis-enone (100 mol%, 0.45 M) was added via syringe. The reaction progress was monitored by TLC. Upon complete consumption of starting materials, the reaction mixture was quenched with methanol/10%$HCl_{(aq)}$ and allowed to stir for 30 minutes. The reaction mixture was partitioned between ethyl acetate and $NH_4Cl_{(aq).}$ The aqueous layer was extracted and the combined organic extracts were dried (Na_2SO_4), filtered and evaporated. Chromatographic purification of the residue on silica gel provided Michael cycloreduction products **3-3.1a** – **3-3.8a**.

General Procedure E [2+2] Cycloaddition. To a solution of $Co(dpm)_2$ (10 mol%) in dichloroethane (0.45 M) at room temperature was added $PhMeSiH_2$ (400 mol%). The reaction mixture was allowed to stir for 30 min., at which point a dichloroethane solution of bis-enone (100 mol%, 0.45 M) was added via syringe. The reaction progress was monitored by TLC. Upon complete consumption of starting materials, the reaction mixture was quenched with methanol/10%$HCl_{(aq)}$ and allowed to stir for 30 minutes. The reaction mixture was partitioned between ethyl acetate and $NH_4Cl_{(aq)}$. The aqueous layer was extracted and the combined organic extracts were dried (Na_2SO_4), filtered and evaporated. Chromatographic purification of the residue on silica gel provided [2+2] cycloaddition products **3-4.1a** – **3-4.10a**.

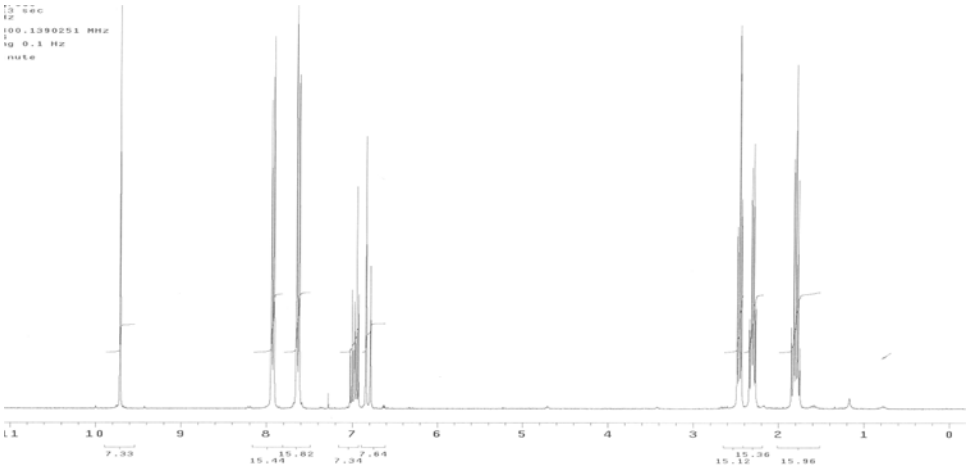
II. Spectroscopic Characterization Data

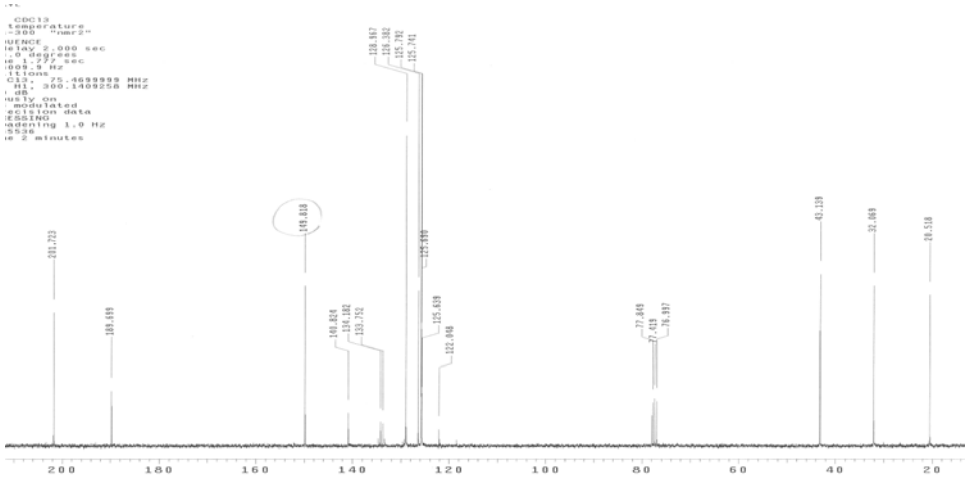
A. Cobalt-Catalyzed Aldol Cyloreduction

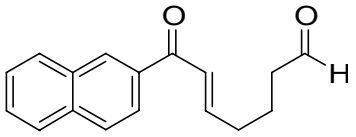


3-2.3

7-Oxo-7-(4-trifluoromethyl-phenyl)-hept-5-enal. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.72 (t, *J* = 1.2 Hz, 1H), 7.98 (m, 2H), 7.62 (m, 2H), 6.97 (m, 1H), 6.80 (d, *J* = 15.3 Hz, 1H), 2.42 (m, 2H), 2.31 (m, 2H), 1.80 (m, 2H). ^{13}C NMR (75 MHz): δ 201.7, 189.7, 149.8, 128.9, 126.4, 125.8, 125.7, 125.6, 125.5, 43.1, 32.0, 20.5. FTIR (neat): 3015, 2969, 1737, 1728, 1665, 1613, 1360, 1208, 1180 cm^{-1}. HRMS: calcd for $C_{14}H_{13}F_3O_2$ [M+1] 271.0946, found 271.0941.

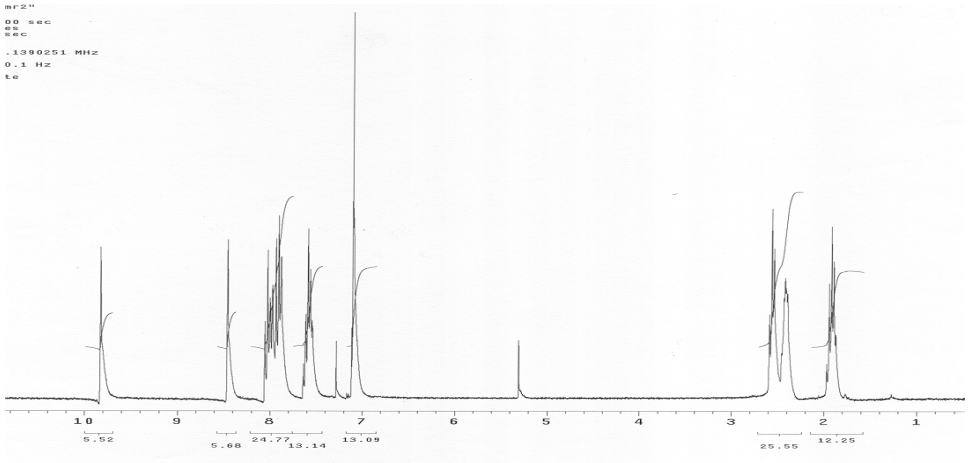


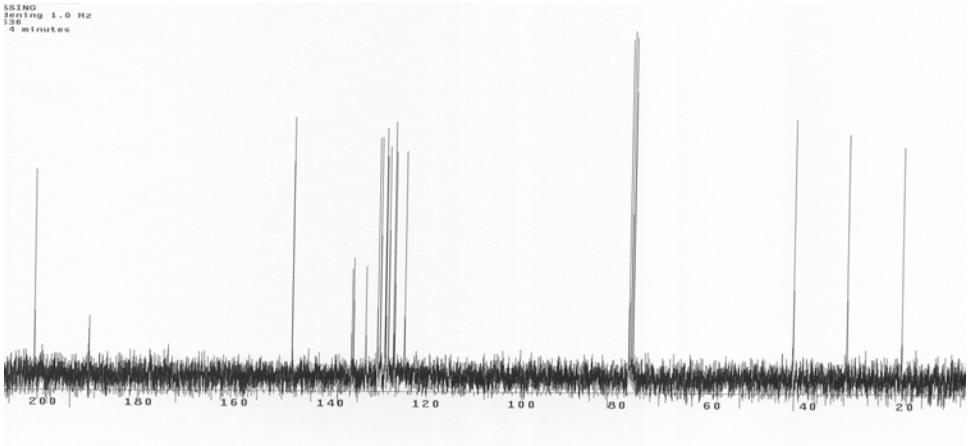


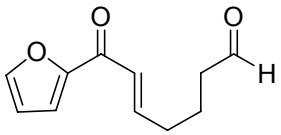


3-2.4

7-Naphthalen-2-yl-7-oxo-hept-5-enal. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.82 (t, J = 1.2 Hz, 1H), 8.45 (s, 1H), 8.03 (m, 4H), 7.58 (m, 2H), 7.10 (m, 2H), 2.56 (m, 2H), 2.42 (m, 2H), 1.87 (m, 2H). ^{13}C NMR (75 MHz): δ 201.9, 190.5, 148.2, 135.7, 135.3, 132.7, 130.3, 129.7, 128.7, 128.6, 128.0, 127.0, 126.7, 124.7, 43.3, 32.2, 20.8. FTIR (neat): 3015, 2969, 1737, 1724, 1665, 1614, 1365, 1216 cm^{-1}. HRMS: calcd for $C_{17}H_{16}O_2$ [M+1] 253.1228, found 253.1227.

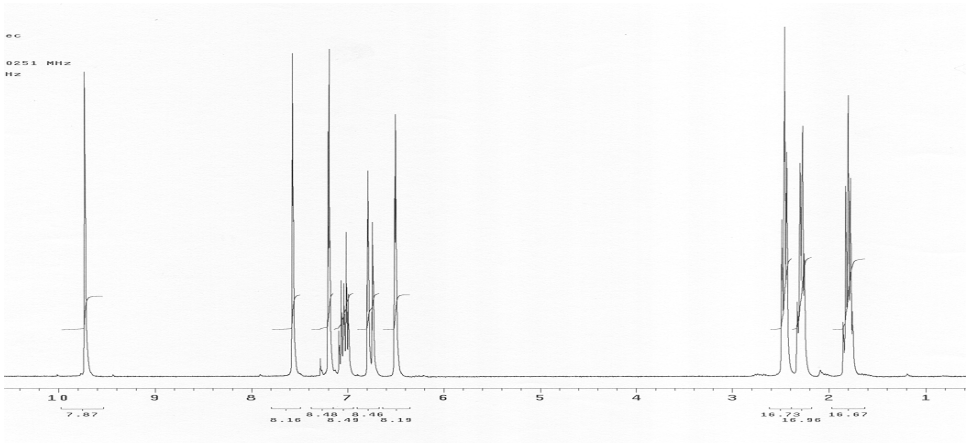


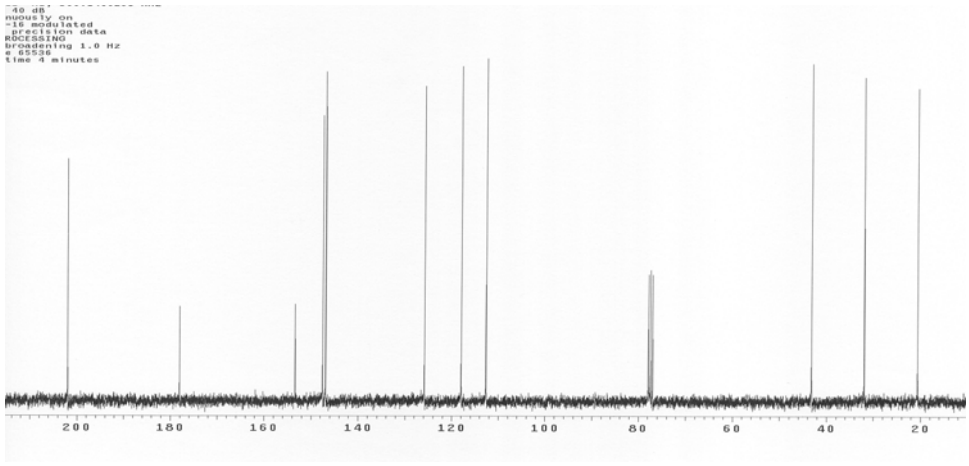


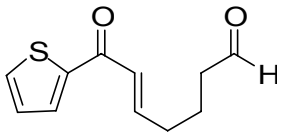


3-2.6

7-Furan-2-yl-7-oxo-hept-5-enal. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.73 (t, *J* = 1.2 Hz, 1H), 7.58 (m, 1H), 7.19 (m, 1H), 7.02 (m, 1H), 6.72 (m, 1H), 6.42 (m, 1H), 2.42 (m, 2H), 2.36 (m, 2H), 1.82 (m, 2H). ^{13}C NMR (75 MHz): δ 201.9, 178.0, 153.4, 147.5, 146.9, 125.8, 117.9, 112.6, 43.2, 31.9, 20.6. FTIR (neat): 3015, 2969, 1737, 1728, 1665, 1620, 1465, 1365, 1216 cm^{-1}. HRMS: calcd for $C_{11}H_{12}O_3$ [M+1] 193.0864, found 193.0864.

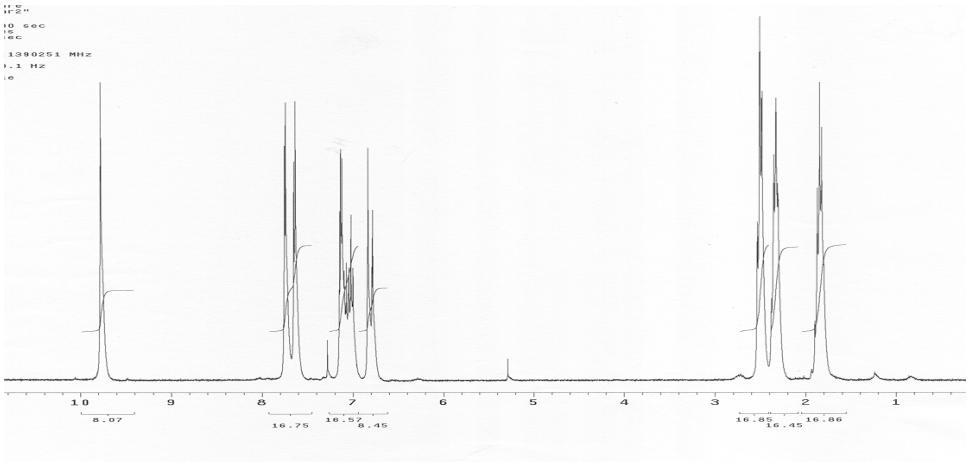


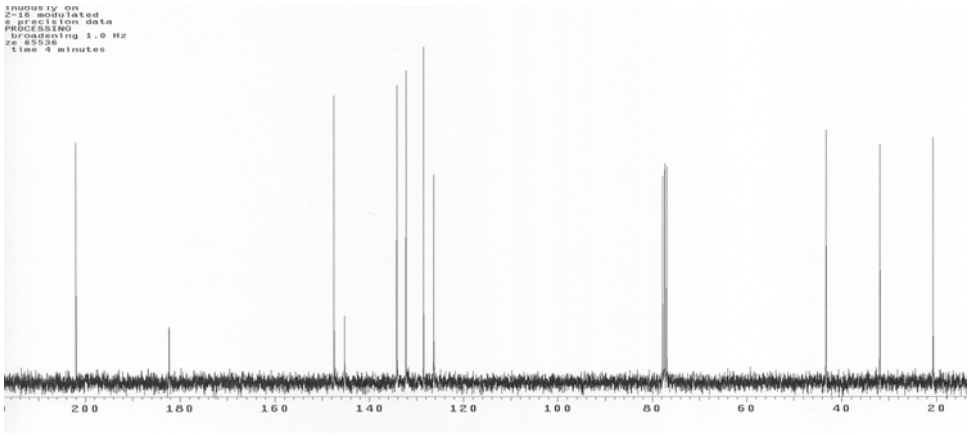


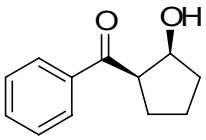


3-2.7

7-Oxo-7-thiophen-2-yl-hept-5-enal. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.77 (t, *J* = 1.2 Hz, 1H), 7.74 (dd, *J* = 1.3, 3.7 Hz, 1H), 7.64 (dd, *J* = 1.1, 4.9 Hz, 1H), 7.07 (m, 2H), 6.83 (d, *J* = 15.3 Hz, 1H), 2.52 (m, 2H), 2.38 (m, 2H), 1.82 (m, 2H). ^{13}C NMR (75 MHz): δ 201.9, 182.2, 147.5, 145.2, 134.1, 132.2, 128.5, 126.3, 43.2, 31.9, 20.7. FTIR (neat): 3015, 2969, 1737, 1724, 1656, 1611, 1414, 1365, 1216 cm^{-1}. HRMS: calcd for $C_{11}H_{12}O_2S$ [M+1] 209.0636, found 209.0642.

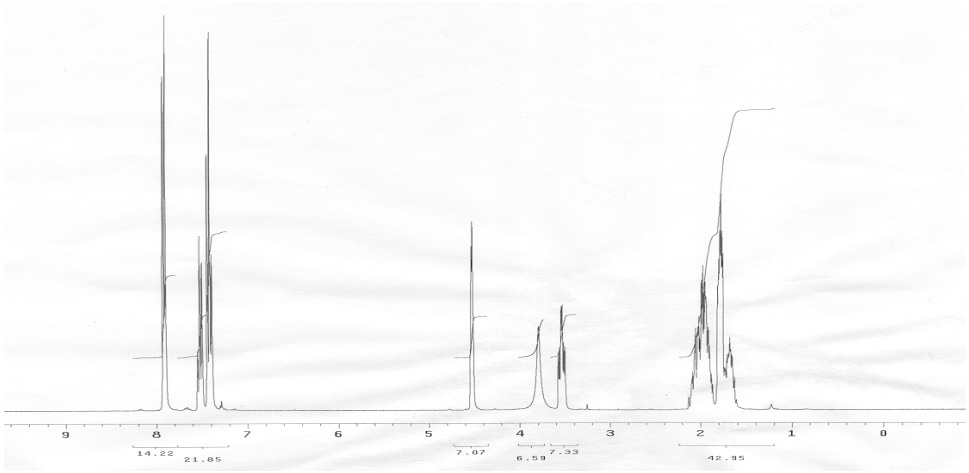


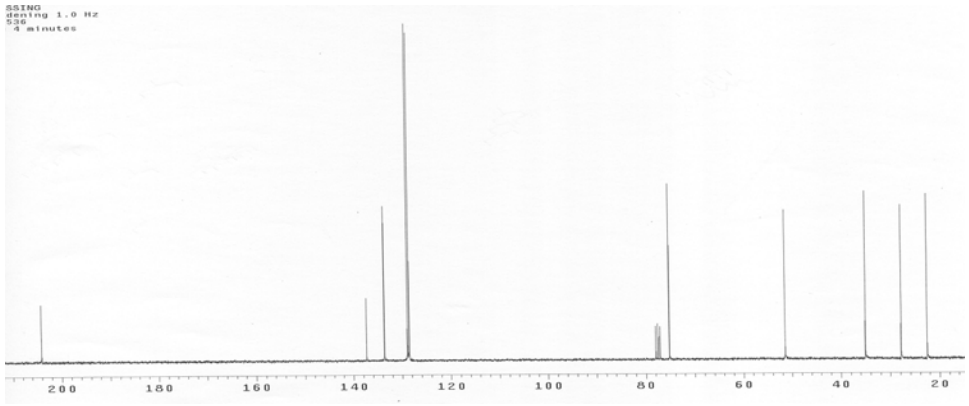


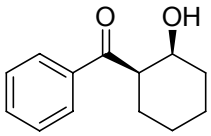


3-2.1a

(2-Hydroxy-cyclopentyl)-phenyl-methanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (m, 2H), 7.48 (m, 3H), 4.52 (s, 1H), 3.80 (brs, 1H), 3.53 (ddd, *J* = 6.9, 7.5, 13.5 Hz, 1H), 2.00 (m, 3H), 1.78 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 204.0, 137.3, 133.6, 128.9, 128.5, 75.2, 51.4, 35.0, 27.8, 22.5. FTIR (neat): 3449, 2957, 2874, 1679, 1596, 1448, 1361, 1222, 1023, 693 cm^{-1}. HRMS: calcd for $C_{12}H_{14}O_2$ [M+1] 191.1072, found 191.1067.

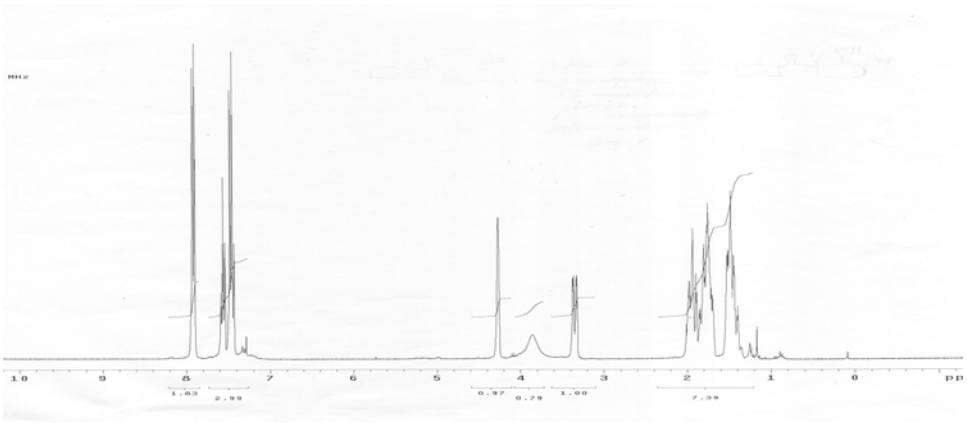


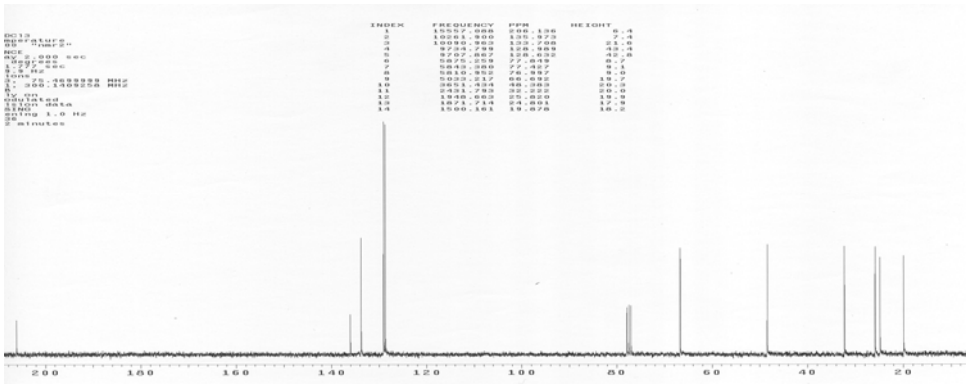


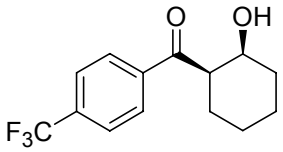


3-2.2a

(2-Hydroxy-cyclohexyl)-phenyl-methanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (m, 2H), 7.52 (m, 3H), 4.23 (m, 1H), 3.8 (brs, 1H), 3.32 (ddd, *J* = 3.1, 3.2, 11.2 Hz, 1H), 1.95 (m, 2H), 1.75 (m, 3H), 1.41 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.1, 135.9, 133.7, 128.9, 128.6, 66.7, 48.4, 32.2, 25.8 24.8, 19.8. FTIR (neat): 3462, 2934, 2857, 1701, 1446, 1355, 1129, 1087, 974, 847, 735, 614 cm^{-1}. HRMS: calcd for $C_{13}H_{16}O_2$ [M+1] 205.1228, found 205.1223. Mp = 72-75ºC.

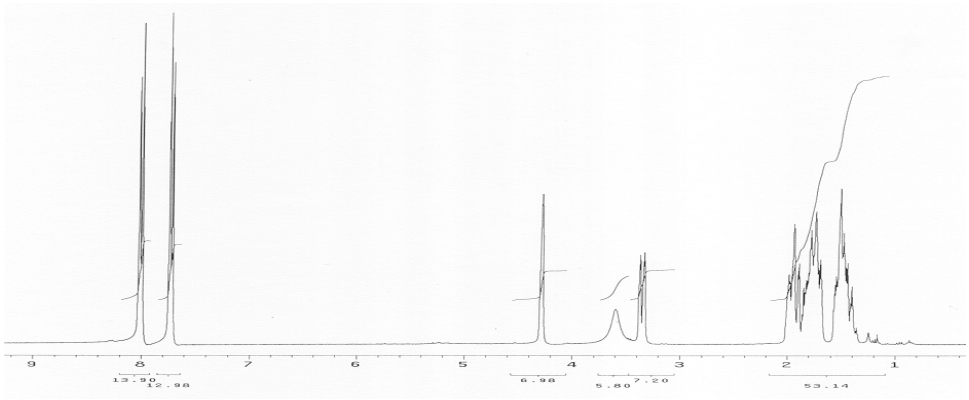


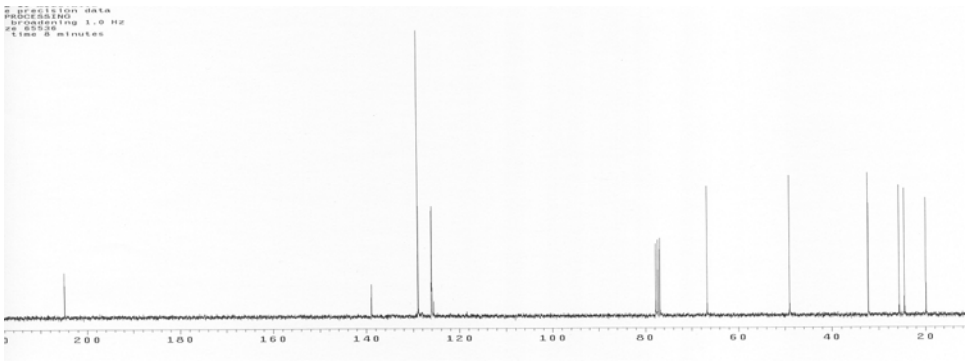


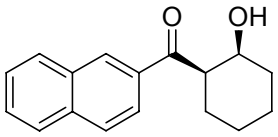


3-2.3a

(2-Hydroxy-cyclohexyl)-(4-trifluoromethyl-phenyl)-methanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02 (m, 2H), 7.73 (m, 2H), 4.29 (m, 1H), 3.60 (brs, 1H), 3.33 (ddd, *J* = 2.4, 3.6, 11.8 Hz, 1H), 1.98 (m, 2H), 1.75 (m, 3H), 1.45 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 294.8, 138.8, 128.9, 126.1, 126.0, 125.9, 66.6, 49.0, 32.2, 25.6, 24.5, 19.8. FTIR (neat): 3526, 2940, 2856, 1673, 1409, 1324, 1265, 1201, 1173, 1133, 1067, 978, 783, 665 cm^{-1}. HRMS: calcd for $C_{14}H_{15}F_3O_2$ [M+1] 273.1102, found 273.1096. Mp = 69-72ºC.

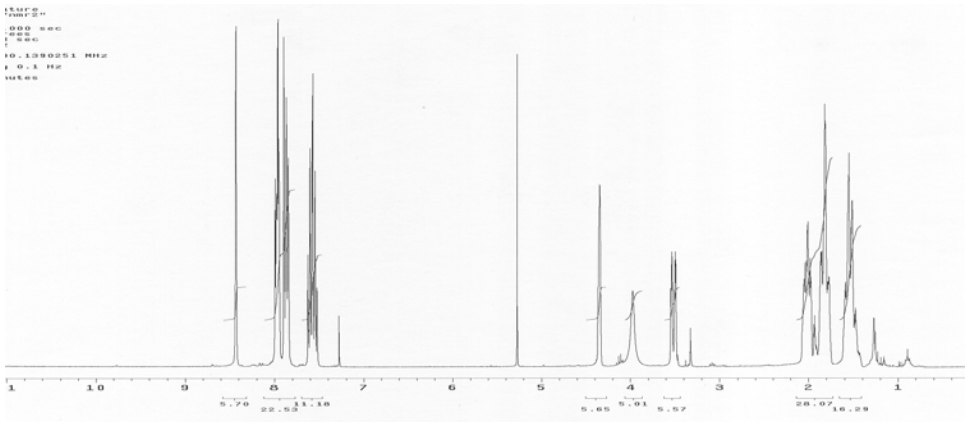


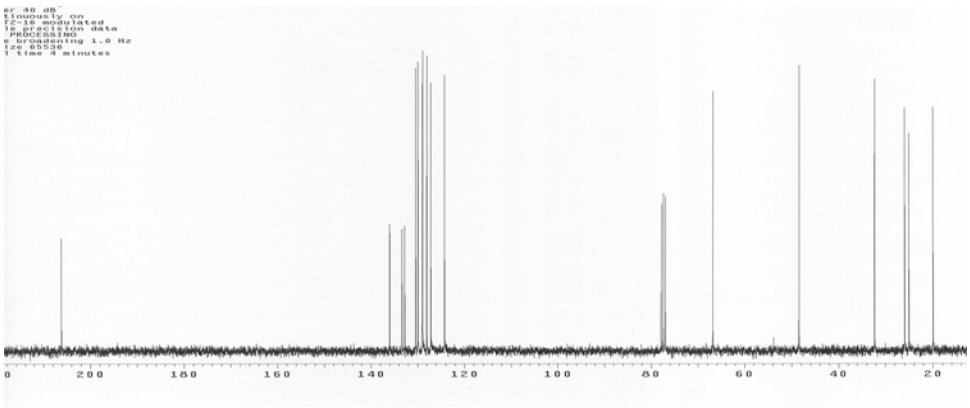


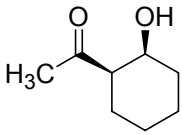


3-2.4a

(2-Hydroxy-cyclohexyl)-naphthalen-2-yl-methanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.43 (s, 1H), 7.97 (m, 4H), 7.56 (m, 2H), 4.34 (s, 1H), 3.97 (brs, 1H), 3.54 (ddd, *J* = 1.8, 3.6, 12.0 Hz, 1H), 2.08 (m, 2H), 1.82 (m, 3H), 1.54 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.1, 135.9, 133.3, 132.7, 130.4, 9.9, 129.0, 128.9, 128.0, 127.1, 124.2, 66.8, 48.4, 32.3, 25.9, 25.0, 19.9. IR (neat): 3462, 2928, 2857, 1712, 1428, 1355, 1127, 1077, 968, 847, 735, 613 cm^{-1}. HRMS: calcd for $C_{17}H_{18}O_2$ [M+1] 255.1385, found 255.1387. Mp = 97-100 ºC.

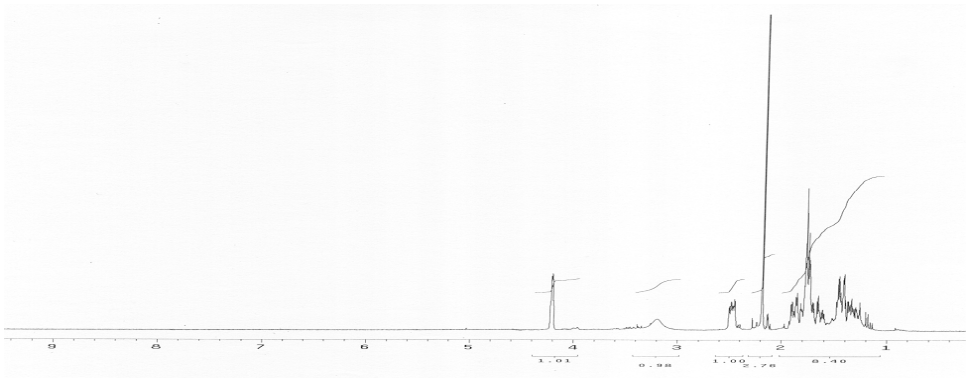


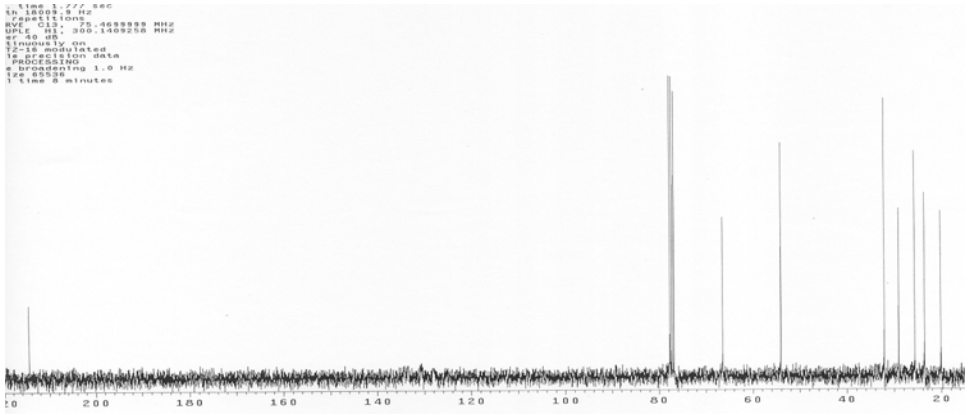


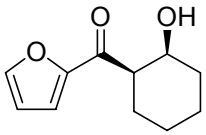


3-2.5a

1-(2-Hydroxy-cyclohexyl)-ethanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.12 (m, 1H), 3.60 (brs, 1H), 2.46 (ddd, *J* = 2.9, 3.6, 11.7 Hz, 1H), 2.28 (s, 3H), 1.72 (m, 4H), 1.43(m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 214.4, 66.5, 54.1, 32.1, 25.6, 23.5, 20.1. FTIR (neat): 3462, 2934, 2857, 1701, 1446, 1355, 1129, 1087, 974, 847, 735 cm^{-1}. HRMS: calcd for $C_8H_{14}O_2$ [M+1] 143.1072, found 143.1068.

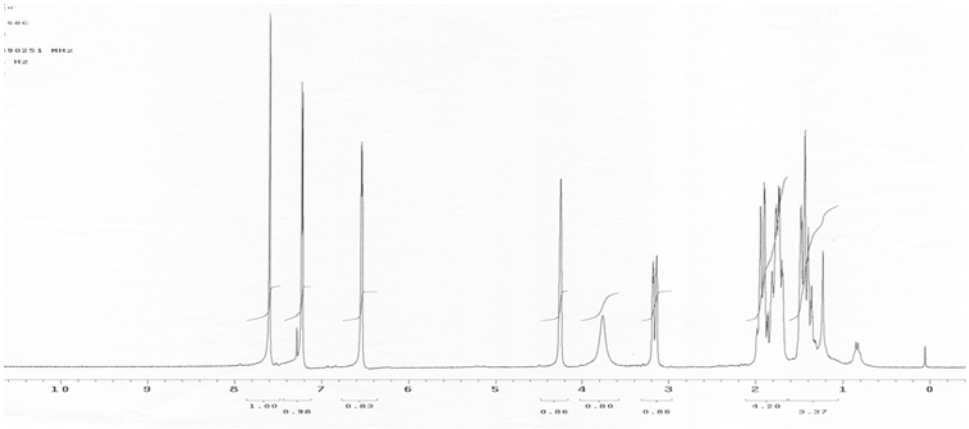


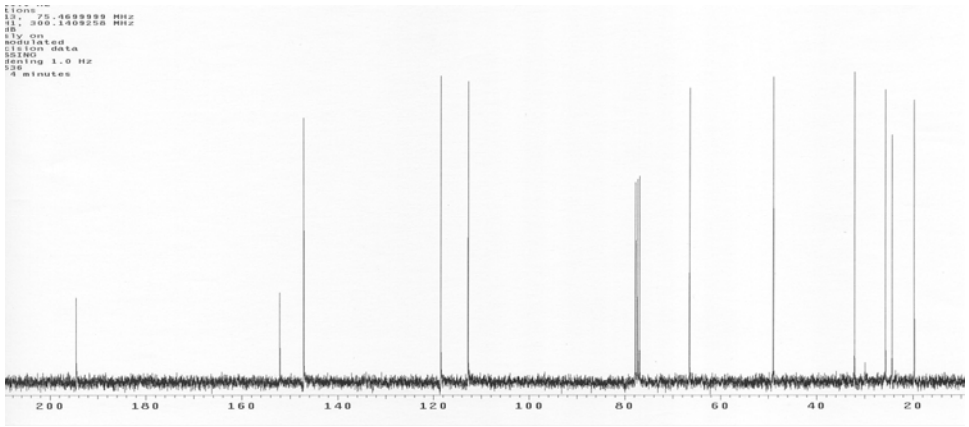


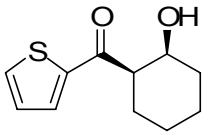


3-2.6a

Furan-2-yl-(2-hydroxy-cyclohexyl)-methanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.60 (s, 1H), 7.23 (d, *J* = 3.5, 1H), 6.54 (dd, *J* = 1.5, 3.5, 1H), 4.25 (m, 1H), 3.76 (brs, 1H), 3.15 (ddd, *J* = 2.5, 2.5, 12.2 Hz, 1H), 1.93 (m, 2H), 1.75 (m, 2H), 1.36 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.5, 152.1, 147.1, 118.4, 112.7, 66.5, 48.9, 32.1, 25.7, 24.3, 19.7. FTIR (neat): 3489, 2935, 2856, 1566, 1466, 1253, 1191, 1117, 883, 769 cm^{-1}. HRMS: calcd for $C_{11}H_{14}O_3$ [M+1] 195.1021, found 195.1017. Mp = 50-52 ºC.

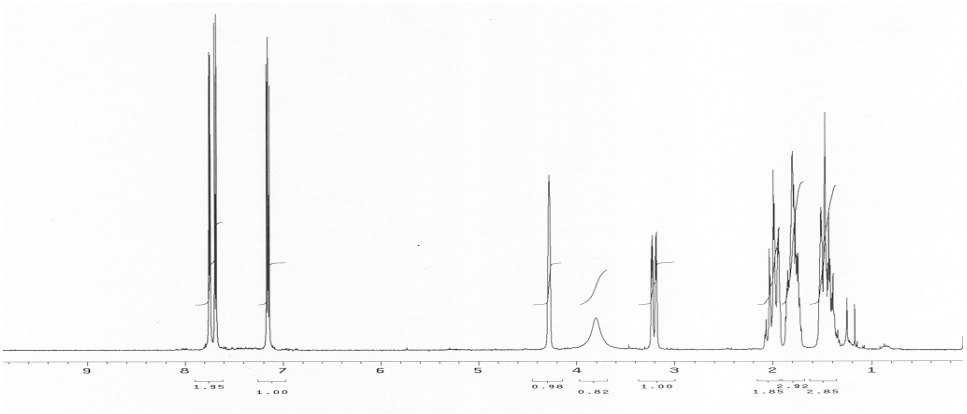


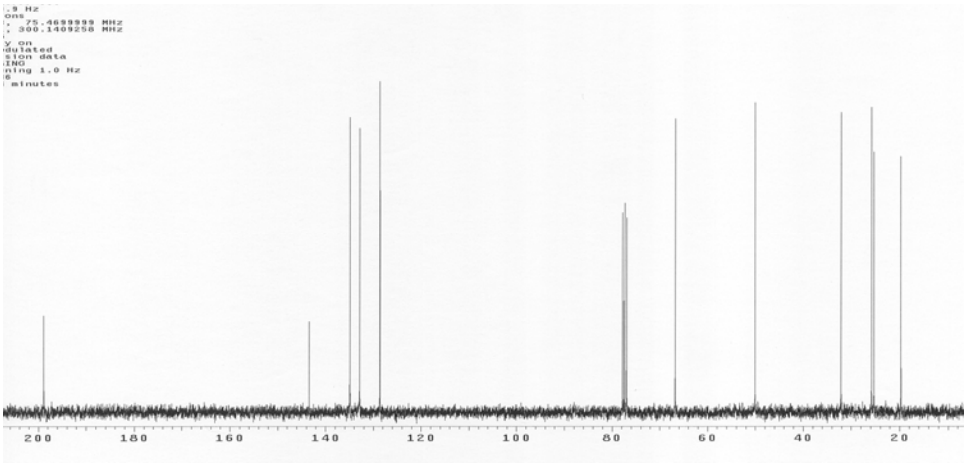


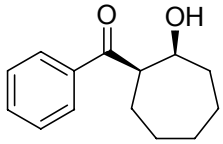


3-2.7a

(2-Hydroxy-cyclohexyl)-thiophene-2-yl-methanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 (m, 2H), 7.15 (m, 1H), 4.25 (m, 1H), 3.80 (brs, 1H), 3.18 (ddd, *J* = 2.4, 2.4, 12.2 Hz, 1H), 1.75 (m, 3H), 2.00 (m, 2H), 1.41 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 198.8, 143.4, 134.9, 132.8, 128.6, 66.7, 50.0, 32.1, 25.8, 25.3, 19.7. FTIR (neat): 3454, 2935, 2848, 1562, 1448, 1253, 1187, 1113, 854, 758 cm^{-1}. HRMS: calcd for $C_{11}H_{14}O_2S$ [M+1] 211.0792, found 211.0790. Mp = 56-58 ºC.

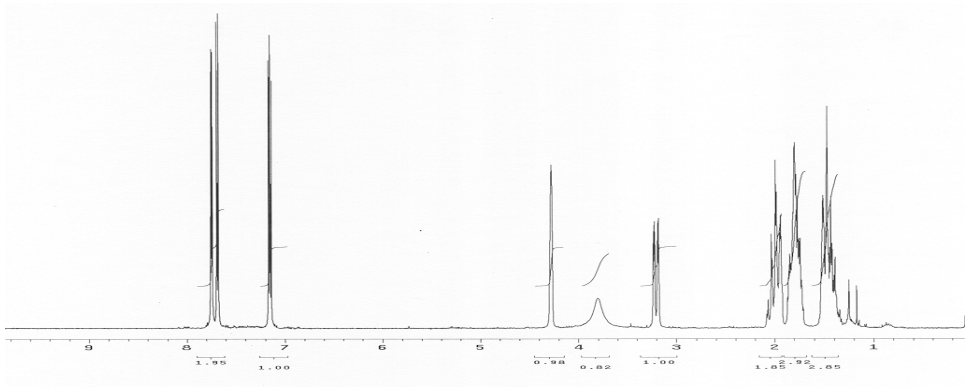


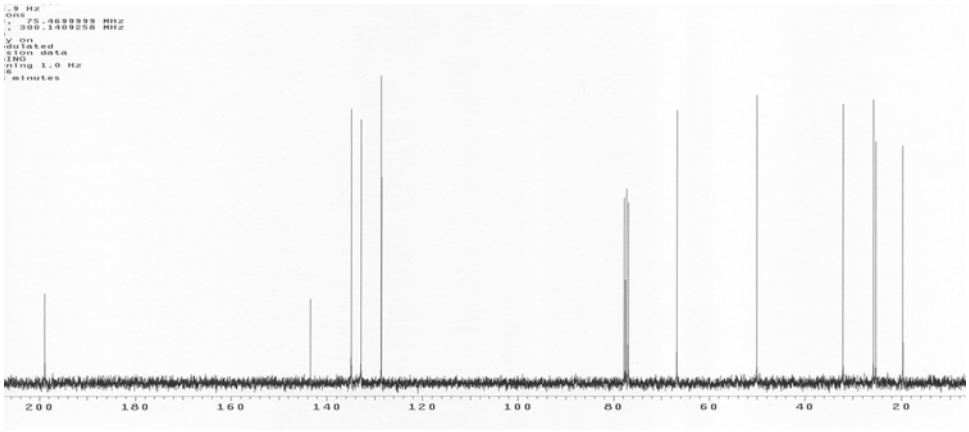




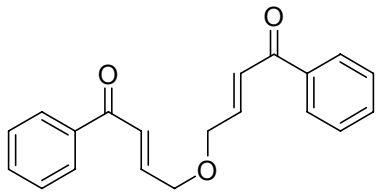
3-2.8a

(2-Hydroxy-cycloheptyl)-phenyl-methanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98 (m, 2H), 7.52 (m, 3H), 4.38 (m, 1H), 3.71 (brs, 1H), 3.46 (ddd, *J* = 1.8, 1.8, 10.2 Hz, 1H), 2.14 (m, 2H), 2.04 (m, 2H), 1.64-1.99 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.1, 135.9, 133.6, 129.0, 128.6, 69.5, 50.1, 36.1, 27.9, 26.8, 24.0, 21.9. FTIR (neat): 3481, 2928, 2859, 1665, 1596, 1447, 1268, 1215, 1129, 848, 739, 697 cm^{-1}. HRMS: calcd for $C_{14}H_{18}O_2$ [M+1] 219.1385, found 219.1384.



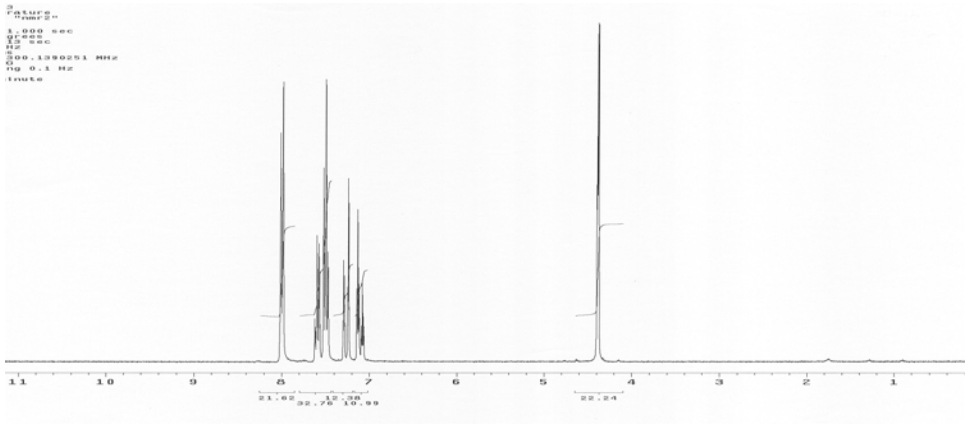


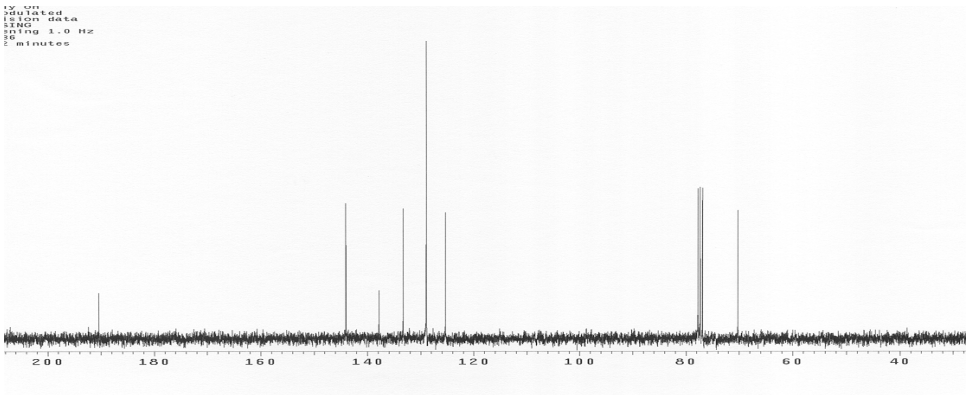
B. Cobalt-Catalyzed Michael Cycloreduction

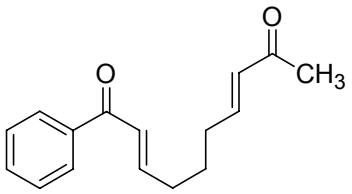


3-3.3

4-(4-Oxo-4-phenyl-but-2-enyloxy)-1-phenyl-but-2-en-1-one. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 (m, 4H), 7.59 (m, 6H), 7.13 (m, 1H), 7.06 (m, 1H), 4.41 (m, 4H). ^{13}C NMR (75 MHz): δ 190.4, 144.0, 137.8, 133.3, 128.9, 128.8, 125.3, 70.2. FTIR (neat): 3015, 2969, 1737, 1666, 1614, 1365, 1228, 1216 cm^{-1}. HRMS: calcd for $C_{20}H_{18}O_3$ [M+1] 307.1334, found 307.1337.

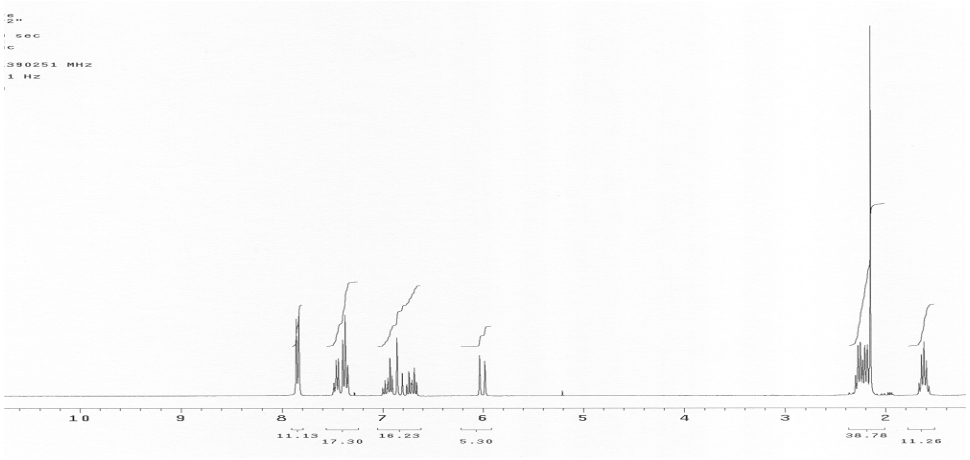


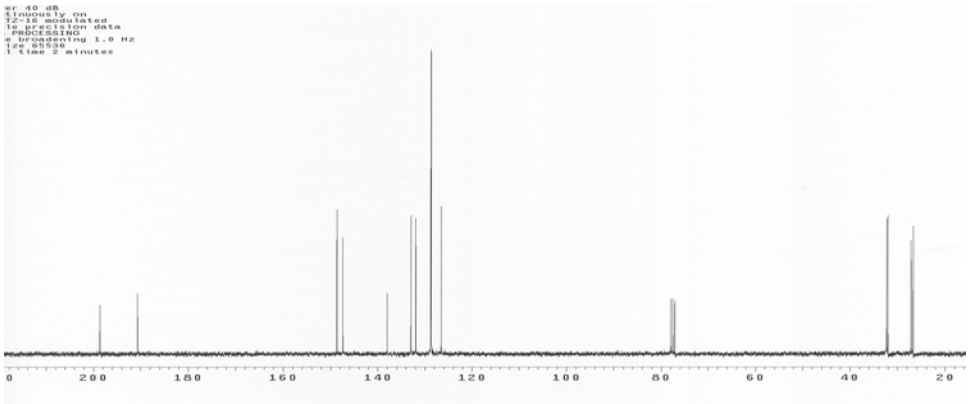


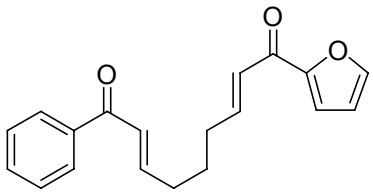


3-3.4

1-Phenyl-2-deca-2,7-diene-1,9-dione. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (m, 2H), 7.42 (m, 3H), 6.92 (m, 1H), 6.81 (d, *J* = 15.1 Hz, 1H), 6.65 (m,1H), 6.01 (d, *J* = 15.1 Hz, 1H), 2.25 (m, 4H), 2.18 (s, 3H), 1.62 (m, 2H). ^{13}C NMR (75 MHz): δ 198.6, 190.6, 148.6, 147.4, 137.9, 132.9, 131.9, 128.7, 128.6, 126.5, 32.3, 31.9, 27.1, 26.7. FTIR (neat): 3015, 2969, 1738, 1671, 1619, 1365, 1216 cm^{-1}. HRMS: calcd for $C_{16}H_{18}O_2$ [M+1] 243.1385, found 243.1383.

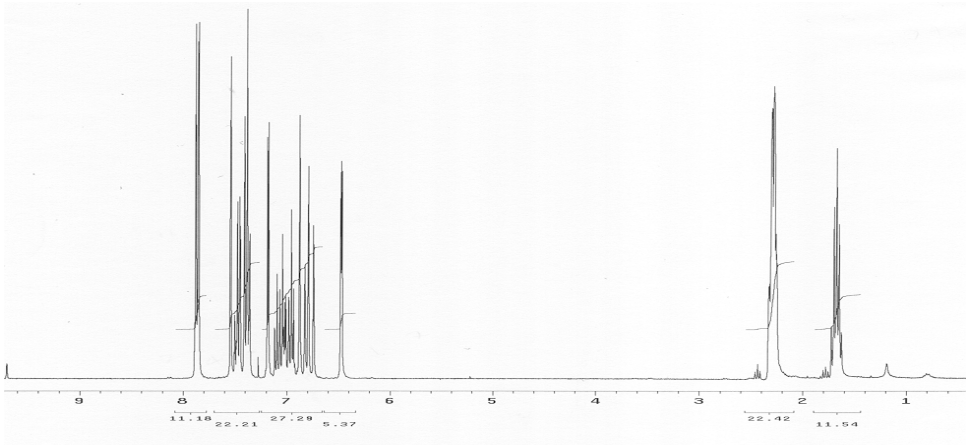


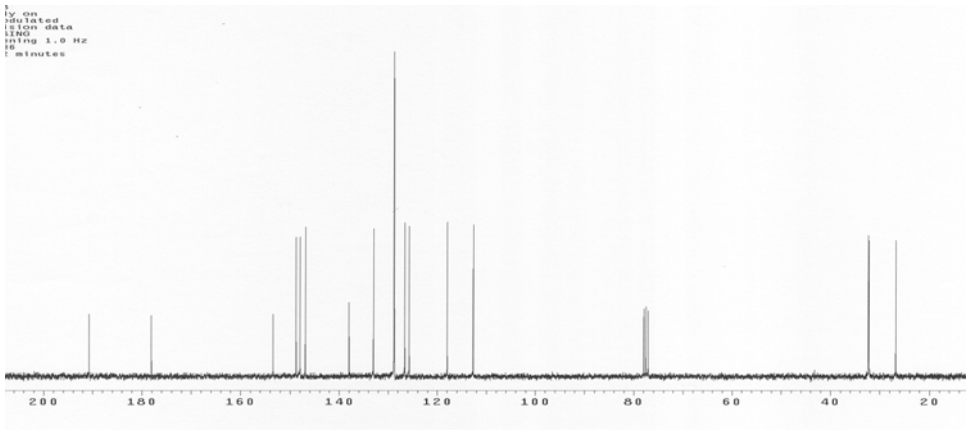


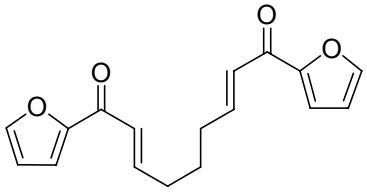


3-3.5

1-Furan-2-yl-9-phenyl-nona-2,7-diene-1,9-dione. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98 (m, 2H), 7.42 (m, 4H), 7.00 (m, 5H), 6.42 (m, 1H), 2.25 (m, 4H), 1.67 (m, 2H). ^{13}C NMR (75 MHz): δ 190.7, 178.0, 153.4, 148.7, 147.9, 146.9, 137.9, 132.9, 128.7, 128.6, 126.6, 125.7, 117.9, 112.6, 32.3, 32.2, 26.7. FTIR (neat): 3015, 2969, 1738, 1666, 1619, 1465, 1365, 1227, 1216 cm^{-1}. HRMS: calcd for $C_{19}H_{18}O_3$ [M+1] 295.1334, found 295.1337.

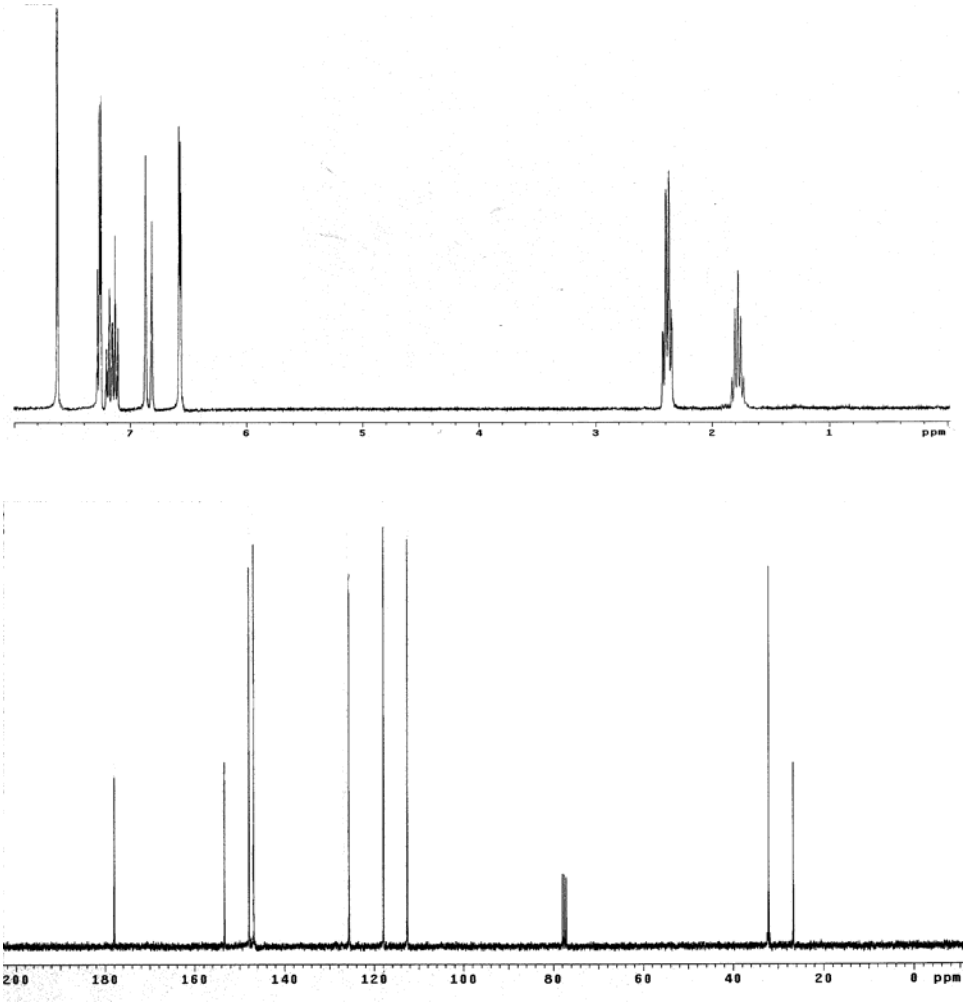


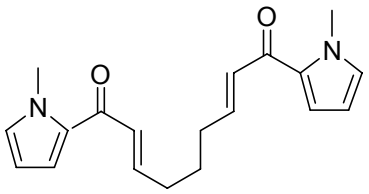




3-3.6

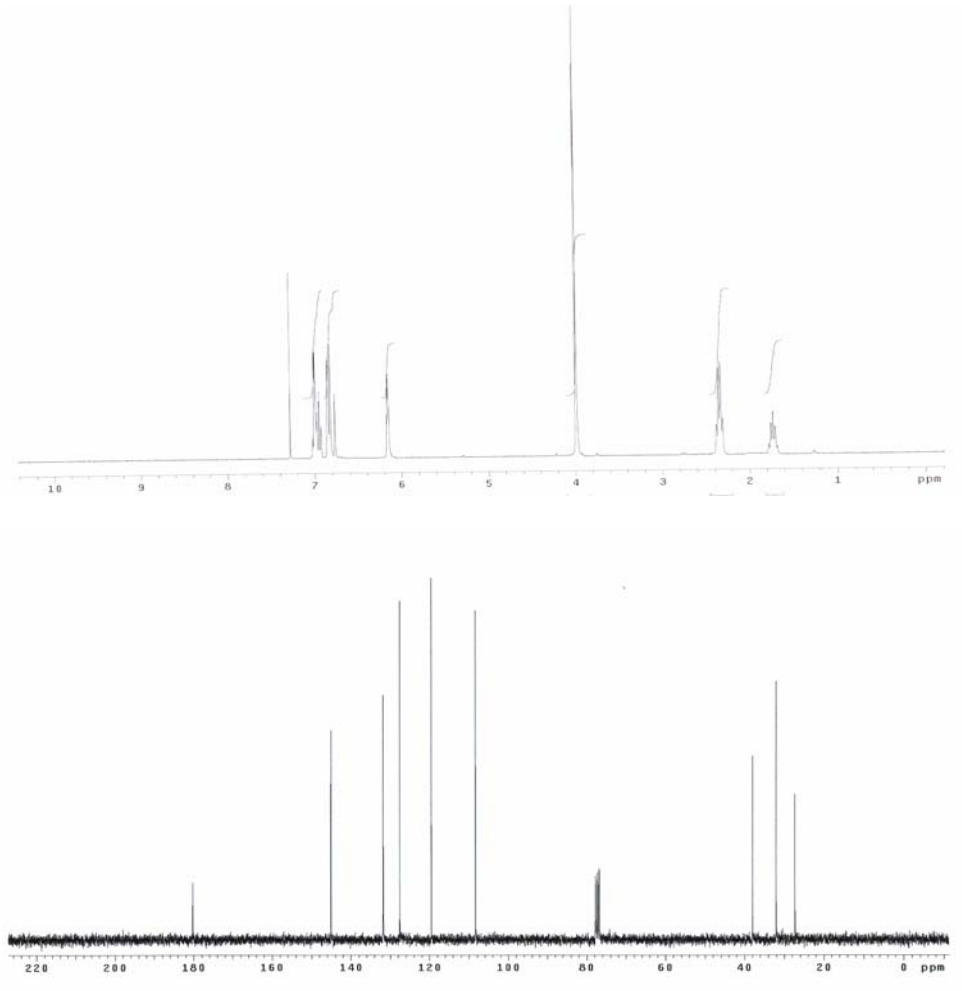
1-Furan-2-yl-9-phenyl-nona-2,7-diene-1,9-dione. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98 (m, 2H), 7.42 (m, 4H), 7.00 (m, 5H), 6.42 (m, 1H), 2.25 (m, 4H), 1.67 (m, 2H). ^{13}C NMR (75 MHz): δ 190.7, 178.0, 153.4, 148.7, 147.9, 146.9, 137.9, 132.9, 128.7, 128.6, 126.6, 125.7, 117.9, 112.6, 32.3, 32.2, 26.7. FTIR (neat): 3015, 2969, 1738, 1666, 1619, 1465, 1365, 1227, 1216 cm^{-1}. HRMS: calcd for $C_{19}H_{18}O_3$ [M+1] 295.1334, found 295.1337.

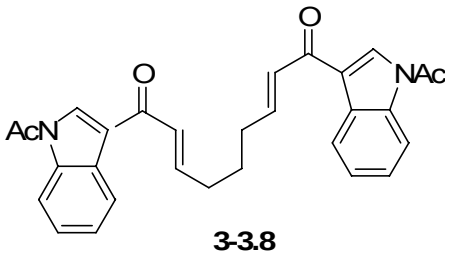




3-3.7

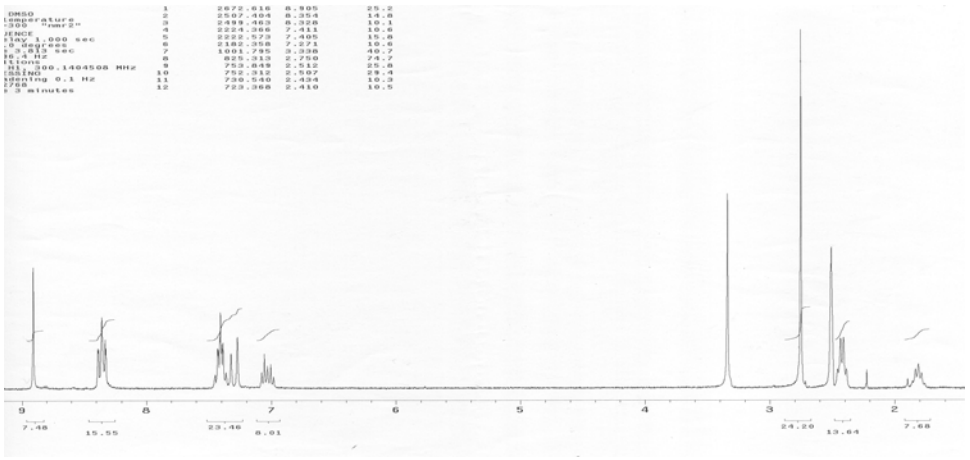
1,9- Bis-(1-methyl-1*H*-pyrrol-2-yl)-nona-2,7-diene-1,9-dione. ^{1}H NMR ($CDCl_3$, 300MHz): δ 6.96 (m, 4H), 6.81 (m, 4H), 6.16 (m, 2H), 3.99 (d, *J* = 2.1 Hz, 6H), 2.34 (dt, *J* = 7.1, 14.3 Hz, 4H), 1.73 (qt, *J* = 7.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 180.2, 145.1, 131.8, 131.7, 127.6, 119.54, 108.4, 38.0, 32.1, 27.3. FTIR (neat): 3053, 2986, 2938, 1658, 1608, 1527, 1460, 1407, 1266, 1095, 1066 cm^{-1}. HRMS: Calcd for $C_{19}H_{22}N_2O_2$ [M+1] 311.1760, found 311.1753.

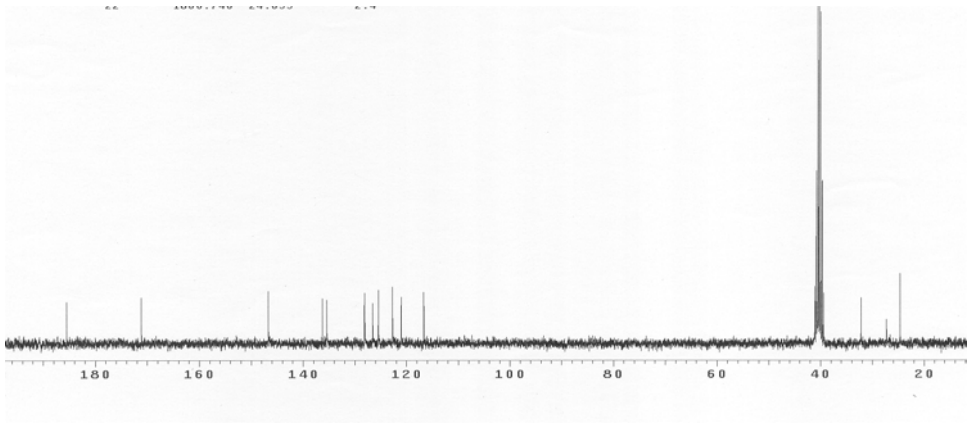


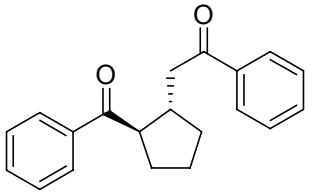


3-3.8

1,9-Bis-(1-acetyl-1*H*-indole-3-carbonyl)-nona-2,7-diene-1,9-dione. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.90 (s, 2H), 8.36 (m, 4H), 7.40 (m, 4H), 7.30 (d, *J* = 15.4 Hz, 2H), 7.09 (dt, *J* = 6.92, 15.4 Hz, 2H), 2.75 (s, 6H), 2.40 (q, *J* = 6.92 Hz, 4H) 1.82 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 185.5, 171.1, 146.7, 136.3, 135.4, 128.1, 128.0, 126.5, 125.4, 122.7, 121.0, 116.6, 32.2, 27.3, 24.7. FTIR (neat): 3015, 2669, 1719, 1659, 1360, 1207cm^{-1}. HRMS: calcd for $C_{29}H_{26}N_2O_4$ [M+1] 467.1971, found 467.1976.

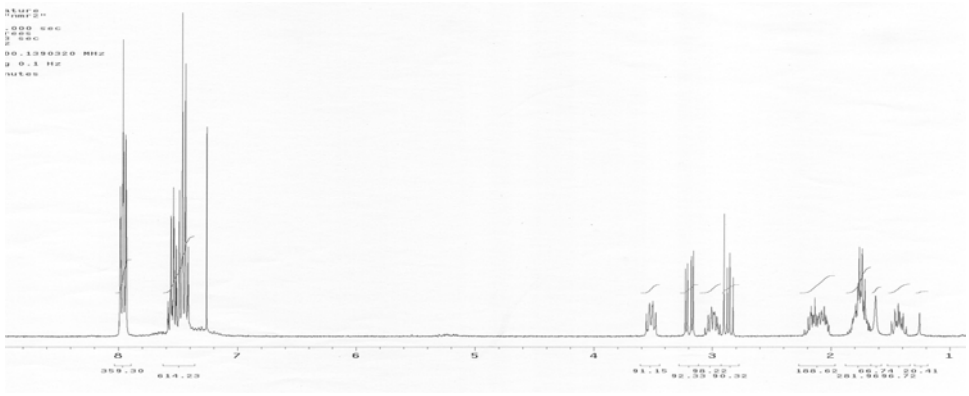


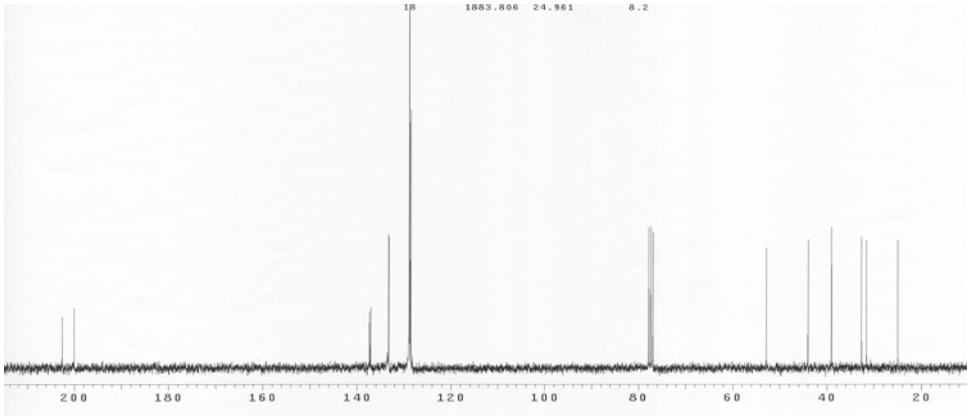


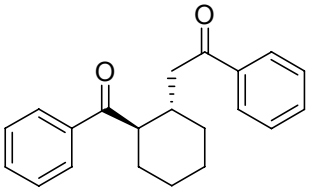


3-3.1a

2-(2-Benzoyl-cyclopentyl)-1-phenyl-ethanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98 (m, 4H), 7.52 (m, 6H), 3.52 (ddd, *J* = 8.7, 15.3, 15.6 Hz, 1H), 3.20 (dd, *J* = 5.4, 14.7 Hz, 1H), 3.00 (m, 1H), 2.92 (m, 1H), 2.08 (m, 2H), 1.78 (m, 3H), 1.42 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 202.5, 200.0, 137.3, 137.1, 133.2, 133.1, 128.8, 128.7, 128.6, 128.5, 52.8, 44.0, 39.0, 32.6, 31.6, 24.9. FTIR (neat): 3059, 2954, 2869, 1685, 1596, 1448, 1375, 1277, 1222, 1129, 1001, 843, 752, 696 cm^{-1}. HRMS: calcd for $C_{20}H_{20}O_2$ [M+1] 293.1541, found 293.1542.

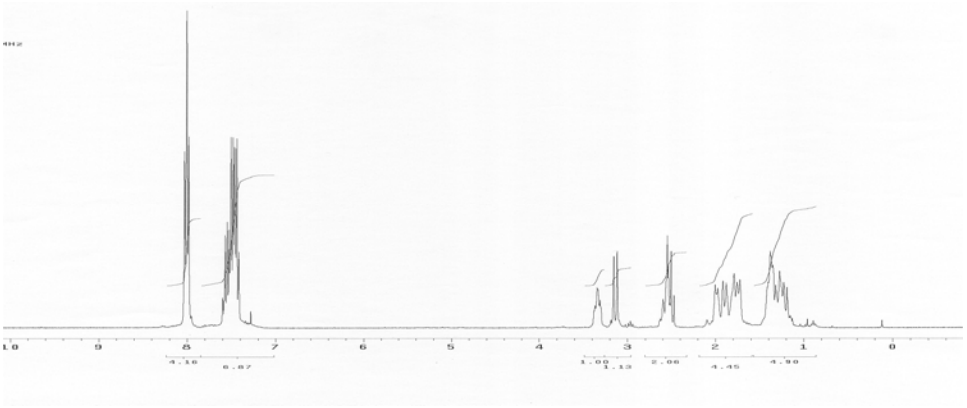


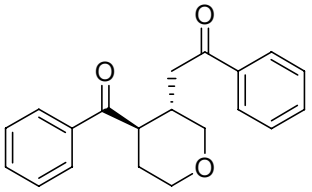




3-3.2a

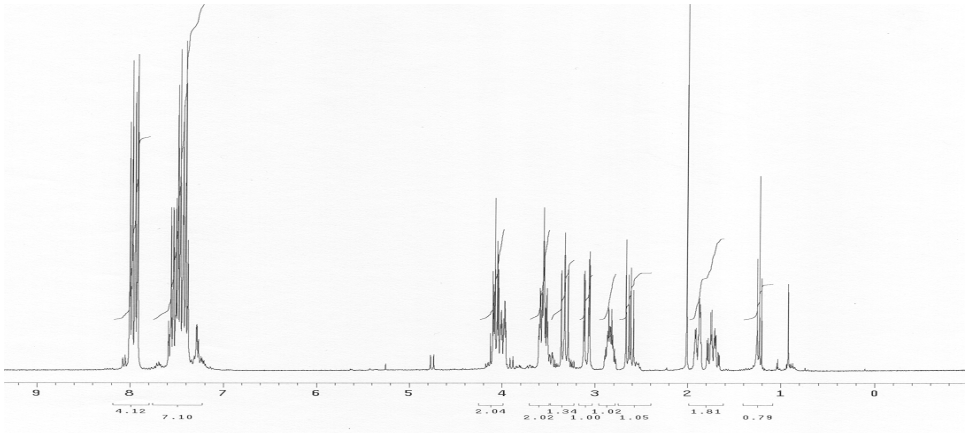
2-(2-Benzoyl-cyclohexyl)-1-phenyl-ethanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01 (m, 4H), 7.45 (m, 6H), 3.34 (ddd, *J* = 3.2, 10.4, 12.8 Hz, 1H), 3.14 (dd, *J* = 2.4, 12.8 Hz, 1H), 2.53 (m, 2H), 1.82 (m, 4H), 1.35 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 203.9, 200.0, 137.1, 137.0, 133.4, 133.2, 129.0, 128.8, 128.7, 128.5, 50.9, 44.5, 36.0, 31.7, 31.5, 26.2, 25.8. FTIR (neat): 3059, 2931, 2855, 1677, 1596, 447, 1372, 1288, 1256, 1209, 1178, 939, 736, 699 cm^{-1} HRMS: calcd for $C_{21}H_{22}O_2$ [M+1] 307.1698, found 307.1706.

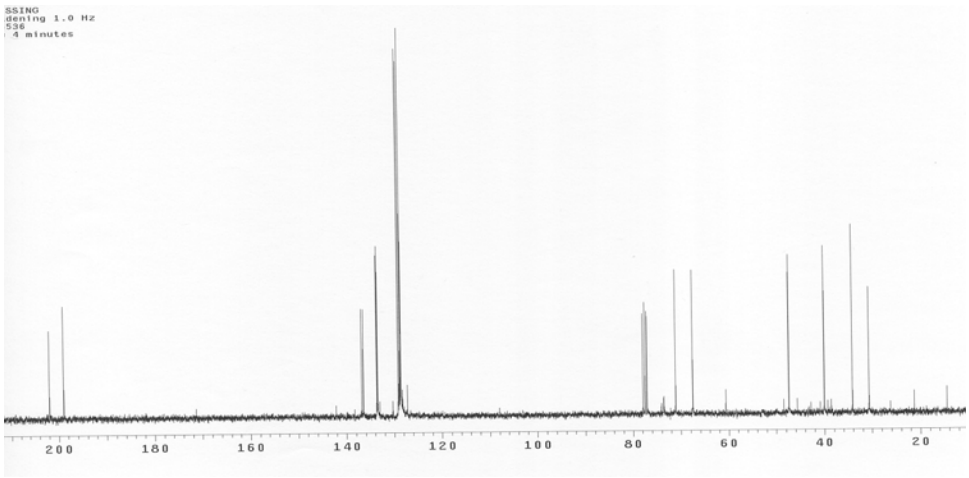


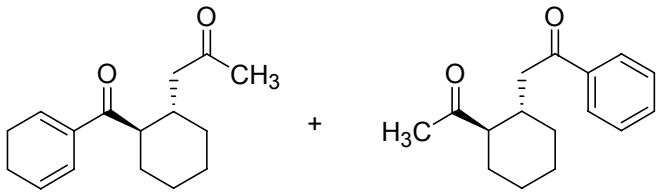


3-3.3a

2-(4-Benzoyl-tetrahydro-pyran-3-yl)-1-phenyl-ethanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02 (m, 4H), 7.52 (m, 6H), 4.10 (m, 2H), 3.62 (m, 2H), 3.37 (t, *J* = 11.1 Hz, 1H), 3.13 (dd, *J* = 3.6, 15.9 Hz, 1H), 2.66 (m, 1H), 2.84 (m, 1H), 1.80 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 201.9, 199.0, 136.8, 136.4, 30.6, 133.6, 133.5, 129.1, 128.8, 128.7, 128.6, 71.1, 67.5, 47.4, 40.0, 34.1. FTIR (neat): 3058, 2954, 2848, 1681, 1596, 1448, 1277, 1213, 1137, 959, 737, 701, 665 cm^{-1}. HRMS: calcd for $C_{20}H_{20}O_3$ [M+1] 309.1490, found 309.1494.

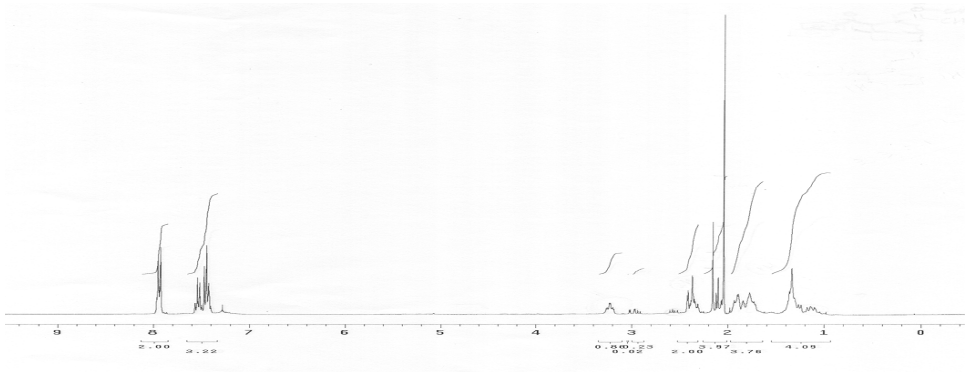


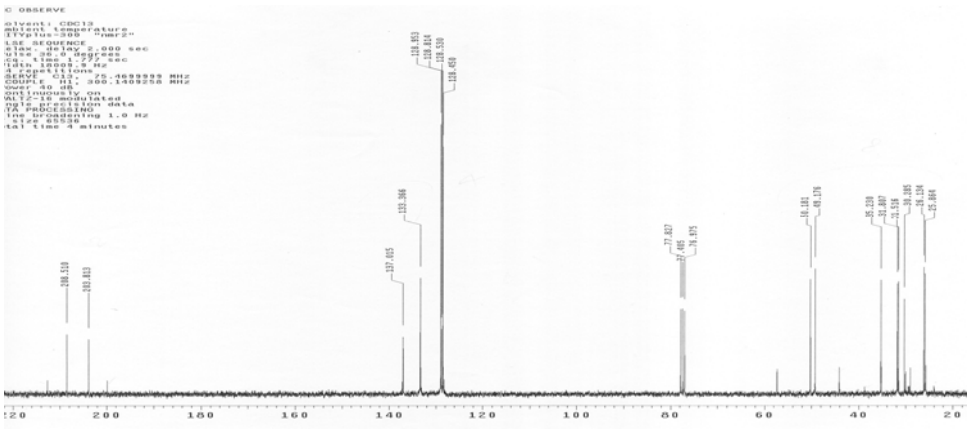


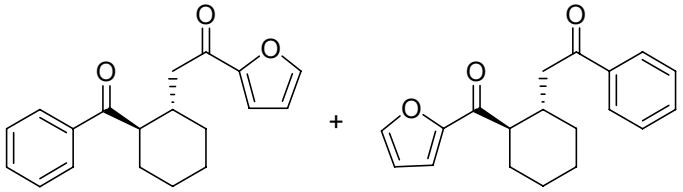


3-3.4a,b

1-(2-Benzoyl-cyclohexyl)-propan-2-one (3-3.4a) and 2-(2-acetyl-cyclohexyl)-1-phenyl-ethanone (3-3.4b). This is an inseparable mixture. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (m, 2H), 7.54 (m, 1H), 7.43 (m, 2H), 3.21 (m, 2H), 2.35 (m, 2H), 2.11 (m, 1H), 2.04 (s, 3H), 1.82 (m, 4H), 1.22 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 208.3, 203.6, 136.7, 133.1, 128.7, 128.1, 49.9, 48.9, 35.0, 31.5, 31.2, 30.0, 25.9, 25.6. HRMS: calcd for $C_{16}H_{20}O_2$ [M+1] 245.1541, found 245.1537.

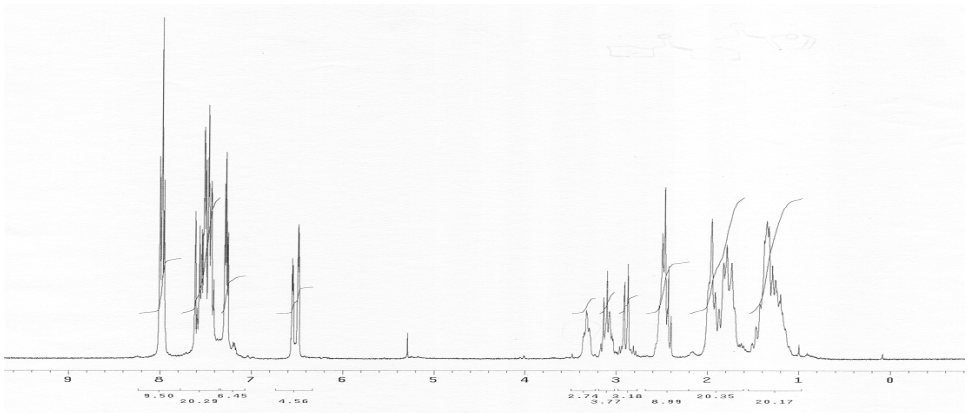


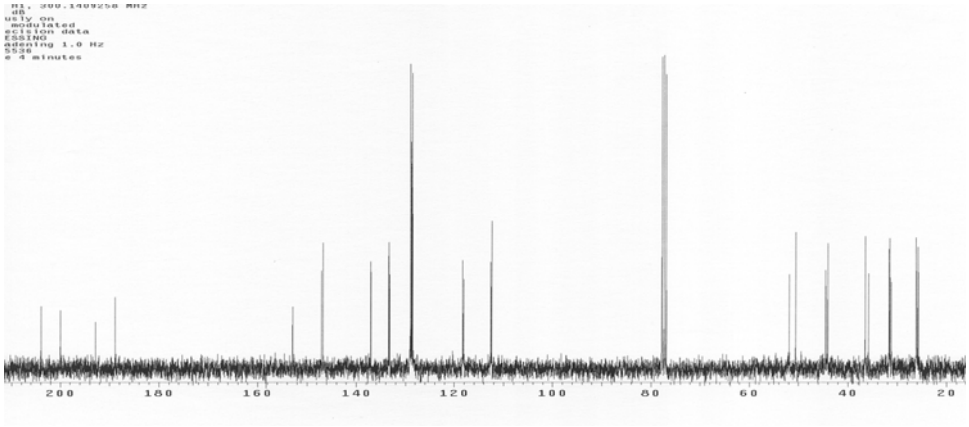


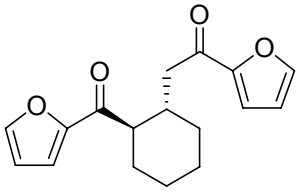


3-3.5a,b

1-(2-Benzoyl-cyclohexyl)-1-furan-2-yl-ethanone (3-3.5a) and 2-[2-(furan-2-carbonyl)-cyclohexyl]-1-phenyl-ethanone (3-3.5b). This is an inseparable mixture. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.99 (m, 4H), 7.51 (m, 8H), 7.28 (m, 2H), 6.53 (m, 2H), 3.32 (m, 1H), 3.08 (m, 2H), 2.88 (m,1H), 2.48 (m, 4H), 1.87 (m, 8H), 1.26 (m, 8H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 203.92, 199.96, 192.81, 188.83, 152.83, 147.00, 146.68, 137.02, 133.37, 133.21, 128.97, 128.81, 128.68, 128.52, 118.25, 118.04, 112.61, 112.41, 51.82, 50.55, 44.44, 44.02, 36.48, 35.84, 31.67, 31.56, 31.47, 32.20, 26.16, 26.09, 25.81, 25.71. FTIR (neat): 3048, 2928, 1665, 1478, 1268, 1207, 1158, 1017, 758, 718 cm^{-1}. HRMS: calcd for $C_{19}H_{20}O_3$ [M+1] 297.1490, found 297.1488.

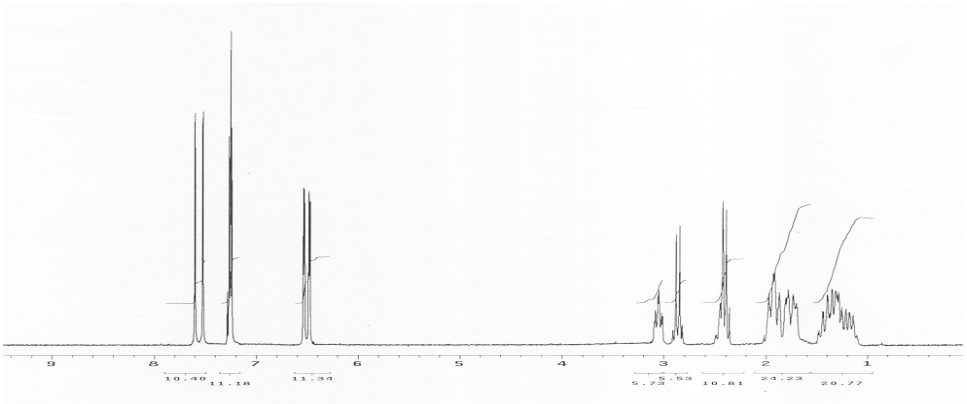


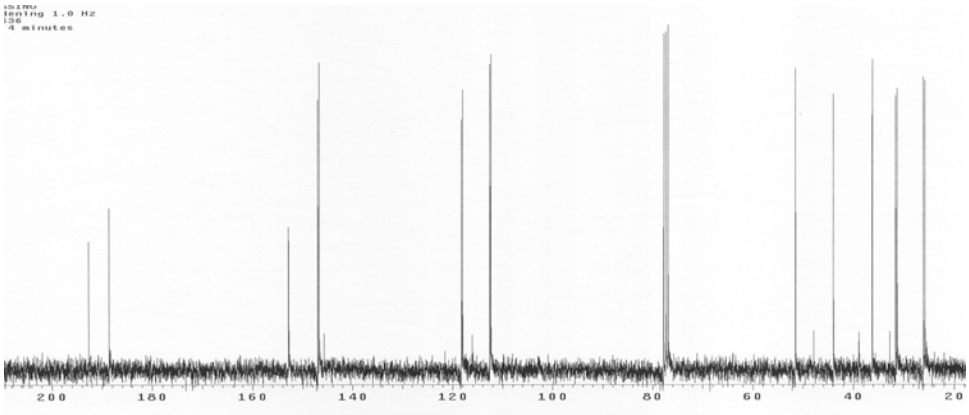


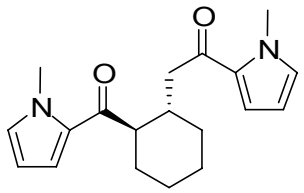


3-3.6a

2-[2-(Furan-2-carbonyl)-cyclohexyl]-1-furan-2-yl-ethanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56 (m, 2H), 7.21 (m, 2H), 6.42 (m, 2H), 3.05 (ddd, *J* = 3.3, 8.7, 10.5 Hz, 1H), 3.07 (dd, *J* = 1.8, 10.5 Hz, 1H), 2.46 (m, 2H), 1.82 (m, 4H), 1.36 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 196.8, 192.9, 144.8, 144.7, 134.5, 133.9, 133.1, 132.3, 128.6, 128.5, 52.7, 45.0, 37.0, 31.9, 31.4, 26.1, 25.7. FTIR (KBr): 3048, 2935, 1665, 1478, 1268, 1207, 1158, 1017, 758, 718 cm^{-1}. HRMS: calcd for $C_{17}H_{18}O_4$ [M+1] 287.1283, found 287.1281. Mp = 113-115 ºC.

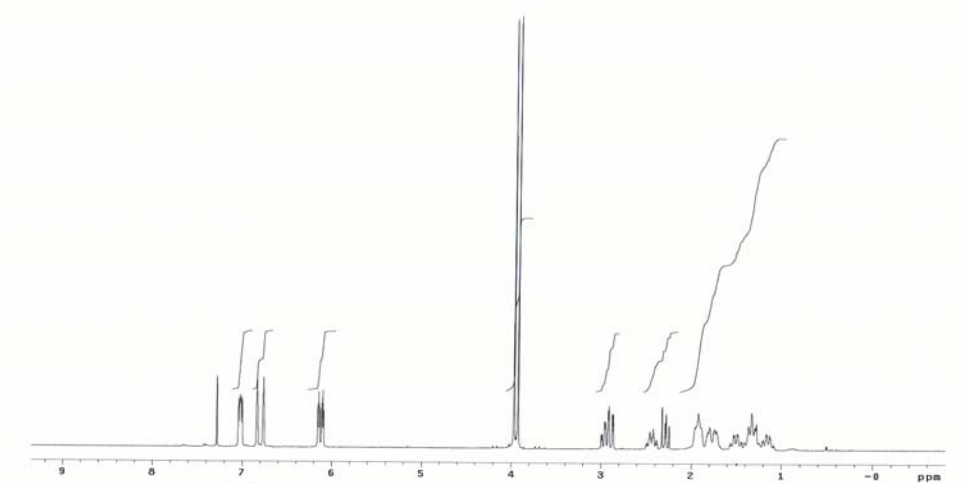


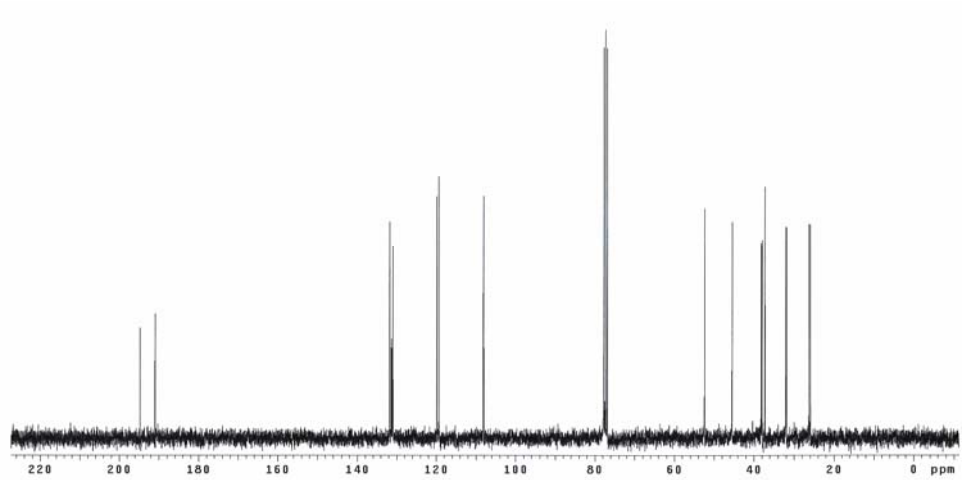


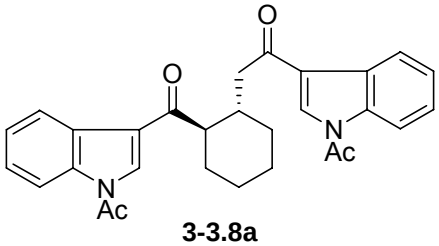


3-3.7a

2-[2-(1-Methyl-1*H*-pyrrole-2-carbonyl)-cyclohexyl]-1-(1-methyl-1*H*-pyrrol-2-yl)-ethanone. ^{1}H NMR ($CDCl_3$, 300MHz): δ 7.02 (m, 2H), 6.83 (s, 1H), 6.76 (s, 1H), 6.12 (m, 2H), 3.97 (s, 3H), 3.93 (s, 3H), 2.93 (m, 2H), 2.35 (m, 2H), 1.54 (m, 8H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 194.7, 191.0, 131.7, 131.3, 131.2, 130.9, 119.8, 119.33, 108.1, 108.0, 52.4, 45.5, 38.1, 37.9, 37.2, 32.0, 31.9, 26.3, 25.9. FTIR (neat): 3108, 2931, 2854, 1647, 1527, 1466, 1407, 1355, 1329, 1302, 1249, 1095, 1066 cm^{-1}. HRMS: Calcd for $C_{19}H_{24}N_2O_2$ [M+1] 313.1916, found 313.1910.

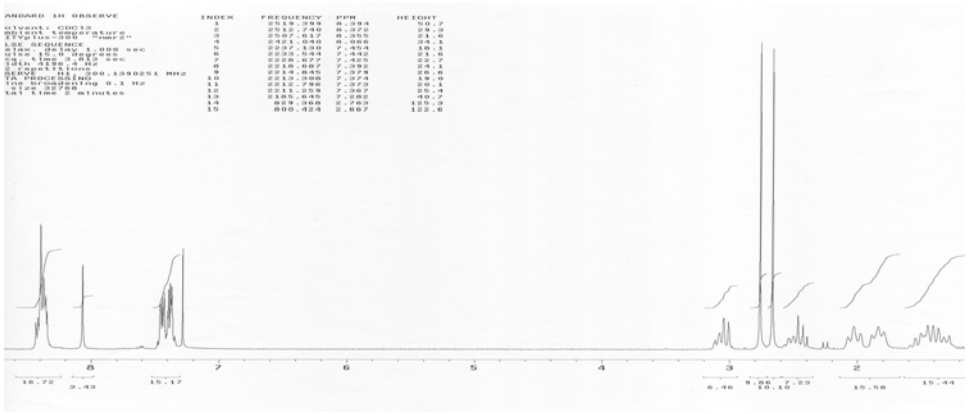


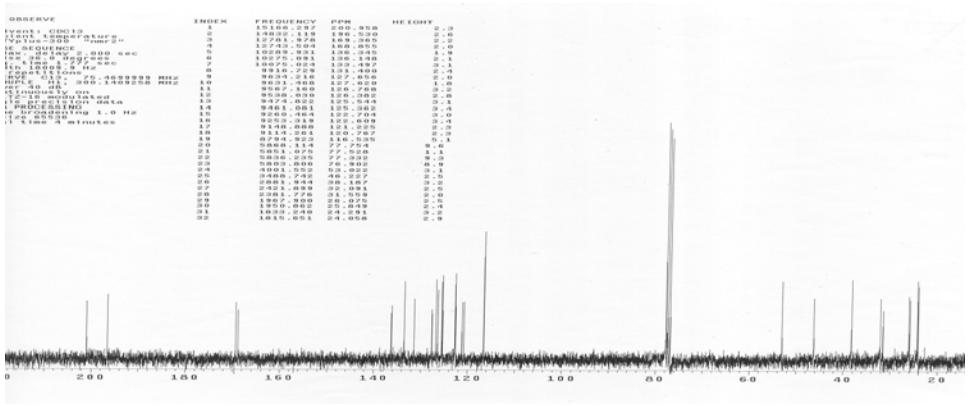




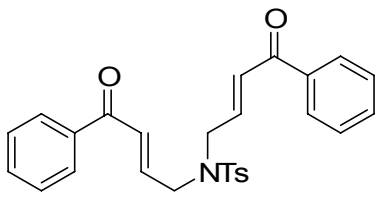
3-3.8a

2-[2-(1-Acetyl-1*H*-indole-3-carbonyl)-cyclohexyl]-1-(1-acetyl-1*H*-indol-3-yl)-ethanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56 (m, 2H), 7.21 (m, 2H), 6.42 (m, 2H), 3.05 (ddd, *J* = 3.3, 8.7, 10.5 Hz, 1H), 3.07 (dd, *J* = 1.8, 10.5 Hz, 1H), 2.46 (m, 2H), 1.82 (m, 4H), 1.36 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 196.8, 192.9, 144.8, 144.7, 134.5, 133.9, 133.1, 132.3, 128.6, 128.5, 52.7, 45.0, 37.0, 31.9, 31.4, 26.1, 25.7. FTIR (neat): 3048, 2935, 1665, 1478, 1268, 1207, 1158, 1017, 758, 718 cm^{-1}. HRMS: calcd for $C_{29}H_{28}N_2O_4$ [M+1] 469.2127, found 469.2128. Mp = 113-115 ºC.



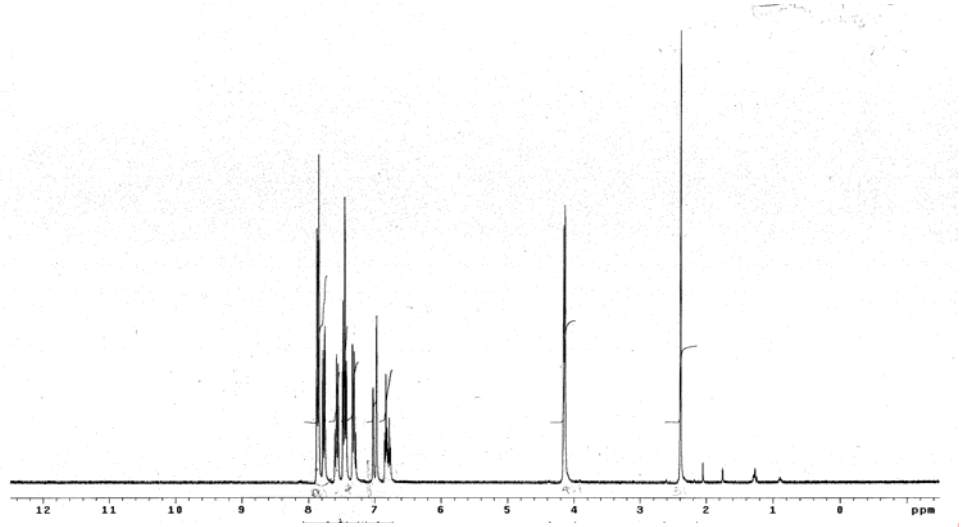


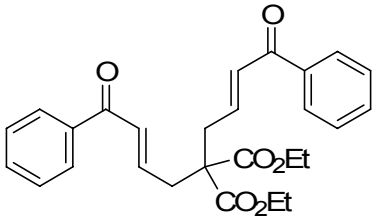
C. Cobalt-Catalyzed [2+2] Cycloaddition



3-4.3

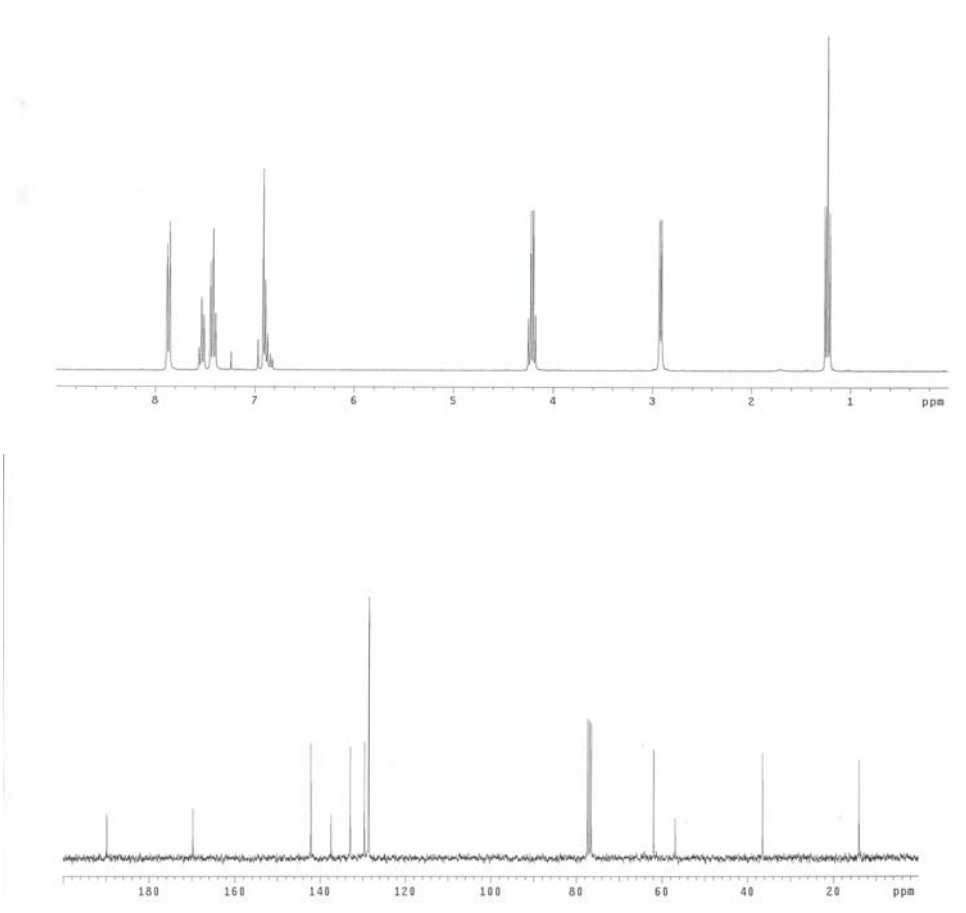
4-Methyl-*N,N*-bis-(4-oxo-4-phenyl-but-2-enyl)-benzenesulfonamide. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.86 (m, 4H), 7.77 (m, 2H), 7.56 (m, 4H), 7.39 (m, 2H), 7.03 (m, 2H), 6.88 (m, 2H), 4.15 (m, 4H), 2.40 (s, 3H). ^{13}C NMR (75 MHz): δ 189.82, 144.38, 141.66, 137.36, 136.83, 133.44, 130.31, 128.94, 128.84, 128.28, 127.51, 49.13, 21.79. FTIR (neat): 1674, 1625, 1597, 1448, 1341, 1283, 1159 cm^{-1}. HRMS: calcd for $C_{27}H_{25}NO_4S$ [M+1] 460.1583, found 460.1583.

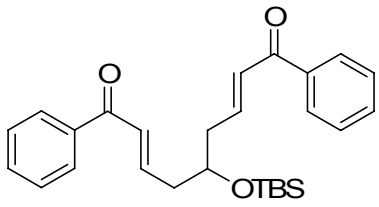




3-4.4

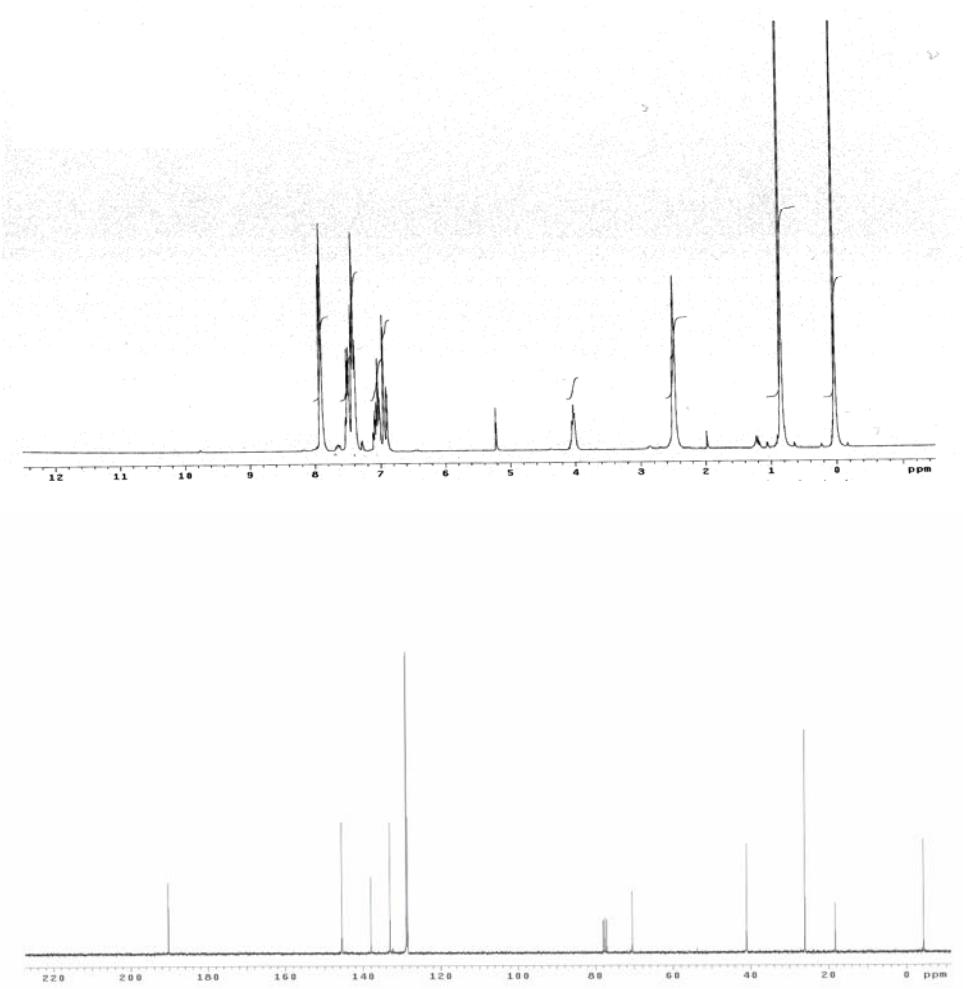
2,2-Bis-(4-oxo-4-phenyl-but-2-enyl)-malonic acid diethyl ester. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.87 (m, 4H), 7.53 (m, 2H), 7.42 (m, 4H), 6.92 (m, 4H), 4.21 (q, *J* = 7.2 Hz, 4H), 5.84 (d, *J* = 6.3 Hz, 4H), 1.23 (t, *J* = 7.2 Hz, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 189.81, 169.71, 142.09, 137.39, 132.89, 129.57, 128.58, 61.94, 56.93, 36.46, 14.04 cm^{-1}. FTIR (neat): 3059, 2981, 2933, 1720, 1671, 1621, 1597, 1579, 1448, 1354, 1279, 1198, 1096, 1015, 694 cm^{-1}. HRMS: calcd for $C_{27}H_{28}O_6$ [M+1] 449.1964, found 449.1970. Mp = 106-107 ºC.

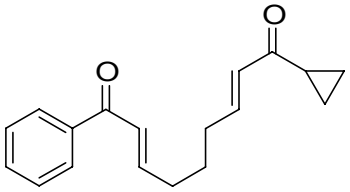




3-4.5

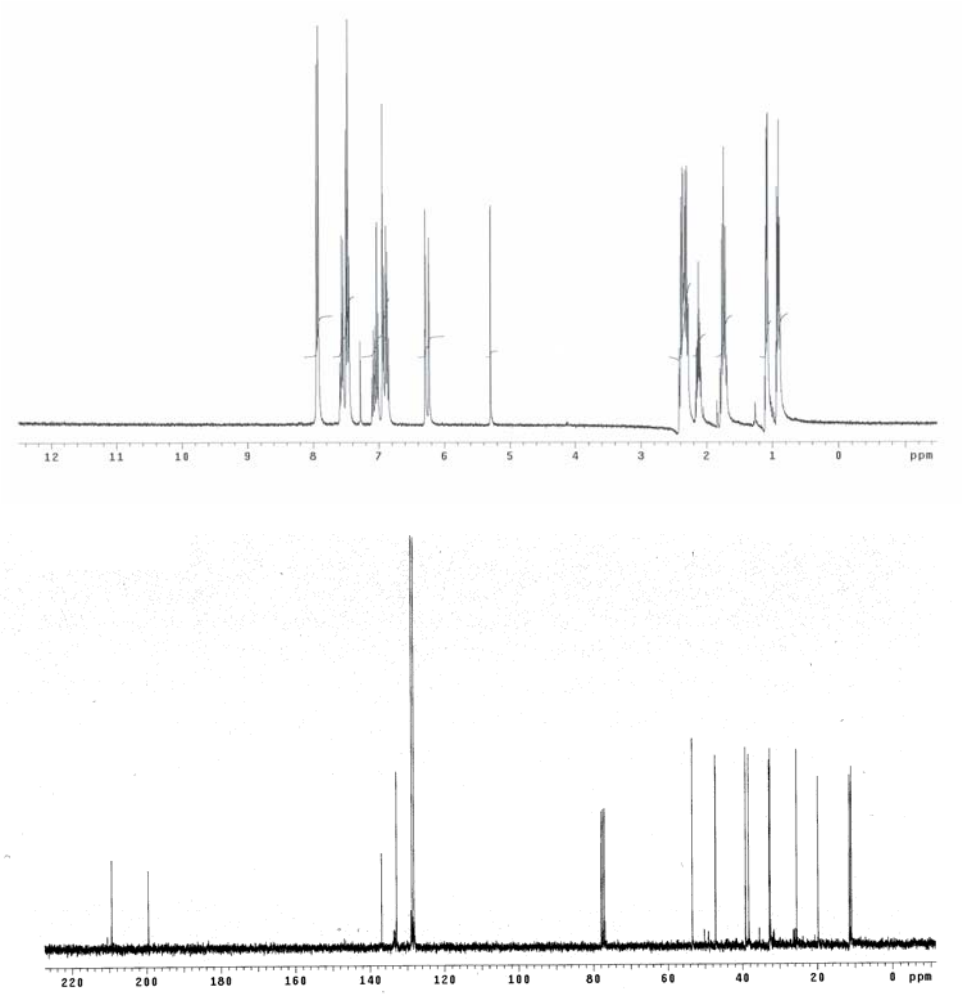
5-(*tert*-Butyl-dimethyl-silanyloxy)-1,9-diphenyl-nona-2,7-diene-1,9-dione. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.91(m, 4H), 7.50 (m, 2H), 7.43 (m, 4H), 7.04 (m, 2H), 6.95 (d, *J* = 2.4 Hz, 2H), 4.04 (m, 1H), 2.49 (m, 4H), 0.86 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (75 MHz): δ 190.27, 145.48, 137.94, 132.99, 128.81, 128.73, 128.47, 70.53, 41.01, 26.01, 18.22, -4.33. FTIR (neat): 2954, 2928, 2856, 1671, 1653, 1623, 1598, 1448, 1337, 1277, 1257, 1096, 1006 cm^{-1}. HRMS: calcd for $C_{27}H_{34}O_3Si$ [M+1] 435.2355, found 435.2352.

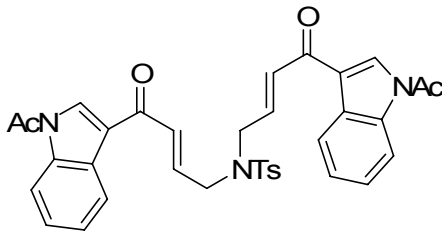




3-4.7

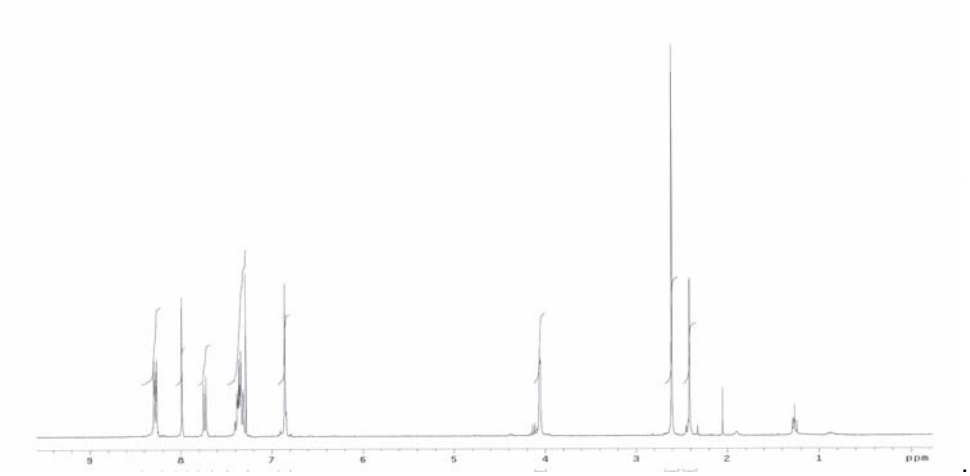
1-Cyclopropyl-9-phenyl-nona-2,7-diene-1,9-dione. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.94 (m, 2H), 7.51 (m, 3H), 6.97 (m, 3H), 6.27 (d, *J* = 15.9 Hz, 1H), 2.34 (m, 4H), 2.12 (m, 1H), 1.73 (m, 2H), 1.08 (m, 2H), 0.913 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 200.35, 190.85, 148.81, 145.77, 138.06, 132.99, 131.20, 128.81, 128.76, 126.64, 32.38, 32.08, 26.88, 19.10, 11.36. FTIR (neat): 1668, 1622, 1447, 1390, 1344, 1294, 1207 cm^{-1}. HRMS: calcd for $C_{18}H_{20}O_2$ [M+1] 269.1542, found 269.1541.

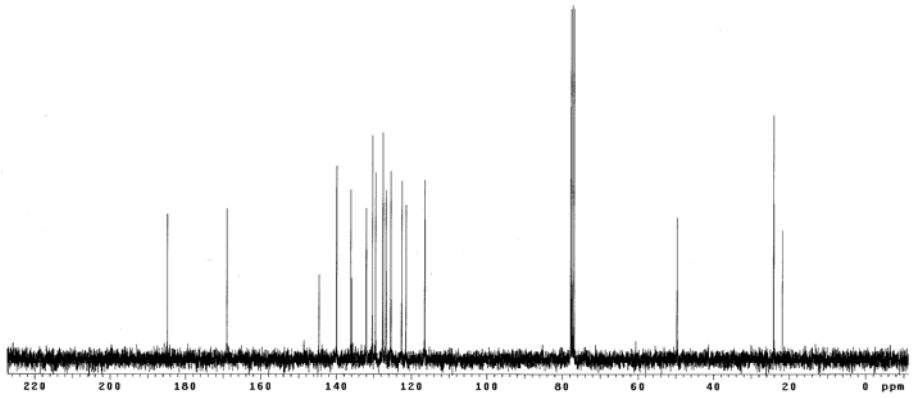


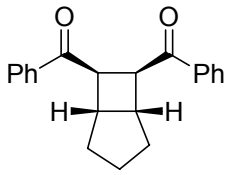


3-4.10

***N,N*-Bis-[4-(1-acetyl-1*H*-indol-3-yl)-4-oxo-but-2-enyl]-4-methyl-benznesulfonamide.** ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.28 (m, 4H), 7.99 (s, 2H), 7.74 (d, *J* = 8.96 Hz, 2H), 7.35 (m, 6H), 6.85 (m, 4H), 4.06 (d, *J* = 3.59 Hz, 4H), 2.61 (s, 6H), 2.41 (s, 3H). ^{13}C NMR (75 MHz): δ 184.81, 168.99, 144.57, 139.92, 136.16, 135.91, 132.00, 130.35, 129.51, 127.55, 127.50, 126.75, 125.46, 122.59, 121.46, 116.46, 49.68, 24.12, 21.82. FTIR (neat): 2958, 1702, 1651, 1261, 1210 cm^{-1}. HRMS: calcd for $C_{35}H_{31}N_3O_6S$ [M+1] 622.2012, found 622.2019. Mp = 173-175 ºC.

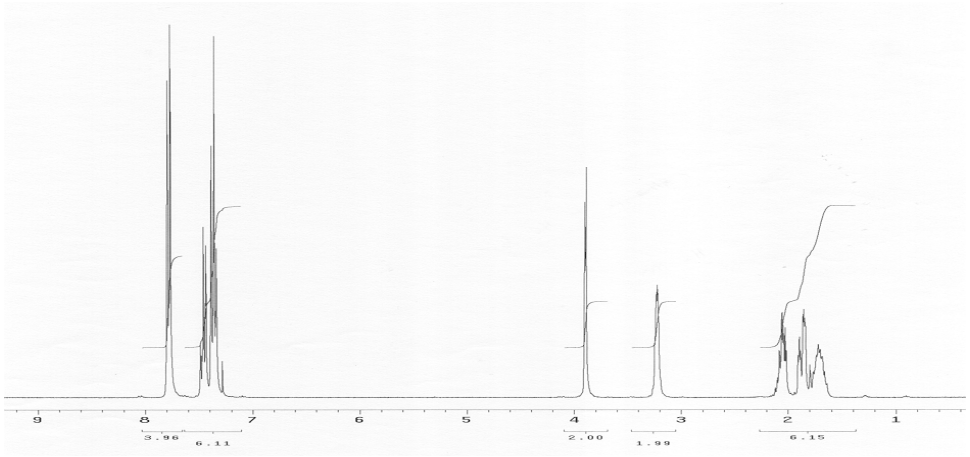


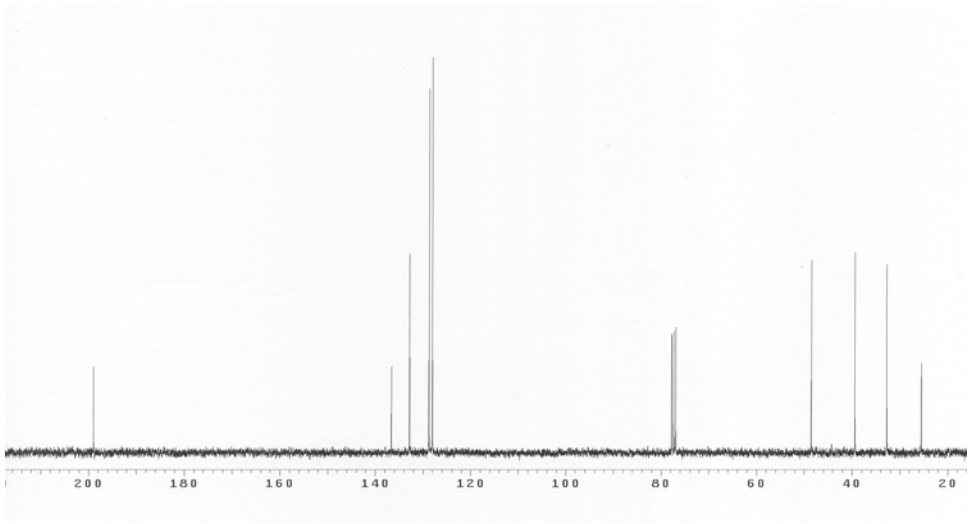


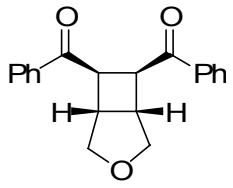


3-4.1a

(3-Benzoyl-octahydro-pentalen-1-yl)-phenyl-methanone. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.78 (m, 4H), 7.42 (m, 6H), 3.90 (d, *J* = 4.2 Hz, 2H), 3.22 (m, 2H), 2.06 (m, 2H), 1.84 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 198.9, 136.6, 128.7, 128.1, 48.6, 39.3, 32.7, 25.5. FTIR (neat): 3054, 2968, 1682, 1447, 1263, 743, 704 cm^{-1}. HRMS: Calcd for $C_{21}H_{20}O_2$ [M+1] 305.1541, found 305.1538. Mp = 155-157^{o}C.

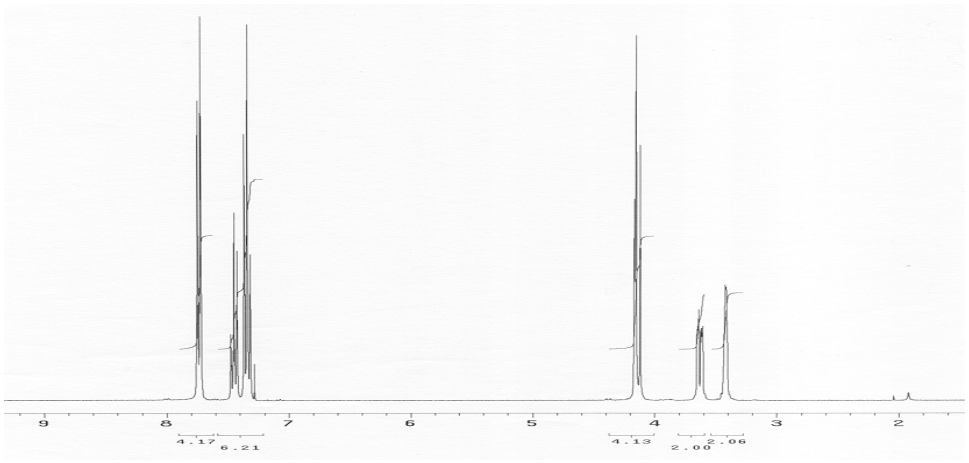


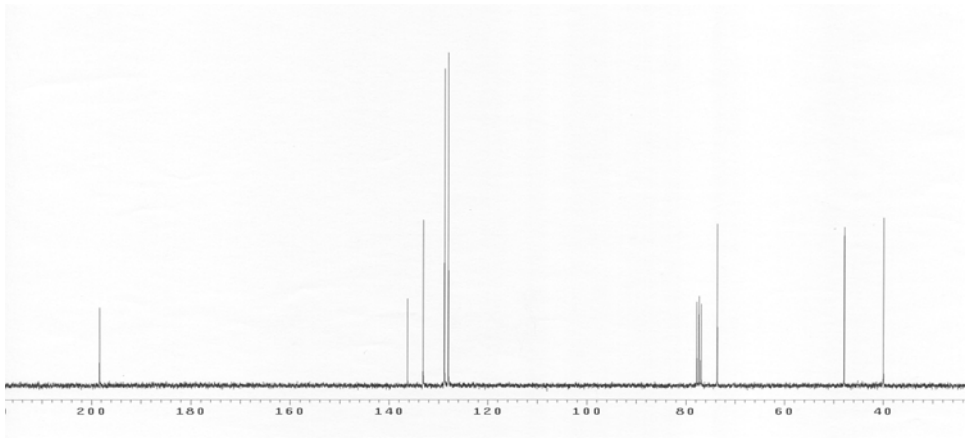


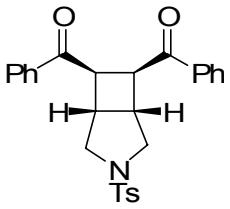


3-4.2a

(6-Benzoyl-hexahydro-cyclopenta[*c*]furan-4-yl)-phenyl-methanone. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.92 (m, 4H), 7.48 (m, 6H), 4.16 (m, 4H), 3.64 (m, 2H), 3.42 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 198.3, 136.2, 133.1, 128.8, 128.0, 73.7, 47.9, 39.9. FTIR (neat): 3055, 2858, 1685, 1448, 1265, 738, 704 cm^{-1}. HRMS: calcd for $C_{20}H_{18}O_3$ [M+1] 307.1334, found 307.1336. Mp = 163-165 ^{o}C.

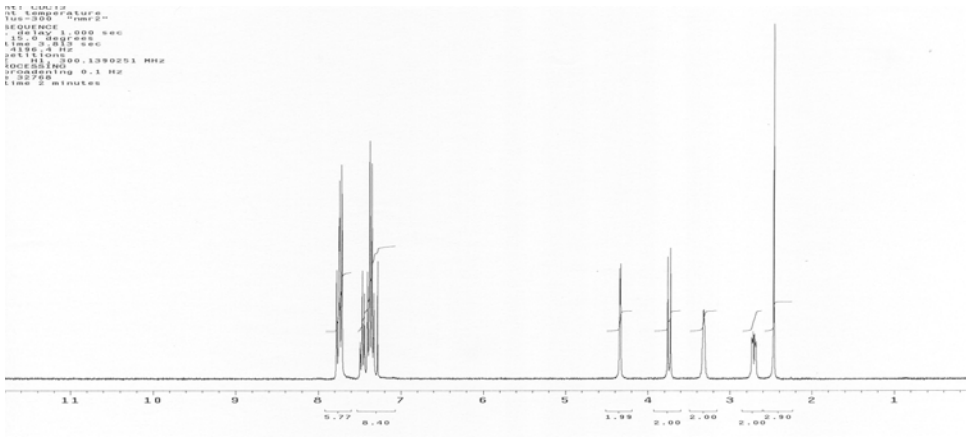


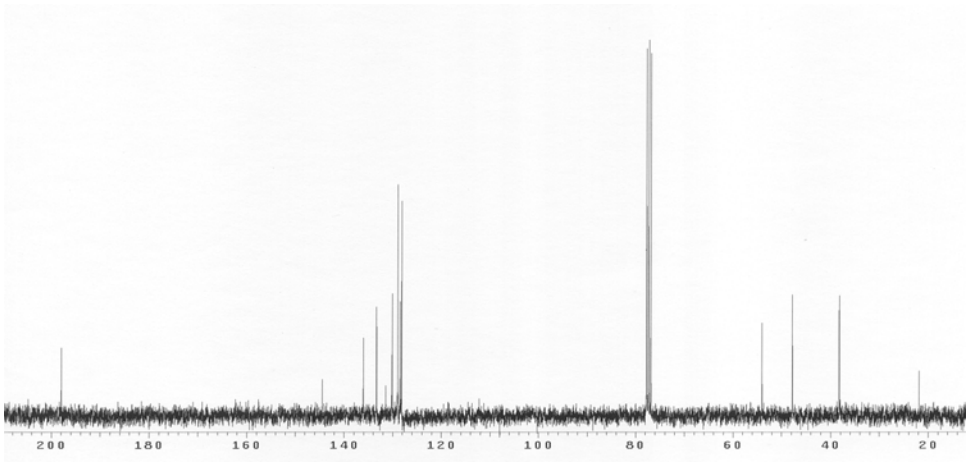


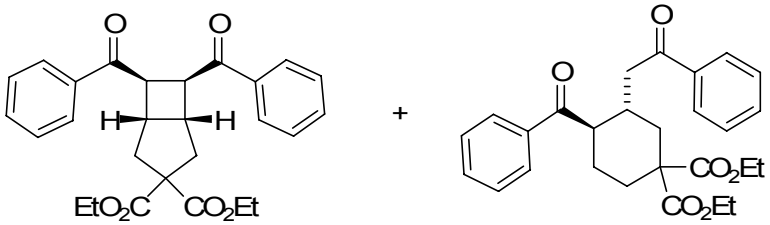


3-4.3a

[6-Benzoyl-2-(toluene-4-sulfonyl)-octahydro-cyclopenta[c]pyrrol-4-yl]-phenyl-methanone. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.70 (m, 6H), 7.42 (m, 8H), 4.33 (d, *J* = 4.2 Hz, 2H), 3.73 (d, *J* = 1.8 Hz, 2H), 3.31 (m, 2H), 2.71 (m, 2H), 2.47 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 197.9, 144.4, 136.0, 133.3, 131.3, 130.0, 128.8, 128.4, 128.1, 54.0, 47.7, 38.2, 21.8. FTIR (neat): 3056, 2985, 1685, 1346, 1265, 1163, 734, 704, 665 cm^{-1}. HRMS: calcd for $C_{27}H_{25}NO_4S$ [M+1] 460.1582, found 460.1587. Mp = 170-172 ^{o}C.





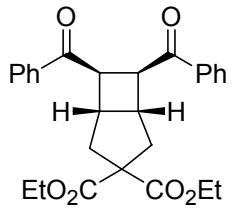


3-4.4a **3-4.4b**

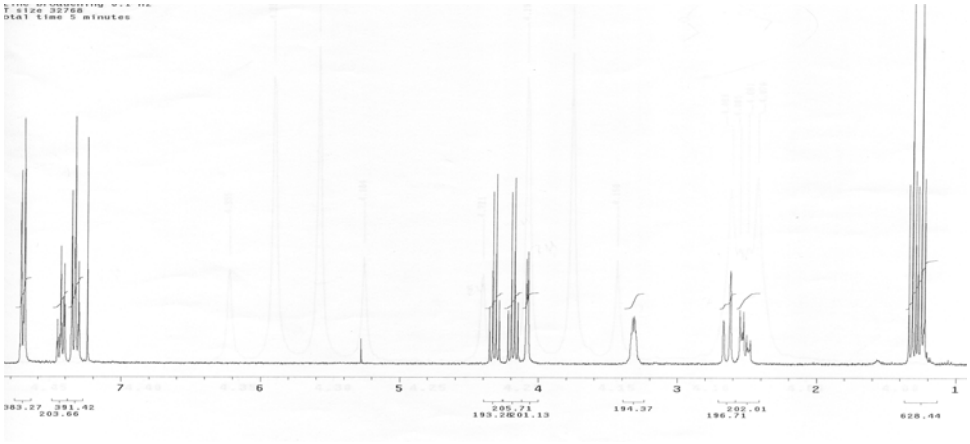
6,7-dibenzoyl-bicyclo[3.2.0]heptane-3,3,-dicarboxylic acid and diethyl ester (3-4.4a) and 4-Benzoyl-3-(2-oxo-2-phenyl-ethyl)-cyclohexane-1,1-dicarboxylic acid diethyl ester (3-4.4b).

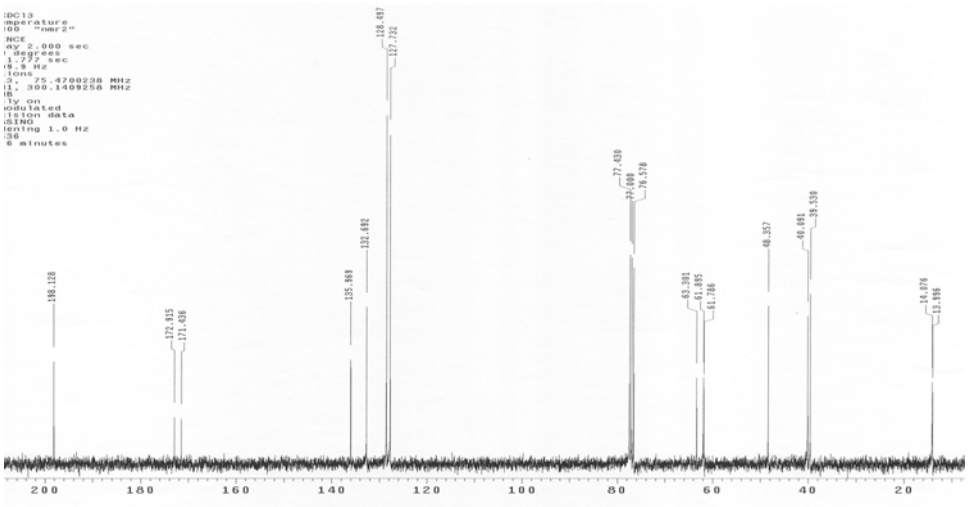
3-4.4a: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72 (m, 4H), 7.42 (m, 6H), 4.30 (q, *J* = 6.3 Hz, 2H), 4.17 (q, *J* = 6.9 Hz, 2H), 4.08 (d, *J* = 3.9 Hz, 2H), 3.32 (m, 2H), 2.62 (m, 4H), 1.27 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 198.1, 172.9, 171.4, 135.9, 132.7, 128.5, 127.7, 63.3, 61.9, 61.8, 48.3, 40.1, 39.5, 14.1, 13.9. FTIR (neat): 3054, 2985, 2306, 1724, 1686, 1597, 1581, 1448, 1272, 758, 697 cm^{-1}. HRMS: calcd for $C_{27}H_{28}O_6$ [M+1] 449.1964, found 449.1957. Mp = 99-101 ^{o}C.

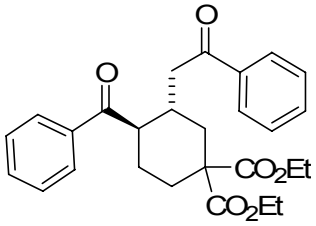
3-4.4b: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90 (m, 4H), 7.53 (m, 2H), 7.43 (m, 4H), 4.16 (m, 4H), 3.18 (m, 2H), 3.04 (m, 2H), 2.58 (m, 2H), 2.38 (m, 2H), 2.03 (m, 2H), 1.21 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.34, 172.35, 137.02, 133.08, 128.60, 128.03, 61.48, 58.93, 42.95, 40.28, 40.22, 14.01. FTIR (neat): 2980, 2927, 2360, 2342, 1727, 1684, 1448, 1258, 1218, 1182, 690, 668 cm^{-1}. HRMS: calcd for $C_{27}H_{30}O_6$ [M+1] 451.2121, found 451.2124. Mp = 116-117 ºC.



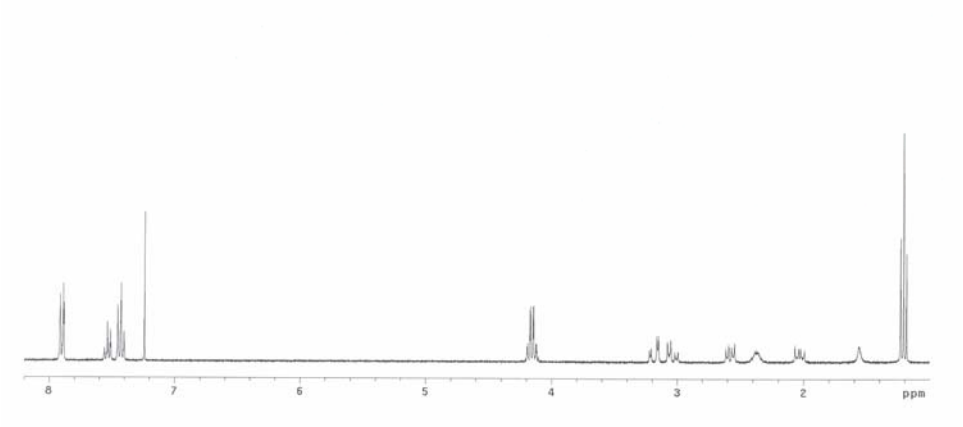
3-4.4a

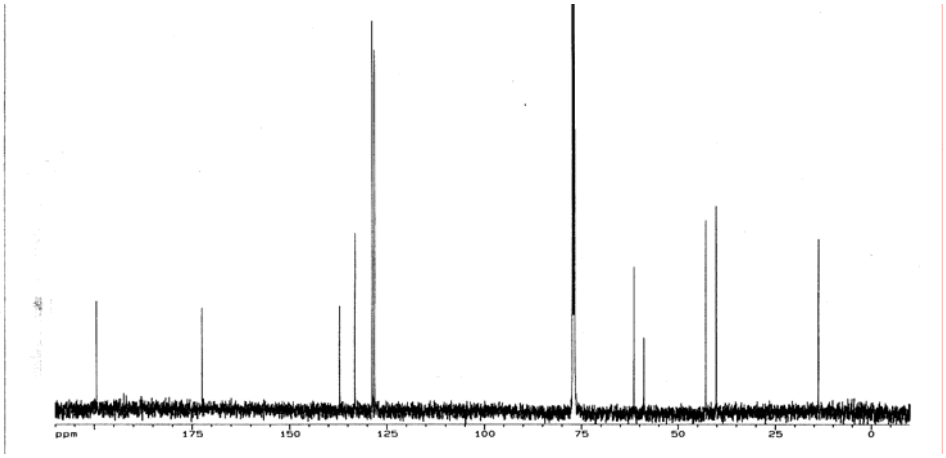


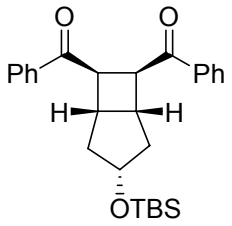




3-4.4b

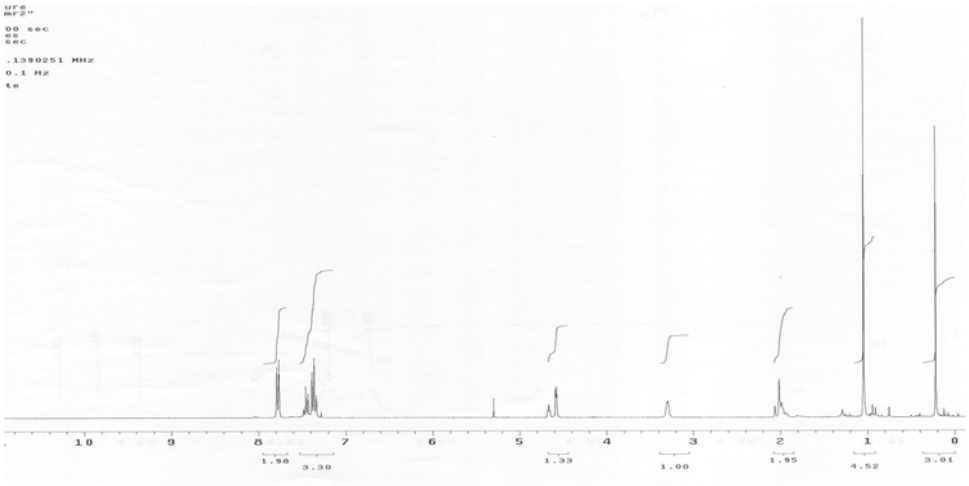


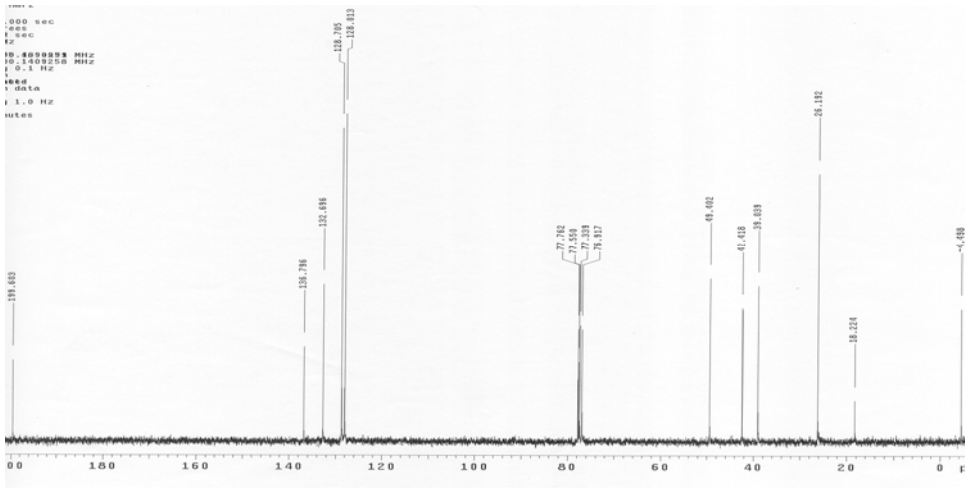


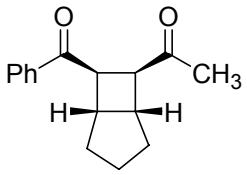


3-4.5a

[7-Benzoyl-3-(*tert*-butyl-dimethyl-silanyloxy)-bicyclo[3.2.0]hept-6-yl]-phenyl-methanone. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.78 (m, 4H), 7.42 (m, 6H), 4.66 (m, 1H), 4.58 (d, J = 3.9 Hz, 2H), 3.29 (d, J = 2.7 Hz, 2H), 1.98 (m, 4H), 1.04 (s, 9H), 0.22 (s, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 199.6, 136.8, 132.7, 128.7, 128.0, 49.4, 42.4, 39.0, 26.2, 18.2, 4.5. FTIR (neat): 3054, 2954, 2929, 2856, 1684, 1448, 1264, 746, 704 cm^{-1}. HRMS: calcd for $C_{27}H_{34}O_3Si$ [M+1] 435.2355, found 435.2360. Mp = 107-109 ^{o}C.

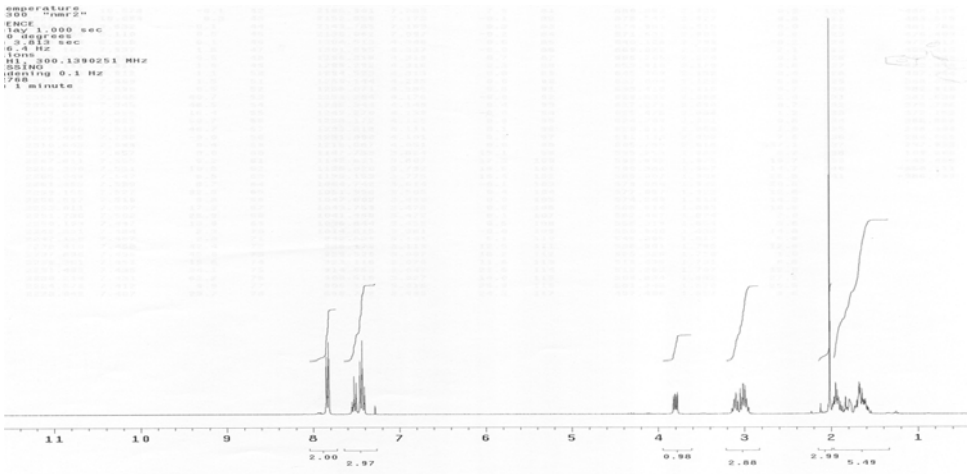


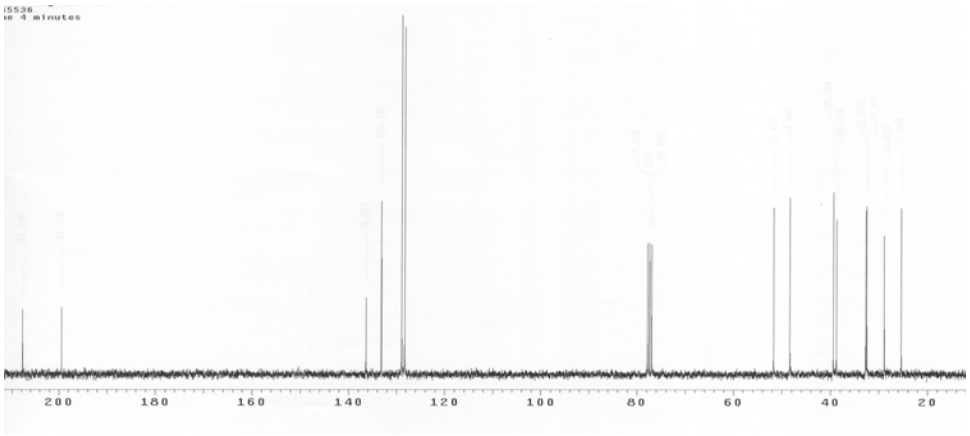


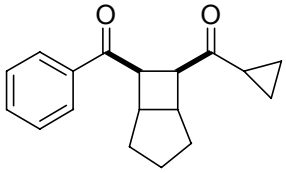


3-4.6a

1-(3-Benzoyl-octahydro-pentalen-1-yl)-ethanone. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.81 (m, 2H), 7.46 (m, 3H), 3.80 (dd, *J* = 5.1, 9.6 Hz, 1H), 3.02 (m, 3H), 2.02 (s, 3H), 1.79 (m, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 207.7, 199.4, 136.4, 133.1, 128.9, 128.2, 51.7, 48.3, 39.4, 38.7, 32.7, 32.5, 28.8, 25.4. FTIR (neat): 3055, 2948, 2858, 1706, 1678, 1448, 1356, 1264, 1218, 739 cm^{-1}. HRMS: Calcd for $C_{16}H_{18}O_2$ [M+1] 243.1385, found 243.1387. Mp = 77-78 ^{o}C.

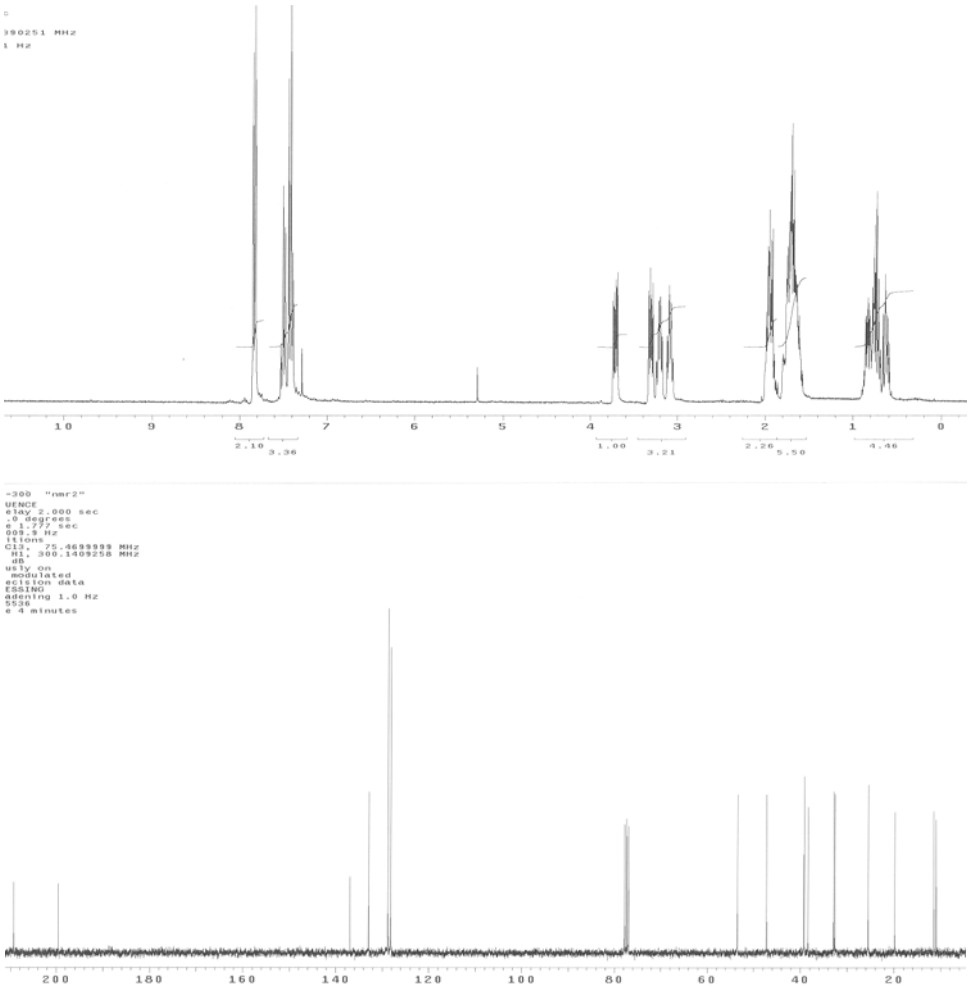


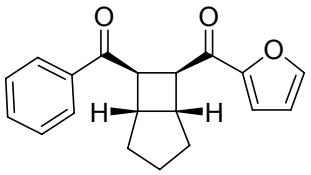




3-4.7a

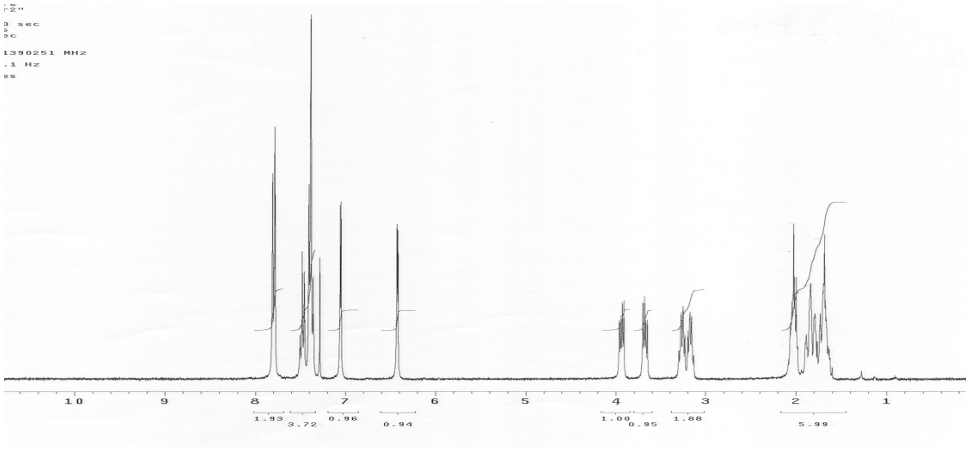
(7-Cyclopropanecarbonyl-bicyclo[3.2.0]hept-6-yl)-phenyl-methanone. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.81 (m, 2H), 7.40 (m, 3H), 3.71 (dd, *J* = 5.2, 9.7 Hz, 1H), 3.31 (dd, *J* = 5.2, 9.7 Hz, 1H), 3.20 (dd, *J* = 7.0, 12.7 Hz, 1H), 3.09 (dd, *J* = 7.0, 12.7 Hz, 1H), 1.98 (m, 2H), 1.65 (m, 5H), 0.82 (s, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 209.4, 199.5, 136.9, 132.8, 128.7, 128.2, 53.5, 47.2, 39.2, 38.3, 32.8, 32.6, 25.5, 19.8, 11.4, 10.9. FTIR (neat): 2944, 1687, 1447, 1385, 1207, 911, 730, 693 cm^{-1}. HRMS: calcd for $C_{18}H_{20}O_2$ [M+1] 269.1541, found 269.1548. Mp = 70-72 ^{o}C.

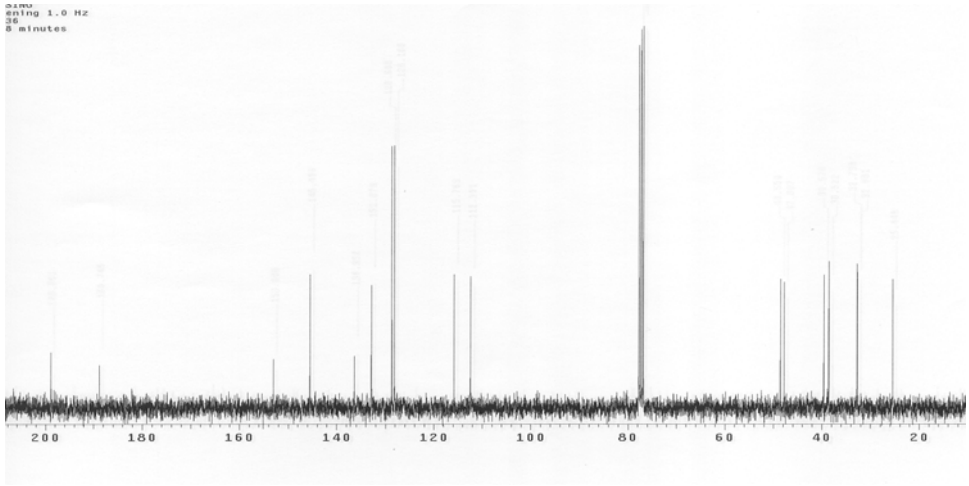


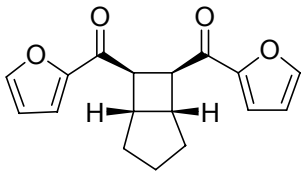


3-4.8a

[3-(furan-2-carbonyl)-octahydro-pentalen-1-yl]-phenyl-methanone. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.70 (m, 2H), 7.40 (m, 4H), 7.05 (dd, *J* = 0.6, 3.6 Hz, 1H), 6.42 (dd, *J* = 1.8, 3.6 Hz, 1H), 3.93 (dd, *J* = 4.8, 9.9 Hz, 1H), 3.61 (dd, *J* = 5.4, 9.9 Hz, 1H), 3.25 (m, 1H), 3.17 (m, 1H), 2.03 (m, 2H), 1.77 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 198.6, 188.7, 153.0, 145.5, 136.3, 132.9, 128.7, 128.2, 115.7, 112.4, 48.5, 47.8, 39.6, 38.5, 32.7, 32.6, 23.4. FTIR (neat): 3054, 2950, 1682, 1467, 1265, 737, 704 cm^{-1}. HRMS: calcd for $C_{19}H_{18}O_3$ [M+1] 295.1334, found 295.1335. Mp = 130-132 ^{o}C.

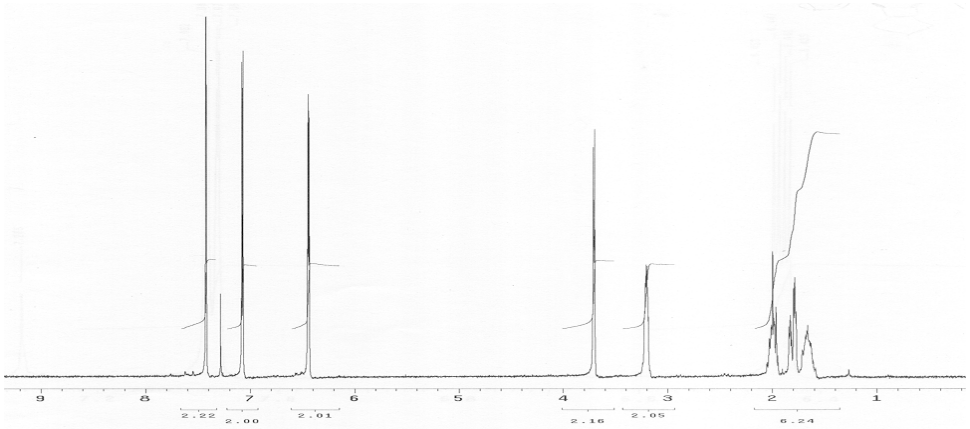


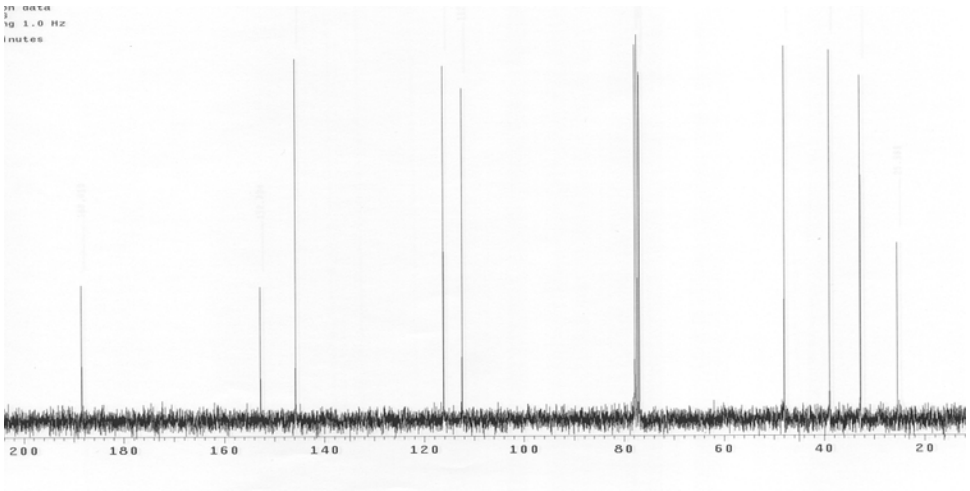


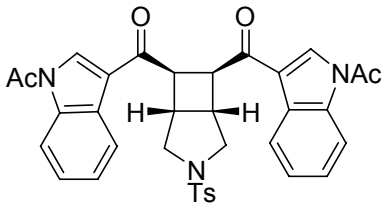


3-4.9a

[3-(furan-2-carbonyl)-octahydro-pentalen-1-yl]-furan-2-yl-methnaone. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.42 (dd, *J* = 0.9, 1.5 Hz, 2H), 7.07 (dd, *J* = 1.6, 3.6 Hz, 2H), 6.44 (dd, *J* = 1.8, 3.6 Hz, 2H), 3.70 (d, *J* = 4.2 Hz, 2H), 3.20 (m, 2H), 1.86 (m, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 188.7, 152.7, 145.7, 116.1, 112.4, 47.9, 38.9, 32.7, 25.4. FTIR (neat): 3054, 2953, 1678, 1570, 1468, 1265, 747, 704 cm^{-1}. HRMS: Calcd for $C_{17}H_{16}O_4$ [M+1] 285.1126, found 285.1128. Mp = 156-157 ºC.

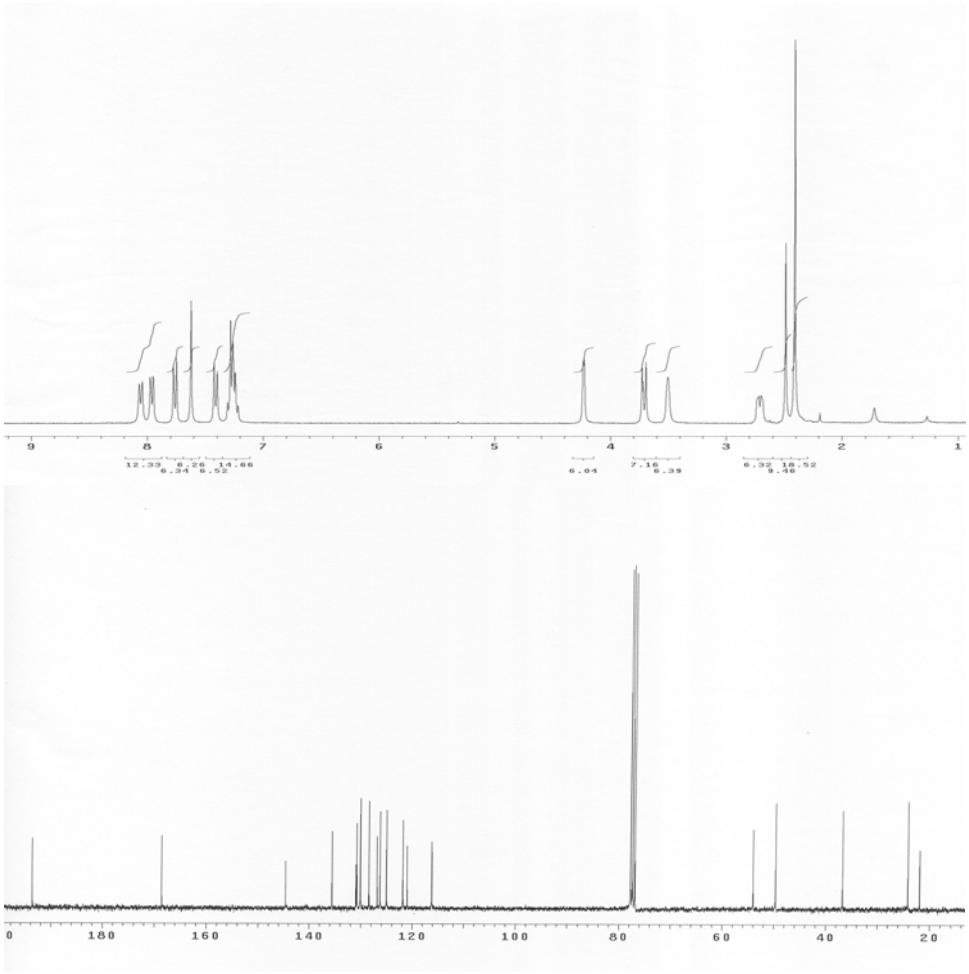






3-4.10a

1-{3-[7-(1-Acetyl-1*H*-indole-3-carbonyl)-3-(toluene-4-sulfonyl)-3-aza-bicyclo[3.2.0]heptane-6-carbonyl]-indol-1-yl}-ethanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.05 (d, *J* = 7.9 Hz, 2H), 7.96 (d, *J* = 6.9 Hz, 2H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.62 (s, 2H), 7.40 (d, *J* = 7.9 Hz, 2H), 7.24 (m, 4H), 4.23 (d, *J* = 2.8 Hz, 2H), 3.72 (d, *J* = 3.0Hz, 2H), 3.50 (s, 2H), 2.70 (m, 2H), 2.48 (s, 3H), 2.41 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.6, 168.5, 144.6, 135.6, 131.0, 130.8, 130.1, 128.4, 126.8, 126.3, 125.0, 121.8, 121.0, 116.2, 53.9, 49.6, 36.7, 24.1, 21.8. FTIR (neat): 3052, 2984, 1723, 1670, 1545, 1447, 1262, 1213, 737, 703 cm^{-1}. HRMS: calcd for $C_{35}H_{31}N_3O_6S$ [M+1] 622.2011, found 622.2012. Mp = 252-253 ºC.



III. Crystallographic Characterization Data

A. X-ray Crystallographic Material for 3-2.2a.

X-ray Experimental

Table 3-8.1. Crystallographic Data for 3-2.2a.

Table 3-8.2. Fractional coordinates and equivalent isotropic thermal parameters ($Å^2$) for the non-hydrogen atoms of 3-2.2a.

Table 3-8.3. Bond Lengths (Å) and Angles (^{o}) for the non-hydrogen atoms of 3-2.2a.

Table 3-8.4. Anisotropic thermal parameters for the non-hydrogen atoms of 3-2.2a.

Table 3-8.5. Fractional coordinates and isotropic thermal parameters ($Å^2$) for the hydrogen atoms of 3-2.2a.

Table 3-8.6. Observed and calculated structure factor amplitudes for 3-2.2a. Values for Fo, Fc and σ (Fo) have been multiplied by 10.

Figure 3-8.1. View of 3-2.2a showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. Hydrogen atoms are drawn to an arbitrary size.

Figure 3-8.2. View of the H-bound dimer formed by 3-2.2a. Displacement ellipsoids are scaled to the 50% probability level. Hydrogen atoms are drawn to an arbitrary size. Dashed lines indicate the H-bonding interactions. The two molecules are related by a crystallographic inversion center at 0, 0, ½. The geometry of the interaction is: O1-H1O···O2 (related by –x, -y, 1-z), O···O 2.859(1)Å, H···O 1.99(2)Å, O-H···O 161(2)□.

Figure 3-8.3. Unit cell packing diagram for 3-2.2a. The view is approximately down the b axis.

X-ray Experimental for $C_{13}H_{16}O_2$: Crystals grew as colorless prisms by slow evaporation from ethylacetate and hexanes. The data crystal was cut into a trigonal prism that had approximate dimensions; 0.33 x 0.33 x 0.10 mm. The data were collected on a Nonius Kappa CCD diffractometer using a graphite monochromator with MoKα radiation (λ = 0.71073Å). A total of 309 frames of data were collected using ω-scans with a scan range of 1° and a counting time of 39 seconds per frame. The data were collected at –120 °C using a Oxford Cryostream low temperature device. Details of crystal data, data collection and structure refinement are listed in Table 3-8.1. Data reduction were performed using DENZO-SMN.[1] The structure was solved by direct methods using SIR92[2] and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms using SHELXL-97.[3] The hydrogen atom positions were located in a ΔF map and refined with isotropic displacement parameters. The function, $\Sigma w(|F_O|^2 - |F_C|^2)^2$, was minimized, where w = $1/[(\sigma (F_O))^2 + (0.0472*P)^2 + (0.1494*P)]$ and P = $(|F_O|^2 + 2|F_C|^2)/3$. $R_W(F^2)$ refined to 0.100, with R(F) equal to 0.0386 and a goodness of fit, S, = 1.033. Definitions used for calculating R(F),$R_W(F^2)$ and the goodness of fit, S, are given below.[4] The data were corrected for secondary extinction effects. The correction takes the form: $F_{corr} = kF_C/[1 + (2.7(5)x10^{-5})* F_C^2 \lambda^3/(\sin 2\theta)]^{0.25}$ where k is the overall scale factor. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).[5] All figures were generated using SHELXTL/PC.[6] Tables of positional and thermal parameters, bond lengths and angles, figures and lists of observed and calculated structure factors are located in Tables 3-8.1 through 3-8.6.

References

1) DENZO-SMN. (1997). Z. Otwinowski and W. Minor, Methods in Enzymology, **276**: Macromolecular Crystallography, part A, 307 – 326, C. W. Carter, Jr. and R. M. Sweets, Editors, Academic Press.

2) SIR92. (1993). A program for crystal structure solution. Altomare, A., Cascarano, G., Giacovazzo, C. & Guagliardi, A. J. Appl. Cryst. 26, 343-350.

3) Sheldrick, G. M. (1994). SHELXL97. Program for the Refinement of Crystal Structures. University of Gottingen, Germany.

4) $R_w(F^2) = \{\Sigma w(|F_o|^2 - |F_c|^2)^2/\Sigma w(|F_o|)^4\}^{1/2}$ where w is the weight given each reflection.
$R(F) = \Sigma (|F_o| - |F_c|)/\Sigma|F_o|\}$ for reflections with $F_o > 4(\Sigma (F_o))$.
$S = [\Sigma w(|F_o|^2 - |F_c|^2)^2/(n - p)]^{1/2}$, where n is the number of reflections and p is the number of refined parameters.

5) International Tables for X-ray Crystallography (1992). Vol. C, Tables 4.2.6.8 and 6.1.1.4, A. J. C. Wilson, editor, Boston: Kluwer Academic Press.

6) Sheldrick, G. M. (1994). SHELXTL/PC (Version 5.03). Siemens Analytical X-ray Instruments, Inc., Madison, Wisconsin, USA.

Table 3-8.1. Crystal data and structure refinement for 3-2.2a.

Empirical formula	C13 H16 O2	
Formula weight	204.26	
Temperature	153(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P21/c	
Unit cell dimensions	a = 9.9320(4) Å	α= 90°.
	b = 9.2240(4) Å	β= 92.967(3)°.
	c = 12.1770(5) Å	γ = 90°.
Volume	1114.07(8) $Å^3$	
Z	4	
Density (calculated)	1.218 Mg/m	
Absorption coefficient	0.081 mm^{-1}	
F(000)	440	
Crystal size	0.33 x 0.33 x 0.10 mm^3	
Theta range for data collection	3.02 to 27.49°.	
Index ranges	-12<=h<=12, -11<=k<=11, -15<=l<=15	
Reflections collected	4501	
Independent reflections	2483 [R(int) = 0.0198]	
Completeness to theta = 27.49°	97.4 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2483 / 0 / 201	
Goodness-of-fit on F^2	1.033	
Final R indices [I>2sigma(I)]	R1 = 0.0386, wR2 = 0.0902	
R indices (all data)	R1 = 0.0614, wR2 = 0.1002	
Extinction coefficient	2.7(5)x10^{-5}	
Largest diff. peak and hole	0.177 and -0.184 e.$Å^{-3}$	

Table 3-8.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 3-2.2a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O1	-662(1)	-26(1)	6708(1)	31(1)
O2	1997(1)	643(1)	5376(1)	36(1)
C1	-390(1)	1407(1)	7101(1)	25(1)
C2	586(1)	2216(1)	6363(1)	24(1)
C3	-117(1)	2620(1)	5255(1)	29(1)
C4	-1373(1)	3527(2)	5420(1)	35(1)
C5	-2356(1)	2708(2)	6113(1)	35(1)
C6	-1674(1)	2293(2)	7219(1)	32(1)
C7	1840(1)	1322(1)	6225(1)	26(1)
C8	2920(1)	1257(1)	7132(1)	26(1)
C9	2870(1)	2071(1)	8092(1)	29(1)
C10	3912(1)	1984(2)	8899(1)	35(1)
C11	5001(1)	1087(2)	8747(1)	39(1)
C12	5060(1)	275(2)	7798(1)	41(1)
C13	4027(1)	356(2)	6993(1)	34(1)

Table 3-8.3. Bond lengths [Å] and angles [°] for 3-2.2a.

O1-C1	1.4270(15)	C5-H5A	0.985(14)
O1-H1O	0.91(2)	C5-H5B	0.997(15)
O2-C7	1.2256(14)	C6-H6A	0.991(15)
C1-C6	1.5271(17)	C6-H6B	0.992(14)
C1-C2	1.5474(16)	C7-C8	1.5006(15)
C1-H1	1.006(12)	C8-C9	1.3916(17)
C2-C7	1.5099(16)	C8-C13	1.3958(17)
C2-C3	1.5322(16)	C9-C10	1.3926(17)
C2-H2	0.982(13)	C9-H9	0.978(13)
C3-C4	1.5238(18)	C10-C11	1.3818(19)
C3-H3A	0.990(14)	C10-H10	0.987(15)
C3-H3B	1.015(15)	C11-C12	1.380(2)
C4-C5	1.524(2)	C11-H11	0.985(15)
C4-H4A	1.008(16)	C12-C13	1.3842(19)
C4-H4B	0.996(16)	C12-H12	1.004(17)
C5-C6	1.5248(18)	C13-H13	0.967(15)

C1-O1-H1O	110.6(11)	C4-C3-H3A	110.3(7)
O1-C1-C6	112.49(10)	C2-C3-H3A	109.2(7)
O1-C1-C2	111.45(9)	C4-C3-H3B	110.2(8)
C6-C1-C2	110.40(10)	C2-C3-H3B	108.4(8)
O1-C1-H1	104.8(7)	H3A-C3-H3B	107.8(11)
C6-C1-H1	108.7(7)	C5-C4-C3	110.70(11)
C2-C1-H1	108.8(7)	C5-C4-H4A	109.7(8)
C7-C2-C3	112.07(10)	C3-C4-H4A	110.4(8)
C7-C2-C1	110.27(9)	C5-C4-H4B	110.5(9)
C3-C2-C1	110.94(9)	C3-C4-H4B	110.9(9)
C7-C2-H2	109.0(7)	H4A-C4-H4B	104.5(12)
C3-C2-H2	108.6(7)	C6-C5-C4	110.22(11)
C1-C2-H2	105.8(7)	C6-C5-H5A	110.0(8)
C4-C3-C2	110.87(10)	C4-C5-H5A	109.7(7)

C6-C5-H5B	109.5(8)
C4-C5-H5B	111.0(8)
H5A-C5-H5B	106.4(11)
C5-C6-C1	112.70(10)
C5-C6-H6A	109.3(8)
C1-C6-H6A	107.6(7)
C5-C6-H6B	111.3(7)
C1-C6-H6B	106.2(8)
H6A-C6-H6B	109.6(11)
O2-C7-C8	118.90(10)
O2-C7-C2	120.96(10)
C8-C7-C2	120.15(10)
C9-C8-C13	119.07(11)
C9-C8-C7	122.77(11)
C13-C8-C7	118.16(11)
C8-C9-C10	120.28(12)
C8-C9-H9	120.2(7)
C10-C9-H9	119.5(8)
C11-C10-C9	119.85(13)
C11-C10-H10	120.4(8)
C9-C10-H10	119.7(8)
C12-C11-C10	120.33(12)
C12-C11-H11	120.7(8)
C10-C11-H11	119.0(9)
C11-C12-C13	120.09(13)
C11-C12-H12	119.6(10)
C13-C12-H12	120.3(10)
C12-C13-C8	120.37(13)
C12-C13-H13	121.4(8)
C8-C13-H13	118.2(8)

Table 3-8.4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 3-2.2a. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O1	39(1)	26(1)	29(1)	3(1)	-4(1)	-5(1)
O2	36(1)	43(1)	30(1)	-12(1)	0(1)	3(1)
C1	29(1)	27(1)	20(1)	0(1)	-2(1)	-2(1)
C2	29(1)	22(1)	22(1)	-2(1)	-1(1)	-2(1)
C3	36(1)	27(1)	24(1)	3(1)	-1(1)	0(1)
C4	44(1)	31(1)	30(1)	1(1)	-7(1)	8(1)
C5	31(1)	41(1)	33(1)	-5(1)	-5(1)	9(1)
C6	30(1)	39(1)	27(1)	-3(1)	2(1)	1(1)
C7	29(1)	24(1)	25(1)	-1(1)	3(1)	-5(1)
C8	25(1)	25(1)	28(1)	1(1)	2(1)	-4(1)
C9	25(1)	33(1)	30(1)	-2(1)	2(1)	-2(1)
C10	32(1)	44(1)	30(1)	-5(1)	-2(1)	-5(1)
C11	28(1)	49(1)	38(1)	3(1)	-7(1)	-3(1)
C12	29(1)	44(1)	50(1)	-2(1)	-2(1)	6(1)
C13	31(1)	35(1)	37(1)	-6(1)	1(1)	1(1)

Table 3-8.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 3-2.2a.

	x	y	z	U(eq)
H1O	-1051(18)	-3(19)	6017(16)	63(5)
H1	66(11)	1269(13)	7850(10)	24(3)
H2	836(11)	3112(15)	6758(10)	24(3)
H3A	-359(12)	1722(16)	4846(10)	28(3)
H3B	544(14)	3183(16)	4810(12)	41(4)
H4A	-1121(13)	4476(17)	5786(11)	39(4)
H4B	-1817(14)	3810(17)	4700(13)	48(4)
H5A	-2676(12)	1832(16)	5719(11)	31(3)
H5B	-3172(14)	3305(16)	6236(11)	41(4)
H6A	-1422(12)	3185(16)	7635(11)	33(3)
H6B	-2275(13)	1688(15)	7656(11)	36(4)
H9	2107(13)	2717(14)	8200(10)	31(3)
H10	3876(13)	2578(15)	9571(12)	39(4)
H11	5732(15)	1040(16)	9323(12)	44(4)
H12	5859(17)	-368(19)	7695(13)	58(5)
H13	4041(13)	-216(15)	6328(13)	38(4)

Table 3-8.6. Observed and calculated structure factors for 3-2.2a

h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s
2	0	0	191	202	1	4	7	0	67	66	2	-9	3	1	53	58	1	6	6	1	56	57	1	-8	0	2	52	54	2
3	0	0	227	241	1	5	7	0	14	20	8	-8	3	1	70	73	2	7	6	1	31	34	1	-7	0	2	119	120	1
4	0	0	327	325	3	6	7	0	75	83	1	-7	3	1	20	21	4	8	6	1	27	28	2	-6	0	2	106	105	1
5	0	0	172	170	1	7	7	0	55	58	1	-6	3	1	33	33	1	9	6	1	49	54	5	-5	0	2	245	234	2
6	0	0	76	74	1	8	7	0	52	53	6	-5	3	1	50	53	1	10	6	1	62	59	7	-4	0	2	366	372	3
7	0	0	113	116	1	9	7	0	11	7	11	-4	3	1	329	324	2	11	6	1	35	28	11	-3	0	2	221	234	2
8	0	0	66	66	1	10	7	0	39	27	6	-3	3	1	24	29	1	-10	7	1	0	6	1	-2	0	2	170	177	2
9	0	0	346	335	6	0	8	0	220	217	3	-2	3	1	53	53	1	-9	7	1	25	34	15	-1	0	2	87	90	1
10	0	0	162	157	2	1	8	0	158	160	2	-1	3	1	298	304	2	-8	7	1	6	11	6	0	0	2	527	533	14
11	0	0	99	96	4	2	8	0	106	105	1	0	3	1	422	431	3	-7	7	1	16	25	7	1	0	2	563	570	10
12	0	0	29	2	13	3	8	0	16	23	6	1	3	1	304	312	3	-6	7	1	151	146	2	2	0	2	148	143	1
1	1	0	171	179	1	4	8	0	86	88	3	2	3	1	114	120	1	-5	7	1	168	170	2	3	0	2	98	98	1
2	1	0	502	511	3	5	8	0	60	59	2	3	3	1	45	43	1	-4	7	1	137	131	1	4	0	2	166	176	1
3	1	0	48	45	1	6	8	0	55	58	2	4	3	1	104	105	1	-3	7	1	16	5	4	5	0	2	425	422	4
4	1	0	160	154	1	7	8	0	0	1	1	5	3	1	90	95	1	-2	7	1	0	2	1	6	0	2	41	43	1
5	1	0	60	57	1	8	8	0	23	18	9	6	3	1	145	146	1	-1	7	1	50	51	1	7	0	2	149	150	1
6	1	0	29	31	1	9	8	0	50	48	4	7	3	1	25	24	2	0	7	1	43	42	2	8	0	2	122	123	1
7	1	0	35	37	1	1	9	0	35	35	2	8	3	1	53	55	1	1	7	1	32	32	3	9	0	2	378	366	5
8	1	0	33	31	1	2	9	0	51	50	2	9	3	1	64	62	2	2	7	1	69	70	1	10	0	2	31	29	3
9	1	0	233	231	2	3	9	0	37	35	3	10	3	1	71	69	1	3	7	1	251	244	3	11	0	2	21	33	9
10	1	0	154	155	2	4	9	0	38	38	5	11	3	1	34	29	5	4	7	1	237	234	3	12	0	2	51	53	6
11	1	0	85	84	2	5	9	0	19	27	13	12	3	1	23	33	23	5	7	1	203	206	2	-12	1	2	0	10	1
12	1	0	0	4	1	6	9	0	0	13	1	-12	4	1	34	33	11	6	7	1	77	82	1	-11	1	2	43	45	3
0	2	0	369	391	5	7	9	0	0	3	1	-11	4	1	120	112	3	7	7	1	12	2	11	-10	1	2	75	75	2
1	2	0	464	476	3	8	9	0	16	16	15	-10	4	1	77	81	3	8	7	1	15	11	15	-9	1	2	32	33	2
2	2	0	368	378	2	0	10	0	33	34	7	-9	4	1	136	140	3	9	7	1	19	1	13	-8	1	2	62	63	1
3	2	0	326	328	2	1	10	0	61	62	3	-8	4	1	66	70	1	10	7	1	35	33	5	-7	1	2	112	112	1
4	2	0	101	106	1	2	10	0	14	17	13	-7	4	1	74	69	1	-9	8	1	43	43	9	-6	1	2	205	203	1
5	2	0	139	138	1	3	10	0	37	42	4	-6	4	1	42	47	1	-8	8	1	12	7	12	-5	1	2	199	196	1
6	2	0	55	52	1	4	10	0	19	0	19	-5	4	1	10	1	3	-7	8	1	9	7	9	-4	1	2	341	337	2
7	2	0	217	220	1	5	10	0	99	97	6	-4	4	1	141	142	1	-6	8	1	43	50	3	-3	1	2	175	179	1
8	2	0	58	57	1	6	10	0	63	63	6	-3	4	1	174	168	1	-5	8	1	154	158	2	-2	1	2	378	388	2
9	2	0	12	3	11	7	10	0	62	57	5	-2	4	1	149	148	1	-4	8	1	87	91	2	0	1	2	479	494	5
10	2	0	90	92	2	1	11	0	74	78	6	-1	4	1	358	353	2	-3	8	1	27	24	4	1	1	2	603	610	8
11	2	0	41	46	5	2	11	0	24	17	23	0	4	1	65	60	1	-2	8	1	52	52	2	2	1	2	29	28	1
12	2	0	25	27	24	3	11	0	38	32	6	1	4	1	0	5	1	-1	8	1	82	78	1	3	1	2	15	13	1
1	3	0	371	378	2	-12	1	1	0	15	1	2	4	1	7	7	3	0	8	1	14	10	13	4	1	2	153	152	1
2	3	0	149	151	1	-11	1	1	120	113	3	3	4	1	197	196	1	1	8	1	17	23	7	5	1	2	25	28	1
3	3	0	373	373	2	-10	1	1	25	26	4	4	4	1	69	73	1	2	8	1	29	28	3	6	1	2	184	179	1
4	3	0	370	361	2	-9	1	1	96	97	1	5	4	1	13	13	2	3	8	1	6	8	6	7	1	2	44	42	1
5	3	0	66	67	1	-8	1	1	91	94	1	6	4	1	121	122	1	4	8	1	7	10	6	8	1	2	169	167	1
6	3	0	107	108	1	-7	1	1	181	181	1	7	4	1	70	70	1	5	8	1	39	38	2	9	1	2	40	41	2
7	3	0	68	70	1	-6	1	1	143	142	1	8	4	1	90	92	1	6	8	1	77	80	1	10	1	2	129	128	2
8	3	0	18	9	2	-5	1	1	42	39	1	9	4	1	11	2	11	7	8	1	38	44	4	11	1	2	60	56	2
9	3	0	77	69	1	-4	1	1	226	238	1	10	4	1	12	15	11	8	8	1	86	83	2	12	1	2	17	5	16
10	3	0	19	25	8	-3	1	1	213	223	1	11	4	1	20	19	20	9	8	1	32	28	8	-12	2	2	60	54	6
11	3	0	14	11	13	-2	1	1	615	612	5	12	4	1	69	62	6	-8	9	1	49	51	8	-11	2	2	159	155	4
12	3	0	54	44	6	-1	1	1	688	680	11	-11	5	1	13	2	12	-7	9	1	0	0	1	-10	2	2	0	1	1
0	4	0	278	284	3	1	1	1	0	2	1	-10	5	1	18	14	17	-6	9	1	55	55	6	-9	2	2	26	26	3
1	4	0	123	126	1	2	1	1	120	125	1	-9	5	1	25	0	6	-5	9	1	12	7	11	-8	2	2	71	68	1
2	4	0	214	209	1	3	1	1	263	266	1	-8	5	1	39	33	1	-4	9	1	31	24	4	-7	2	2	70	73	1
3	4	0	156	155	1	4	1	1	258	266	1	-7	5	1	125	137	3	-3	9	1	57	58	3	-6	2	2	57	57	1
4	4	0	6	2	6	5	1	1	413	413	2	-6	5	1	7	8	7	-2	9	1	19	26	19	-5	2	2	90	83	1
5	4	0	92	86	1	6	1	1	7	3	2	-5	5	1	123	119	1	-1	9	1	81	82	3	-4	2	2	462	454	2
6	4	0	189	188	1	7	1	1	15	12	3	-4	5	1	37	38	1	0	9	1	32	24	8	-3	2	2	560	563	3
7	4	0	99	99	1	8	1	1	286	281	2	-3	5	1	23	23	1	1	9	1	33	31	6	-1	2	2	559	569	6
8	4	0	18	17	2	9	1	1	78	77	1	-2	5	1	4	2	4	2	9	1	86	82	2	0	2	2	199	204	2
9	4	0	29	27	7	10	1	1	11	12	11	-1	5	1	24	23	1	3	9	1	89	86	4	1	2	2	263	271	3
10	4	0	28	33	5	11	1	1	0	17	1	0	5	1	54	51	1	4	9	1	130	128	3	2	2	2	201	203	2
11	4	0	10	5	10	12	1	1	41	42	8	1	5	1	67	66	1	5	9	1	103	102	3	3	2	2	79	80	1
12	4	0	91	79	6	-12	2	1	39	41	9	2	5	1	426	416	4	6	9	1	0	6	1	4	2	2	325	322	2
1	5	0	55	65	1	-11	2	1	36	29	4	3	5	1	26	22	1	7	9	1	10	1	10	5	2	2	114	117	1
2	5	0	48	48	1	-10	2	1	98	91	2	4	5	1	14	17	2	8	9	1	68	63	4	6	2	2	55	58	1
3	5	0	210	205	1	-9	2	1	136	136	2	5	5	1	180	173	1	-7	10	1	14	10	14	7	2	2	146	145	1
4	5	0	33	32	2	-8	2	1	26	26	1	6	5	1	41	44	1	-5	10	1	68	67	5	8	2	2	207	206	1
5	5	0	40	40	1	-7	2	1	83	80	1	7	5	1	32	33	1	-4	10	1	32	7	11	9	2	2	31	33	1
6	5	0	113	114	1	-6	2	1	68	65	1	8	5	1	67	70	1	-3	10	1	36	33	5	10	2	2	83	82	2
7	5	0	17	21	4	-5	2	1	85	90	1	9	5	1	79	75	2	-2	10	1	0	5	1	11	2	2	21	24	11
8	5	0	35	31	2	-4	2	1	503	495	3	10	5	1	100	91	3	-1	10	1	45	41	4	12	2	2	60	56	3
9	5	0	9	7	8	-3	2	1	156	157	1	11	5	1	67	62	3	0	10	1	164	161	2	-12	3	2	115	112	7
10	5	0	58	57	3	-2	2	1	314	317	2	-11	6	1	0	8	1	1	10	1	25	36	6	-11	3	2	19	12	11
11	5	0	3	10	2	-1	2	1	560	556	5	-10	6	1	16	20	15	2	10	1	30	38	9	-10	3	2	45	47	5
0	6	0	49	44	1	1	2	1	338	355	3	-9	6	1	72	79	3	3	10	1	0	19	1	-9	3	2	29	29	2
1	6	0	40	40	1	2	2	1	414	426	3	-8	6	1	76	79	2	4	10	1	35	39	6	-8	3	2	7	0	6
2	6	0	132	130	1	3	2	1	62	65	1	-7	6	1	21	16	3	5	10	1	0	3	1	-7	3	2	36	38	1
3	6	0	63	61	1	4	2	1	8	15	3	-6	6	1	147	146	2	6	10	1	53	64	3	-6	3	2	151	145	1
4	6	0	147	142	1	5	2	1	109	107	1	-5	6	1	108	107	1	7	10	1	0	17	1	-5	3	2	29	31	1
5	6	0	132	131	1	6	2	1	115	114	1	-4	6	1	145	141	1	-1	11	1	35	40	7	-4	3	2	269	267	2
6	6	0	90	86	1	7	2	1	75	76	1	-3	6	1	27	28	1	0	11	1	0	4	1	-3	3	2	201	206	1
7	6	0	4	3	4	8	2	1	84	88	1	-2	6	1	10	14	5	1	11	1	89	93	5	-2	3	2	401	406	3
8	6	0	26	30	3	9	2	1	227	221	2	-1	6	1	83	82	1	2	11	1	23	24	10	-1	3	2	58	53	1
9	6	0	65	72	2	10	2	1	107	105	1	0	6	1	44	44	1	3	11	1	32	26	9	0	3	2	23	20	1
10	6	0	26	28	7	11	2	1	18	10	8	1	6	1	153	148	1	4	11	1	45	50	5	1	3	2	72	65	1
11	6	0	30	33	11	12	2	1	25	17	11	2	6	1	79	77	1	-12	0	2	45	38	7	2	3	2	188	182	1
1	7	0	55	53	2	-12	3	1	16	24	15	3	6	1	34	41	1	-11	0	2	61	58	4	3	3	2	86	89	1
2	7	0	44	41	1	-11	3	1	53	55	8	4	6	1	90	89	1	-10	0	2	46	50	5	4	3	2	180	180	1
3	7	0	64	66	1	-10	3	1	132	129	3	5	6	1	127	126	1	-9	0	2	125	122	2	5	3	2	294	296	2

Table 3-8.6. Observed and calculated structure factors for 3-2.2a

h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s
6	3	2	115	117	1	1	7	2	72	76	1	11	1	3	7	4	7	0	5	3	117	115	1	5	9	3	40	40	3
7	3	2	190	191	1	2	7	2	64	61	1	12	1	3	22	9	13	1	5	3	284	270	2	6	9	3	51	50	2
8	3	2	151	149	1	3	7	2	115	111	3	-12	2	3	22	33	22	2	5	3	210	199	2	7	9	3	55	49	4
9	3	2	8	15	7	4	7	2	19	16	2	-11	2	3	30	15	5	3	5	3	13	15	3	8	9	3	93	95	3
10	3	2	114	111	2	5	7	2	1	6	1	-10	2	3	13	6	8	4	5	3	13	0	3	-6	10	3	32	32	7
11	3	2	128	117	4	6	7	2	0	7	1	-9	2	3	57	60	1	5	5	3	53	54	1	-5	10	3	9	28	9
12	3	2	44	39	5	7	7	2	16	16	5	-8	2	3	43	45	2	6	5	3	14	5	3	-4	10	3	49	51	4
-12	4	2	83	76	7	8	7	2	8	7	7	-7	2	3	160	158	1	7	5	3	154	151	1	-3	10	3	22	14	10
-11	4	2	29	28	17	9	7	2	23	20	9	-6	2	3	5	0	5	8	5	3	35	34	1	-2	10	3	30	35	4
-10	4	2	75	76	3	10	7	2	0	24	1	-5	2	3	196	189	1	9	5	3	16	7	5	-1	10	3	79	79	2
-9	4	2	146	140	3	-9	8	2	31	17	13	-4	2	3	11	12	2	10	5	3	60	59	2	0	10	3	103	101	2
-8	4	2	44	33	1	-8	8	2	120	117	4	-3	2	3	312	312	2	11	5	3	39	38	4	1	10	3	50	51	3
-7	4	2	62	63	1	-7	8	2	66	59	3	-2	2	3	144	146	1	-11	6	3	66	61	7	2	10	3	0	16	1
-6	4	2	14	10	2	-6	8	2	28	30	4	-1	2	3	259	265	2	-10	6	3	23	30	11	3	10	3	0	8	1
-5	4	2	28	27	1	-5	8	2	53	57	2	0	2	3	85	86	2	-9	6	3	82	81	3	4	10	3	30	23	8
-4	4	2	239	227	1	-4	8	2	63	67	3	1	2	3	104	105	1	-8	6	3	55	67	2	5	10	3	34	30	5
-3	4	2	512	495	3	-3	8	2	40	39	3	2	2	3	155	152	1	-7	6	3	11	7	6	6	10	3	44	39	5
-2	4	2	81	84	1	-2	8	2	50	52	2	3	2	3	190	193	1	-6	6	3	0	1	1	-4	11	3	25	25	11
-1	4	2	195	198	1	-1	8	2	24	20	4	4	2	3	88	84	1	-5	6	3	74	76	1	-3	11	3	0	2	1
0	4	2	152	154	1	0	8	2	115	111	2	5	2	3	112	111	1	-4	6	3	19	19	2	-2	11	3	75	74	8
1	4	2	400	395	4	1	8	2	47	48	6	6	2	3	46	52	1	-3	6	3	354	345	3	-1	11	3	27	22	9
2	4	2	123	124	1	2	8	2	135	130	2	7	2	3	145	150	1	-2	6	3	39	44	1	0	11	3	80	86	4
3	4	2	199	197	1	3	8	2	77	75	2	8	2	3	7	8	6	-1	6	3	0	3	1	1	11	3	77	79	3
4	4	2	162	161	1	4	8	2	26	25	3	9	2	3	43	41	1	0	6	3	26	23	3	2	11	3	105	108	8
5	4	2	99	103	1	5	8	2	72	75	2	10	2	3	93	94	4	1	6	3	227	219	2	3	11	3	29	18	15
6	4	2	48	47	2	6	8	2	43	44	2	11	2	3	59	58	5	2	6	3	37	42	1	-12	0	4	28	30	13
7	4	2	83	88	1	7	8	2	50	51	2	12	2	3	53	54	3	3	6	3	19	19	2	-11	0	4	8	0	8
8	4	2	8	4	8	8	8	2	47	38	3	-12	3	3	28	6	13	4	6	3	122	120	1	-10	0	4	22	27	5
9	4	2	20	24	3	9	8	2	99	95	3	-11	3	3	19	28	19	5	6	3	82	82	1	-9	0	4	6	10	5
10	4	2	45	44	5	-8	9	2	20	11	20	-10	3	3	54	54	3	6	6	3	144	142	1	-8	0	4	21	18	4
11	4	2	23	26	6	-7	9	2	0	7	1	-9	3	3	15	14	11	7	6	3	70	69	1	-7	0	4	455	443	4
-11	5	2	31	34	10	-5	9	2	0	23	1	-8	3	3	61	70	1	8	6	3	20	16	4	-6	0	4	370	377	3
-10	5	2	55	57	4	-4	9	2	48	53	3	-7	3	3	45	48	1	9	6	3	70	66	2	-5	0	4	173	191	2
-9	5	2	63	66	3	-3	9	2	18	19	15	-6	3	3	47	51	1	10	6	3	107	96	4	-4	0	4	137	140	1
-8	5	2	65	74	1	-2	9	2	50	52	3	-5	3	3	91	93	1	-10	7	3	0	12	1	-3	0	4	120	125	1
-7	5	2	90	94	1	-1	9	2	58	58	2	-4	3	3	157	154	1	-9	7	3	74	69	5	-2	0	4	339	345	3
-6	5	2	20	20	2	0	9	2	153	152	2	-3	3	3	431	425	3	-8	7	3	78	74	3	-1	0	4	271	277	3
-5	5	2	231	227	2	1	9	2	41	38	3	-2	3	3	227	228	2	-7	7	3	33	33	2	0	0	4	24	18	1
-4	5	2	182	182	1	2	9	2	28	29	4	-1	3	3	0	5	1	-6	7	3	9	6	9	1	0	4	119	120	1
-3	5	2	159	155	1	3	9	2	0	1	1	0	3	3	19	22	2	-5	7	3	11	11	11	2	0	4	403	394	9
-2	5	2	107	107	1	4	9	2	16	15	15	1	3	3	300	298	3	-4	7	3	31	35	1	3	0	4	154	157	1
-1	5	2	174	169	1	5	9	2	79	78	2	2	3	3	33	30	1	-3	7	3	52	54	1	4	0	4	13	12	2
0	5	2	48	50	2	6	9	2	16	13	8	3	3	3	6	3	5	-2	7	3	146	142	1	5	0	4	58	54	1
1	5	2	158	160	1	7	9	2	92	90	5	4	3	3	28	29	1	-1	7	3	144	139	3	6	0	4	50	50	1
2	5	2	171	165	2	8	9	2	0	12	1	5	3	3	20	21	1	0	7	3	260	251	3	7	0	4	18	19	3
3	5	2	135	130	1	-4	10	2	17	1	16	6	3	3	365	360	3	1	7	3	0	2	1	8	0	4	46	46	2
4	5	2	94	94	1	-3	10	2	17	13	16	7	3	3	38	38	1	2	7	3	88	78	2	9	0	4	136	130	3
5	5	2	66	69	1	-2	10	2	45	41	3	8	3	3	58	57	2	3	7	3	18	22	3	10	0	4	96	95	4
6	5	2	189	192	2	-1	10	2	108	106	2	9	3	3	65	64	2	4	7	3	26	28	1	11	0	4	81	71	4
7	5	2	21	18	2	0	10	2	63	60	5	10	3	3	0	3	1	5	7	3	36	36	1	12	0	4	101	94	7
8	5	2	18	14	2	1	10	2	0	7	1	11	3	3	22	13	7	6	7	3	93	87	1	-12	1	4	23	6	8
9	5	2	11	6	10	2	10	2	0	4	1	12	3	3	53	53	3	7	7	3	27	29	2	-11	1	4	12	18	12
10	5	2	64	60	2	3	10	2	21	25	9	-12	4	3	39	36	7	8	7	3	20	27	4	-10	1	4	20	23	7
11	5	2	37	32	3	4	10	2	0	11	1	-11	4	3	53	54	5	9	7	3	12	14	12	-9	1	4	100	102	1
-11	6	2	25	6	25	5	10	2	36	32	4	-10	4	3	33	34	4	10	7	3	43	39	6	-8	1	4	207	205	2
-10	6	2	29	28	5	6	10	2	0	6	1	-9	4	3	76	80	3	-9	8	3	29	14	11	-7	1	4	175	177	1
-9	6	2	0	22	1	-3	11	2	0	17	1	-8	4	3	65	76	1	-8	8	3	0	13	1	-6	1	4	188	184	1
-8	6	2	20	0	5	-2	11	2	31	34	31	-7	4	3	39	42	1	-7	8	3	29	33	4	-5	1	4	108	111	1
-7	6	2	31	38	2	-1	11	2	66	71	4	-6	4	3	29	30	1	-6	8	3	0	6	1	-4	1	4	127	124	1
-6	6	2	23	26	2	0	11	2	55	54	4	-5	4	3	7	3	7	-5	8	3	22	14	8	-3	1	4	312	305	3
-5	6	2	116	114	1	1	11	2	44	34	6	-4	4	3	180	183	1	-4	8	3	32	30	3	-2	1	4	70	70	1
-4	6	2	258	253	2	2	11	2	19	9	18	-3	4	3	13	17	2	-3	8	3	36	33	4	-1	1	4	197	202	1
-3	6	2	235	230	2	3	11	2	38	38	6	-2	4	3	373	370	3	-2	8	3	234	222	3	0	1	4	69	72	1
-2	6	2	192	191	1	4	11	2	41	36	10	-1	4	3	178	173	1	-1	8	3	76	78	1	1	1	4	80	82	1
-1	6	2	114	111	1	-12	1	3	29	20	7	0	4	3	98	100	1	0	8	3	73	73	2	2	1	4	465	461	4
0	6	2	194	191	2	-11	1	3	18	17	9	1	4	3	152	152	1	1	8	3	11	7	3	3	1	4	469	456	4
1	6	2	34	29	1	-10	1	3	60	62	2	2	4	3	39	41	1	2	8	3	56	52	2	4	1	4	177	171	1
2	6	2	31	27	2	-9	1	3	82	86	1	3	4	3	215	215	2	3	8	3	20	24	3	5	1	4	30	34	1
3	6	2	76	76	1	-8	1	3	60	60	1	4	4	3	65	66	1	4	8	3	69	69	1	6	1	4	92	94	1
4	6	2	10	14	4	-7	1	3	33	32	1	5	4	3	68	69	1	5	8	3	72	73	1	7	1	4	76	75	1
5	6	2	7	4	7	-6	1	3	344	337	2	6	4	3	176	178	1	6	8	3	23	28	3	8	1	4	50	51	1
6	6	2	56	58	1	-5	1	3	22	16	1	7	4	3	70	70	1	7	8	3	49	53	2	9	1	4	68	69	1
7	6	2	112	108	1	-4	1	3	87	87	1	8	4	3	159	155	1	8	8	3	68	69	3	10	1	4	92	93	2
8	6	2	17	16	5	-3	1	3	229	235	1	9	4	3	22	25	5	9	8	3	96	88	3	11	1	4	22	22	21
9	6	2	43	38	2	-2	1	3	173	176	1	10	4	3	7	9	7	-8	9	3	86	85	5	12	1	4	0	4	1
10	6	2	79	68	5	-1	1	3	187	198	1	11	4	3	0	17	1	-7	9	3	59	40	6	-12	2	4	33	27	8
-10	7	2	27	9	11	0	1	3	316	325	3	-11	5	3	0	14	1	-6	9	3	67	65	4	-11	2	4	107	100	4
-9	7	2	21	0	12	1	1	3	654	648	7	-10	5	3	8	29	7	-5	9	3	0	4	1	-10	2	4	34	39	3
-8	7	2	60	59	8	2	1	3	478	475	4	-9	5	3	21	31	17	-4	9	3	12	22	12	-9	2	4	25	26	2
-7	7	2	34	47	2	3	1	3	316	306	2	-8	5	3	58	63	1	-3	9	3	0	0	1	-8	2	4	85	88	1
-6	7	2	26	31	5	4	1	3	406	399	3	-7	5	3	110	114	1	-2	9	3	9	6	8	-7	2	4	121	122	1
-5	7	2	64	69	1	5	1	3	11	2	2	-6	5	3	58	56	1	-1	9	3	145	138	2	-6	2	4	40	40	1
-4	7	2	68	70	1	6	1	3	37	38	1	-5	5	3	12	3	4	0	9	3	103	103	2	-5	2	4	162	159	1
-3	7	2	9	2	8	7	1	3	164	163	1	-4	5	3	41	38	1	1	9	3	151	151	2	-4	2	4	148	152	1
-2	7	2	46	43	1	8	1	3	156	157	1	-3	5	3	99	97	1	2	9	3	67	70	4	-3	2	4	35	33	1
-1	7	2	72	76	1	9	1	3	34	35	1	-2	5	3	290	288	2	3	9	3	66	64	2	-2	2	4	148	142	1
0	7	2	74	75	1	10	1	3	72	73	2	-1	5	3	135	130	1	4	9	3	19	10	7	-1	2	4	244	249	2

Table 3-8.6. Observed and calculated structure factors for 3-2.2a

h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s
0	2	4	140	132	1	-6	6	4	10	13	6	-1	11	4	17	0	17	0	4	5	232	220	2	5	8	5	1	14	1
1	2	4	336	336	3	-5	6	4	26	23	2	0	11	4	18	30	18	1	4	5	264	257	2	6	8	5	55	57	2
2	2	4	399	395	4	-4	6	4	244	241	2	1	11	4	23	24	10	2	4	5	59	53	1	7	8	5	90	96	2
3	2	4	173	167	2	-3	6	4	64	63	1	2	11	4	31	5	18	3	4	5	99	101	1	8	8	5	0	7	1
4	2	4	62	60	1	-2	6	4	44	48	2	-12	1	5	34	33	5	4	4	5	9	13	9	-7	9	5	48	47	4
5	2	4	75	79	1	-1	6	4	142	141	1	-11	1	5	41	45	5	5	4	5	139	140	1	-6	9	5	35	30	9
6	2	4	299	297	2	0	6	4	18	26	3	-10	1	5	13	25	12	6	4	5	36	38	1	-5	9	5	18	13	17
7	2	4	166	166	1	1	6	4	18	12	4	-9	1	5	100	95	1	7	4	5	39	41	1	-4	9	5	70	67	4
8	2	4	115	116	2	2	6	4	16	21	4	-8	1	5	81	81	1	8	4	5	13	8	4	-3	9	5	13	16	12
9	2	4	32	34	2	3	6	4	121	121	1	-7	1	5	3	4	3	9	4	5	51	52	2	-2	9	5	71	75	2
10	2	4	10	1	9	4	6	4	127	127	1	-6	1	5	87	86	1	10	4	5	8	12	8	-1	9	5	74	76	3
11	2	4	41	37	4	5	6	4	242	237	2	-5	1	5	88	89	2	11	4	5	0	2	1	0	9	5	33	31	12
12	2	4	0	6	1	6	6	4	85	90	1	-4	1	5	17	17	1	-11	5	5	15	18	14	1	9	5	52	52	2
-12	3	4	31	30	14	7	6	4	67	67	1	-3	1	5	187	188	1	-10	5	5	41	35	5	2	9	5	30	28	20
-11	3	4	17	17	16	8	6	4	65	63	2	-2	1	5	305	315	3	-9	5	5	15	25	14	3	9	5	72	61	3
-10	3	4	23	8	6	9	6	4	24	27	5	-1	1	5	209	210	1	-8	5	5	20	28	4	4	9	5	63	60	2
-9	3	4	50	49	3	10	6	4	37	36	3	0	1	5	340	331	3	-7	5	5	38	38	2	5	9	5	65	66	5
-8	3	4	109	107	1	-10	7	4	18	5	18	1	1	5	138	140	1	-6	5	5	55	61	1	6	9	5	28	28	10
-7	3	4	193	190	1	-9	7	4	0	19	1	2	1	5	181	174	2	-5	5	5	215	209	2	7	9	5	16	5	16
-6	3	4	28	26	1	-8	7	4	68	60	2	3	1	5	118	115	1	-4	5	5	135	140	1	-5	10	5	4	24	4
-5	3	4	70	71	1	-7	7	4	72	67	2	4	1	5	101	92	1	-3	5	5	42	44	1	-4	10	5	37	42	10
-4	3	4	153	149	1	-6	7	4	11	17	11	5	1	5	35	36	1	-2	5	5	42	44	1	-3	10	5	0	25	1
-3	3	4	470	458	4	-5	7	4	68	74	1	6	1	5	156	152	1	-1	5	5	17	16	5	-2	10	5	56	62	4
-2	3	4	29	27	1	-4	7	4	63	67	1	7	1	5	31	32	2	0	5	5	26	18	2	-1	10	5	18	6	10
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0	3	4	35	24	3	-2	7	4	135	133	1	9	1	5	23	21	2	2	5	5	78	73	1	1	10	5	96	92	3
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3	3	4	161	164	1	1	7	4	0	2	1	-12	2	5	0	12	1	5	5	5	175	169	2	4	10	5	31	32	10
4	3	4	85	88	1	2	7	4	12	10	9	-11	2	5	30	26	5	6	5	5	115	111	1	5	10	5	27	38	11
5	3	4	32	34	1	3	7	4	39	34	1	-10	2	5	16	17	10	7	5	5	52	54	1	-2	11	5	78	80	6
6	3	4	137	139	1	4	7	4	15	21	5	-9	2	5	72	73	2	8	5	5	8	9	8	-1	11	5	46	53	6
7	3	4	76	76	1	5	7	4	117	114	1	-8	2	5	59	60	1	9	5	5	27	23	18	-12	0	6	87	76	5
8	3	4	43	49	1	6	7	4	105	104	1	-7	2	5	86	87	1	10	5	5	45	49	3	-11	0	6	94	92	4
9	3	4	54	53	1	7	7	4	48	50	1	-6	2	5	27	31	1	-10	6	5	0	5	1	-10	0	6	30	30	5
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11	3	4	30	24	5	9	7	4	60	56	2	-4	2	5	170	170	1	-8	6	5	7	7	7	-8	0	6	222	218	3
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-10	4	4	27	24	5	-8	8	4	51	41	8	-2	2	5	80	78	1	-6	6	5	61	66	1	-6	0	6	69	67	1
-9	4	4	76	83	3	-7	8	4	107	95	2	-1	2	5	26	21	1	-5	6	5	47	49	1	-5	0	6	30	29	2
-8	4	4	56	61	1	-6	8	4	83	79	3	0	2	5	38	33	1	-4	6	5	115	117	1	-4	0	6	169	164	1
-7	4	4	35	34	1	-5	8	4	31	28	5	1	2	5	23	25	1	-3	6	5	415	407	4	-3	0	6	7	14	7
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-5	4	4	10	13	7	-3	8	4	261	253	4	3	2	5	72	73	1	-1	6	5	16	22	4	-1	0	6	360	352	4
-4	4	4	148	148	1	-2	8	4	87	89	1	4	2	5	37	37	1	0	6	5	69	73	1	0	0	6	137	132	1
-3	4	4	291	290	2	-1	8	4	64	60	1	5	2	5	15	15	2	1	6	5	94	86	1	1	0	6	223	220	3
-2	4	4	231	237	2	0	8	4	26	21	4	6	2	5	118	121	2	2	6	5	121	116	1	2	0	6	626	600	10
-1	4	4	41	43	1	1	8	4	37	37	1	7	2	5	136	137	1	3	6	5	71	69	1	3	0	6	410	399	5
0	4	4	42	43	3	2	8	4	16	7	7	8	2	5	74	72	1	4	6	5	121	118	1	4	0	6	259	252	3
1	4	4	367	354	4	3	8	4	16	17	3	9	2	5	13	0	5	5	6	5	10	10	7	5	0	6	72	70	1
2	4	4	60	64	1	4	8	4	54	54	1	10	2	5	20	0	7	6	6	5	263	253	2	6	0	6	86	91	1
3	4	4	168	165	2	5	8	4	37	40	2	11	2	5	60	62	5	7	6	5	47	47	1	7	0	6	169	178	3
4	4	4	49	49	1	6	8	4	63	68	2	-12	3	5	24	11	24	8	6	5	36	40	3	8	0	6	36	26	3
5	4	4	112	115	1	7	8	4	96	94	2	-11	3	5	20	30	19	9	6	5	14	20	13	9	0	6	66	64	2
6	4	4	404	392	3	8	8	4	50	49	3	-10	3	5	59	60	6	10	6	5	47	44	4	10	0	6	32	24	10
7	4	4	0	0	1	-8	9	4	61	51	5	-9	3	5	51	56	3	-9	7	5	29	29	11	11	0	6	57	54	7
8	4	4	42	44	1	-7	9	4	57	63	5	-8	3	5	99	99	1	-8	7	5	8	8	8	-12	1	6	0	13	1
9	4	4	33	35	3	-6	9	4	72	66	5	-7	3	5	92	95	1	-7	7	5	4	11	4	-11	1	6	18	13	18
10	4	4	196	181	4	-5	9	4	0	17	1	-6	3	5	86	88	1	-6	7	5	98	100	2	-10	1	6	81	77	2
11	4	4	89	76	3	-4	9	4	45	47	6	-5	3	5	150	151	1	-5	7	5	95	101	1	-9	1	6	25	21	2
-11	5	4	17	7	16	-3	9	4	50	55	7	-4	3	5	52	48	1	-4	7	5	203	203	2	-8	1	6	77	79	1
-10	5	4	0	7	1	-2	9	4	175	166	6	-3	3	5	55	53	1	-3	7	5	329	318	3	-7	1	6	81	84	2
-9	5	4	29	20	19	-1	9	4	46	44	4	-2	3	5	39	40	1	-2	7	5	151	149	2	-6	1	6	167	166	1
-8	5	4	14	1	6	0	9	4	38	43	4	-1	3	5	335	327	2	-1	7	5	132	134	2	-5	1	6	28	28	1
-7	5	4	21	28	2	1	9	4	0	7	1	0	3	5	17	13	1	0	7	5	25	31	3	-4	1	6	92	89	1
-6	5	4	24	27	1	2	9	4	52	53	3	1	3	5	24	28	1	1	7	5	33	36	3	-3	1	6	60	58	1
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-4	5	4	406	396	3	4	9	4	0	9	1	3	3	5	23	25	1	3	7	5	91	87	1	-1	1	6	179	167	1
-3	5	4	131	129	1	5	9	4	6	3	5	4	3	5	156	154	1	4	7	5	42	42	1	0	1	6	215	214	2
-2	5	4	64	63	1	6	9	4	0	5	1	5	3	5	95	97	1	5	7	5	166	162	2	1	1	6	187	186	2
-1	5	4	59	57	1	7	9	4	118	116	3	6	3	5	247	247	2	6	7	5	13	4	6	2	1	6	294	286	3
0	5	4	145	137	1	-6	10	4	54	53	5	7	3	5	35	36	2	7	7	5	82	77	2	3	1	6	103	104	1
1	5	4	223	215	2	-5	10	4	23	3	22	8	3	5	77	79	1	8	7	5	92	89	2	4	1	6	72	70	1
2	5	4	67	66	2	-4	10	4	25	30	11	9	3	5	87	92	1	9	7	5	65	58	2	5	1	6	128	128	1
3	5	4	24	21	1	-3	10	4	15	10	15	10	3	5	52	54	3	-8	8	5	30	21	14	6	1	6	131	131	1
4	5	4	85	83	1	-2	10	4	69	72	6	11	3	5	90	85	3	-7	8	5	23	18	11	7	1	6	115	118	2
5	5	4	26	24	1	-1	10	4	20	12	7	-11	4	5	24	8	17	-6	8	5	31	25	5	8	1	6	76	79	3
6	5	4	105	103	1	0	10	4	107	105	2	-10	4	5	38	40	6	-5	8	5	49	54	4	9	1	6	41	50	2
7	5	4	94	96	1	1	10	4	63	64	3	-9	4	5	10	11	9	-4	8	5	91	102	3	10	1	6	42	40	4
8	5	4	50	53	2	2	10	4	79	81	3	-8	4	5	65	71	1	-3	8	5	96	101	2	11	1	6	68	58	5
9	5	4	8	1	8	3	10	4	50	47	4	-7	4	5	96	98	1	-2	8	5	137	134	3	-11	2	6	15	10	15
10	5	4	75	72	3	4	10	4	34	42	4	-6	4	5	10	4	6	-1	8	5	79	81	1	-10	2	6	76	78	2
11	5	4	16	19	16	5	10	4	16	18	15	-5	4	5	10	13	5	0	8	5	53	52	2	-9	2	6	85	80	1
-10	6	4	0	34	1	6	10	4	38	42	9	-4	4	5	16	10	2	1	8	5	71	68	2	-8	2	6	60	64	1
-9	6	4	19	5	12	-4	11	4	19	10	19	-3	4	5	9	4	4	2	8	5	106	99	2	-7	2	6	73	76	1
-8	6	4	44	51	2	-3	11	4	19	11	18	-2	4	5	96	93	1	3	8	5	63	62	1	-6	2	6	60	58	1
-7	6	4	16	18	4	-2	11	4	24	17	9	-1	4	5	98	94	1	4	8	5	64	65	1	-5	2	6	63	63	1

Table 3-8.6. Observed and calculated structure factors for 3-2.2a

h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s
-4	2	6	150	153	1	-5	6	6	56	60	1	3	1	7	19	18	2	1	5	7	45	46	1	-6	0	8	276	267	3
-3	2	6	28	24	1	-4	6	6	11	2	8	4	1	7	154	155	1	2	5	7	132	132	1	-5	0	8	79	82	1
-2	2	6	105	100	1	-3	6	6	63	62	1	5	1	7	43	45	1	3	5	7	155	155	1	-4	0	8	85	82	1
-1	2	6	272	265	2	-2	6	6	67	65	5	6	1	7	58	64	1	4	5	7	133	130	1	-3	0	8	224	217	2
0	2	6	99	108	1	-1	6	6	15	14	4	7	1	7	38	47	2	5	5	7	106	104	2	-2	0	8	166	154	2
1	2	6	167	168	2	0	6	6	33	33	2	8	1	7	0	14	1	6	5	7	94	91	2	-1	0	8	43	44	1
2	2	6	197	193	2	1	6	6	135	129	1	9	1	7	12	13	10	7	5	7	105	103	2	0	0	8	18	21	3
3	2	6	127	121	1	2	6	6	90	87	1	10	1	7	65	64	4	8	5	7	66	65	2	1	0	8	162	158	2
4	2	6	81	76	1	3	6	6	57	58	1	11	1	7	19	27	18	9	5	7	75	76	3	2	0	8	31	29	1
5	2	6	50	54	2	4	6	6	67	65	2	-11	2	7	24	36	23	-9	6	7	21	20	21	3	0	8	41	38	1
6	2	6	127	130	1	5	6	6	45	45	2	-10	2	7	0	5	1	-8	6	7	42	49	4	4	0	8	205	210	2
7	2	6	221	218	3	6	6	6	45	47	2	-9	2	7	11	18	10	-7	6	7	0	6	1	5	0	8	60	65	1
8	2	6	144	142	2	7	6	6	37	36	3	-8	2	7	69	70	1	-6	6	7	102	101	2	6	0	8	79	88	2
9	2	6	2	10	2	8	6	6	76	74	2	-7	2	7	91	94	2	-5	6	7	10	15	9	7	0	8	155	166	3
10	2	6	27	4	7	9	6	6	15	14	14	-6	2	7	193	194	2	-4	6	7	68	74	1	8	0	8	72	77	3
11	2	6	41	43	5	-9	7	6	20	15	19	-5	2	7	0	0	1	-3	6	7	52	55	1	9	0	8	0	9	1
-11	3	6	128	113	6	-8	7	6	60	47	4	-4	2	7	70	66	2	-2	6	7	159	153	1	10	0	8	0	6	1
-10	3	6	16	11	16	-7	7	6	41	36	5	-3	2	7	50	49	1	-1	6	7	64	67	1	-11	1	8	34	24	7
-9	3	6	43	45	3	-6	7	6	99	104	2	-2	2	7	284	270	2	0	6	7	115	116	2	-10	1	8	65	64	3
-8	3	6	34	33	1	-5	7	6	105	117	1	-1	2	7	9	3	9	1	6	7	31	34	4	-9	1	8	45	44	3
-7	3	6	60	59	1	-4	7	6	145	148	2	0	2	7	74	72	1	2	6	7	115	116	1	-8	1	8	52	52	1
-6	3	6	173	169	2	-3	7	6	12	14	9	1	2	7	13	12	4	3	6	7	175	171	2	-7	1	8	55	54	1
-5	3	6	86	84	1	-2	7	6	63	65	1	2	2	7	1	5	1	4	6	7	137	129	1	-6	1	8	89	89	1
-4	3	6	138	140	2	-1	7	6	0	9	1	3	2	7	127	129	1	5	6	7	4	4	4	-5	1	8	83	78	1
-3	3	6	74	78	1	0	7	6	0	12	1	4	2	7	88	85	2	6	6	7	79	77	2	-4	1	8	2	1	2
-2	3	6	61	58	1	1	7	6	14	9	9	5	2	7	82	82	1	7	6	7	12	10	12	-3	1	8	159	150	1
-1	3	6	41	46	1	2	7	6	77	78	3	6	2	7	39	44	1	8	6	7	17	11	17	-2	1	8	49	53	1
0	3	6	298	291	2	3	7	6	9	6	9	7	2	7	71	81	1	9	6	7	16	13	15	-1	1	8	82	80	1
1	3	6	127	120	1	4	7	6	84	84	1	8	2	7	50	53	2	-9	7	7	116	94	5	0	1	8	26	25	1
2	3	6	168	171	2	5	7	6	155	149	2	9	2	7	80	77	2	-8	7	7	26	15	21	1	1	8	12	15	10
3	3	6	89	83	1	6	7	6	137	138	3	10	2	7	0	0	1	-7	7	7	109	109	3	2	1	8	212	208	2
4	3	6	88	87	1	7	7	6	21	4	7	11	2	7	0	6	1	-6	7	7	16	22	16	3	1	8	224	216	2
5	3	6	117	118	1	8	7	6	31	26	6	-11	3	7	0	6	1	-5	7	7	19	24	18	4	1	8	49	52	1
6	3	6	87	89	1	-8	8	6	15	12	14	-10	3	7	0	5	1	-4	7	7	66	72	2	5	1	8	2	1	2
7	3	6	92	90	3	-7	8	6	102	92	6	-9	3	7	68	68	2	-3	7	7	104	108	2	6	1	8	92	102	1
8	3	6	36	35	2	-6	8	6	152	153	6	-8	3	7	14	12	7	-2	7	7	87	88	1	7	1	8	39	42	2
9	3	6	28	30	3	-5	8	6	24	34	7	-7	3	7	50	47	1	-1	7	7	86	85	1	8	1	8	75	77	2
10	3	6	37	34	5	-4	8	6	81	85	5	-6	3	7	164	166	2	0	7	7	22	26	3	9	1	8	23	33	7
11	3	6	52	56	5	-3	8	6	42	50	13	-5	3	7	152	150	1	1	7	7	33	37	2	10	1	8	34	19	6
-11	4	6	19	14	19	-2	8	6	35	27	4	-4	3	7	84	85	1	2	7	7	33	33	2	-11	2	8	90	87	3
-10	4	6	48	54	6	-1	8	6	0	8	1	-3	3	7	24	24	2	3	7	7	158	149	2	-10	2	8	88	81	4
-9	4	6	25	23	8	0	8	6	39	39	4	-2	3	7	21	22	3	4	7	7	30	33	4	-9	2	8	36	32	3
-8	4	6	92	91	1	1	8	6	125	124	4	-1	3	7	25	27	1	5	7	7	103	104	3	-8	2	8	12	14	5
-7	4	6	51	51	1	2	8	6	185	182	2	0	3	7	114	111	1	6	7	7	101	99	2	-7	2	8	110	109	1
-6	4	6	26	28	2	3	8	6	120	124	2	1	3	7	42	40	1	7	7	7	89	88	3	-6	2	8	60	55	1
-5	4	6	59	60	1	4	8	6	108	102	1	2	3	7	231	226	3	8	7	7	47	46	9	-5	2	8	187	189	2
-4	4	6	136	134	1	5	8	6	10	14	10	3	3	7	67	66	1	-8	8	7	20	25	20	-4	2	8	10	13	5
-3	4	6	198	198	2	6	8	6	102	100	2	4	3	7	298	293	4	-7	8	7	20	14	10	-3	2	8	158	155	2
-2	4	6	172	173	1	7	8	6	35	27	5	5	3	7	69	70	1	-6	8	7	16	1	16	-2	2	8	86	88	1
-1	4	6	172	170	1	-7	9	6	116	112	4	6	3	7	53	56	3	-5	8	7	35	51	6	-1	2	8	215	215	3
0	4	6	145	146	1	-6	9	6	32	35	7	7	3	7	0	7	1	-4	8	7	32	34	3	0	2	8	226	228	2
1	4	6	137	133	1	-5	9	6	28	25	11	8	3	7	41	43	2	-3	8	7	64	69	2	1	2	8	16	20	4
2	4	6	67	74	1	-4	9	6	0	13	1	9	3	7	0	15	1	-2	8	7	110	109	3	2	2	8	76	77	3
3	4	6	90	94	1	-3	9	6	63	66	3	10	3	7	15	2	14	-1	8	7	47	48	3	3	2	8	99	99	1
4	4	6	169	167	2	-2	9	6	44	46	3	-11	4	7	0	6	1	0	8	7	7	13	7	4	2	8	96	96	3
5	4	6	5	4	5	-1	9	6	81	81	3	-10	4	7	12	12	12	1	8	7	82	87	3	5	2	8	45	49	1
6	4	6	134	136	1	0	9	6	64	62	2	-9	4	7	10	25	10	2	8	7	84	81	3	6	2	8	132	136	1
7	4	6	44	45	1	1	9	6	61	55	2	-8	4	7	28	33	4	3	8	7	27	30	14	7	2	8	69	71	2
8	4	6	31	33	2	2	9	6	25	17	7	-7	4	7	16	22	7	4	8	7	8	0	8	8	2	8	63	62	2
9	4	6	93	88	2	3	9	6	133	133	6	-6	4	7	26	31	2	5	8	7	35	35	10	9	2	8	0	14	1
10	4	6	51	56	3	4	9	6	0	21	1	-5	4	7	223	225	2	6	8	7	21	12	12	10	2	8	50	40	5
-10	5	6	107	98	5	5	9	6	33	34	6	-4	4	7	103	103	1	7	8	7	0	12	1	-10	3	8	22	26	9
-9	5	6	59	56	6	6	9	6	0	6	1	-3	4	7	24	22	1	-6	9	7	118	122	5	-9	3	8	21	1	21
-8	5	6	70	74	2	-5	10	6	70	85	6	-2	4	7	17	15	3	-5	9	7	26	23	13	-8	3	8	8	4	8
-7	5	6	12	11	9	-4	10	6	25	2	24	-1	4	7	157	152	1	-4	9	7	0	16	1	-7	3	8	97	100	1
-6	5	6	60	61	3	-3	10	6	48	45	7	0	4	7	168	168	2	-3	9	7	0	3	1	-6	3	8	91	93	2
-5	5	6	248	241	2	-2	10	6	44	37	6	1	4	7	61	64	3	-2	9	7	27	24	6	-5	3	8	40	45	1
-4	5	6	50	54	1	-1	10	6	40	38	6	2	4	7	20	25	3	-1	9	7	30	27	5	-4	3	8	7	2	6
-3	5	6	77	80	2	0	10	6	25	37	7	3	4	7	108	108	1	0	9	7	0	10	1	-3	3	8	154	150	2
-2	5	6	98	98	1	1	10	6	44	34	9	4	4	7	142	139	2	1	9	7	123	116	3	-2	3	8	225	226	2
-1	5	6	64	67	1	2	10	6	39	44	8	5	4	7	133	134	2	2	9	7	93	89	4	-1	3	8	92	95	1
0	5	6	12	12	2	3	10	6	63	52	8	6	4	7	15	21	10	3	9	7	53	61	6	0	3	8	10	1	4
1	5	6	88	90	1	4	10	6	20	17	19	7	4	7	48	47	2	4	9	7	24	29	14	1	3	8	15	28	5
2	5	6	69	65	1	-11	1	7	77	73	3	8	4	7	63	62	2	5	9	7	37	40	12	2	3	8	107	112	1
3	5	6	77	75	1	-10	1	7	18	19	13	9	4	7	0	2	1	6	9	7	0	6	1	3	3	8	379	381	5
4	5	6	100	99	1	-9	1	7	14	14	14	10	4	7	64	55	4	-4	10	7	8	15	8	4	3	8	37	45	2
5	5	6	265	256	3	-8	1	7	0	11	1	-10	5	7	20	6	20	-3	10	7	8	4	8	5	3	8	28	27	4
6	5	6	73	76	1	-7	1	7	83	82	1	-9	5	7	60	59	7	-2	10	7	104	108	5	6	3	8	3	4	2
7	5	6	0	9	1	-6	1	7	13	13	3	-8	5	7	43	44	3	-1	10	7	58	62	5	7	3	8	52	56	2
8	5	6	59	54	2	-5	1	7	106	108	1	-7	5	7	14	6	8	0	10	7	54	51	8	8	3	8	0	6	1
9	5	6	24	27	4	-4	1	7	160	164	3	-6	5	7	110	111	1	1	10	7	36	32	8	9	3	8	56	54	5
10	5	6	56	56	3	-3	1	7	232	226	2	-5	5	7	222	219	2	2	10	7	56	59	6	10	3	8	0	0	1
-10	6	6	64	59	6	-2	1	7	4	7	3	-4	5	7	91	87	1	-11	0	8	0	30	1	-10	4	8	111	101	6
-9	6	6	22	27	14	-1	1	7	127	123	1	-3	5	7	37	38	3	-10	0	8	20	15	12	-9	4	8	12	24	12
-8	6	6	0	10	1	0	1	7	26	25	1	-2	5	7	42	42	1	-9	0	8	0	3	1	-8	4	8	60	60	2
-7	6	6	35	41	2	1	1	7	21	26	1	-1	5	7	60	62	1	-8	0	8	31	27	2	-7	4	8	11	18	10
-6	6	6	69	70	1	2	1	7	90	85	1	0	5	7	110	109	1	-7	0	8	68	65	1	-6	4	8	162	156	2

Table 3-8.6. Observed and calculated structure factors for 3-2.2a

h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s
-5	4	8	93	92	2	-1	9	8	17	21	16	-9	5	9	39	44	8	-10	1	10	0	17	1	2	5	10	80	72	2
-4	4	8	63	62	1	0	9	8	48	60	7	-8	5	9	0	0	1	-9	1	10	0	4	1	3	5	10	70	75	3
-3	4	8	41	41	2	1	9	8	0	22	1	-7	5	9	48	53	10	-8	1	10	140	139	2	4	5	10	83	84	3
-2	4	8	16	13	10	2	9	8	99	104	5	-6	5	9	69	74	2	-7	1	10	111	111	1	5	5	10	88	90	3
-1	4	8	167	174	2	3	9	8	63	61	8	-5	5	9	28	30	3	-6	1	10	174	170	1	6	5	10	0	18	1
0	4	8	47	46	1	4	9	8	27	16	23	-4	5	9	64	66	2	-5	1	10	152	153	1	7	5	10	34	19	5
1	4	8	40	43	2	-10	1	9	23	18	11	-3	5	9	16	14	5	-4	1	10	77	79	1	-8	6	10	0	1	1
2	4	8	0	11	1	-9	1	9	18	21	8	-2	5	9	22	29	3	-3	1	10	14	19	3	-7	6	10	20	16	12
3	4	8	216	216	3	-8	1	9	69	70	2	-1	5	9	73	76	3	-2	1	10	9	10	5	-6	6	10	18	0	17
4	4	8	68	71	3	-7	1	9	229	224	2	0	5	9	132	133	1	-1	1	10	166	163	1	-5	6	10	53	46	8
5	4	8	134	132	3	-6	1	9	94	94	1	1	5	9	19	24	8	0	1	10	263	259	2	-4	6	10	26	31	5
6	4	8	81	78	4	-5	1	9	44	46	1	2	5	9	47	45	3	1	1	10	258	255	2	-3	6	10	39	41	3
7	4	8	88	81	4	-4	1	9	101	98	1	3	5	9	132	124	3	2	1	10	184	181	2	-2	6	10	55	55	3
8	4	8	25	23	6	-3	1	9	56	54	1	4	5	9	80	76	3	3	1	10	4	15	4	-1	6	10	0	12	1
9	4	8	75	68	3	-2	1	9	56	57	1	5	5	9	37	39	8	4	1	10	42	53	2	0	6	10	25	21	9
-10	5	8	68	56	6	-1	1	9	104	102	1	6	5	9	55	52	3	5	1	10	28	22	1	1	6	10	24	39	9
-9	5	8	13	15	12	0	1	9	84	83	1	7	5	9	24	28	9	6	1	10	63	66	4	2	6	10	0	15	1
-8	5	8	0	2	1	1	1	9	24	27	1	8	5	9	22	29	8	7	1	10	14	8	14	3	6	10	0	15	1
-7	5	8	28	26	3	2	1	9	292	288	3	-8	6	9	0	4	1	8	1	10	9	15	9	4	6	10	0	4	1
-6	5	8	95	98	2	3	1	9	55	61	2	-7	6	9	6	11	5	9	1	10	46	43	7	5	6	10	0	7	1
-5	5	8	15	8	5	4	1	9	49	44	3	-6	6	9	0	7	1	-10	2	10	26	15	6	6	6	10	25	7	8
-4	5	8	57	57	1	5	1	9	23	34	1	-5	6	9	92	90	2	-9	2	10	0	10	1	7	6	10	28	26	8
-3	5	8	76	76	1	6	1	9	53	59	1	-4	6	9	66	67	2	-8	2	10	8	11	7	-6	7	10	44	40	7
-2	5	8	99	104	1	7	1	9	69	70	3	-3	6	9	24	25	6	-7	2	10	29	31	4	-5	7	10	43	46	8
-1	5	8	189	188	2	8	1	9	14	11	13	-2	6	9	17	3	12	-6	2	10	73	72	1	-4	7	10	0	6	1
0	5	8	95	98	1	9	1	9	21	15	9	-1	6	9	170	176	3	-5	2	10	11	14	6	-3	7	10	60	59	4
1	5	8	67	69	2	10	1	9	24	32	23	0	6	9	4	8	4	-4	2	10	109	108	1	-2	7	10	38	36	5
2	5	8	33	38	3	-10	2	9	56	55	3	1	6	9	26	30	2	-3	2	10	61	61	1	-1	7	10	60	68	6
3	5	8	109	112	2	-9	2	9	71	68	3	2	6	9	31	25	4	-2	2	10	200	197	2	0	7	10	99	101	4
4	5	8	273	264	5	-8	2	9	17	13	4	3	6	9	31	36	5	-1	2	10	101	98	2	1	7	10	27	25	8
5	5	8	20	14	9	-7	2	9	141	139	1	4	6	9	32	42	9	0	2	10	76	79	3	2	7	10	24	25	7
6	5	8	22	10	9	-6	2	9	115	111	1	5	6	9	49	45	4	1	2	10	126	131	2	3	7	10	32	25	14
7	5	8	46	46	5	-5	2	9	48	43	1	6	6	9	27	36	9	2	2	10	29	32	1	4	7	10	37	43	6
8	5	8	80	71	5	-4	2	9	19	13	2	7	6	9	70	64	3	3	2	10	55	49	1	5	7	10	43	43	6
9	5	8	0	16	1	-3	2	9	28	28	1	8	6	9	70	71	4	4	2	10	21	8	4	6	7	10	17	9	17
-9	6	8	59	53	6	-2	2	9	27	28	1	-7	7	9	27	20	9	5	2	10	46	38	2	-5	8	10	0	11	1
-8	6	8	0	14	1	-1	2	9	24	26	2	-6	7	9	46	43	6	6	2	10	60	64	2	-4	8	10	82	73	5
-7	6	8	28	25	5	0	2	9	24	22	4	-5	7	9	44	42	9	7	2	10	28	8	7	-3	8	10	13	18	12
-6	6	8	0	17	1	1	2	9	0	0	1	-4	7	9	0	14	1	8	2	10	0	1	1	-2	8	10	50	36	6
-5	6	8	48	54	3	2	2	9	78	72	1	-3	7	9	0	0	1	9	2	10	16	24	16	-1	8	10	27	39	17
-4	6	8	12	8	11	3	2	9	286	274	4	-2	7	9	70	73	3	-9	3	10	14	16	14	0	8	10	34	25	8
-3	6	8	17	11	5	4	2	9	55	55	3	-1	7	9	2	6	2	-8	3	10	71	72	2	1	8	10	24	9	13
-2	6	8	173	171	4	5	2	9	54	58	1	0	7	9	74	79	3	-7	3	10	25	24	3	2	8	10	22	21	21
-1	6	8	187	185	4	6	2	9	12	20	11	1	7	9	20	29	7	-6	3	10	18	24	4	3	8	10	43	44	8
0	6	8	108	115	1	7	2	9	118	123	2	2	7	9	77	74	3	-5	3	10	27	32	4	-9	1	11	84	86	6
1	6	8	43	46	3	8	2	9	56	59	5	3	7	9	7	5	7	-4	3	10	94	95	1	-8	1	11	86	90	2
2	6	8	41	40	1	9	2	9	49	53	5	4	7	9	0	2	1	-3	3	10	32	31	3	-7	1	11	38	39	2
3	6	8	27	22	5	-10	3	9	12	14	12	5	7	9	99	93	3	-2	3	10	113	117	2	-6	1	11	12	16	6
4	6	8	89	91	3	-9	3	9	28	39	8	6	7	9	55	54	4	-1	3	10	43	38	2	-5	1	11	81	77	2
5	6	8	17	26	17	-8	3	9	65	62	1	7	7	9	38	35	12	0	3	10	85	83	1	-4	1	11	45	42	1
6	6	8	29	25	6	-7	3	9	9	5	8	-6	8	9	38	43	6	1	3	10	16	7	8	-3	1	11	0	0	1
7	6	8	37	40	7	-6	3	9	128	131	1	-5	8	9	38	38	5	2	3	10	108	109	3	-2	1	11	133	130	2
8	6	8	35	30	7	-5	3	9	80	77	2	-4	8	9	84	78	4	3	3	10	20	24	5	-1	1	11	100	97	1
-8	7	8	0	3	1	-4	3	9	0	9	1	-3	8	9	16	15	16	4	3	10	83	86	5	0	1	11	0	8	1
-7	7	8	6	10	5	-3	3	9	70	69	1	-2	8	9	16	23	16	5	3	10	53	56	2	1	1	11	163	164	2
-6	7	8	55	52	4	-2	3	9	90	90	1	-1	8	9	0	5	1	6	3	10	61	64	2	2	1	11	152	145	2
-5	7	8	43	46	3	-1	3	9	193	188	2	0	8	9	62	72	3	7	3	10	18	22	10	3	1	11	33	37	2
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-3	7	8	52	53	3	1	3	9	162	165	2	2	8	9	88	90	3	9	3	10	29	33	14	5	1	11	99	94	3
-2	7	8	63	68	3	2	3	9	36	34	2	3	8	9	32	35	7	-9	4	10	42	42	7	6	1	11	24	25	7
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2	7	8	85	83	3	6	3	9	12	4	11	-3	9	9	57	53	6	-5	4	10	108	106	2	-8	2	11	36	35	9
3	7	8	98	104	3	7	3	9	14	27	14	-2	9	9	46	42	8	-4	4	10	93	90	2	-7	2	11	13	18	10
4	7	8	17	15	16	8	3	9	129	123	4	-1	9	9	33	30	10	-3	4	10	62	65	2	-6	2	11	11	11	9
5	7	8	47	46	4	9	3	9	103	100	5	0	9	9	27	10	9	-2	4	10	38	36	2	-5	2	11	0	9	1
6	7	8	0	2	1	-10	4	9	44	45	7	1	9	9	24	9	13	-1	4	10	148	156	2	-4	2	11	19	19	3
7	7	8	33	38	6	-9	4	9	22	15	11	2	9	9	73	71	5	0	4	10	19	0	14	-3	2	11	37	39	1
-7	8	8	6	2	5	-8	4	9	39	44	5	-10	0	10	41	31	6	1	4	10	15	0	15	-2	2	11	43	43	1
-6	8	8	45	42	7	-7	4	9	36	37	3	-9	0	10	205	188	5	2	4	10	86	88	2	-1	2	11	110	114	1
-5	8	8	17	20	16	-6	4	9	69	71	3	-8	0	10	7	8	7	3	4	10	223	225	4	0	2	11	210	204	2
-4	8	8	26	26	9	-5	4	9	29	32	3	-7	0	10	139	131	2	4	4	10	183	183	4	1	2	11	133	129	2
-3	8	8	53	57	3	-4	4	9	72	75	1	-6	0	10	45	48	2	5	4	10	70	65	3	2	2	11	50	48	2
-2	8	8	52	57	4	-3	4	9	136	134	2	-5	0	10	88	86	1	6	4	10	29	17	6	3	2	11	22	26	4
-1	8	8	97	98	2	-2	4	9	42	47	1	-4	0	10	115	115	1	7	4	10	43	45	3	4	2	11	44	52	4
0	8	8	32	38	4	-1	4	9	43	42	1	-3	0	10	89	89	1	8	4	10	112	99	4	5	2	11	41	43	3
1	8	8	58	58	4	0	4	9	79	85	1	-2	0	10	35	36	2	-8	5	10	18	20	18	6	2	11	63	64	4
2	8	8	46	49	4	1	4	9	23	17	5	-1	0	10	30	27	2	-7	5	10	6	3	5	7	2	11	29	30	6
3	8	8	52	51	4	2	4	9	109	113	2	0	0	10	123	118	1	-6	5	10	15	25	11	8	2	11	43	48	8
4	8	8	59	71	4	3	4	9	73	70	3	1	0	10	228	225	3	-5	5	10	37	38	3	-9	3	11	64	65	6
5	8	8	43	36	6	4	4	9	54	56	2	2	0	10	82	82	1	-4	5	10	11	5	11	-8	3	11	61	60	3
6	8	8	46	44	7	5	4	9	54	57	3	3	0	10	166	161	2	-3	5	10	40	41	2	-7	3	11	15	9	8
-5	9	8	22	17	21	6	4	9	57	61	3	4	0	10	6	13	5	-2	5	10	94	89	2	-6	3	11	23	24	3
-4	9	8	0	8	1	7	4	9	15	17	15	5	0	10	54	52	1	-1	5	10	146	151	2	-5	3	11	14	12	13
-3	9	8	0	10	1	8	4	9	69	69	3	7	0	10	0	2	1	0	5	10	39	37	3	-4	3	11	78	74	2
-2	9	8	7	17	7	9	4	9	26	37	14	8	0	10	96	85	6	1	5	10	22	25	6	-3	3	11	146	149	2

Table 3-8.6. Observed and calculated structure factors for 3-2.2a

h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s
-2	3	11	73	73	2	1	7	11	69	72	4	0	3	12	63	67	2	5	1	13	61	65	4	-2	0	14	0	8	1
-1	3	11	38	39	1	2	7	11	33	33	7	1	3	12	120	119	2	6	1	13	0	15	1	-1	0	14	48	41	6
0	3	11	128	126	3	3	7	11	50	44	5	2	3	12	29	27	4	-7	2	13	31	33	4	0	0	14	56	45	7
1	3	11	88	89	3	4	7	11	0	18	1	3	3	12	39	43	3	-6	2	13	12	4	11	1	0	14	9	18	9
2	3	11	0	9	1	-3	8	11	10	1	10	4	3	12	0	29	1	-5	2	13	26	24	4	2	0	14	111	110	5
3	3	11	34	33	4	-2	8	11	60	68	6	5	3	12	20	16	20	-4	2	13	154	153	2	3	0	14	88	89	6
4	3	11	17	13	16	-1	8	11	36	43	6	6	3	12	0	15	1	-3	2	13	31	37	3	4	0	14	12	1	12
5	3	11	79	80	2	-8	0	12	0	0	1	7	3	12	31	33	8	-2	2	13	53	53	2	5	0	14	77	66	6
6	3	11	97	94	3	-7	0	12	0	14	1	-7	4	12	5	12	5	-1	2	13	32	31	4	-6	1	14	64	64	2
7	3	11	52	57	4	-6	0	12	80	88	2	-6	4	12	18	15	16	0	2	13	128	126	2	-5	1	14	48	52	4
8	3	11	54	61	5	-5	0	12	183	177	2	-5	4	12	130	121	4	1	2	13	104	99	4	-4	1	14	21	23	15
-8	4	11	30	35	6	-4	0	12	184	176	2	-4	4	12	36	29	6	2	2	13	125	122	3	-3	1	14	41	45	3
-7	4	11	15	4	14	-3	0	12	71	72	1	-3	4	12	19	23	18	3	2	13	14	8	14	-2	1	14	16	6	15
-6	4	11	39	38	3	-2	0	12	82	84	1	-2	4	12	14	18	14	4	2	13	24	13	23	-1	1	14	14	24	14
-5	4	11	10	3	9	-1	0	12	71	70	1	-1	4	12	23	32	10	5	2	13	65	64	4	0	1	14	0	3	1
-4	4	11	47	45	3	0	0	12	355	346	5	0	4	12	106	100	3	6	2	13	44	49	7	1	1	14	31	39	8
-3	4	11	96	98	2	1	0	12	57	54	2	1	4	12	110	102	4	-7	3	13	11	22	10	2	1	14	32	35	16
-2	4	11	31	34	2	2	0	12	21	7	15	2	4	12	40	41	4	-6	3	13	57	57	2	3	1	14	0	5	1
-1	4	11	20	3	7	3	0	12	90	91	4	3	4	12	0	8	1	-5	3	13	38	34	3	4	1	14	78	79	4
0	4	11	34	24	7	4	0	12	50	50	5	4	4	12	59	57	3	-4	3	13	21	11	6	5	1	14	40	20	8
1	4	11	10	12	10	5	0	12	58	41	5	5	4	12	0	12	1	-3	3	13	55	61	2	-6	2	14	10	7	9
2	4	11	29	31	5	6	0	12	83	87	7	6	4	12	85	83	3	-2	3	13	0	3	1	-5	2	14	23	11	6
3	4	11	0	9	1	7	0	12	37	41	7	-6	5	12	36	39	4	-1	3	13	30	29	5	-4	2	14	7	17	7
4	4	11	124	116	3	-8	1	12	48	55	4	-5	5	12	59	46	4	0	3	13	124	120	2	-3	2	14	30	28	5
5	4	11	37	34	4	-7	1	12	5	18	4	-4	5	12	69	66	7	1	3	13	48	47	3	-2	2	14	27	34	5
6	4	11	26	22	6	-6	1	12	27	23	2	-3	5	12	107	111	8	2	3	13	9	22	9	-1	2	14	128	126	3
7	4	11	58	57	5	-5	1	12	60	59	1	-2	5	12	60	58	9	3	3	13	83	83	4	0	2	14	13	3	13
-7	5	11	62	66	4	-4	1	12	62	64	1	-1	5	12	6	9	6	4	3	13	33	37	5	1	2	14	47	45	4
-6	5	11	39	40	7	-3	1	12	34	38	1	0	5	12	47	50	6	5	3	13	50	53	4	2	2	14	46	46	5
-5	5	11	69	71	5	-2	1	12	21	23	2	1	5	12	20	26	9	6	3	13	69	69	4	3	2	14	27	23	6
-4	5	11	53	51	5	-1	1	12	58	57	1	2	5	12	0	0	1	-6	4	13	31	28	9	4	2	14	42	34	6
-3	5	11	73	72	2	0	1	12	56	57	1	3	5	12	35	44	4	-5	4	13	34	32	26	5	2	14	47	33	9
-2	5	11	22	25	7	1	1	12	11	12	10	4	5	12	32	34	7	-4	4	13	0	14	1	-5	3	14	12	12	12
-1	5	11	33	42	7	2	1	12	80	81	2	5	5	12	0	13	1	-3	4	13	8	18	7	-4	3	14	16	11	16
0	5	11	23	19	7	3	1	12	6	9	6	-5	6	12	27	32	15	-2	4	13	50	53	5	-3	3	14	10	11	9
1	5	11	8	7	7	4	1	12	74	70	3	-4	6	12	71	62	5	-1	4	13	128	122	5	-2	3	14	71	73	5
2	5	11	38	36	4	5	1	12	50	45	3	-3	6	12	0	6	1	0	4	13	21	22	10	-1	3	14	26	24	6
3	5	11	68	66	3	6	1	12	20	9	20	-2	6	12	24	3	11	1	4	13	40	36	4	0	3	14	74	72	7
4	5	11	34	42	7	7	1	12	27	15	17	-1	6	12	21	14	12	2	4	13	61	62	4	1	3	14	32	36	11
5	5	11	36	34	5	-7	2	12	46	39	3	0	6	12	48	51	5	3	4	13	22	15	22	2	3	14	30	30	7
6	5	11	36	47	10	-6	2	12	0	10	1	1	6	12	41	48	7	4	4	13	22	23	13	3	3	14	22	16	17
7	5	11	39	30	13	-5	2	12	47	46	3	2	6	12	18	8	12	5	4	13	12	5	11	-4	4	14	96	101	3
-7	6	11	24	21	7	-4	2	12	28	32	3	3	6	12	24	6	8	-5	5	13	0	6	1	-3	4	14	188	174	3
-6	6	11	14	13	14	-3	2	12	56	60	2	4	6	12	11	9	10	-4	5	13	47	46	9	-2	4	14	43	41	8
-5	6	11	83	80	6	-2	2	12	18	20	5	-4	7	12	56	61	6	-3	5	13	54	60	5	-1	4	14	31	30	7
-4	6	11	29	26	9	-1	2	12	200	193	2	-3	7	12	32	25	14	-2	5	13	110	104	3	0	4	14	47	49	5
-3	6	11	24	13	9	0	2	12	85	91	2	-2	7	12	0	7	1	-1	5	13	50	51	6	1	4	14	19	26	16
-2	6	11	14	1	14	1	2	12	52	56	3	-1	7	12	23	20	23	0	5	13	92	91	5	-2	5	14	0	2	1
-1	6	11	80	88	3	2	2	12	88	89	2	0	7	12	16	13	16	1	5	13	26	21	10	-1	5	14	85	94	6
0	6	11	37	35	5	3	2	12	64	62	2	1	7	12	15	26	14	2	5	13	0	13	1	0	5	14	22	33	21
1	6	11	58	58	4	4	2	12	43	43	4	2	7	12	0	14	1	3	5	13	92	89	6	-4	1	15	18	22	18
2	6	11	0	15	1	5	2	12	91	88	3	-7	1	13	35	38	4	-4	6	13	0	11	1	-3	1	15	11	19	11
3	6	11	12	16	11	6	2	12	79	80	3	-6	1	13	8	1	7	-3	6	13	17	13	16	-2	1	15	0	18	1
4	6	11	167	155	4	7	2	12	43	39	5	-5	1	13	82	83	3	-2	6	13	0	24	1	-1	1	15	47	51	5
5	6	11	56	62	5	-8	3	12	54	53	5	-4	1	13	31	31	2	-1	6	13	33	35	11	0	1	15	22	5	14
6	6	11	86	85	6	-7	3	12	6	2	5	-3	1	13	23	20	3	0	6	13	0	2	1	1	1	15	20	10	14
-5	7	11	68	63	5	-6	3	12	16	7	8	-2	1	13	16	11	6	1	6	13	22	12	22	-4	2	15	17	18	17
-4	7	11	19	20	19	-5	3	12	41	37	3	-1	1	13	46	44	8	2	6	13	33	27	11	-3	2	15	31	24	9
-3	7	11	18	26	17	-4	3	12	159	152	2	0	1	13	25	30	6	-6	0	14	36	42	6	-2	2	15	42	43	4
-2	7	11	26	25	25	-3	3	12	138	138	2	1	1	13	64	62	3	-5	0	14	62	67	4	-1	2	15	50	51	8
-1	7	11	50	52	5	-2	3	12	16	4	7	2	1	13	40	43	4	-4	0	14	59	61	6						
0	7	11	118	113	4	-1	3	12	54	55	4	3	1	13	58	56	4	-3	0	14	0	19	1						

Figure 3-8.1. View of 3-2.2a showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. Hydrogen atoms are drawn to an arbitrary size.

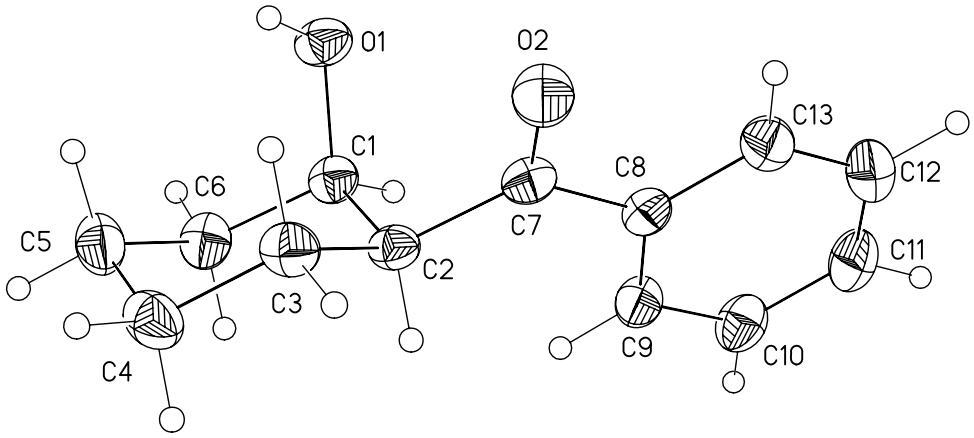


Figure 3-8.2. View of the H-bound dimer formed by 3-2.2a. Displacement ellipsoids are scaled to the 50% probability level. Hydrogen atoms are drawn to an arbitrary size. Dashed lines indicate the H-bonding interactions. The two molecules are related by a crystallographic inversion center at 0, 0, ½. The geometry of the interaction is: O1-H1O···O2 (related by –x, -y, 1-z), O···O 2.859(1)Å, H···O 1.99(2)Å, O-H···O 161(2)°.

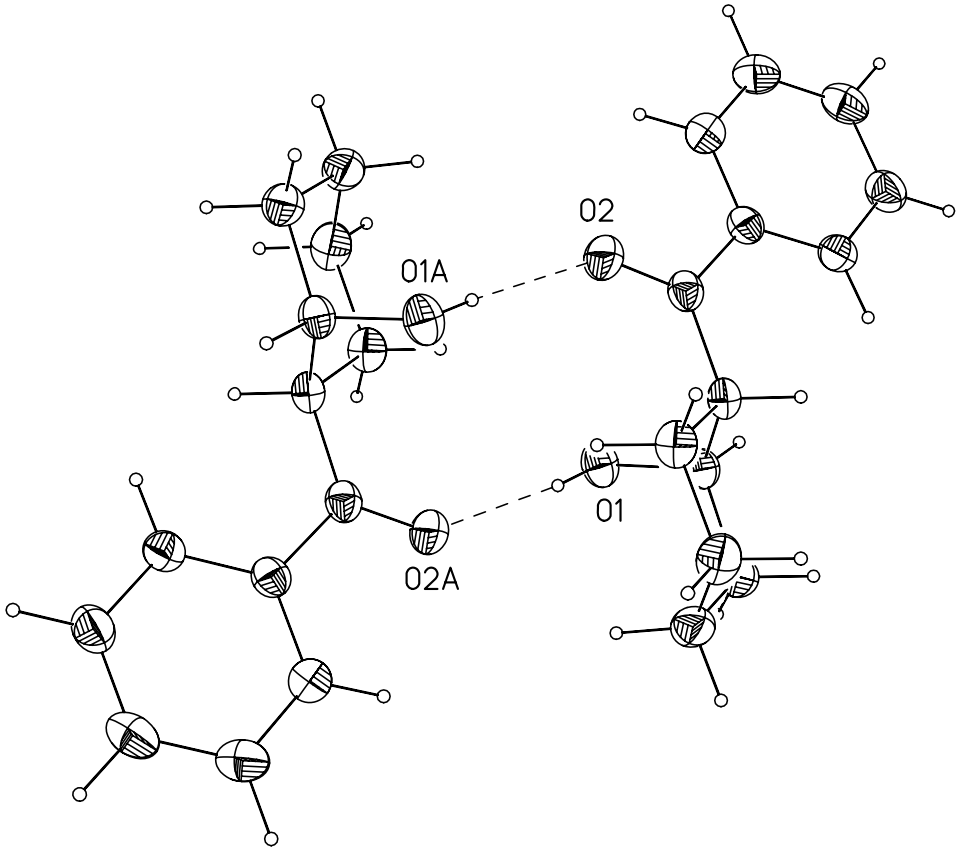
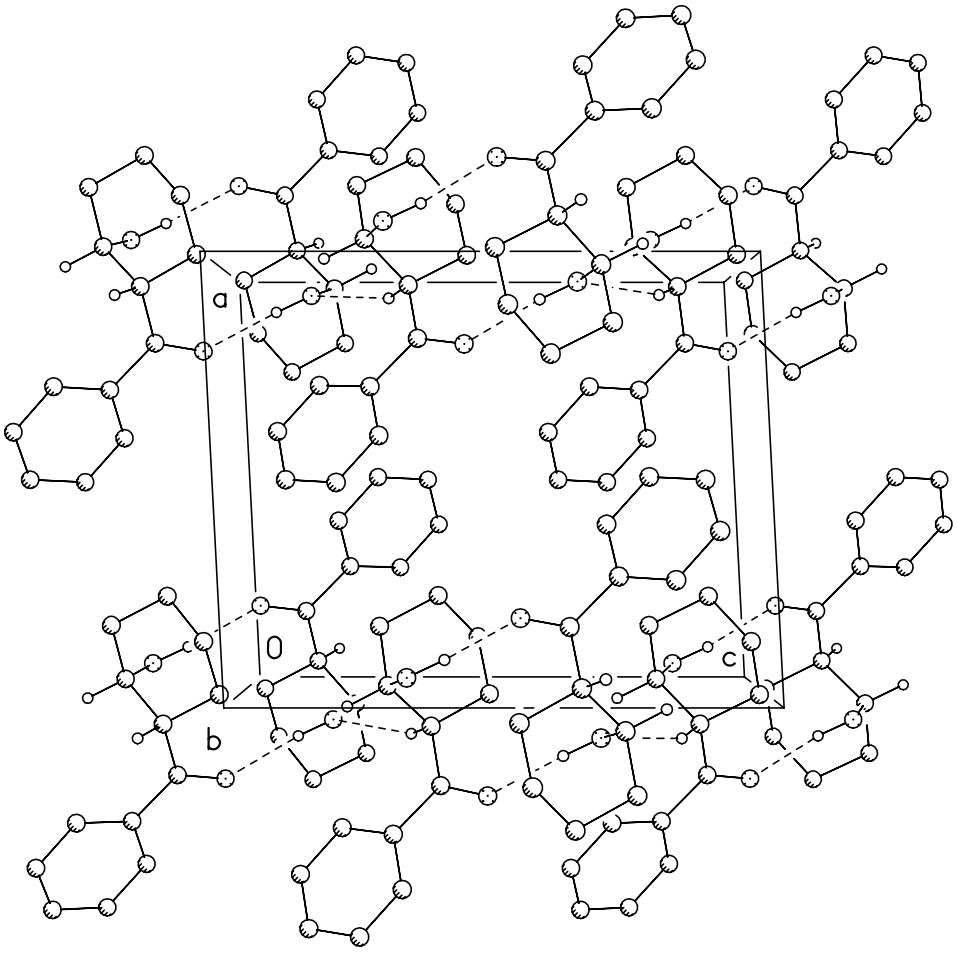


Figure 3-8.3. Unit cell packing diagram for 3-2.2a. The view is approximately down the b axis.



B. X-ray Crystallographic Material for 3-4.1a

X-Ray Experimental

Table 3-8.7. Crystallographic Data for 3-4.1a.

Table 3-8.8. Fractional coordinates and equivalent isotropic thermal parameters ($Å^2$) for the non-hydrogen atoms of 3-4.1a.

Table 3-8.9. Bond Lengths (Å) and Angles (^{o}) for the non-hydrogen atoms of 3-4.1a.

Table 3-8.10. Anisotropic thermal parameters for the non-hydrogen atoms of 3-4.1a.

Table 3-8.11. Fractional coordinates and isotropic thermal parameters ($Å^2$) for the hydrogen atoms of 3-4.1a.

Table 3-8.12. Observed and calculated structure factor amplitudes for 3-4.1a. Values for Fo, Fc and σ (Fo) have been multiplied by 10.

Figure 3-8.4. View of 3-4.1a showing the atom labeling scheme. Thermal ellipsoids are scaled to the 50% probability level. Hydrogen atoms shown are drawn to an arbitrary scale.

Figure 3-8.5. Unit cell packing diagram for 3-4.1a. The view is approximately down the c axis.

X-ray Experimental for $C_{21}H_{20}O_2$: Crystals grew as colorless by slow evaporation from ethylacetate and hexane. The data crystal was a long needle that had approximate dimensions; 0.45x0.08x0.08 mm. The data were collected on a Nonius Kappa CCD diffractometer using a graphite monochromator with MoKα radiation (λ = 0.71073Å). A total of 366 frames of data were collected using ω-scans with a scan range of 1° and a counting time of 151 seconds per frame. The data were collected at –120 °C using a Oxford Cryostream low temperature device. Details of crystal data, data collection and structure refinement are listed in Table 3-8.7. Data reduction were performed using DENZO-SMN.[1] The structure was solved by direct methods using SIR92[2] and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms using SHELXL-97.[3] The hydrogen atoms on carbon were calculated in ideal positions with isotropic displacement parameters set to 1.2xUeq of the attached. The function, $\Sigma w(|F_O|^2 - |F_C|^2)^2$, was minimized, where $w = 1/[(\sigma(F_O))^2 + (0.019*P)^2 + (0.7511*P)]$ and $P = (|F_O|^2 + 2|F_C|^2)/3$. $R_W(F^2)$ refined to 0.114, with R(F) equal to 0.0553 and a goodness of fit, S, = 1.008. Definitions used for calculating R(F),$R_W(F^2)$ and the goodness of fit, S, are given below.[4] The data were corrected for secondary extinction effects. The correction takes the form: $F_{corr} = kF_C/[1 + (8.4(12)x10^{-6})* F_C^2 \lambda^3/(\sin 2\theta)]^{0.25}$ where k is the overall scale factor. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).[5] All figures were generated using SHELXTL/PC.[6] Tables of positional and thermal parameters, bond lengths and angles, figures and lists of observed and calculated structure factors are located in Tables 3-8.7 through 3-8.12.

References

1) DENZO-SMN. (1997). Z. Otwinowski and W. Minor, Methods in Enzymology, **276**: Macromolecular Crystallography, part A, 307 – 326, C. W. Carter, Jr. and R. M. Sweets, Editors, Academic Press.

2) SIR92. (1993). A program for crystal structure solution. Altomare, A., Cascarano, G., Giacovazzo, C. & Guagliardi, A. J. Appl. Cryst. 26, 343-350.

3) Sheldrick, G. M. (1994). SHELXL97. Program for the Refinement of Crystal Structures. University of Gottingen, Germany.

4) $R_w(F^2) = \{\Sigma w(|F_o|^2 - |F_c|^2)^2/\Sigma w(|F_o|)^4\}^{1/2}$ where w is the weight given each reflection.
$R(F) = \Sigma (|F_o| - |F_c|)/\Sigma|F_o|\}$ for reflections with $F_o > 4(\Sigma(F_o))$.
$S = [\Sigma w(|F_o|^2 - |F_c|^2)^2/(n - p)]^{1/2}$, where n is the number of reflections and p is the number of refined parameters.

5) International Tables for X-ray Crystallography (1992). Vol. C, Tables 4.2.6.8 and 6.1.1.4, A. J. C. Wilson, editor, Boston: Kluwer Academic Press.

6) Sheldrick, G. M. (1994). SHELXTL/PC (Version 5.03). Siemens Analytical X-ray Instruments, Inc., Madison, Wisconsin, USA.

Table 3-8.7. Crystal data and structure refinement for 3-4.1a.

Empirical formula	C21 H20 O2	
Formula weight	304.37	
Temperature	153(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P21/c	
Unit cell dimensions	a = 14.4375(5) Å	α= 90°.
	b = 10.6909(4) Å	β= 108.223(2)°.
	c = 10.8075(5) Å	γ = 90°.
Volume	1584.47(11) $Å^3$	
Z	4	
Density (calculated)	1.276 Mg/m^3	
Absorption coefficient	0.081 mm^{-1}	
F(000)	648	
Crystal size	0.45 x 0.08 x 0.08 mm	
Theta range for data collection	3.0 to 27.5°.	
Index ranges	-18<=h<=18, -13<=k<=11, -14<=l<=13	
Reflections collected	5650	
Independent reflections	3606 [R(int) = 0.0413]	
Completeness to theta = 27.48°	99.4 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3606 / 0 / 209	
Goodness-of-fit on F^2	1.082	
Final R indices [I>2sigma(I)]	R1 = 0.0553, wR2 = 0.0999	
R indices (all data)	R1 = 0.0973, wR2 = 0.1140	
Extinction coefficient	$8.4(12)x10^{-6}$	
Largest diff. peak and hole	0.25 and -0.24 $e.Å^{-3}$	

Table 3-8.8. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 3-4.1a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C1	1922(1)	2801(2)	923(2)	24(1)
C2	2975(1)	3018(2)	1870(2)	25(1)
C3	2649(1)	4270(2)	2323(2)	30(1)
C4	3093(2)	5446(2)	1944(2)	43(1)
C5	2602(2)	5554(2)	481(2)	45(1)
C6	1550(2)	5177(2)	285(2)	38(1)
C7	1624(1)	4140(2)	1273(2)	29(1)
C8	1301(1)	1880(2)	1343(2)	26(1)
O9	1569(1)	1420(1)	2432(1)	35(1)
C10	283(1)	1681(2)	453(2)	26(1)
C11	9(1)	1951(2)	-871(2)	31(1)
C12	-946(1)	1749(2)	-1652(2)	35(1)
C13	-1632(1)	1303(2)	-1109(2)	36(1)
C14	-1366(1)	1046(2)	205(2)	36(1)
C15	-410(1)	1215(2)	981(2)	31(1)
C16	3453(1)	2052(2)	2888(2)	26(1)
O17	3646(1)	2277(1)	4051(1)	34(1)
C18	3763(1)	828(2)	2454(2)	23(1)
C19	3726(1)	608(2)	1173(2)	28(1)
C20	4030(1)	-538(2)	826(2)	32(1)
C21	4358(1)	-1465(2)	1746(2)	33(1)
C22	4412(1)	-1250(2)	3032(2)	34(1)
C23	4124(1)	-102(2)	3388(2)	29(1)

Table 3-8.9. Bond lengths [Å] and angles [°] for 3-4.1a.

C1-C8	1.494(2)	C10-C11	1.391(3)
C1-C2	1.562(2)	C11-C12	1.389(3)
C1-C7	1.574(2)	C11-H11	0.96
C1-H1	0.96	C12-C13	1.385(3)
C2-C16	1.509(3)	C12-H12	0.96
C2-C3	1.549(2)	C13-C14	1.378(3)
C2-H2	0.96	C13-H13	0.96
C3-C4	1.524(3)	C14-C15	1.384(3)
C3-C7	1.564(3)	C14-H14	0.96
C3-H3	0.96	C15-H15	0.96
C4-C5	1.522(3)	C16-O17	1.224(2)
C4-H4A	0.96	C16-C18	1.504(2)
C4-H4B	0.96	C18-C19	1.388(3)
C5-C6	1.521(3)	C18-C23	1.396(3)
C5-H5A	0.96	C19-C20	1.392(2)
C5-H5B	0.96	C19-H19	0.96
C6-C7	1.519(3)	C20-C21	1.378(3)
C6-H6A	0.96	C20-H20	0.96
C6-H6B	0.96	C21-C22	1.387(3)
C7-H7	0.96	C21-H21	0.96
C8-O9	1.222(2)	C22-C23	1.389(3)
C8-C10	1.499(3)	C22-H22	0.96
C10-C15	1.390(3)	C23-H23	0.96
C8-C1-C2	116.86(16)	C16-C2-H2	108.8
C8-C1-C7	106.89(14)	C3-C2-H2	108.0
C2-C1-C7	89.49(13)	C1-C2-H2	109.4
C8-C1-H1	113.6	C4-C3-C2	115.67(16)
C2-C1-H1	114.2	C4-C3-C7	105.13(16)
C7-C1-H1	113.1	C2-C3-C7	90.36(14)
C16-C2-C3	118.45(16)	C4-C3-H3	114.6
C16-C2-C1	120.39(15)	C2-C3-H3	113.7
C3-C2-C1	90.30(13)	C7-C3-H3	114.6

C5-C4-C3	104.05(17)	C13-C12-C11	120.1(2)
C5-C4-H4A	111.4	C13-C12-H12	119.9
C3-C4-H4A	110.8	C11-C12-H12	120.0
C5-C4-H4B	110.2	C14-C13-C12	119.98(19)
C3-C4-H4B	111.3	C14-C13-H13	120.0
H4A-C4-H4B	109.0	C12-C13-H13	120.0
C6-C5-C4	104.18(18)	C13-C14-C15	120.15(19)
C6-C5-H5A	110.4	C13-C14-H14	119.6
C4-C5-H5A	110.3	C15-C14-H14	120.3
C6-C5-H5B	111.3	C14-C15-C10	120.5(2)
C4-C5-H5B	111.5	C14-C15-H15	120.1
H5A-C5-H5B	109.0	C10-C15-H15	119.4
C7-C6-C5	104.37(17)	O17-C16-C18	119.78(17)
C7-C6-H6A	110.6	O17-C16-C2	121.32(17)
C5-C6-H6A	111.4	C18-C16-C2	118.74(16)
C7-C6-H6B	111.1	C19-C18-C23	119.32(17)
C5-C6-H6B	110.4	C19-C18-C16	122.37(16)
H6A-C6-H6B	108.9	C23-C18-C16	118.29(17)
C6-C7-C3	106.69(16)	C18-C19-C20	120.02(18)
C6-C7-C1	117.30(17)	C18-C19-H19	119.2
C3-C7-C1	89.27(13)	C20-C19-H19	120.8
C6-C7-H7	113.8	C21-C20-C19	120.34(19)
C3-C7-H7	114.2	C21-C20-H20	120.1
C1-C7-H7	113.0	C19-C20-H20	119.6
O9-C8-C1	121.30(17)	C20-C21-C22	120.16(18)
O9-C8-C10	120.77(16)	C20-C21-H21	119.7
C1-C8-C10	117.37(16)	C22-C21-H21	120.1
C15-C10-C11	119.12(17)	C21-C22-C23	119.76(19)
C15-C10-C8	118.37(17)	C21-C22-H22	119.7
C11-C10-C8	122.51(17)	C23-C22-H22	120.5
C12-C11-C10	120.17(19)	C22-C23-C18	120.36(19)
C12-C11-H11	120.3	C22-C23-H23	120.4
C10-C11-H11	119.6	C18-C23-H23	119.2

Table 3-8.10. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 3-4.1a. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C1	24(1)	23(1)	25(1)	-2(1)	8(1)	0(1)
C2	25(1)	23(1)	27(1)	-2(1)	9(1)	-2(1)
C3	34(1)	24(1)	31(1)	-5(1)	9(1)	-1(1)
C4	33(1)	25(1)	68(2)	-2(1)	11(1)	-1(1)
C5	56(1)	27(1)	62(2)	8(1)	32(1)	7(1)
C6	45(1)	26(1)	40(1)	-1(1)	7(1)	8(1)
C7	27(1)	24(1)	39(1)	-3(1)	13(1)	4(1)
C8	28(1)	21(1)	28(1)	-3(1)	9(1)	0(1)
O9	33(1)	40(1)	30(1)	5(1)	7(1)	-5(1)
C10	26(1)	19(1)	33(1)	-3(1)	10(1)	0(1)
C11	30(1)	28(1)	35(1)	-1(1)	9(1)	-1(1)
C12	33(1)	30(1)	38(1)	0(1)	3(1)	-2(1)
C13	27(1)	25(1)	50(2)	-4(1)	4(1)	-2(1)
C14	28(1)	31(1)	50(1)	-3(1)	14(1)	-5(1)
C15	31(1)	27(1)	38(1)	-2(1)	13(1)	-3(1)
C16	21(1)	27(1)	27(1)	-2(1)	6(1)	-3(1)
O17	37(1)	36(1)	28(1)	-4(1)	6(1)	2(1)
C18	18(1)	25(1)	27(1)	1(1)	6(1)	-3(1)
C19	27(1)	25(1)	30(1)	2(1)	8(1)	-1(1)
C20	31(1)	30(1)	37(1)	-4(1)	13(1)	1(1)
C21	25(1)	25(1)	48(1)	-2(1)	8(1)	4(1)
C22	27(1)	31(1)	40(1)	9(1)	6(1)	5(1)
C23	22(1)	35(1)	28(1)	3(1)	6(1)	2(1)

Table 3-8.11. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 3-4.1a.

	x	y	z	U(eq)
H1	1887	2720	24	29
H2	3405	3206	1374	30
H3	2639	4257	3207	36
H4A	3787	5362	2154	51
H4B	2952	6171	2379	51
H5A	2899	4990	26	54
H5B	2642	6390	178	54
H6A	1240	4877	-583	46
H6B	1186	5875	448	46
H7	1090	4122	1624	35
H11	483	2275	-1242	38
H12	-1128	1909	-2571	42
H13	-2295	1183	-1645	43
H14	-1847	746	578	43
H15	-220	1005	1890	38
H19	3481	1250	533	33
H20	4018	-676	-56	39
H21	4555	-2257	1494	40
H22	4635	-1902	3666	41
H23	4177	66	4280	35

Figure 3-8.4. View of 3-4.1a showing the atom labeling scheme. Thermal ellipsoids are scaled to the 50% probability level. Hydrogen atoms shown are drawn to an arbitrary scale.

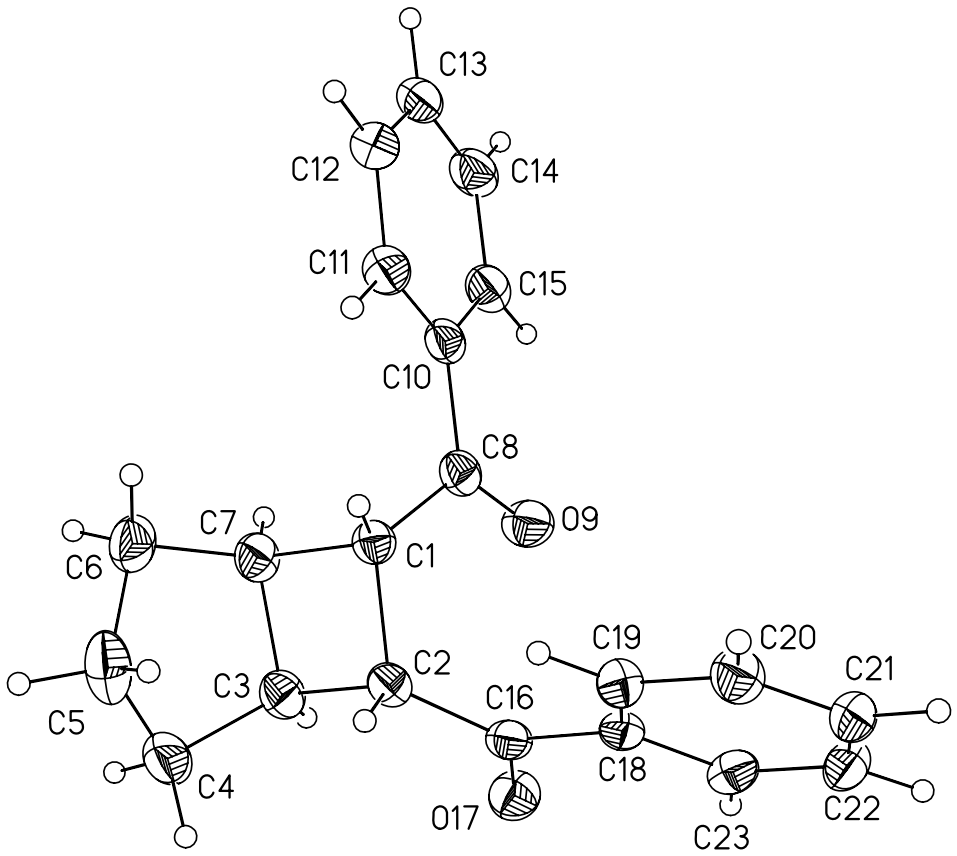


Figure 3-8.5. Unit cell packing diagram for 3-4.1a. The view is approximately down the c axis.

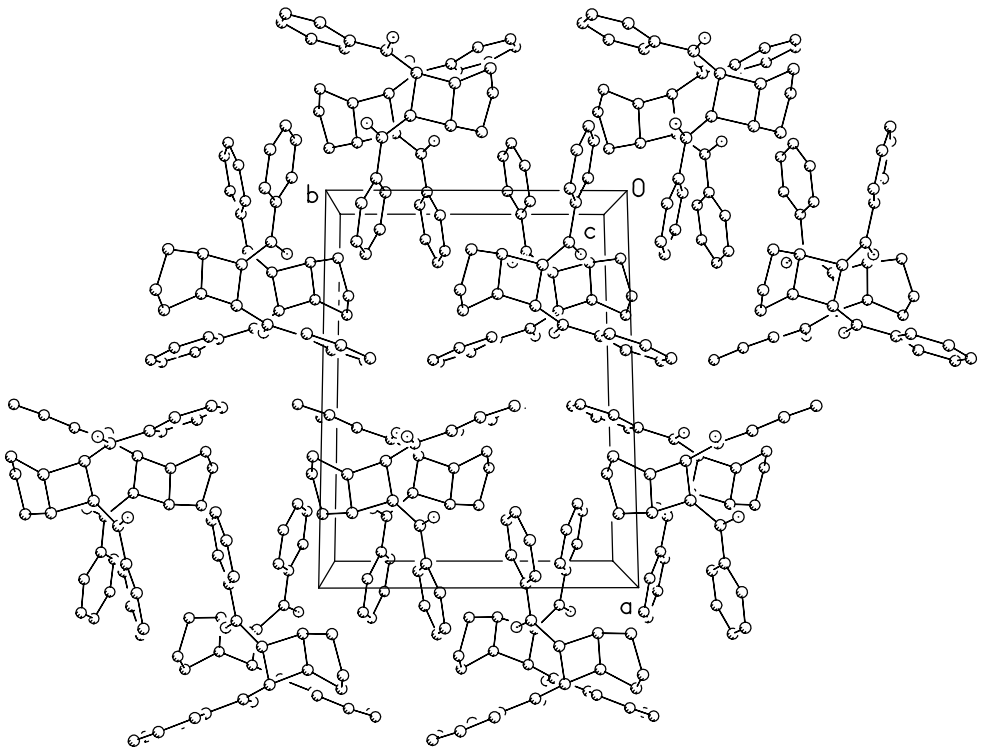


Table 3-8.12. Observed and calculated structure factors for 3-4.1a

h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s
2	0	0	371	384	5	3	5	0	209	221	2	1	11	0	51	52	3	11	2	1	61	60	3	-4	5	1	432	432	4
3	0	0	172	161	1	4	5	0	89	86	1	2	11	0	86	80	3	12	2	1	93	97	2	-3	5	1	234	241	3
4	0	0	1132	1112	12	5	5	0	45	42	2	3	11	0	89	83	3	13	2	1	35	30	5	-2	5	1	400	388	3
5	0	0	559	550	5	6	5	0	173	174	2	4	11	0	59	57	4	14	2	1	18	8	17	-1	5	1	304	306	2
6	0	0	399	396	4	7	5	0	41	38	4	5	11	0	0	9	1	15	2	1	0	10	1	0	5	1	357	359	3
7	0	0	734	704	9	8	5	0	236	231	3	6	11	0	67	64	4	16	2	1	53	40	10	1	5	1	100	94	1
8	0	0	192	183	2	9	5	0	46	42	6	7	11	0	38	29	11	17	2	1	62	53	19	2	5	1	84	87	3
9	0	0	284	273	3	10	5	0	180	179	6	8	11	0	148	145	6	-17	3	1	59	60	14	3	5	1	104	95	2
10	0	0	248	241	3	11	5	0	50	57	4	9	11	0	161	152	6	-16	3	1	0	12	1	4	5	1	132	136	1
11	0	0	134	123	3	12	5	0	238	223	5	10	11	0	10	29	10	-15	3	1	5	14	5	5	5	1	83	81	1
12	0	0	12	0	11	13	5	0	155	157	8	0	12	0	84	89	5	-14	3	1	117	119	5	6	5	1	63	61	3
13	0	0	33	28	7	14	5	0	71	76	5	1	12	0	45	48	4	-13	3	1	8	11	8	7	5	1	189	184	3
14	0	0	68	71	6	15	5	0	76	79	7	2	12	0	56	54	4	-12	3	1	171	174	2	8	5	1	94	92	4
15	0	0	146	152	6	16	5	0	29	39	28	3	12	0	46	38	5	-11	3	1	325	323	3	9	5	1	30	20	6
16	0	0	20	11	19	0	6	0	1	7	1	4	12	0	51	37	7	-10	3	1	72	72	6	10	5	1	19	34	18
17	0	0	62	75	15	1	6	0	266	260	2	5	12	0	35	14	10	-9	3	1	208	200	2	11	5	1	154	153	4
2	1	0	255	258	2	2	6	0	335	326	2	6	12	0	80	82	7	-8	3	1	20	13	4	12	5	1	0	8	1
3	1	0	321	318	2	3	6	0	123	126	2	7	12	0	38	19	17	-7	3	1	516	514	4	13	5	1	53	57	8
4	1	0	288	294	2	4	6	0	51	51	2	8	12	0	113	109	9	-6	3	1	192	191	1	14	5	1	146	135	5
5	1	0	842	841	9	5	6	0	100	87	4	1	13	0	25	33	25	-5	3	1	220	226	3	15	5	1	80	79	7
6	1	0	478	464	4	6	6	0	28	12	12	2	13	0	13	23	13	-4	3	1	98	97	2	16	5	1	38	15	20
7	1	0	144	136	1	7	6	0	255	249	5	3	13	0	21	9	20	-3	3	1	179	172	2	-16	6	1	85	68	11
8	1	0	31	33	3	8	6	0	175	173	3	4	13	0	37	15	9	-2	3	1	639	645	6	-15	6	1	20	44	19
9	1	0	277	272	5	9	6	0	200	196	4	5	13	0	124	120	7	-1	3	1	1243	1239	12	-14	6	1	0	6	1
10	1	0	183	174	2	10	6	0	65	61	6	6	13	0	22	2	21	0	3	1	775	781	8	-13	6	1	34	5	14
11	1	0	116	118	2	11	6	0	140	137	4	-18	1	1	34	22	34	1	3	1	210	202	2	-12	6	1	60	57	6
12	1	0	62	61	6	12	6	0	124	116	3	-17	1	1	21	20	21	2	3	1	0	25	1	-11	6	1	123	122	3
13	1	0	68	71	2	13	6	0	13	23	13	-16	1	1	42	1	41	3	3	1	379	392	4	-10	6	1	230	220	6
14	1	0	10	22	10	14	6	0	43	47	11	-15	1	1	49	44	7	4	3	1	192	197	4	-9	6	1	31	21	4
15	1	0	41	51	10	15	6	0	57	38	8	-14	1	1	66	65	3	5	3	1	230	232	4	-8	6	1	179	177	2
16	1	0	21	14	20	16	6	0	89	101	8	-13	1	1	45	55	3	6	3	1	361	353	7	-7	6	1	120	116	1
17	1	0	75	74	8	1	7	0	98	96	1	-12	1	1	98	94	1	7	3	1	242	240	3	-6	6	1	155	154	2
0	2	0	16	30	15	2	7	0	169	163	2	-11	1	1	136	128	1	8	3	1	164	156	2	-5	6	1	42	44	3
1	2	0	530	547	4	3	7	0	52	44	2	-10	1	1	62	53	2	9	3	1	144	144	2	-4	6	1	223	221	2
2	2	0	334	333	3	4	7	0	74	72	3	-9	1	1	63	49	1	10	3	1	109	105	2	-3	6	1	40	41	3
3	2	0	176	173	2	5	7	0	69	61	4	-8	1	1	89	88	2	11	3	1	103	98	2	-2	6	1	304	307	3
4	2	0	119	115	2	6	7	0	65	58	9	-7	1	1	294	292	3	12	3	1	12	15	11	-1	6	1	391	401	4
5	2	0	80	81	1	7	7	0	166	157	8	-6	1	1	261	252	2	13	3	1	31	32	13	0	6	1	74	69	2
6	2	0	457	449	4	8	7	0	74	70	2	-5	1	1	41	39	2	14	3	1	103	110	8	1	6	1	220	220	2
7	2	0	296	299	2	9	7	0	205	197	4	-4	1	1	893	896	7	15	3	1	45	39	9	2	6	1	267	266	2
8	2	0	56	58	4	10	7	0	176	170	4	-3	1	1	1392	1346	30	16	3	1	73	74	20	3	6	1	79	78	1
9	2	0	340	329	7	11	7	0	50	52	7	-2	1	1	212	228	1	-17	4	1	81	73	81	4	6	1	172	166	2
10	2	0	0	1	1	12	7	0	27	28	20	1	1	1	110	123	1	-16	4	1	191	191	8	5	6	1	32	27	6
11	2	0	200	197	2	13	7	0	138	134	4	2	1	1	980	987	19	-15	4	1	94	93	5	6	6	1	94	91	2
12	2	0	101	102	2	14	7	0	40	34	14	3	1	1	743	749	14	-14	4	1	49	59	5	7	6	1	50	39	6
13	2	0	87	95	2	15	7	0	33	0	32	4	1	1	442	463	13	-13	4	1	192	203	6	8	6	1	166	163	4
14	2	0	90	98	3	0	8	0	189	193	2	5	1	1	437	440	5	-12	4	1	223	229	3	9	6	1	313	313	6
15	2	0	0	19	1	1	8	0	0	1	1	6	1	1	159	159	2	-11	4	1	151	147	2	10	6	1	117	115	4
16	2	0	39	27	23	2	8	0	134	137	1	7	1	1	89	81	1	-10	4	1	466	461	5	11	6	1	32	27	18
17	2	0	65	48	12	3	8	0	341	337	7	8	1	1	149	137	2	-9	4	1	131	133	1	12	6	1	105	94	5
1	3	0	674	684	5	4	8	0	81	71	8	9	1	1	13	4	13	-8	4	1	88	81	1	13	6	1	25	23	24
2	3	0	137	137	1	5	8	0	141	132	7	10	1	1	20	20	6	-7	4	1	20	17	20	14	6	1	82	81	7
3	3	0	211	218	2	6	8	0	57	51	10	11	1	1	18	1	18	-6	4	1	82	85	3	15	6	1	46	58	12
4	3	0	0	9	1	7	8	0	48	46	4	12	1	1	130	136	2	-5	4	1	13	11	6	-15	7	1	33	49	19
5	3	0	50	47	2	8	8	0	239	237	10	13	1	1	25	38	13	-4	4	1	35	31	3	-14	7	1	0	3	1
6	3	0	42	36	5	9	8	0	25	21	25	14	1	1	73	81	4	-3	4	1	515	510	4	-13	7	1	0	13	1
7	3	0	235	234	3	10	8	0	202	195	4	15	1	1	25	30	25	-2	4	1	420	430	4	-12	7	1	40	13	11
8	3	0	55	54	2	11	8	0	82	96	4	16	1	1	34	23	24	-1	4	1	371	369	3	-11	7	1	67	50	5
9	3	0	91	94	1	12	8	0	53	42	8	17	1	1	11	23	11	0	4	1	195	190	2	-10	7	1	64	66	6
10	3	0	256	251	3	13	8	0	0	17	1	-17	2	1	75	63	10	1	4	1	168	175	1	-9	7	1	223	224	4
11	3	0	30	14	6	14	8	0	0	30	1	-16	2	1	50	45	9	2	4	1	191	190	2	-8	7	1	122	121	3
12	3	0	27	23	7	1	9	0	343	334	27	-15	2	1	45	42	8	3	4	1	54	53	1	-7	7	1	61	61	8
13	3	0	63	66	2	2	9	0	139	132	3	-14	2	1	27	33	7	4	4	1	171	180	1	-6	7	1	206	203	5
14	3	0	114	116	3	3	9	0	67	69	2	-13	2	1	41	45	3	5	4	1	108	109	2	-5	7	1	160	154	6
15	3	0	25	9	19	4	9	0	42	41	6	-12	2	1	223	224	2	6	4	1	0	1	1	-4	7	1	158	153	1
16	3	0	0	14	1	5	9	0	0	18	1	-11	2	1	235	228	2	7	4	1	83	86	2	-3	7	1	140	138	4
17	3	0	38	36	37	6	9	0	57	55	4	-10	2	1	141	142	3	8	4	1	300	302	5	-2	7	1	67	67	7
0	4	0	365	365	5	7	9	0	80	81	10	-9	2	1	280	275	2	9	4	1	47	23	6	-1	7	1	311	311	3
1	4	0	453	454	4	8	9	0	138	144	3	-8	2	1	390	376	3	10	4	1	73	69	3	0	7	1	152	153	1
2	4	0	250	245	2	9	9	0	37	24	12	-7	2	1	168	164	2	11	4	1	55	54	4	1	7	1	170	167	1
3	4	0	425	427	3	10	9	0	25	4	25	-6	2	1	445	451	3	12	4	1	31	31	9	2	7	1	377	376	3
4	4	0	51	48	3	11	9	0	50	51	8	-5	2	1	167	171	1	13	4	1	86	87	4	3	7	1	112	108	1
5	4	0	48	40	2	12	9	0	40	25	23	-4	2	1	678	679	6	14	4	1	55	49	7	4	7	1	311	304	4
6	4	0	39	45	3	13	9	0	44	48	15	-3	2	1	679	694	6	15	4	1	164	154	5	5	7	1	201	200	2
7	4	0	309	297	4	0	10	0	43	45	5	-2	2	1	232	225	2	16	4	1	90	87	9	6	7	1	374	378	16
8	4	0	59	64	3	1	10	0	130	129	2	-1	2	1	532	545	5	-16	5	1	18	13	17	7	7	1	226	223	3
9	4	0	50	52	4	2	10	0	0	16	1	0	2	1	113	120	4	-15	5	1	105	108	5	8	7	1	329	334	5
10	4	0	298	292	4	3	10	0	16	17	15	1	2	1	131	122	3	-14	5	1	201	194	4	9	7	1	113	112	3
11	4	0	0	8	1	4	10	0	53	57	3	2	2	1	428	437	5	-13	5	1	127	136	4	10	7	1	109	107	4
12	4	0	18	19	17	5	10	0	44	43	4	3	2	1	118	121	2	-12	5	1	134	131	3	11	7	1	207	200	4
13	4	0	59	54	4	6	10	0	131	132	3	4	2	1	139	145	1	-11	5	1	8	19	7	12	7	1	19	40	18
14	4	0	18	15	17	7	10	0	40	34	6	5	2	1	275	270	3	-10	5	1	175	178	2	13	7	1	110	122	8
15	4	0	143	139	4	8	10	0	71	63	5	6	2	1	375	377	4	-9	5	1	275	271	3	14	7	1	95	80	6
16	4	0	0	13	1	9	10	0	66	64	6	7	2	1	343	337	5	-8	5	1	59	51	2	-14	8	1	49	47	12
17	4	0	118	141	16	10	10	0	0	24	1	8	2	1	173	169	2	-7	5	1	53	53	1	-13	8	1	68	75	8
1	5	0	135	126	1	11	10	0	40	19	18	9	2	1	74	68	2	-6	5	1	93	94	1	-12	8	1	0	5	1
2	5	0	164	164	2	12	10	0	13	29	13	10	2	1	61	61	4	-5	5	1	88	87	2	-11	8	1	68	54	6

Table 3-8.12. Observed and calculated structure factors for 3-4.1a

h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s
-10	8	1	31	39	16	0	11	1	56	55	3	-6	1	2	82	80	1	11	3	2	102	101	4	-1	6	2	25	39	5
-9	8	1	197	199	3	1	11	1	91	96	2	-5	1	2	513	525	4	12	3	2	34	24	6	0	6	2	32	43	3
-8	8	1	164	166	2	2	11	1	34	32	6	-4	1	2	228	233	3	13	3	2	24	0	17	1	6	2	45	48	2
-7	8	1	31	37	5	3	11	1	49	51	4	-3	1	2	635	650	5	14	3	2	70	73	8	2	6	2	101	102	1
-6	8	1	62	65	10	4	11	1	61	66	4	-2	1	2	87	83	3	15	3	2	82	54	14	3	6	2	88	91	1
-5	8	1	67	55	2	5	11	1	62	61	4	-1	1	2	716	747	7	16	3	2	70	59	12	4	6	2	21	10	12
-4	8	1	181	182	3	6	11	1	18	21	17	0	1	2	52	12	13	-17	4	2	41	42	15	5	6	2	55	44	3
-3	8	1	121	121	6	7	11	1	0	24	1	1	1	2	141	132	3	-16	4	2	107	110	6	6	6	2	109	107	2
-2	8	1	252	255	8	8	11	1	130	128	5	2	1	2	263	266	5	-15	4	2	168	181	4	7	6	2	69	64	5
-1	8	1	65	62	9	9	11	1	143	127	7	3	1	2	94	103	2	-14	4	2	38	30	8	8	6	2	159	161	3
0	8	1	29	23	7	10	11	1	27	11	27	4	1	2	47	49	2	-13	4	2	0	17	1	9	6	2	139	137	3
1	8	1	430	434	4	-9	12	1	76	69	8	5	1	2	278	280	4	-12	4	2	0	14	1	10	6	2	98	94	4
2	8	1	91	81	3	-8	12	1	52	47	11	6	1	2	205	203	3	-11	4	2	307	309	5	11	6	2	42	21	8
3	8	1	134	133	8	-7	12	1	15	11	14	7	1	2	171	176	2	-10	4	2	41	39	2	12	6	2	82	89	7
4	8	1	147	139	6	-6	12	1	79	67	4	8	1	2	293	297	4	-9	4	2	111	116	5	13	6	2	83	81	5
5	8	1	195	204	5	-5	12	1	55	46	5	9	1	2	234	233	3	-8	4	2	56	49	4	14	6	2	96	98	6
6	8	1	203	197	13	-4	12	1	136	128	3	10	1	2	94	89	2	-7	4	2	225	226	2	15	6	2	0	14	1
7	8	1	235	241	8	-3	12	1	130	128	2	11	1	2	69	76	4	-6	4	2	17	24	6	-16	7	2	0	5	1
8	8	1	41	19	10	-2	12	1	19	3	18	12	1	2	37	51	7	-5	4	2	421	412	3	-15	7	2	0	2	1
9	8	1	24	18	23	-1	12	1	28	27	7	13	1	2	42	55	5	-4	4	2	35	21	5	-14	7	2	30	8	29
10	8	1	0	19	1	0	12	1	22	20	15	14	1	2	27	17	15	-3	4	2	541	540	4	-13	7	2	41	32	11
11	8	1	13	14	13	1	12	1	33	34	7	15	1	2	26	21	25	-2	4	2	58	67	2	-12	7	2	95	83	6
12	8	1	20	26	19	2	12	1	8	12	8	16	1	2	42	35	13	-1	4	2	305	310	3	-11	7	2	113	116	2
13	8	1	58	54	11	3	12	1	17	19	16	-18	2	2	41	21	20	0	4	2	359	356	3	-10	7	2	107	104	10
14	8	1	13	29	13	4	12	1	69	74	4	-17	2	2	16	8	15	1	4	2	96	110	1	-9	7	2	66	69	4
-13	9	1	40	29	14	5	12	1	21	24	20	-16	2	2	98	103	7	2	4	2	209	220	3	-8	7	2	59	56	2
-12	9	1	40	29	16	6	12	1	13	9	13	-15	2	2	35	8	8	3	4	2	74	78	1	-7	7	2	52	56	7
-11	9	1	137	139	4	7	12	1	47	59	11	-14	2	2	147	151	2	4	4	2	224	228	3	-6	7	2	19	5	18
-10	9	1	86	82	6	8	12	1	0	5	1	-13	2	2	23	12	7	5	4	2	54	61	2	-5	7	2	13	5	13
-9	9	1	22	5	22	-6	13	1	22	17	21	-12	2	2	46	35	2	6	4	2	32	38	4	-4	7	2	192	190	3
-8	9	1	27	22	9	-5	13	1	40	48	11	-11	2	2	157	158	4	7	4	2	29	23	8	-3	7	2	119	110	1
-7	9	1	74	72	4	-4	13	1	101	108	5	-10	2	2	341	333	4	8	4	2	18	3	18	-2	7	2	182	182	2
-6	9	1	68	72	2	-3	13	1	84	84	7	-9	2	2	286	281	3	9	4	2	27	18	9	-1	7	2	104	101	2
-5	9	1	172	165	6	-2	13	1	121	114	5	-8	2	2	77	70	1	10	4	2	133	136	4	0	7	2	114	116	2
-4	9	1	169	169	9	-1	13	1	47	61	11	-7	2	2	58	64	2	11	4	2	19	27	19	1	7	2	102	100	1
-3	9	1	142	143	8	0	13	1	104	100	7	-6	2	2	276	283	2	12	4	2	53	56	5	2	7	2	44	34	3
-2	9	1	249	252	10	1	13	1	86	94	5	-5	2	2	583	582	4	13	4	2	119	119	4	3	7	2	103	111	1
-1	9	1	122	119	7	2	13	1	88	93	6	-4	2	2	46	56	2	14	4	2	92	90	5	4	7	2	25	12	6
0	9	1	188	192	3	3	13	1	29	2	13	-3	2	2	348	365	3	15	4	2	12	31	11	5	7	2	33	24	5
1	9	1	59	57	2	4	13	1	25	6	24	-2	2	2	703	717	6	-17	5	2	16	16	15	6	7	2	63	55	9
2	9	1	101	93	9	5	13	1	29	49	28	-1	2	2	225	223	2	-16	5	2	81	82	7	7	7	2	33	32	5
3	9	1	49	53	12	-17	0	2	20	48	19	0	2	2	148	154	5	-15	5	2	62	70	10	8	7	2	120	119	4
4	9	1	133	131	8	-16	0	2	22	2	21	1	2	2	70	81	2	-14	5	2	21	15	20	9	7	2	18	13	17
5	9	1	169	171	7	-15	0	2	84	84	6	2	2	2	351	365	4	-13	5	2	63	69	4	10	7	2	23	23	23
6	9	1	61	56	2	-14	0	2	106	108	3	3	2	2	282	288	5	-12	5	2	248	242	3	11	7	2	53	50	7
7	9	1	52	43	4	-13	0	2	23	22	9	4	2	2	386	395	6	-11	5	2	138	139	5	12	7	2	106	103	4
8	9	1	34	31	9	-12	0	2	70	76	2	5	2	2	47	47	2	-10	5	2	75	75	4	13	7	2	0	4	1
9	9	1	0	9	1	-11	0	2	48	53	3	6	2	2	200	201	4	-9	5	2	54	56	2	14	7	2	72	52	8
10	9	1	77	75	6	-10	0	2	115	110	2	7	2	2	157	165	2	-8	5	2	68	64	1	-15	8	2	0	30	1
11	9	1	18	31	17	-9	0	2	219	213	2	8	2	2	28	24	10	-7	5	2	194	195	2	-14	8	2	0	30	1
12	9	1	54	9	9	-8	0	2	488	479	5	9	2	2	198	208	3	-6	5	2	17	19	17	-13	8	2	50	46	10
13	9	1	68	19	17	-7	0	2	37	36	4	10	2	2	55	59	3	-5	5	2	449	445	3	-12	8	2	65	68	6
-12	10	1	147	139	8	-6	0	2	219	231	2	11	2	2	0	16	1	-4	5	2	64	64	2	-11	8	2	131	125	4
-11	10	1	92	82	6	-5	0	2	0	19	1	12	2	2	86	82	3	-3	5	2	243	249	2	-10	8	2	41	43	5
-10	10	1	0	3	1	-4	0	2	77	73	2	13	2	2	53	34	6	-2	5	2	250	249	3	-9	8	2	73	71	1
-9	10	1	69	76	5	-3	0	2	357	380	4	14	2	2	39	40	14	-1	5	2	128	125	1	-8	8	2	56	60	6
-8	10	1	34	39	7	-2	0	2	894	918	10	15	2	2	22	9	21	0	5	2	105	107	3	-7	8	2	40	48	3
-7	10	1	47	46	9	-1	0	2	2104	1975	37	16	2	2	70	63	13	1	5	2	0	9	1	-6	8	2	46	42	1
-6	10	1	161	150	16	0	0	2	335	362	7	-18	3	2	54	39	20	2	5	2	119	127	1	-5	8	2	241	241	5
-5	10	1	117	119	6	1	0	2	249	263	7	-17	3	2	46	4	46	3	5	2	359	360	4	-4	8	2	216	212	2
-4	10	1	93	93	6	2	0	2	359	372	7	-16	3	2	31	58	16	4	5	2	74	65	2	-3	8	2	136	135	5
-3	10	1	84	89	13	3	0	2	23	40	8	-15	3	2	117	123	6	5	5	2	234	240	3	-2	8	2	51	46	4
-2	10	1	69	67	2	4	0	2	394	398	8	-14	3	2	24	19	7	6	5	2	29	0	3	-1	8	2	216	216	5
-1	10	1	174	171	2	5	0	2	581	578	13	-13	3	2	43	42	3	7	5	2	129	131	4	0	8	2	64	64	5
0	10	1	19	24	10	6	0	2	440	432	8	-12	3	2	49	52	5	8	5	2	65	65	5	1	8	2	271	267	7
1	10	1	24	23	7	7	0	2	84	85	2	-11	3	2	149	140	3	9	5	2	49	44	4	2	8	2	265	271	9
2	10	1	77	75	6	8	0	2	0	3	1	-10	3	2	421	418	8	10	5	2	0	19	1	3	8	2	255	256	5
3	10	1	39	37	4	9	0	2	67	72	3	-9	3	2	240	239	1	11	5	2	144	142	6	4	8	2	27	15	15
4	10	1	20	1	19	10	0	2	129	129	3	-8	3	2	448	455	3	12	5	2	39	46	8	5	8	2	102	110	4
5	10	1	115	115	12	11	0	2	136	144	3	-7	3	2	493	484	3	13	5	2	28	6	17	6	8	2	68	75	3
6	10	1	108	108	3	12	0	2	27	3	5	-6	3	2	298	298	2	14	5	2	41	33	12	7	8	2	169	172	7
7	10	1	64	73	6	13	0	2	110	115	8	-5	3	2	39	46	2	15	5	2	15	22	14	8	8	2	126	127	4
8	10	1	22	8	22	14	0	2	173	174	6	-4	3	2	466	470	3	-16	6	2	0	23	1	9	8	2	34	34	12
9	10	1	141	128	5	15	0	2	112	126	10	-3	3	2	366	374	3	-15	6	2	0	16	1	10	8	2	0	33	1
10	10	1	0	22	1	16	0	2	43	46	19	-2	3	2	729	733	7	-14	6	2	0	8	1	11	8	2	94	102	5
11	10	1	77	58	8	-18	1	2	37	48	16	-1	3	2	560	569	6	-13	6	2	43	54	9	12	8	2	70	58	6
-11	11	1	169	163	7	-17	1	2	69	83	7	0	3	2	273	278	3	-12	6	2	21	14	20	13	8	2	47	21	18
-10	11	1	74	74	9	-16	1	2	41	30	7	1	3	2	474	479	4	-11	6	2	101	97	9	-14	9	2	17	7	16
-9	11	1	45	52	9	-15	1	2	87	81	3	2	3	2	30	26	7	-10	6	2	71	73	5	-13	9	2	45	30	20
-8	11	1	32	8	14	-14	1	2	127	128	2	3	3	2	265	276	4	-9	6	2	34	23	5	-12	9	2	49	23	14
-7	11	1	100	94	3	-13	1	2	92	96	1	4	3	2	22	19	5	-8	6	2	14	6	13	-11	9	2	25	29	24
-6	11	1	47	56	5	-12	1	2	387	376	3	5	3	2	281	278	4	-7	6	2	13	1	13	-10	9	2	25	47	25
-5	11	1	0	11	1	-11	1	2	298	298	3	6	3	2	21	17	4	-6	6	2	44	31	2	-9	9	2	114	114	3
-4	11	1	177	177	2	-10	1	2	100	103	1	7	3	2	58	54	4	-5	6	2	66	60	1	-8	9	2	81	77	11
-3	11	1	58	50	4	-9	1	2	42	44	2	8	3	2	27	16	4	-4	6	2	392	389	4	-7	9	2	37	33	15
-2	11	1	12	11	11	-8	1	2	36	40	4	9	3	2	203	204	3	-3	6	2	305	311	3	-6	9	2	55	53	3
-1	11	1	32	41	6	-7	1	2	56	60	3	10	3	2	0	8	1	-2	6	2	142	146	1	-5	9	2	12	13	12

Table 3-8.12. Observed and calculated structure factors for 3-4.1a

h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s
-4	9	2	58	56	2	2	13	2	41	10	13	-3	3	3	19	25	19	-13	6	3	117	120	4	-13	9	3	46	44	15
-3	9	2	134	141	5	3	13	2	30	29	14	-2	3	3	79	88	2	-12	6	3	49	48	3	-12	9	3	33	1	32
-2	9	2	436	436	15	4	13	2	59	61	9	-1	3	3	176	180	2	-11	6	3	128	122	4	-11	9	3	30	38	14
-1	9	2	91	93	2	-18	1	3	0	11	1	0	3	3	56	62	1	-10	6	3	116	111	2	-10	9	3	81	80	3
0	9	2	170	172	7	-17	1	3	72	85	8	1	3	3	142	144	2	-9	6	3	256	238	4	-9	9	3	68	65	4
1	9	2	134	134	1	-16	1	3	40	24	8	2	3	3	248	244	3	-8	6	3	222	217	5	-8	9	3	15	27	14
2	9	2	101	110	9	-15	1	3	36	55	12	3	3	3	302	297	4	-7	6	3	41	41	3	-7	9	3	67	71	3
3	9	2	164	167	3	-14	1	3	60	57	4	4	3	3	18	5	17	-6	6	3	121	122	1	-6	9	3	196	197	7
4	9	2	209	210	6	-13	1	3	48	44	3	5	3	3	29	23	4	-5	6	3	124	125	1	-5	9	3	48	46	3
5	9	2	112	106	7	-12	1	3	30	5	4	6	3	3	263	260	5	-4	6	3	222	226	2	-4	9	3	137	140	3
6	9	2	105	108	4	-11	1	3	16	1	14	7	3	3	30	9	9	-3	6	3	107	109	1	-3	9	3	135	145	1
7	9	2	150	148	4	-10	1	3	152	151	1	8	3	3	45	48	6	-2	6	3	301	300	3	-2	9	3	22	25	7
8	9	2	21	16	20	-9	1	3	100	100	1	9	3	3	131	129	4	-1	6	3	62	62	2	-1	9	3	175	182	2
9	9	2	55	74	8	-8	1	3	182	190	2	10	3	3	89	94	2	0	6	3	20	15	7	0	9	3	140	143	2
10	9	2	63	66	7	-7	1	3	73	70	1	11	3	3	15	12	14	1	6	3	76	79	2	1	9	3	0	1	1
11	9	2	50	53	15	-6	1	3	69	80	1	12	3	3	76	85	9	2	6	3	244	242	7	2	9	3	34	37	5
12	9	2	105	94	6	-5	1	3	135	131	1	13	3	3	25	17	24	3	6	3	249	241	5	3	9	3	24	21	8
-12	10	2	51	16	15	-4	1	3	147	153	1	14	3	3	20	24	20	4	6	3	130	129	3	4	9	3	134	136	6
-11	10	2	0	6	1	-3	1	3	130	156	1	15	3	3	41	22	40	5	6	3	116	119	2	5	9	3	35	38	9
-10	10	2	75	59	8	-2	1	3	463	482	4	-17	4	3	29	34	28	6	6	3	32	29	2	6	9	3	36	29	12
-9	10	2	42	40	9	-1	1	3	315	330	3	-16	4	3	0	22	1	7	6	3	44	48	2	7	9	3	61	73	7
-8	10	2	64	63	4	0	1	3	85	97	2	-15	4	3	153	150	4	8	6	3	89	99	2	8	9	3	90	93	5
-7	10	2	138	142	2	1	1	3	187	202	3	-14	4	3	153	154	11	9	6	3	123	123	4	9	9	3	45	47	12
-6	10	2	0	11	1	2	1	3	462	472	7	-13	4	3	100	105	4	10	6	3	159	153	4	10	9	3	19	41	18
-5	10	2	88	96	17	3	1	3	169	168	10	-12	4	3	191	191	4	11	6	3	0	16	1	11	9	3	93	97	7
-4	10	2	6	8	6	4	1	3	173	173	3	-11	4	3	306	307	9	12	6	3	44	48	10	-13	10	3	107	119	15
-3	10	2	245	248	3	5	1	3	110	97	2	-10	4	3	54	50	2	13	6	3	66	64	9	-12	10	3	47	3	15
-2	10	2	195	196	2	6	1	3	0	11	1	-9	4	3	88	91	3	14	6	3	47	25	17	-11	10	3	6	11	6
-1	10	2	39	42	3	7	1	3	266	257	4	-8	4	3	30	25	6	-16	7	3	41	37	29	-10	10	3	37	1	12
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2	10	2	139	142	10	10	1	3	59	52	3	-5	4	3	0	0	1	-13	7	3	40	34	9	-7	10	3	56	63	4
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9	10	2	33	21	19	-18	2	3	41	43	16	2	4	3	171	177	2	-6	7	3	70	67	4	0	10	3	36	30	5
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-6	11	2	143	132	3	-10	2	3	54	51	2	10	4	3	97	103	3	2	7	3	41	36	3	8	10	3	0	15	1
-5	11	2	131	128	3	-9	2	3	179	176	2	11	4	3	58	54	4	3	7	3	147	143	5	9	10	3	84	71	8
-4	11	2	62	64	3	-8	2	3	30	38	4	12	4	3	61	64	4	4	7	3	76	74	7	10	10	3	25	46	25
-3	11	2	18	14	12	-7	2	3	189	192	2	13	4	3	45	38	8	5	7	3	108	115	3	-11	11	3	28	12	28
-2	11	2	75	78	2	-6	2	3	561	551	4	14	4	3	43	32	13	6	7	3	206	207	10	-10	11	3	15	16	14
-1	11	2	32	30	5	-5	2	3	507	509	4	15	4	3	74	66	13	7	7	3	113	121	6	-9	11	3	95	90	7
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3	11	2	99	97	3	-1	2	3	231	236	2	-14	5	3	73	85	4	11	7	3	34	47	12	-5	11	3	239	238	3
4	11	2	37	45	7	0	2	3	51	55	9	-13	5	3	158	158	10	12	7	3	69	74	7	-4	11	3	31	36	8
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-6	12	2	130	122	4	9	2	3	57	54	2	-4	5	3	234	231	3	-8	8	3	50	44	7	5	11	3	41	48	13
-5	12	2	31	19	12	10	2	3	132	140	2	-3	5	3	764	742	6	-7	8	3	23	16	23	6	11	3	55	55	9
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1	12	2	32	31	8	-18	3	3	40	17	40	3	5	3	137	149	2	-1	8	3	95	96	3	-6	12	3	31	5	22
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5	12	2	91	93	6	-14	3	3	77	76	2	7	5	3	87	86	3	3	8	3	87	79	4	-2	12	3	0	11	1
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-4	13	2	83	82	6	-9	3	3	40	31	3	12	5	3	40	45	10	8	8	3	24	20	23	3	12	3	172	178	7
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-1	13	2	15	33	14	-6	3	3	241	243	2	-16	6	3	19	42	18	11	8	3	47	34	11	6	12	3	85	86	8
0	13	2	48	56	9	-5	3	3	18	5	17	-15	6	3	172	152	9	12	8	3	0	38	1	-6	13	3	44	39	7
1	13	2	16	10	15	-4	3	3	325	324	2	-14	6	3	33	39	15	-14	9	3	96	102	8	-5	13	3	129	134	7

Table 3-8.12. Observed and calculated structure factors for 3-4.1a

h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s
-4	13	3	63	66	7	-7	2	4	276	276	2	14	4	4	54	47	54	8	7	4	92	89	5	-3	11	4	24	5	23
-3	13	3	51	45	9	-6	2	4	21	16	10	-17	5	4	39	17	39	9	7	4	38	20	12	-2	11	4	22	9	21
-2	13	3	59	35	15	-5	2	4	63	54	3	-16	5	4	0	0	1	10	7	4	16	12	15	-1	11	4	40	37	5
-1	13	3	44	45	10	-4	2	4	76	82	2	-15	5	4	0	34	1	11	7	4	54	52	9	0	11	4	64	67	4
0	13	3	23	21	23	-3	2	4	201	204	1	-14	5	4	183	183	5	12	7	4	0	16	1	1	11	4	77	67	5
1	13	3	110	111	7	-2	2	4	338	335	3	-13	5	4	109	110	3	-15	8	4	34	34	33	2	11	4	168	161	3
2	13	3	57	53	8	-1	2	4	326	332	3	-12	5	4	12	15	12	-14	8	4	145	136	9	3	11	4	15	15	14
3	13	3	34	38	14	0	2	4	351	356	4	-11	5	4	76	78	4	-13	8	4	100	79	8	4	11	4	17	21	16
-18	0	4	58	76	16	1	2	4	18	30	18	-10	5	4	52	48	3	-12	8	4	43	44	9	5	11	4	43	18	17
-17	0	4	184	192	8	2	2	4	60	47	9	-9	5	4	170	172	4	-11	8	4	6	2	6	6	11	4	60	64	9
-16	0	4	65	64	5	3	2	4	230	225	4	-8	5	4	43	45	3	-10	8	4	32	32	7	7	11	4	68	65	8
-15	0	4	114	119	3	4	2	4	98	83	8	-7	5	4	190	188	2	-9	8	4	92	95	2	-9	12	4	19	42	18
-14	0	4	137	141	3	5	2	4	85	88	4	-6	5	4	379	368	5	-8	8	4	54	60	2	-8	12	4	131	134	6
-13	0	4	228	232	3	6	2	4	109	106	3	-5	5	4	336	330	5	-7	8	4	118	116	5	-7	12	4	49	64	8
-12	0	4	107	105	2	7	2	4	201	204	3	-4	5	4	80	76	1	-6	8	4	84	92	12	-6	12	4	35	3	12
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-9	0	4	0	3	1	10	2	4	0	36	1	-1	5	4	258	259	2	-3	8	4	159	165	6	-3	12	4	24	25	23
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-7	0	4	205	204	3	12	2	4	32	17	12	1	5	4	260	256	3	-1	8	4	115	119	8	-1	12	4	29	6	18
-6	0	4	325	319	4	13	2	4	27	21	26	2	5	4	311	305	3	0	8	4	47	39	4	0	12	4	57	55	5
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1	0	4	55	61	8	-14	3	4	111	112	3	9	5	4	24	21	11	7	8	4	64	54	6	-4	13	4	26	5	26
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3	0	4	71	67	4	-12	3	4	203	203	4	11	5	4	47	57	8	9	8	4	173	163	4	-2	13	4	125	120	6
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7	0	4	74	78	3	-8	3	4	63	58	2	-16	6	4	104	86	11	-13	9	4	52	29	15	-18	1	5	27	5	27
8	0	4	37	22	6	-7	3	4	9	15	9	-15	6	4	73	65	8	-12	9	4	33	6	32	-17	1	5	68	77	6
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11	0	4	53	53	4	-4	3	4	41	37	3	-12	6	4	10	5	10	-9	9	4	25	9	15	-14	1	5	172	178	4
12	0	4	41	52	9	-3	3	4	241	245	2	-11	6	4	20	24	19	-8	9	4	137	141	3	-13	1	5	0	0	1
13	0	4	90	87	6	-2	3	4	164	158	4	-10	6	4	59	57	3	-7	9	4	0	11	1	-12	1	5	60	56	3
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5	1	4	133	135	4	-8	4	4	69	58	3	-14	7	4	38	17	38	-4	10	4	132	140	7	14	1	5	50	58	50
6	1	4	7	3	6	-7	4	4	55	53	2	-13	7	4	46	40	11	-3	10	4	96	110	4	-18	2	5	50	54	15
7	1	4	69	61	3	-6	4	4	72	61	2	-12	7	4	38	42	7	-2	10	4	53	47	10	-17	2	5	38	8	37
8	1	4	40	37	10	-5	4	4	107	103	3	-11	7	4	93	92	2	-1	10	4	118	121	6	-16	2	5	0	28	1
9	1	4	61	59	9	-4	4	4	0	2	1	-10	7	4	60	64	2	0	10	4	24	23	9	-15	2	5	111	124	8
10	1	4	44	52	3	-3	4	4	18	17	11	-9	7	4	140	149	2	1	10	4	92	98	2	-14	2	5	54	64	3
11	1	4	102	116	2	-2	4	4	205	212	2	-8	7	4	45	41	3	2	10	4	43	45	5	-13	2	5	38	23	5
12	1	4	20	9	20	-1	4	4	276	264	3	-7	7	4	109	111	4	3	10	4	40	27	9	-12	2	5	85	86	2
13	1	4	27	22	20	0	4	4	194	188	2	-6	7	4	47	35	3	4	10	4	29	40	18	-11	2	5	115	105	5
14	1	4	36	11	19	1	4	4	72	69	4	-5	7	4	75	72	4	5	10	4	34	33	12	-10	2	5	124	123	2
15	1	4	5	38	5	2	4	4	146	152	2	-4	7	4	47	38	8	6	10	4	0	18	1	-9	2	5	77	77	2
-18	2	4	56	24	55	3	4	4	108	97	2	-3	7	4	29	12	8	7	10	4	134	137	5	-8	2	5	247	242	2
-17	2	4	50	55	11	4	4	4	250	245	3	-2	7	4	85	82	3	8	10	4	89	95	7	-7	2	5	133	119	1
-16	2	4	78	70	4	5	4	4	97	95	5	-1	7	4	22	15	7	9	10	4	34	23	22	-6	2	5	0	4	1
-15	2	4	104	105	4	6	4	4	22	14	6	0	7	4	16	1	15	-11	11	4	0	2	1	-5	2	5	36	31	3
-14	2	4	85	80	2	7	4	4	34	35	14	1	7	4	60	63	4	-10	11	4	43	31	18	-4	2	5	45	33	8
-13	2	4	8	2	8	8	4	4	169	168	2	2	7	4	47	39	4	-9	11	4	37	22	15	-3	2	5	241	247	2
-12	2	4	156	154	2	9	4	4	27	39	7	3	7	4	84	88	2	-8	11	4	98	100	5	-2	2	5	113	114	1
-11	2	4	93	89	2	10	4	4	63	74	4	4	7	4	64	61	2	-7	11	4	151	147	5	-1	2	5	59	42	2
-10	2	4	104	103	1	11	4	4	14	23	14	5	7	4	31	36	5	-6	11	4	97	102	3	0	2	5	612	603	9
-9	2	4	24	22	18	12	4	4	65	70	5	6	7	4	16	4	8	-5	11	4	25	24	15	1	2	5	192	195	2
-8	2	4	309	304	4	13	4	4	25	27	25	7	7	4	108	97	4	-4	11	4	55	55	4	2	2	5	73	60	9

Table 3-8.12. Observed and calculated structure factors for 3-4.1a

h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s
3	2	5	78	84	4	-6	5	5	189	184	4	-5	8	5	56	47	3	1	12	5	82	83	8	2	2	6	66	48	4
4	2	5	327	321	6	-5	5	5	279	275	2	-4	8	5	0	2	1	2	12	5	45	36	13	3	2	6	83	69	3
5	2	5	69	68	5	-4	5	5	240	238	2	-3	8	5	14	12	13	3	12	5	0	24	1	4	2	6	23	18	15
6	2	5	217	216	4	-3	5	5	232	229	5	-2	8	5	26	41	8	4	12	5	40	30	18	5	2	6	191	193	4
7	2	5	253	248	4	-2	5	5	37	33	4	-1	8	5	61	63	3	-18	0	6	106	108	12	6	2	6	262	254	6
8	2	5	86	79	2	-1	5	5	148	148	2	0	8	5	74	84	8	-17	0	6	23	42	23	7	2	6	0	7	1
9	2	5	81	88	2	0	5	5	85	83	3	1	8	5	130	131	3	-16	0	6	51	40	11	8	2	6	11	5	11
10	2	5	119	125	3	1	5	5	28	15	7	2	8	5	27	20	7	-15	0	6	43	50	10	9	2	6	33	34	7
11	2	5	26	20	16	2	5	5	154	157	2	3	8	5	89	88	13	-14	0	6	107	99	4	10	2	6	49	49	7
12	2	5	22	8	22	3	5	5	118	119	2	4	8	5	163	166	8	-13	0	6	87	74	3	11	2	6	79	75	6
13	2	5	104	108	8	4	5	5	116	121	2	5	8	5	0	2	1	-12	0	6	0	18	1	12	2	6	55	48	10
14	2	5	0	47	1	5	5	5	34	29	5	6	8	5	130	129	3	-11	0	6	86	73	4	13	2	6	41	46	16
-18	3	5	103	88	9	6	5	5	117	121	3	7	8	5	73	76	6	-10	0	6	133	82	3	-18	3	6	0	40	1
-17	3	5	114	107	14	7	5	5	207	217	6	8	8	5	15	18	14	-9	0	6	281	278	4	-17	3	6	37	40	23
-16	3	5	19	18	18	8	5	5	31	39	10	9	8	5	10	15	10	-8	0	6	90	82	3	-16	3	6	42	31	9
-15	3	5	83	87	3	9	5	5	81	86	4	10	8	5	47	49	11	-7	0	6	250	238	4	-15	3	6	115	111	5
-14	3	5	20	1	20	10	5	5	61	53	7	11	8	5	35	15	34	-6	0	6	280	272	4	-14	3	6	139	140	6
-13	3	5	92	94	3	11	5	5	56	64	6	-14	9	5	36	12	17	-5	0	6	85	64	3	-13	3	6	170	172	8
-12	3	5	6	9	5	12	5	5	105	99	5	-13	9	5	0	0	1	-4	0	6	419	411	5	-12	3	6	22	36	21
-11	3	5	82	74	2	13	5	5	49	35	14	-11	9	5	19	21	18	-3	0	6	477	455	6	-11	3	6	55	59	4
-10	3	5	16	9	15	-16	6	5	93	94	11	-10	9	5	16	23	15	-2	0	6	115	71	2	-10	3	6	45	22	6
-9	3	5	59	57	2	-15	6	5	0	2	1	-9	9	5	0	34	1	-1	0	6	130	87	4	-9	3	6	211	206	2
-8	3	5	257	260	2	-14	6	5	0	14	1	-8	9	5	15	13	14	0	0	6	298	285	6	-8	3	6	71	63	2
-7	3	5	67	62	2	-13	6	5	75	85	3	-7	9	5	157	156	2	1	0	6	107	100	3	-7	3	6	11	19	11
-6	3	5	43	40	3	-12	6	5	69	68	3	-6	9	5	23	19	13	2	0	6	182	183	3	-6	3	6	237	233	2
-5	3	5	24	15	23	-11	6	5	41	30	4	-5	9	5	67	66	11	3	0	6	0	4	1	-5	3	6	32	28	5
-4	3	5	199	197	2	-10	6	5	0	14	1	-4	9	5	22	20	10	4	0	6	208	205	4	-4	3	6	30	33	6
-3	3	5	205	204	2	-9	6	5	115	117	3	-3	9	5	44	50	5	5	0	6	598	577	14	-3	3	6	204	208	3
-2	3	5	164	159	1	-8	6	5	30	9	7	-2	9	5	139	139	5	6	0	6	234	241	11	-2	3	6	52	29	8
-1	3	5	26	9	26	-7	6	5	21	22	10	-1	9	5	43	36	10	7	0	6	131	140	7	-1	3	6	80	85	2
0	3	5	58	61	3	-6	6	5	151	145	5	0	9	5	68	69	3	8	0	6	308	309	16	0	3	6	75	83	3
1	3	5	287	272	3	-5	6	5	27	15	8	1	9	5	93	91	11	9	0	6	227	214	6	1	3	6	55	41	7
2	3	5	10	22	10	-4	6	5	232	228	4	2	9	5	93	88	5	10	0	6	32	47	12	2	3	6	27	39	13
3	3	5	52	37	6	-3	6	5	160	165	2	3	9	5	78	77	7	11	0	6	230	206	5	3	3	6	112	106	5
4	3	5	154	156	3	-2	6	5	26	19	18	4	9	5	145	140	4	12	0	6	49	43	17	4	3	6	47	0	20
5	3	5	114	107	2	-1	6	5	52	48	3	5	9	5	41	46	9	-18	1	6	88	94	11	5	3	6	36	12	6
6	3	5	200	195	7	0	6	5	138	135	2	6	9	5	54	55	8	-17	1	6	57	34	11	6	3	6	145	146	2
7	3	5	150	151	4	1	6	5	93	89	2	7	9	5	21	27	20	-16	1	6	44	33	8	7	3	6	78	74	5
8	3	5	157	163	3	2	6	5	65	58	4	8	9	5	174	166	5	-15	1	6	88	86	3	8	3	6	65	60	3
9	3	5	128	132	1	3	6	5	82	89	4	9	9	5	51	57	16	-14	1	6	86	84	2	9	3	6	38	43	7
10	3	5	35	57	21	4	6	5	19	7	14	-12	10	5	8	24	8	-13	1	6	39	30	15	10	3	6	48	42	6
11	3	5	28	25	14	5	6	5	103	103	4	-11	10	5	29	43	28	-12	1	6	97	103	2	11	3	6	25	12	24
12	3	5	34	28	16	6	6	5	35	15	26	-10	10	5	23	20	23	-11	1	6	58	46	3	12	3	6	53	59	52
13	3	5	63	45	29	7	6	5	151	157	12	-9	10	5	25	27	25	-10	1	6	73	70	2	13	3	6	62	11	37
14	3	5	54	37	16	8	6	5	34	37	8	-8	10	5	0	13	1	-9	1	6	44	27	5	-17	4	6	77	26	19
-17	4	5	102	98	15	9	6	5	69	71	5	-7	10	5	54	49	4	-8	1	6	149	142	2	-16	4	6	114	123	5
-16	4	5	162	160	9	10	6	5	40	35	14	-6	10	5	15	25	14	-7	1	6	96	85	4	-15	4	6	25	30	14
-15	4	5	64	32	9	11	6	5	69	65	8	-5	10	5	19	3	18	-6	1	6	82	85	2	-14	4	6	37	26	9
-14	4	5	20	4	20	12	6	5	26	21	26	-4	10	5	9	7	9	-5	1	6	111	103	2	-13	4	6	19	26	18
-13	4	5	31	24	5	-16	7	5	44	78	28	-3	10	5	124	124	3	-4	1	6	93	76	2	-12	4	6	12	18	11
-12	4	5	83	86	3	-15	7	5	37	23	36	-2	10	5	63	63	3	-3	1	6	271	260	2	-11	4	6	214	220	4
-11	4	5	12	3	12	-14	7	5	0	13	1	-1	10	5	206	201	3	-2	1	6	73	52	2	-10	4	6	84	88	5
-10	4	5	142	145	8	-13	7	5	49	40	7	0	10	5	45	34	7	-1	1	6	327	324	3	-9	4	6	234	223	3
-9	4	5	152	143	10	-12	7	5	74	63	4	1	10	5	119	118	5	0	1	6	42	38	5	-8	4	6	47	44	5
-8	4	5	68	58	4	-11	7	5	22	9	12	2	10	5	41	39	6	1	1	6	233	242	3	-7	4	6	119	121	5
-7	4	5	23	20	12	-10	7	5	41	53	4	3	10	5	23	5	23	2	1	6	128	117	2	-6	4	6	66	64	2
-6	4	5	277	271	2	-9	7	5	220	217	2	4	10	5	64	58	8	3	1	6	121	118	3	-5	4	6	137	140	4
-5	4	5	57	52	3	-8	7	5	74	92	2	5	10	5	0	9	1	4	1	6	236	235	6	-4	4	6	146	140	2
-4	4	5	168	176	1	-7	7	5	51	56	7	6	10	5	51	34	15	5	1	6	148	143	4	-3	4	6	38	22	6
-3	4	5	278	270	2	-6	7	5	101	106	8	7	10	5	113	102	6	6	1	6	94	82	4	-2	4	6	29	11	28
-2	4	5	36	44	3	-5	7	5	62	57	3	8	10	5	45	39	20	7	1	6	114	113	5	-1	4	6	249	251	2
-1	4	5	64	58	4	-4	7	5	107	110	6	-10	11	5	85	86	7	8	1	6	42	52	8	0	4	6	49	38	4
0	4	5	53	51	4	-3	7	5	55	36	11	-9	11	5	0	16	1	9	1	6	81	79	3	1	4	6	31	26	8
1	4	5	169	179	2	-2	7	5	170	164	4	-8	11	5	31	31	19	10	1	6	98	88	5	2	4	6	67	68	7
2	4	5	118	110	1	-1	7	5	71	70	2	-7	11	5	86	84	6	11	1	6	68	63	5	3	4	6	57	58	3
3	4	5	108	110	2	0	7	5	16	3	15	-6	11	5	65	67	4	12	1	6	107	112	6	4	4	6	133	129	2
4	4	5	34	7	33	1	7	5	87	78	7	-5	11	5	24	22	15	13	1	6	63	75	8	5	4	6	105	96	11
5	4	5	53	44	5	2	7	5	134	139	2	-4	11	5	0	23	1	-18	2	6	18	22	18	6	4	6	152	156	12
6	4	5	104	107	9	3	7	5	315	320	9	-3	11	5	74	57	74	-17	2	6	53	49	11	7	4	6	61	71	8
7	4	5	103	101	2	4	7	5	0	9	1	-2	11	5	28	51	28	-16	2	6	85	76	5	8	4	6	62	67	10
8	4	5	111	122	2	5	7	5	128	132	6	-1	11	5	32	7	31	-15	2	6	29	26	22	9	4	6	127	137	5
9	4	5	105	108	3	6	7	5	0	10	1	0	11	5	35	37	8	-14	2	6	74	72	13	10	4	6	18	7	18
10	4	5	67	73	4	7	7	5	0	42	1	1	11	5	23	14	23	-13	2	6	31	32	6	11	4	6	27	28	27
11	4	5	44	47	7	8	7	5	62	58	7	2	11	5	76	73	7	-12	2	6	53	59	3	12	4	6	84	84	6
12	4	5	87	85	7	9	7	5	40	18	12	3	11	5	29	41	29	-11	2	6	106	87	4	-17	5	6	84	101	11
13	4	5	80	75	6	10	7	5	42	63	16	4	11	5	63	29	11	-10	2	6	64	47	6	-16	5	6	13	13	13
-17	5	5	52	78	15	11	7	5	46	27	12	5	11	5	61	62	8	-9	2	6	49	46	4	-15	5	6	30	14	18
-16	5	5	36	49	35	-15	8	5	71	49	13	6	11	5	97	85	6	-8	2	6	50	35	3	-14	5	6	33	8	16
-15	5	5	64	72	6	-14	8	5	37	11	31	-8	12	5	0	20	1	-7	2	6	44	47	4	-13	5	6	122	124	2
-14	5	5	150	149	11	-13	8	5	91	86	9	-7	12	5	0	24	1	-6	2	6	99	99	2	-12	5	6	34	27	6
-13	5	5	145	148	14	-12	8	5	167	179	5	-6	12	5	22	25	21	-5	2	6	172	176	1	-11	5	6	79	71	4
-12	5	5	17	2	17	-11	8	5	18	13	17	-5	12	5	54	67	7	-4	2	6	74	64	4	-10	5	6	26	45	11
-11	5	5	111	117	7	-10	8	5	99	103	2	-4	12	5	24	20	23	-3	2	6	113	102	2	-9	5	6	152	150	2
-10	5	5	10	8	9	-9	8	5	0	1	1	-3	12	5	54	24	11	-2	2	6	90	74	6	-8	5	6	37	11	12
-9	5	5	30	2	30	-8	8	5	113	117	4	-2	12	5	22	17	22	-1	2	6	201	202	2	-7	5	6	71	67	3
-8	5	5	135	132	3	-7	8	5	78	93	3	-1	12	5	45	37	8	0	2	6	142	135	2	-6	5	6	51	45	7
-7	5	5	179	175	3	-6	8	5	87	93	3	0	12	5	32	21	20	1	2	6	70	69	4	-5	5	6	150	144	3

Table 3-8.12. Observed and calculated structure factors for 3-4.1a

h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s
-4	5	6	166	169	2	2	8	6	44	39	5	-7	1	7	62	63	3	-10	4	7	37	39	10	-5	7	7	164	170	9
-3	5	6	57	65	3	3	8	6	79	70	3	-6	1	7	48	27	10	-9	4	7	42	17	8	-4	7	7	152	155	7
-2	5	6	49	48	4	4	8	6	45	37	12	-5	1	7	177	177	2	-8	4	7	134	125	4	-3	7	7	97	103	8
-1	5	6	36	22	6	5	8	6	279	279	6	-4	1	7	64	61	3	-7	4	7	304	299	3	-2	7	7	193	196	8
0	5	6	253	244	2	6	8	6	158	156	5	-3	1	7	74	67	2	-6	4	7	155	153	8	-1	7	7	54	57	4
1	5	6	73	77	3	7	8	6	89	98	5	-2	1	7	150	150	2	-5	4	7	450	451	4	0	7	7	148	147	14
2	5	6	149	146	2	8	8	6	100	106	8	-1	1	7	276	269	5	-4	4	7	0	15	1	1	7	7	14	11	13
3	5	6	107	104	3	9	8	6	27	35	27	0	1	7	48	40	4	-3	4	7	197	191	2	2	7	7	372	390	22
4	5	6	77	67	6	-13	9	6	0	37	1	1	1	7	162	159	4	-2	4	7	172	171	3	3	7	7	210	229	19
5	5	6	22	9	10	-12	9	6	0	10	1	2	1	7	108	89	10	-1	4	7	108	111	5	4	7	7	70	71	12
6	5	6	197	212	9	-11	9	6	36	22	13	3	1	7	9	1	8	0	4	7	151	154	7	5	7	7	67	60	12
7	5	6	73	70	5	-10	9	6	34	32	9	4	1	7	27	8	12	1	4	7	96	103	4	6	7	7	71	80	7
8	5	6	65	52	11	-9	9	6	35	36	8	5	1	7	445	429	11	2	4	7	200	198	3	7	7	7	130	131	6
9	5	6	33	18	14	-8	9	6	74	76	4	6	1	7	0	29	1	3	4	7	71	73	8	8	7	7	19	2	18
10	5	6	90	89	5	-7	9	6	49	44	4	7	1	7	67	64	6	4	4	7	52	67	4	9	7	7	32	20	31
11	5	6	75	75	12	-6	9	6	43	39	5	8	1	7	71	67	10	5	4	7	65	58	14	-13	8	7	58	30	19
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-13	6	6	47	31	8	-1	9	6	52	44	4	-18	2	7	78	81	12	10	4	7	36	43	24	-8	8	7	0	10	1
-12	6	6	72	61	3	0	9	6	49	50	5	-17	2	7	24	27	24	11	4	7	18	27	17	-7	8	7	0	16	1
-11	6	6	79	82	2	1	9	6	32	37	8	-16	2	7	62	57	7	-16	5	7	64	24	26	-6	8	7	68	69	6
-10	6	6	68	72	13	2	9	6	15	10	14	-15	2	7	158	166	3	-15	5	7	52	36	13	-5	8	7	0	5	1
-9	6	6	57	59	3	3	9	6	81	92	6	-14	2	7	76	83	4	-14	5	7	50	54	50	-4	8	7	102	99	6
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11	6	6	0	43	1	2	10	6	0	12	1	6	2	7	169	166	3	6	5	7	0	21	1	-6	9	7	99	103	4
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-13	7	6	65	62	5	5	10	6	54	47	11	9	2	7	23	0	22	9	5	7	23	16	23	-3	9	7	26	17	26
-12	7	6	30	21	11	6	10	6	59	50	13	10	2	7	15	14	14	10	5	7	38	15	18	-2	9	7	39	55	24
-11	7	6	41	38	6	7	10	6	55	63	13	11	2	7	0	4	1	11	5	7	39	25	22	-1	9	7	39	6	30
-10	7	6	106	108	3	-10	11	6	62	63	10	12	2	7	107	86	9	-16	6	7	52	1	13	0	9	7	21	15	21
-9	7	6	100	94	3	-9	11	6	58	43	8	-17	3	7	57	51	12	-15	6	7	6	10	6	1	9	7	45	54	11
-8	7	6	91	87	3	-8	11	6	36	36	12	-16	3	7	41	23	12	-14	6	7	31	15	14	2	9	7	92	91	8
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-13	8	6	33	52	33	-1	12	6	60	71	9	4	3	7	233	235	6	6	6	7	0	6	1	3	10	7	64	60	12
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-9	8	6	95	103	3	-18	1	7	40	0	21	8	3	7	35	34	11	10	6	7	62	26	16	-8	11	7	97	93	6
-8	8	6	29	32	6	-17	1	7	107	116	7	9	3	7	59	32	8	-15	7	7	103	87	10	-7	11	7	10	10	10
-7	8	6	54	51	13	-16	1	7	80	89	5	10	3	7	71	52	12	-14	7	7	22	30	22	-6	11	7	23	30	23
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-3	8	6	170	174	2	-12	1	7	46	59	5	-15	4	7	25	19	13	-10	7	7	117	125	3	-2	11	7	52	11	15
-2	8	6	84	85	3	-11	1	7	54	47	5	-14	4	7	37	6	7	-9	7	7	47	45	5	-1	11	7	86	95	10
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0	8	6	42	45	7	-9	1	7	36	35	4	-12	4	7	97	79	3	-7	7	7	68	75	7	1	11	7	10	14	10
1	8	6	114	123	11	-8	1	7	21	21	20	-11	4	7	73	83	3	-6	7	7	50	54	4	2	11	7	0	0	1

Table 3-8.12. Observed and calculated structure factors for 3-4.1a

h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s
3	11	7	43	23	18	11	2	8	82	68	7	-10	6	8	34	12	9	-5	10	8	62	73	8	1	3	9	42	15	8
-4	12	7	70	75	12	-17	3	8	0	24	1	-9	6	8	87	90	3	-4	10	8	16	30	15	2	3	9	252	253	4
-3	12	7	55	9	18	-16	3	8	33	9	33	-8	6	8	35	10	9	-3	10	8	37	30	14	3	3	9	48	50	8
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-17	0	8	78	92	8	-14	3	8	153	159	2	-6	6	8	42	32	7	-1	10	8	0	27	1	5	3	9	0	5	1
-16	0	8	54	54	20	-13	3	8	38	34	12	-5	6	8	49	64	18	0	10	8	71	22	15	6	3	9	83	95	7
-15	0	8	8	16	8	-12	3	8	0	6	1	-4	6	8	45	38	19	1	10	8	0	10	1	7	3	9	0	11	1
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-13	0	8	46	51	8	-10	3	8	320	320	4	-2	6	8	74	75	3	3	10	8	43	27	34	9	3	9	88	81	12
-12	0	8	101	122	5	-9	3	8	0	15	1	-1	6	8	128	134	8	-7	11	8	0	4	1	-16	4	9	38	16	14
-11	0	8	62	46	8	-8	3	8	244	238	3	0	6	8	142	145	12	-6	11	8	0	20	1	-15	4	9	26	12	26
-10	0	8	120	124	4	-7	3	8	87	76	3	1	6	8	34	42	8	-5	11	8	82	81	7	-14	4	9	61	53	7
-9	0	8	25	25	16	-6	3	8	37	32	7	2	6	8	114	127	17	-4	11	8	75	6	15	-13	4	9	25	28	24
-8	0	8	86	76	4	-5	3	8	9	19	9	3	6	8	107	115	5	-3	11	8	33	19	33	-12	4	9	0	26	1
-7	0	8	56	55	9	-4	3	8	0	2	1	4	6	8	43	9	43	-2	11	8	70	69	21	-11	4	9	57	58	7
-6	0	8	269	257	3	-3	3	8	243	240	3	5	6	8	62	68	12	-1	11	8	41	63	30	-10	4	9	82	71	5
-5	0	8	115	119	3	-2	3	8	174	176	5	6	6	8	61	53	13	0	11	8	52	45	17	-9	4	9	104	109	3
-4	0	8	76	61	4	-1	3	8	176	180	4	7	6	8	45	16	20	-17	1	9	74	81	19	-8	4	9	169	174	9
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1	0	8	124	120	3	4	3	8	36	45	8	-12	7	8	33	31	19	-12	1	9	39	44	14	-3	4	9	13	2	13
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6	0	8	106	110	4	9	3	8	0	0	1	-7	7	8	130	124	3	-7	1	9	67	75	4	2	4	9	51	63	13
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8	0	8	279	273	5	-17	4	8	20	26	20	-5	7	8	125	139	3	-5	1	9	60	41	5	4	4	9	116	117	11
9	0	8	308	286	9	-16	4	8	87	74	8	-4	7	8	99	93	11	-4	1	9	43	23	17	5	4	9	42	37	11
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-10	1	8	2	5	1	-7	4	8	101	102	3	5	7	8	0	34	1	5	1	9	90	82	4	-10	5	9	141	141	3
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-2	1	8	0	5	1	1	4	8	112	123	7	-9	8	8	30	32	11	-13	2	9	150	157	4	-2	5	9	85	89	3
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2	1	8	88	73	5	5	4	8	174	192	13	-5	8	8	0	12	1	-9	2	9	127	125	2	2	5	9	108	109	6
3	1	8	302	292	4	6	4	8	74	59	5	-4	8	8	68	73	4	-8	2	9	192	193	3	3	5	9	27	0	26
4	1	8	217	212	4	8	4	8	0	20	1	-3	8	8	47	43	31	-7	2	9	275	275	3	4	5	9	102	107	5
5	1	8	21	2	20	9	4	8	65	10	34	-2	8	8	146	143	3	-6	2	9	100	94	5	5	5	9	60	62	10
6	1	8	100	103	4	10	4	8	63	75	14	-1	8	8	63	76	7	-5	2	9	115	114	10	6	5	9	87	66	10
7	1	8	67	63	9	-16	5	8	59	30	16	0	8	8	42	24	10	-4	2	9	66	65	3	7	5	9	91	70	11
8	1	8	132	129	10	-15	5	8	41	10	12	1	8	8	87	85	11	-3	2	9	171	170	3	8	5	9	83	63	12
9	1	8	65	64	9	-14	5	8	49	18	11	2	8	8	0	31	1	-2	2	9	84	92	3	-15	6	9	70	77	17
11	1	8	74	62	8	-13	5	8	54	46	11	3	8	8	19	35	18	-1	2	9	63	51	7	-14	6	9	98	104	7
-17	2	8	34	18	34	-12	5	8	33	13	10	4	8	8	39	54	28	0	2	9	220	224	4	-13	6	9	8	17	8
-16	2	8	33	37	19	-11	5	8	150	151	3	5	8	8	84	85	12	1	2	9	54	48	8	-12	6	9	39	55	18
-15	2	8	152	162	9	-10	5	8	109	113	3	6	8	8	42	26	41	2	2	9	0	17	1	-11	6	9	108	111	5
-14	2	8	48	50	7	-9	5	8	16	6	15	7	8	8	26	26	26	3	2	9	24	3	23	-10	6	9	142	138	4
-13	2	8	24	47	12	-8	5	8	141	137	5	-12	9	8	22	7	22	4	2	9	106	106	8	-9	6	9	58	74	6
-12	2	8	80	73	3	-7	5	8	0	13	1	-11	9	8	33	27	16	5	2	9	63	60	6	-8	6	9	41	18	12
-11	2	8	99	96	2	-6	5	8	213	215	5	-10	9	8	0	7	1	6	2	9	46	29	21	-7	6	9	30	25	14
-10	2	8	40	44	11	-5	5	8	0	17	1	-9	9	8	36	38	16	7	2	9	39	42	19	-6	6	9	0	11	1
-9	2	8	111	111	6	-4	5	8	242	239	7	-8	9	8	0	14	1	8	2	9	60	38	15	-5	6	9	83	88	5
-8	2	8	54	27	4	-3	5	8	104	110	2	-7	9	8	153	137	3	9	2	9	72	55	19	-4	6	9	27	32	13
-7	2	8	97	95	2	-2	5	8	225	222	5	-6	9	8	42	24	10	-16	3	9	34	28	33	-3	6	9	23	28	22
-6	2	8	0	22	1	-1	5	8	192	202	9	-5	9	8	81	88	5	-15	3	9	44	39	31	-2	6	9	70	70	14
-5	2	8	73	75	3	0	5	8	34	36	10	-4	9	8	15	19	14	-14	3	9	26	2	26	-1	6	9	141	141	8
-4	2	8	100	99	3	1	5	8	21	19	20	-3	9	8	55	20	55	-13	3	9	128	128	9	0	6	9	56	39	7
-3	2	8	114	119	2	2	5	8	12	1	11	-2	9	8	37	17	9	-12	3	9	101	99	3	1	6	9	88	67	6
-2	2	8	281	278	3	3	5	8	29	18	29	-1	9	8	42	38	8	-11	3	9	31	17	10	2	6	9	56	76	17
-1	2	8	155	148	3	4	5	8	27	15	26	0	9	8	73	72	7	-10	3	9	40	25	17	3	6	9	43	41	43
0	2	8	56	60	15	5	5	8	35	17	35	1	9	8	82	69	10	-9	3	9	38	45	8	4	6	9	91	88	13
1	2	8	112	106	3	6	5	8	52	32	15	2	9	8	127	118	7	-8	3	9	186	177	8	5	6	9	56	26	16
2	2	8	251	249	3	7	5	8	17	50	16	3	9	8	15	7	14	-7	3	9	110	105	3	6	6	9	57	1	27
3	2	8	273	272	4	8	5	8	39	12	24	4	9	8	43	9	26	-6	3	9	73	73	4	7	6	9	29	28	28
4	2	8	95	97	5	9	5	8	49	71	23	5	9	8	43	37	43	-5	3	9	109	112	2	-14	7	9	65	61	11
5	2	8	0	3	1	-15	6	8	82	82	25	-10	10	8	31	47	31	-4	3	9	27	28	27	-13	7	9	41	51	13
6	2	8	71	78	9	-14	6	8	10	13	10	-9	10	8	42	37	15	-3	3	9	85	87	3	-12	7	9	62	73	12
7	2	8	134	132	13	-13	6	8	21	22	20	-8	10	8	34	9	23	-2	3	9	131	136	3	-11	7	9	115	108	6
8	2	8	0	5	1	-12	6	8	64	71	5	-7	10	8	40	51	14	-1	3	9	206	193	5	-10	7	9	40	44	8
9	2	8	0	15	1	-11	6	8	56	41	6	-6	10	8	26	31	26	0	3	9	127	127	4	-9	7	9	34	19	12

Table 3-8.12. Observed and calculated structure factors for 3-4.1a

h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s
-8	7	9	0	14	1	-10	1	10	51	56	7	5	4	10	0	12	1	-12	1	11	180	187	9	-6	5	11	57	54	7
-7	7	9	30	30	18	-9	1	10	112	119	3	6	4	10	116	98	12	-11	1	11	31	18	11	-5	5	11	69	58	7
-6	7	9	113	117	4	-8	1	10	308	313	4	7	4	10	0	14	1	-10	1	11	78	82	5	-4	5	11	46	41	11
-5	7	9	13	12	13	-7	1	10	136	134	2	-14	5	10	0	43	1	-9	1	11	39	17	11	-3	5	11	28	23	28
-4	7	9	0	16	1	-6	1	10	90	74	4	-13	5	10	52	46	12	-8	1	11	85	91	4	-2	5	11	62	71	10
-3	7	9	40	39	30	-5	1	10	84	92	4	-12	5	10	86	91	6	-7	1	11	46	52	9	-1	5	11	6	33	6
-2	7	9	65	54	5	-4	1	10	131	131	4	-11	5	10	65	71	7	-6	1	11	48	45	13	0	5	11	107	109	10
-1	7	9	35	26	25	-3	1	10	0	39	1	-10	5	10	24	23	23	-5	1	11	64	65	9	1	5	11	32	21	31
0	7	9	59	60	32	-2	1	10	186	193	3	-9	5	10	233	215	5	-4	1	11	104	104	6	2	5	11	80	70	10
1	7	9	0	24	1	-1	1	10	33	17	10	-8	5	10	0	11	1	-3	1	11	94	97	6	3	5	11	27	17	26
2	7	9	72	78	11	0	1	10	125	125	3	-7	5	10	119	127	5	-2	1	11	47	52	47	4	5	11	8	28	8
3	7	9	54	55	18	1	1	10	86	86	3	-6	5	10	80	75	4	-1	1	11	89	63	89	-12	6	11	74	69	10
4	7	9	0	53	1	2	1	10	52	35	7	-5	5	10	64	54	7	0	1	11	47	44	10	-11	6	11	118	99	7
5	7	9	56	37	15	3	1	10	93	83	7	-4	5	10	45	44	9	1	1	11	83	91	8	-10	6	11	66	70	9
6	7	9	30	16	30	4	1	10	17	10	16	-3	5	10	33	33	17	2	1	11	39	26	29	-9	6	11	37	41	28
-12	8	9	0	46	1	5	1	10	25	30	24	-2	5	10	91	99	6	3	1	11	76	60	8	-8	6	11	0	13	1
-11	8	9	56	60	7	6	1	10	33	11	32	-1	5	10	167	168	14	4	1	11	0	8	1	-7	6	11	63	38	9
-10	8	9	117	97	5	7	1	10	20	24	19	0	5	10	21	7	20	5	1	11	0	22	1	-6	6	11	38	43	11
-9	8	9	30	41	30	-16	2	10	57	66	9	1	5	10	38	34	16	-15	2	11	47	46	31	-5	6	11	15	13	14
-8	8	9	70	72	6	-15	2	10	28	5	28	2	5	10	33	3	16	-14	2	11	42	14	41	-4	6	11	140	131	5
-7	8	9	26	19	26	-14	2	10	21	15	21	3	5	10	110	103	11	-13	2	11	104	106	5	-3	6	11	43	2	12
-6	8	9	24	26	23	-13	2	10	62	63	6	4	5	10	64	53	12	-12	2	11	43	20	10	-2	6	11	27	27	26
-5	8	9	79	76	5	-12	2	10	27	23	17	5	5	10	59	6	15	-11	2	11	32	48	31	-1	6	11	24	28	23
-4	8	9	6	0	6	-11	2	10	162	158	4	6	5	10	45	31	39	-10	2	11	74	86	5	0	6	11	121	123	11
-3	8	9	55	48	10	-10	2	10	90	83	4	-14	6	10	97	73	8	-9	2	11	105	113	4	1	6	11	116	97	8
-2	8	9	45	15	45	-9	2	10	40	9	11	-13	6	10	60	46	9	-8	2	11	114	125	4	2	6	11	0	5	1
-1	8	9	60	66	8	-8	2	10	22	4	22	-12	6	10	61	66	10	-7	2	11	18	27	17	3	6	11	0	4	1
0	8	9	38	39	14	-7	2	10	74	75	4	-11	6	10	84	88	8	-6	2	11	27	16	27	-11	7	11	56	49	10
1	8	9	38	75	37	-6	2	10	45	24	24	-10	6	10	93	104	5	-5	2	11	30	40	29	-10	7	11	24	13	23
2	8	9	0	6	1	-5	2	10	84	93	4	-9	6	10	0	3	1	-4	2	11	16	20	15	-9	7	11	20	31	19
3	8	9	29	0	28	-4	2	10	0	0	1	-8	6	10	69	66	7	-3	2	11	183	184	8	-8	7	11	66	67	9
4	8	9	74	47	17	-3	2	10	72	80	5	-7	6	10	31	0	19	-2	2	11	74	64	7	-7	7	11	31	50	31
5	8	9	46	20	28	-2	2	10	43	49	32	-6	6	10	46	39	9	-1	2	11	82	92	7	-6	7	11	0	11	1
-11	9	9	32	47	11	-1	2	10	183	190	3	-5	6	10	80	83	5	0	2	11	21	15	20	-5	7	11	0	19	1
-10	9	9	35	11	19	0	2	10	132	135	4	-4	6	10	25	36	25	1	2	11	63	66	13	-4	7	11	83	69	13
-9	9	9	98	105	6	1	2	10	16	35	15	-3	6	10	50	57	8	2	2	11	26	2	25	-3	7	11	59	40	15
-8	9	9	24	28	23	2	2	10	79	84	9	-2	6	10	40	12	14	3	2	11	47	9	15	-2	7	11	52	1	19
-7	9	9	61	67	7	3	2	10	55	46	10	-1	6	10	77	74	5	4	2	11	46	10	14	-1	7	11	94	68	16
-6	9	9	23	10	23	4	2	10	30	31	18	0	6	10	84	89	5	5	2	11	0	26	1	0	7	11	0	19	1
-5	9	9	87	80	6	5	2	10	56	61	7	1	6	10	0	17	1	6	2	11	62	73	13	1	7	11	0	18	1
-4	9	9	0	4	1	6	2	10	41	26	23	2	6	10	118	97	9	-14	3	11	26	36	25	-8	8	11	40	29	40
-3	9	9	80	73	6	7	2	10	44	15	18	3	6	10	43	12	32	-13	3	11	57	54	8	-7	8	11	29	4	28
-2	9	9	69	66	7	8	2	10	0	16	1	4	6	10	96	85	10	-12	3	11	74	64	8	-6	8	11	92	80	7
-1	9	9	62	47	16	-16	3	10	49	32	13	5	6	10	0	1	1	-11	3	11	29	13	28	-5	8	11	83	71	7
0	9	9	76	35	16	-15	3	10	0	19	1	-12	7	10	32	22	19	-10	3	11	48	50	10	-4	8	11	0	24	1
1	9	9	91	100	11	-14	3	10	45	44	9	-11	7	10	66	65	10	-9	3	11	41	42	14	-3	8	11	0	32	1
2	9	9	84	78	13	-13	3	10	36	37	17	-10	7	10	100	105	6	-8	3	11	16	6	15	-2	8	11	36	39	36
3	9	9	61	20	14	-12	3	10	21	21	20	-9	7	10	66	57	9	-7	3	11	51	36	11	-1	8	11	52	37	19
-8	10	9	136	141	7	-11	3	10	0	37	1	-8	7	10	23	15	23	-6	3	11	40	9	16	-14	0	12	65	52	11
-7	10	9	38	43	15	-10	3	10	72	73	6	-7	7	10	35	1	15	-5	3	11	0	1	1	-13	0	12	82	50	17
-6	10	9	59	62	9	-9	3	10	76	79	5	-6	7	10	29	27	12	-4	3	11	15	18	14	-12	0	12	25	5	24
-5	10	9	67	78	7	-8	3	10	46	38	10	-5	7	10	0	11	1	-3	3	11	47	63	12	-11	0	12	48	56	15
-4	10	9	46	37	14	-7	3	10	112	108	4	-4	7	10	0	11	1	-2	3	11	35	8	35	-10	0	12	111	132	9
-3	10	9	60	66	8	-6	3	10	84	86	5	-3	7	10	52	18	8	-1	3	11	35	1	27	-9	0	12	188	201	11
-2	10	9	85	72	11	-5	3	10	73	62	5	-2	7	10	87	82	13	0	3	11	87	83	11	-8	0	12	44	32	26
-1	10	9	41	49	28	-4	3	10	76	69	7	-1	7	10	34	16	16	1	3	11	24	31	23	-7	0	12	44	62	25
0	10	9	0	14	1	-3	3	10	79	86	5	0	7	10	51	24	8	2	3	11	131	135	5	-6	0	12	87	96	11
-16	0	10	38	54	37	-2	3	10	154	155	7	1	7	10	58	52	22	3	3	11	18	18	18	-5	0	12	97	78	10
-15	0	10	73	21	17	-1	3	10	126	119	5	2	7	10	71	53	12	4	3	11	54	67	11	-4	0	12	70	56	12
-14	0	10	113	111	6	0	3	10	141	141	4	3	7	10	0	42	1	5	3	11	0	16	1	-3	0	12	60	44	20
-13	0	10	22	6	22	1	3	10	206	214	13	4	7	10	0	0	1	-14	4	11	62	33	9	-2	0	12	0	10	1
-12	0	10	67	88	10	2	3	10	0	21	1	-11	8	10	0	11	1	-13	4	11	64	71	9	-1	0	12	56	42	14
-11	0	10	30	17	29	3	3	10	52	50	10	-10	8	10	85	82	7	-12	4	11	76	72	7	0	0	12	52	67	17
-10	0	10	0	59	1	4	3	10	40	30	10	-9	8	10	118	114	7	-11	4	11	108	110	7	1	0	12	0	16	1
-9	0	10	258	259	6	5	3	10	71	68	15	-8	8	10	12	43	11	-10	4	11	29	2	23	2	0	12	70	59	17
-8	0	10	0	21	1	6	3	10	63	50	15	-7	8	10	49	19	16	-9	4	11	67	63	7	3	0	12	54	47	16
-7	0	10	111	118	4	7	3	10	45	39	44	-6	8	10	47	50	11	-8	4	11	58	64	7	4	0	12	30	4	29
-6	0	10	156	160	3	-15	4	10	18	2	17	-5	8	10	35	17	22	-7	4	11	12	10	11	-14	1	12	29	40	29
-5	0	10	48	47	22	-14	4	10	43	1	12	-4	8	10	46	19	11	-6	4	11	61	59	7	-13	1	12	10	9	10
-4	0	10	59	64	10	-13	4	10	0	6	1	-3	8	10	0	12	1	-5	4	11	0	18	1	-12	1	12	42	37	10
-3	0	10	143	143	5	-12	4	10	33	30	14	-2	8	10	0	10	1	-4	4	11	13	11	13	-11	1	12	0	22	1
-2	0	10	68	64	6	-11	4	10	95	87	7	-1	8	10	85	57	16	-3	4	11	32	9	15	-10	1	12	153	154	6
-1	0	10	0	2	1	-10	4	10	85	93	5	0	8	10	37	39	36	-2	4	11	100	105	10	-9	1	12	10	31	10
0	0	10	54	65	9	-9	4	10	39	23	11	1	8	10	45	37	28	-1	4	11	108	123	6	-8	1	12	97	96	9
1	0	10	162	155	5	-8	4	10	34	52	14	2	8	10	10	33	10	0	4	11	50	10	14	-7	1	12	0	14	1
2	0	10	62	64	6	-7	4	10	155	154	4	-8	9	10	88	85	8	1	4	11	79	83	7	-6	1	12	67	38	19
3	0	10	106	93	6	-6	4	10	78	74	5	-7	9	10	67	51	8	2	4	11	46	40	20	-5	1	12	33	0	33
4	0	10	90	83	5	-5	4	10	41	33	19	-6	9	10	77	63	9	3	4	11	43	34	42	-4	1	12	126	132	6
5	0	10	117	103	11	-4	4	10	87	87	10	-5	9	10	40	26	14	4	4	11	45	25	20	-3	1	12	72	81	7
6	0	10	55	51	20	-3	4	10	114	113	5	-4	9	10	58	49	11	5	4	11	65	18	16	-2	1	12	43	0	42
7	0	10	32	37	31	-2	4	10	110	118	8	-3	9	10	33	32	32	-13	5	11	13	21	13	-1	1	12	21	13	20
-16	1	10	64	65	33	-1	4	10	30	10	23	-2	9	10	56	30	19	-12	5	11	92	82	8	0	1	12	30	16	29
-15	1	10	22	5	21	0	4	10	78	72	18	-1	9	10	69	49	15	-11	5	11	61	44	10	1	1	12	34	3	33
-14	1	10	66	78	16	1	4	10	40	20	35	0	9	10	71	80	12	-10	5	11	25	7	25	2	1	12	13	17	13
-13	1	10	61	63	6	2	4	10	47	62	8	-15	1	11	38	6	22	-9	5	11	191	188	6	3	1	12	73	45	13
-12	1	10	61	65	7	3	4	10	29	15	29	-14	1	11	38	35	14	-8	5	11	35	6	14	4	1	12	29	23	29
-11	1	10	23	20	23	4	4	10	51	28	14	-13	1	11	56	71	29	-7	5	11	23	7	23	-13	2	12	75	65	15

Table 3-8.12. Observed and calculated structure factors for 3-4.1a

h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s	h	k	l	10Fo	10Fc	10s
-12	2	12	32	31	31	-3	3	12	63	59	19	-7	5	12	0	5	1	-11	1	13	29	40	29	-9	3	13	46	9	27
-11	2	12	123	135	7	-2	3	12	87	72	11	-6	5	12	44	11	18	-10	1	13	27	51	27	-8	3	13	22	23	22
-10	2	12	23	23	23	-1	3	12	0	0	1	-5	5	12	54	30	23	-9	1	13	44	31	15	-7	3	13	0	14	1
-9	2	12	68	66	7	0	3	12	28	15	27	-4	5	12	86	86	15	-8	1	13	74	11	25	-6	3	13	82	50	10
-8	2	12	29	10	28	1	3	12	0	7	1	-3	5	12	0	33	1	-7	1	13	32	14	31	-5	3	13	53	47	32
-7	2	12	53	1	14	2	3	12	74	81	12	-2	5	12	0	21	1	-6	1	13	37	45	29	-4	3	13	59	43	16
-6	2	12	49	35	14	3	3	12	33	10	33	-1	5	12	44	14	16	-5	1	13	19	31	18	-3	3	13	0	14	1
-5	2	12	82	71	8	-12	4	12	0	5	1	0	5	12	0	6	1	-4	1	13	34	67	34	-2	3	13	36	25	28
-4	2	12	59	46	16	-11	4	12	0	8	1	1	5	12	0	23	1	-3	1	13	33	12	32	-1	3	13	27	56	26
-3	2	12	122	123	5	-10	4	12	89	91	7	-10	6	12	0	20	1	-2	1	13	81	52	13	0	3	13	35	30	35
-2	2	12	20	34	19	-9	4	12	0	13	1	-9	6	12	30	28	30	-1	1	13	49	30	15	-9	4	13	47	32	16
-1	2	12	63	66	10	-8	4	12	78	46	8	-8	6	12	22	0	21	0	1	13	0	8	1	-8	4	13	34	47	34
0	2	12	43	20	16	-7	4	12	45	53	12	-7	6	12	0	16	1	1	1	13	0	8	1	-7	4	13	50	26	20
1	2	12	52	51	12	-6	4	12	40	34	22	-6	6	12	61	42	12	-11	2	13	0	2	1	-5	4	13	35	5	34
2	2	12	16	39	15	-5	4	12	81	79	7	-5	6	12	0	2	1	-10	2	13	35	56	34	-4	4	13	29	17	28
3	2	12	0	32	1	-4	4	12	0	4	1	-4	6	12	33	6	32	-9	2	13	73	67	15	-3	4	13	50	42	15
-13	3	12	0	0	1	-3	4	12	17	21	16	-3	6	12	37	45	23	-8	2	13	58	16	20	-2	4	13	74	60	9
-12	3	12	62	60	13	-2	4	12	40	69	40	-2	6	12	38	37	38	-7	2	13	64	58	15	-7	5	13	0	22	1
-11	3	12	0	3	1	-1	4	12	42	36	16	-1	6	12	43	57	30	-6	2	13	56	64	16	-6	5	13	58	24	20
-10	3	12	78	64	8	0	4	12	0	10	1	0	6	12	39	2	39	-5	2	13	98	94	8	-5	5	13	51	12	44
-9	3	12	0	9	1	1	4	12	81	79	11	-7	7	12	89	87	8	-4	2	13	40	23	15	-4	5	13	58	67	18
-8	3	12	83	91	7	2	4	12	41	22	40	-6	7	12	33	29	33	-3	2	13	65	6	27	-6	0	14	8	34	8
-7	3	12	27	15	27	-11	5	12	37	43	26	-5	7	12	0	13	1	-2	2	13	52	47	21						
-6	3	12	49	56	13	-10	5	12	34	11	33	-4	7	12	0	4	1	-1	2	13	22	16	22						
-5	3	12	0	15	1	-9	5	12	52	21	11	-3	7	12	137	120	10	0	2	13	50	11	14						
-4	3	12	111	96	9	-8	5	12	46	34	12	-12	1	13	32	12	32	-10	3	13	32	28	32						

Chapter 4. Tandem Catalytic Reactions Enabled by the Nucleophilic Activation of Enones via Organocatalysis

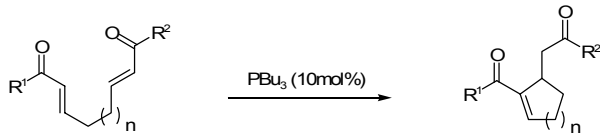
Part 1. Respective Contributions

The phosphine-catalyzed Michael cycloisomerization was developed by the author in partnership with Dr. Long-Cheng Wang, Kyriacos Agapiou and Dr. Hye-Young Jang. Studies to expand the scope by including vinyl sulfones as reacting partners were performed by the author.

Part 2. Tertiary Phosphine-Catalyzed Michael Cycloisomerization

As demonstrated by the Morita-Baylis-Hillman and Rauhut Currier reactions, tertiary amines and phosphines may also serve as efficient catalysts for the nucleophilic activation of enones. While the intermolecular Rauhut Currier reaction is well-known, related catalytic intramolecular condensations were undescribed until recently. In 2001, an intramolecular variant of the Rauhut-Currier reaction was simultaneously developed by Krische and Roush.[1] Trialkylphosphines turned out to be far better catalysts than triarylphosphines and amines for this intramolecular variant. The kinetic bias in favor of intramolecular addition suppresses polymerization, a common problem in the intermolecular process. In studies done by Krische, bis-enones afforded five- and six-membered ring adducts in high yield over short reaction times using 10 mol% PBu_3 (Scheme 4-2.1).

Scheme 4-2.1

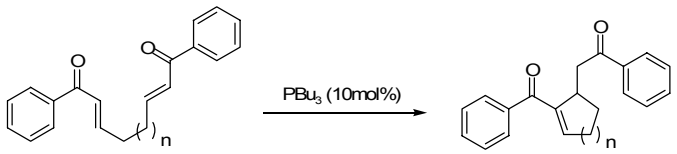


Initial studies focused on finding optimal conditions for the catalytic cycloisomerization of substrate **3-3.2**. The tertiary amines DABCO, DMAP and piperidine were first assayed in benzene-d_6 at ambient temperature by placing **3-3.2** and 30 mol % of the corresponding amine in three NMR tubes. The reactions were not complete after 24 hours, but judging from disappearance of starting material, DMAP was identified as the best

of the amine catalysts. Next, the efficiency of DMAP was compared to that of PBu_3. Numerous experiments varying the catalyst (10 mol%) were conducted in $CDCl_3$, d^6-acetone and d^6-DMSO and analyzed by ^1H NMR. Through this preliminary screen, tributylphosphine was identified as the catalyst of choice. Reactions employing DMAP as catalyst were sluggish in all solvents, resulting in very low conversions to the desired product. The use of PBu_3 resulted in much faster reactions. Additionally, a dramatic increase in reaction rate with increasing solvent polarity was observed for these reactions.

The reaction of **3-3.2** using 10 mol% PBu_3 in DMSO (0.1M) was complete in less than 5 minutes but gave substantial quantities of oligomerized products, and consequently, a poor yield of the corresponding Michael cycloisomerization adduct (Table 4-2.1). Oligomerization was suppressed in a less polar medium. Exposing **3-3.2** to 10 mol% PBu_3 in acetone (0.1M) at room temperature for 2 hours afforded cyclization product **4-2.3a** in 82% yield. Five-membered ring formations occur at much faster rates than six-membered ring formations, as exemplified by the faster cyclization of **3-3.1** (1 h). It was reasoned that the rather low yield obtained was due to competitive oligomerization in acetone. This prompted the use of a less polar solvent, ethyl acetate, which improved the yield of **4-2.1a**. However, a higher temperature of 50ºC was required to obtain an acceptable reaction time (5 h).

Table 4-2.1



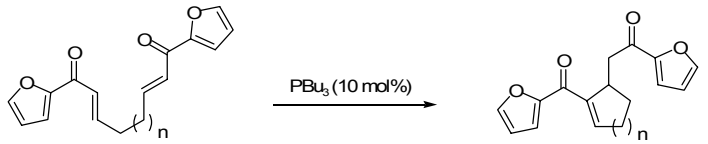
3-3.1, n=1
3-3.2, n=2

4-2.1a
4-2.3a

Substrate	Solvent	Temperature (ºC)	Time	Yield (%)
3-3.1	Acetone	25	1 h	62
3-3.1	Ethyl acetate	50	5 h	86
3-3.2	DMSO	25	< 5 min	5
3-3.2	Acetone	25	2 h	82

For substrate **3-3.2**, acetone proved to be the most effective medium at ambient temperature. Exposure of furyl-substituted bis-enone **3-3.6** to these conditions afforded Michael cycloisomerization adduct **4-2.8a** in a low 40% yield (Table 4-2.2). Conducting the reaction in ethyl acetate at 50ºC increased the yield to 90%. For highly electrophilic substrates, a less polar medium like ethyl acetate promoted cleaner conversions. As expected, the homologous substrate **4-2.2** underwent cycloisomerization smoothly in ethyl acetate.

Table 4-2.2



4-2.2, n=1
3-3.6, n=2

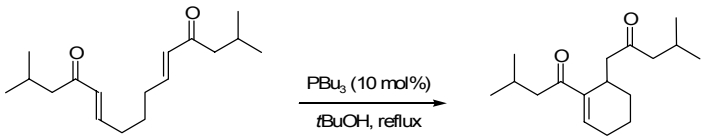
4-2.2a
4-2.10a

Substrate	Solvent	Temperature (ºC)	Time	Yield (%)
4-2.2	Ethyl acetate	40	1 h	95
3-3.6	Acetone	25	45 min	40
3-3.6	Ethyl acetate	50	5 h	90

Under these optimized conditions, other aroyl- and heteroaroyl-containing bis(enones) underwent cycloisomerization in good to excellent yields (Table 4-2.3, entries 2-4). This methodology tolerates substrates having heteroatoms in the tether such as bis-enones **3-3.3** and **3-4.3**.

Aliphatic bis-enones were also viable substrates (Table 4-4.3, entry 5). However, because of their reduced electrophilicity, more forcing conditions were needed to induce cycloisomerization. Exposure of isovaleryl-containing bis-enone **4-2.12** to 10 mol% PBu_3 in refluxing *tert*-butanol for 12 hours afforded a 70% yield of product (Scheme 4-2.2).

Scheme 4-2.2

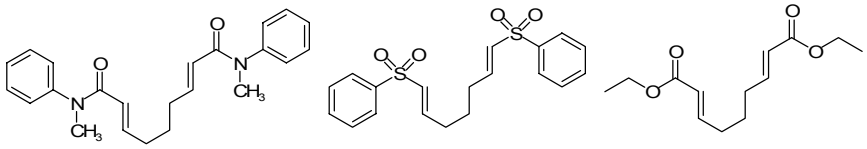


4-2.12

4-2.12a, 70%

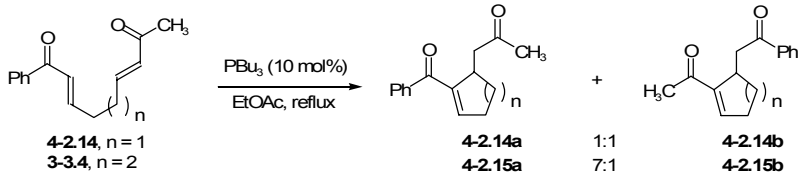
Less electrophilic bis-enones do not undergo Michael cycloisomerization (Figure 4-4.1). These substrates fail to react in refluxing acetone and even refluxing DMSO. Mixed bis-enones incorporating enoate moieties are viable substrates though (Table 4-4.3, entry 8).

Figure 4-4.1



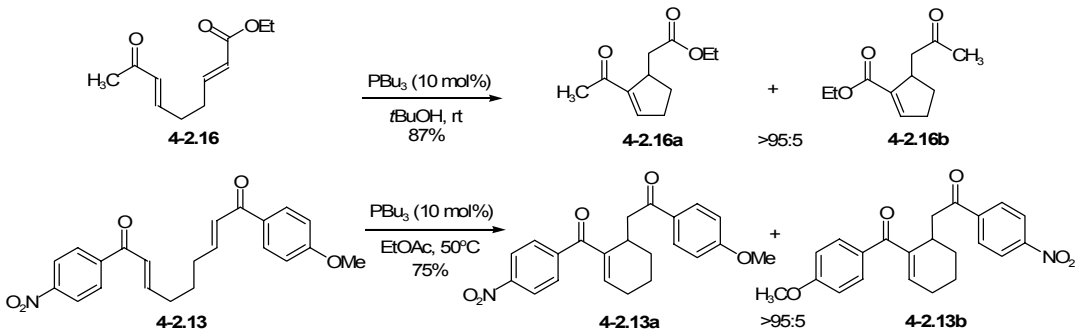
Chemoselective cross-Michael cycloisomerization of unsymmetrical substrates was the next focus. The aromatic-aliphatic mixed bis-enone **4-2.14** affords the corresponding cyclopentene adducts as a 1:1 mixture of isomers in 79% yield in refluxing ethyl acetate (Scheme 4-2.3). The homologous substrate **3-3.4** provides a 77% yield of cyclohexenes **4-2.15a** and **4-2.15b** in a 7:1 ratio, respectively, under the same conditions.

Scheme 4-2.3



Further electronic differentiation of the reacting partners, as illustrated by the enone-enoate **4-2.16**, results in a completely chemoselective cyclization for which a single product, **4-2.16a**, is obtained (Scheme 4-2.4). The ability to completely suppress a cyclization manifold on the basis of electronic effects is emphasized by the cycloisomerization of aromatic bis-enone **4-2.13**. In this case, remote para substituents direct the formation of a single cycloisomerization product **4-2.13a**. In both cases, the product derived from conjugate addition of PBu_3 to the less electrophilic enone partner is obtained.

Scheme 4-2.4



In the absence of a significant electronic bias, steric factors direct selectivity. Substrates bearing a gem-dimethyl substituent in the tether afford products formed by initial conjugate addition of PBu_3 to the less hindered enone, as illustrated by the cycloisomerizations of **4-2.17**and **4-2.18** (Scheme 4-2.5).

Scheme 4-2.5

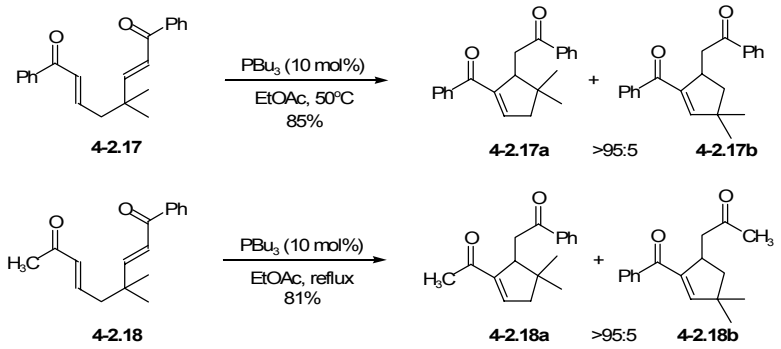
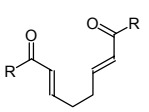
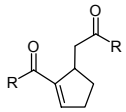
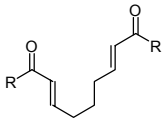
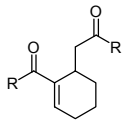
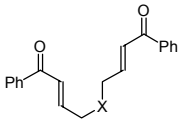
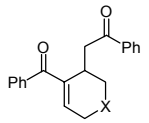
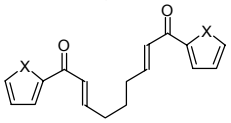
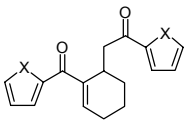
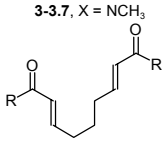
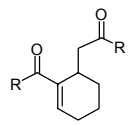
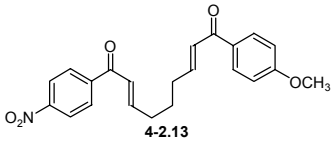
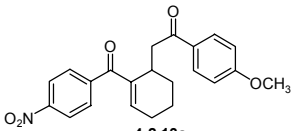
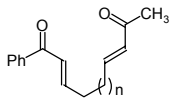
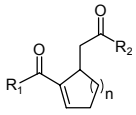
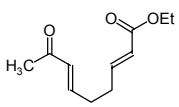
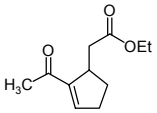
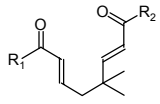
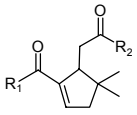


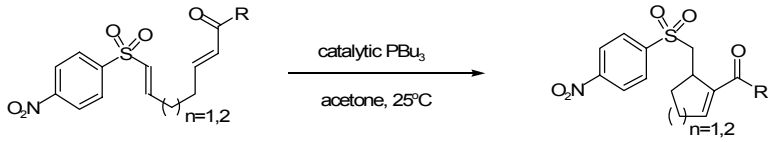
Table 4-2.3. Phosphine-catalyzed Michael cycloisomerization

Entry	Substrate	Product	T (°C)	Solvent	Yield (%)
1					
	3-3.1, R = Ph	**4-2.1a**	50	EtOAc	86
	4-2.2, R = 2-furyl	**4-2.2a**	40	EtOAc	95
2					
	3-3.2, R = phenyl	**4-2.3a**	25	Acetone	82
	4-2.4, R = 4-methoxyphenyl	**4-2.4a**	50	Acetone	78
	4-2.5, R = 2-naphthyl	**4-2.5a**	50	EtOAc	88
3					
	3-3.3, X = O	**4-2.6a**	25	Acetone	95
	3-4.3, X = NTs	**4-2.7a**	25	EtOAc:Acetone (1:1)	90
4					
	3-3.6, X = O	**4-2.8a**	50	EtOAc	90
	4-2.9, X = S	**4-2.9a**	25	EtOAc	82
	3-3.7, X = NCH_3	**4-2.10a**	56	Acetone	88
5					
	4-2.11, R = CH_3	**4-2.11a**	84	tBuOH	61
	4-2.12, R = $CH_2CH(CH_3)_2$	**4-2.12a**	84	tBuOH	70
6					
	4-2.13	**4-2.13a**	50	EtOAc	75
7					
	4-2.14, n = 1	**4-2.14a/4-2.14b**, R_1 = Ph, R_2 = CH_3	76	EtOAc	79
	3-3.4, n = 2	**4-2.15a/4-2.15b**, R_1 = CH_3, R_2 = Ph	76	EtOAc	77
		4-2.14a/4-2.14b (1:1)			
		4-2.15a/4-2.15b (7:1)			
8					
	4-2.16	**4-2.16a**	25	tBuOH	87
9					
	4-2.17, R_1 = R_2 = Ph	**4-2.17a**	50	EtOAc	85
	4-2.18, R_1 = CH_3, R_2 = Ph	**4-2.18a**	76	EtOAc	81

Part 3. Vinyl Sulfones as Reacting Partners in the Cross-Michael Cycloisomerization[2]

Unlike the parent transformation, the intramolecular process is amenable to cross-condensation. To extend the scope of this process, subsequent studies focused on expanding the variety of reacting partners viable for this cross-Michael cycloisomerization reaction. Inspired by the versatility of the sulfone moiety in organic syntheses,[3] conditions for cycloisomerization of vinylsulfones with appendant ketone and enoate partners were explored using PBu_3 as catalyst. To favor cyclization, substrates bearing a *para* nitro group in the benzene-sulfonyl moiety were utilized. All substrates were first submitted to the standard Baylis-Hillman conditions for the cycloisomerization of bis-enones. These are 10 mol% tributylphosphine in acetone at room temperature (Scheme 4-3.1).

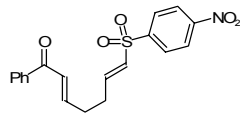
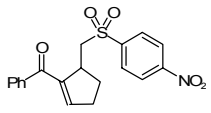
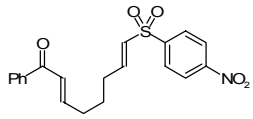
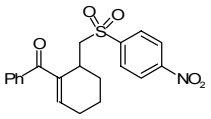
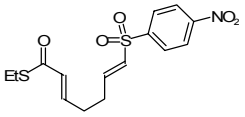
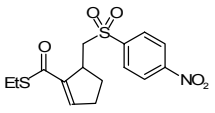
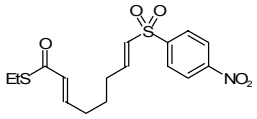
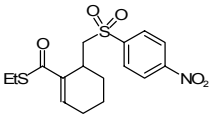
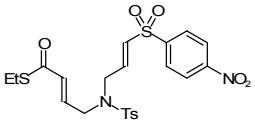
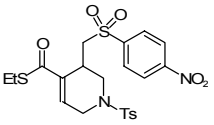
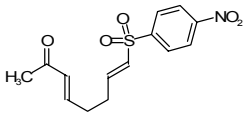
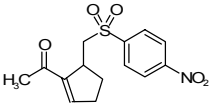
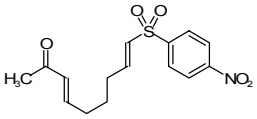
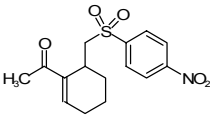
Scheme 4-3.1



Reaction conditions were modified as needed to drive the reaction to completion and/or improve the yield for each substrate. As previously observed, the ideal choice of temperature and reaction solvent was highly substrate dependant. Indeed, optimal reaction conditions were unique for each substrate. However, upon identification of suitable conditions, the cycloisomerization products **4-3.1a – 4-3.6a** were produced in good to excellent yields using 10-20 mol% of tributylphosphine as catalyst (Table 4-3.1).

In each case, the vinyl sulfone moiety acted as the electrophilic partner while the enone moiety acted as the pronucleophilic partner. As expected, substrates bearing more electrophilic enone partners cyclized in less polar solvents with lower catalyst loadings. Also, organocatalytic cycloisomerizations leading to five-membered ring products were faster and gave higher yields than the corresponding processes to six-membered cycloadducts.

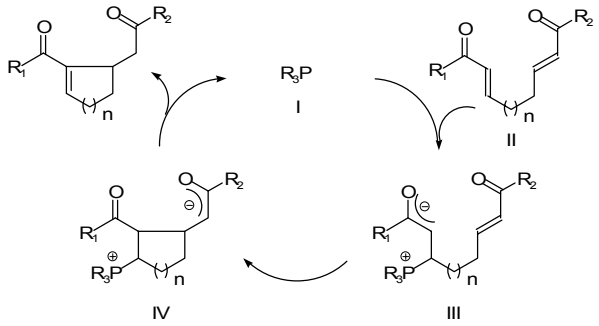
Table 4-3.1. Phosphine-Catalyzed cross-Michael Cycloisomerization

Entry	Substrate	Product	PBu_3 (mol%)	T (°C)	Solvent	Yield (%)
1	 **4-3.1**	 **4-3.1a**	10	50	EtOAc	97
2	 **4-3.2**	 **4-3.2a**	10	25	Acetone	74
3	 **4-3.3**	 **4-3.3a**	10	50	*t*-AmylOH	89
4	 **4-3.4**	 **4-3.4a**	10	25	Acetonitrile	86
5	 **4-3.5**	 **4-3.5a**	20	130	*t*-AmylOH	76
6	 **4-3.6**	 **4-3.6a**	20	82	*t*-BuOH	84
	 **4-3.7**	 **4-3.7a**	20	60	*t*-AmylOH	80

Part 4. Mechanistic Details for the Phosphine-Catalyzed Michael Cycloisomerization

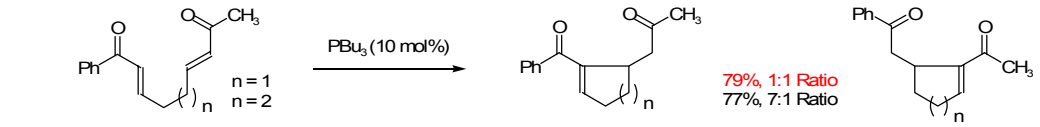
Mechanistic studies of the intermolecular reaction suggest the following catalytic cycle for the phosphine-catalyzed cycloisomerization of bis-enones (Scheme 4-4.1).[4] Conjugate addition of tributylphosphine **I** to the bis-enone **II** results in the formation of enolate **III**. Subsequent intramolecular conjugate addition to the appendant enone yields zwitterionic intermediate **IV**. Finally, proton transfer enables β-elimination of tributylphosphine to complete the catalytic cycle. Cycloisomerization performed in d^6-acetone did not result in products incorporating deuterium, indicating proton transfer occurs either inter- or, more likely, intramolecularly.

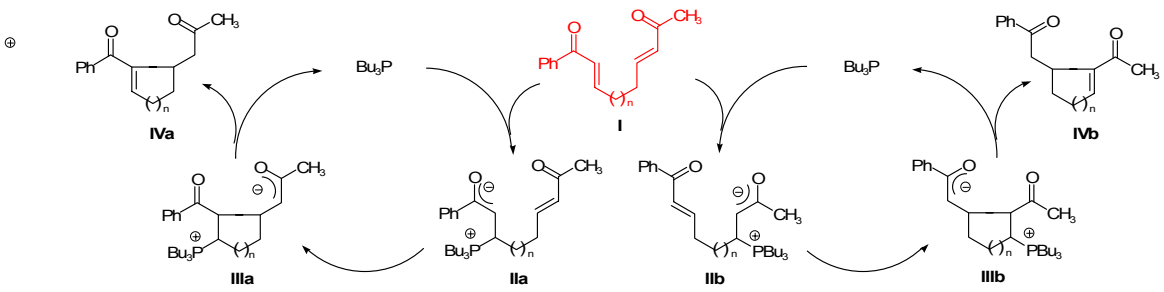
Scheme 4-4.1

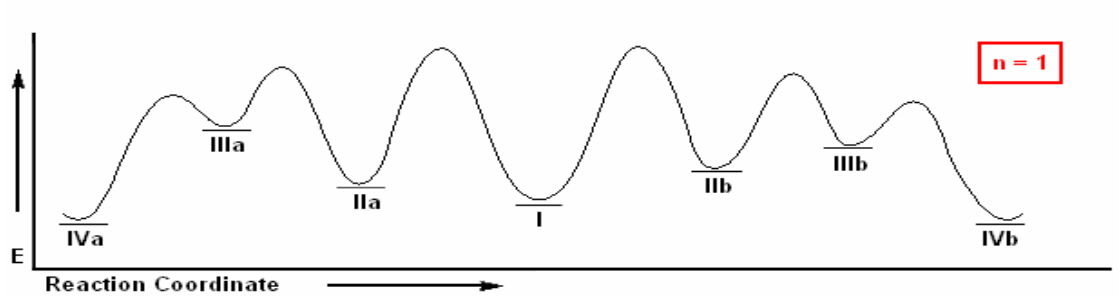


As discussed in Chapter 4 Part 2, whereas the aromatic-aliphatic mixed bis-enone **4-2.14** affords the corresponding cyclopentene products as a 1:1 mixture of isomers, the homologous substrate **3-3.4** provides the corresponding cyclohexenes in a 7:1 ratio. This result suggests that initial conjugate addition of tributylphosphine is indiscriminate and in the case of five-membered ring formation, the kinetic phosphine adducts are trapped *via* cyclization (Scheme 4-4.2).

Scheme 4-4.2

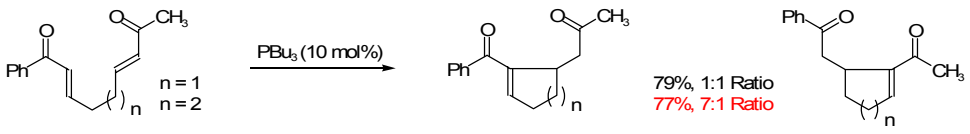


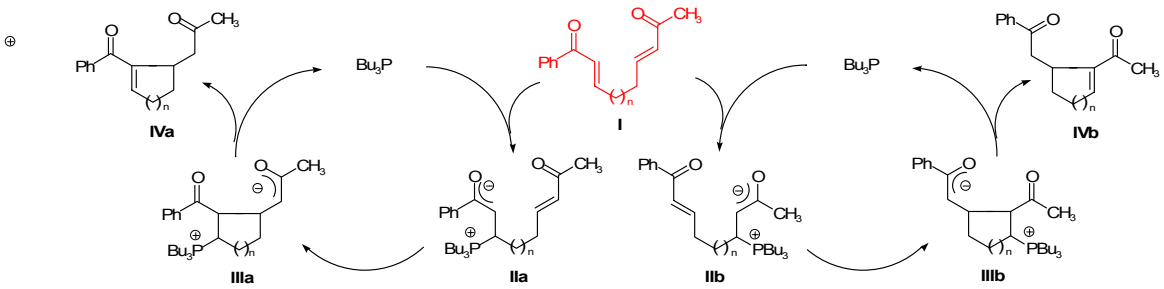


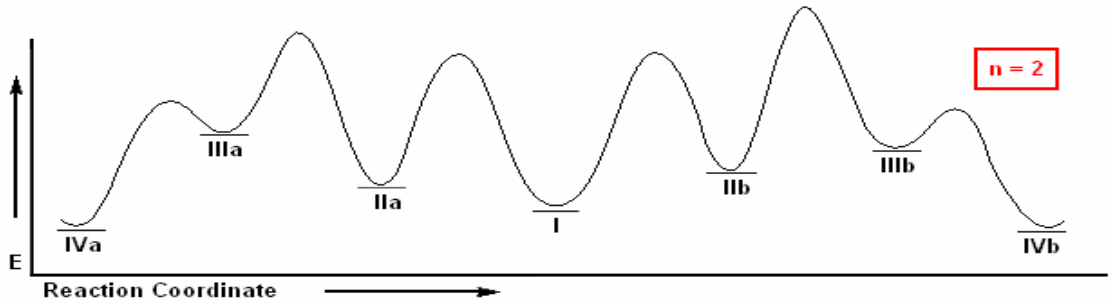


In the case of six-membered ring formation, a slower cyclization rate results in the establishment of a pre-equilibrium of phosphine adducts. As a result, cyclization now becomes the product- and rate-determining step (Scheme 4-4.3).

Scheme 4-4.3







Part 5. Conclusion

The Michael Cycloisomerization reaction represents the first intramolecular variant of the Rauhut-Currier reaction and underscores the utility of enolate generation *via* nucleophilic organocatalysis. This transformation is viable for five- and six-membered cyclizations of both aromatic and aliphatic bis-enones. The remarkable sensitivity of this reaction with respect to the electrophilicity of the reacting partners enables highly selective "crossed" cycloisomerizations of non-symmetric bis-enones, giving rise to single isomeric products. Most importantly, organocatalytic approaches avoid the use of terminal reductants, permitting the development of environmentally benign, atom economical processes.

Part 6. References

[1] (a) "Organocatalytic Michael Cycloisomerization of Bis(enones): The Intramolecular Rauhut-Currier Reaction," Wang, L. C.; Luis, A. L.; Agapiou, K.; Jang, H.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2002**, 124, 2402. (b) "The Vinylogous Intramolecular Morita-Baylis-Hillman Reaction: Synthesis of Functionalized Cyclopentenes and Cyclohexenes Using Trialkylphosphines as Nucleophilic Catalysts," Frank, S. A.; Mergott, D. J.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, 124, 2404.

[2] "Nucleophilic Catalysis via Phosphine Conjugate Addition: Vinyl Sulfones as Reacting Partners in Catalytic Cross-Michael Cycloisomerization," Luis, A. L.; Krische, M. J. *Synthesis*, **2004**, 2579.

[3] For a review, see: (a) "Desulfonylation reactions: Recent developments ," Najera, C.; Yus, M. *Tetrahedron* 1999, *55*, 10547. (b) "Rearrangements of sulfoxides and sulfones in the total synthesis of natural compounds," Prilezhaeva, E. N. *Russ. Chem. Rev.* 2001, *70*, 897. (c) "Recent applications of vinyl sulfones and vinyl sulfoxides in asymmetric synthesis," Carretero, J. C.; Arrayas, R. G.; Buezo, N. D.; Garrido, J. L.; Alonso, I.; Adrio, J. *Phosphorus, Sulfur Silicon Relat. Elem.* 1999, *153*, 259. (d) "Recent developments in sulfone chemistry," Magnus, P. D. *Tetrahedron* 1977, *33*, 2019.

[4] For a mechanistic study, see: "The Kinetics and Mechanism of the Phosphorus-Catalyzed Dimerization of Acrylonitrile," Hall, C. D.; Lowther, N.; Tweedy, B. R.; Hall, A. C.; Shaw, G. *J. Chem. Soc., Perkin Trans. II* **1998**, 2047.

Part 5. Experimentals

I. General Procedures

All reactions were run with solvents purchased commercially without purification, unless otherwise indicated. For reactions requiring anhydrous conditions, flasks were flame-dried and cooled under a stream of nitrogen. Dichloromethane (DCM) was distilled from calcium hydride. Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone ketyl. Anhydrous solvents were transferred by an oven-dried syringe.

Analytical thin-layer chromatography (TLC) was carried out using 0.2-mm commercial silica gel plates (DC-Fertigplatten Krieselgel 60 F_{254}). Preparative column chromatography employing silica gel was performed according to the method of Still.[1] Solvents for chromatography are listed as volume/volume ratios. Melting points were determined on a Thomas-Hoover melting point apparatus in open capillaries and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 1420 spectrometer. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported as m/e (relative intensity). Accurate masses are reported for the molecular ion (M+1) or a suitable fragment ion.

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with a Varian Gemini (300 MHz) spectrometer. Chemical shifts are reported in delta (δ) units, parts per million (ppm) downfield from trimethylsilane. Coupling constants are reported in Hertz (Hz). Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded with a Varian Gemini 300 (75 MHz) spectrometer. Chemical shifts are reported in delta (δ) units, parts per million (ppm) relative to the center of the triplet at 77.00 ppm for deuteriochloroform. ^{13}C NMR spectra were routinely run with broadbrand decoupling.

([1]) Still, W. C.; Kahn, M; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

General Procedure A for the Preparation of Substrates 4-2.2, 4-2.4, 4-2.5, 4-2.9, 4-2.11, 4-2.17. To a solution of dialdehyde (100 mol%) in dichloromethane (0.3 M) at room temperature, was added Wittig reagent (300-400 mol%) followed by stirring for 12-24 h at room temperature. The volatiles were removed under reduced pressure by rotary evaporation and the residue was purified via flash chromatography on silica. Charaterization data for substrate **4-2.5**,[2] **4-2.9**[3] and **4-2.11**[4] was consistent with that reported in the literature. Succinaldehyde was generated from 2,5-dimethoxyfuran.[5]

General Procedure B for the Preparation of Substrates 4-2.13, 4-2.14, 4-2.16, 4-2.18. To a solution of dialdehyde (100 mol%) in dichloromethane (0.3 M) at room temperature, was added Wittig reagent (20-30 mol%) followed by stirring for 12-24 h at room temperature. The volatiles were removed under reduced pressure by rotary evaporation and the residue was purified via flash chromatography on silica to give desired enone-aldehyde.

To a solution of this enone-aldehyde (100 mol%) in dichloromethane (0.3 M) at room temperature, was added Wittig reagent (100 mol%) followed by stirring for 12-24 h at room temperature. The volatiles were removed under reduced pressure by rotary evaporation and the residue was purified via flash chromatography on silica to afford the desired mixed bis-enones. Charaterization data for substrate **4-2.16**,[6] was consistent with that reported in the literature. Succinaldehyde was generated from 2,5-dimethoxyfuran.[7]

Procedure for the Preparation of Substrates 4-2.12.

To a solution of sodium hydride (2.00 g, 50.0 mmol, 220 mol%) in dry tetrahydrofuran (0.5M) at 0 ^{o}C was added (4-methyl-2-oxo-pentyl)-phosphonic acid dimethyl ester (9.46 g, 45.4

(2)Yang, Jingkui; Felton, Greg A. N.; Bauld, Nathan L.; Krische, Michael J. *J. Am. Chem. Soc.* **2004**, *126*, 1634.
(3) Montgomery, J. Savchenko, A. V.; Zhao, Y. *J. Org. Chem.* **1995**, *60*, 5699.
(4) Montgomery, J. Savchenko, A. V.; Zhao, Y. *J. Org. Chem.* **1995**, *60*, 5699.
(5) Fakstorp, J.; Raleigh, D.; Schniepp, L. E. *J. Am. Chem. Soc.* **1950**, *72*, 869.
(6) Pandey, Ganesh; Hajra, Saumen; Ghorai, Manas K.; Kumar, K. Ravi *J. Am. Chem. Soc.***1997**, *119*, 8777.

mmol, 200 mol%) in dry tetrahydrofuran (2.3 M) dropwise. Reaction is stirred at 0 ^{o}C for 15 min and then allowed to warm to room temperature over a period of 45 min. This is added via cannula to a solution of glutaric dialdehyde (2.27 g, 22.7 mmol, 100 mol%) in dry tetrahydrofuran (0.2M) at 0 ^{o}C. Reaction is allowed to warm to room temperature over a period of 30 min, quenched with sat. aq. NH_4Cl and extracted with ethyl acetate. The solvent is evaporated and the reaction purified via flash chromatography (SiO_2: 15:1 hexane:ethyl acetate) to provide **4-2.12** (4.14 g, 15.7 mmol) as a yellowish oil in 69% yield.

General Procedure C for the Preparation of Substrates 4-3.1, 4-3.2, 4-3.6, 4-3.7.

To a stirred solution of **(**4-Nitro-benzenesulfonylmethyl)-phosphonic acid dimethyl ester (100 mol%) in dry tetrahydrofuran (0.2 M) under argon at –65^{o}C was added lithium hexamethyldisilazide (1.0 M in tetrahydrofuran, 100 mol%). The solution was stirred at –78^{o}C for 1 h. Pentenal or hexenal (130 mol%) in dry dichloromethane (1.6 M) was added. The reaction was allowed to warm to room temperature over a period of 1 h. Solution was poured into saturated ammonium chloride. The aqueous layer was extracted with ether (3X). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified via flash chromatography on silica to give the vinylsulfone-alkene compound.

To tricyclohexylphosphine[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene][benzylidine]ruthenium(IV) dichloride (3 mol%) in dry dichloromethane (0.007 M) under argon was added the vinylsulfone-alkene (100 mol%) in 5.0 mL dry dichloromethane and the corresponding vinyl ketone (124 mol%). The solution was refluxed for 6 h and allowed to cool to room temperature. The reaction was stirred open to air for 20 min. and concentrated under vacuum. The residue was purified via flash chromatography on silica.

General Procedure D for the Preparation of Substrates 4-3.3 and 4-3.4.

To succinic or glutaric dialdehyde (100 mol%) in dichloromethane (0.13 M) was added (triphenyl-λ^5-phosphanylidene)-thioacetic acid *S*-ethyl ester (20 mol%) in dichloromethane (0.07 M) dropwise over a period of 5 hours. Reaction was stirred at room temperature overnight and concentrated under vacuum. The residue was purified via flash chromatography on silica to provide a thioenoate-aldehyde compound.

To (4-Nitro-benzenesulfonylmethyl)-phosphonic acid dimethyl ester (100 mol%) in dry tetrahydrofuran (0.20 M) under argon at -78˚C was added *n*-butyllithium (2.5 M in tetrahydrofuran, 100 mol%) dropwise. After 1 h, the thioenoate-aldehyde (105 mol%) was added in dry tetrahydrofuran (0.7M) dropwise. Reaction was allowed to warm to room temperature over a period of 1 h and poured into saturated ammonium chloride solution. Aqueous layer was extracted with ether (3X). Combined organic extracts were dried (Na_2SO_4) and concentrated under vacuum. The residue was purified via flash chromatography on silica.

Procedure for the Preparation of Substrate 4-3.5.

To a stirred solution of **(**4-Nitro-benzenesulfonylmethyl)-phosphonic acid dimethyl ester (1.43 g, 4.62 mmol, 100 mol%) in dry tetrahydrofuran (36 mL, 0.15 M) under argon at –78^{o}C was added *n*-butyl lithium (1.85 mL, 2.5 M in hexanes, 100 mol%). The solution was stirred at –78^{o}C for 1 h. N-(2,2-diethoxy-ethyl)-4-methyl-N-(2-oxo-ethyl)-benzenesulfonamide (1.50 g, 4.62 mmol, 100 mol%) in dry tetrahydrofuran (12 mL) was added dropwise. The reaction was allowed to warm to room temperature over a period of 45 min. Solution was poured into saturated ammonium chloride. The aqueous layer was extracted with ether (3 X 150 mL). The organic extracts were combined, washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified via flash chromatography (SiO_3 9:1 hexane:ethyl acetate) to provide N-(2,2-diethoxy-ethyl)-4-methyl-N-[3-(4-nitro-

benzenesulfonyl)-allyl]-benzenesulfonamide (1.54 g, 3.01 mmol) as a yellow oil in 65.0% yield.

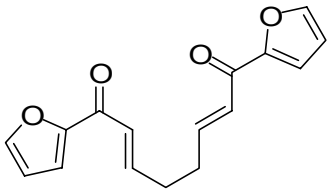
To a solution of N-(2,2-diethoxy-ethyl)-4-methyl-N-[3-(4-nitro-benzenesulfonyl)-allyl]-benzenesulfonamide (1.50 g, 2.93 mmol, 100 mol%) in dichloromethane (9.0 mL, 0.33M) at 0°C was added a solution of trifluoroacetic acid (3.00 mL, 50% aq.) dropwise. Reaction stirred at ambient temperature for 24 hrs. Resulting mixture was filtered and solid dried under vacuum to give 4-methyl-N-[3-(4-nitro-benzenesulfonyl)-allyl]-N-(2-oxo-ethyl)-benzenesulfonamide (1.02 g, 2.34 mmol) as a white solid in 80.0% yield.

To a solution of 4-methyl-N-[3-(4-nitro-benzenesulfonyl)-allyl]-N-(2-oxo-ethyl)-benzenesulfonamide (1.00 g, 2.28 mmol, 100 mol%) in tetrahydrofuran (24 mL, 0.1M) was added (triphenyl-λ^5-phosphanylidene)-thioacetic acid *S*-ethyl ester (1.20g, 3.42 mmol, 150 mol%) and reaction refluxed overnight. Reaction concentrated under vacuum and purified via flash chromatography (SiO_3 9:1 hexane:ethyl acetate) to provide **9a** (0.970 g, 1.85 mmol) as a white solid in 81.0% yield.

General Procedure E for the Michael Cycloisomerization.

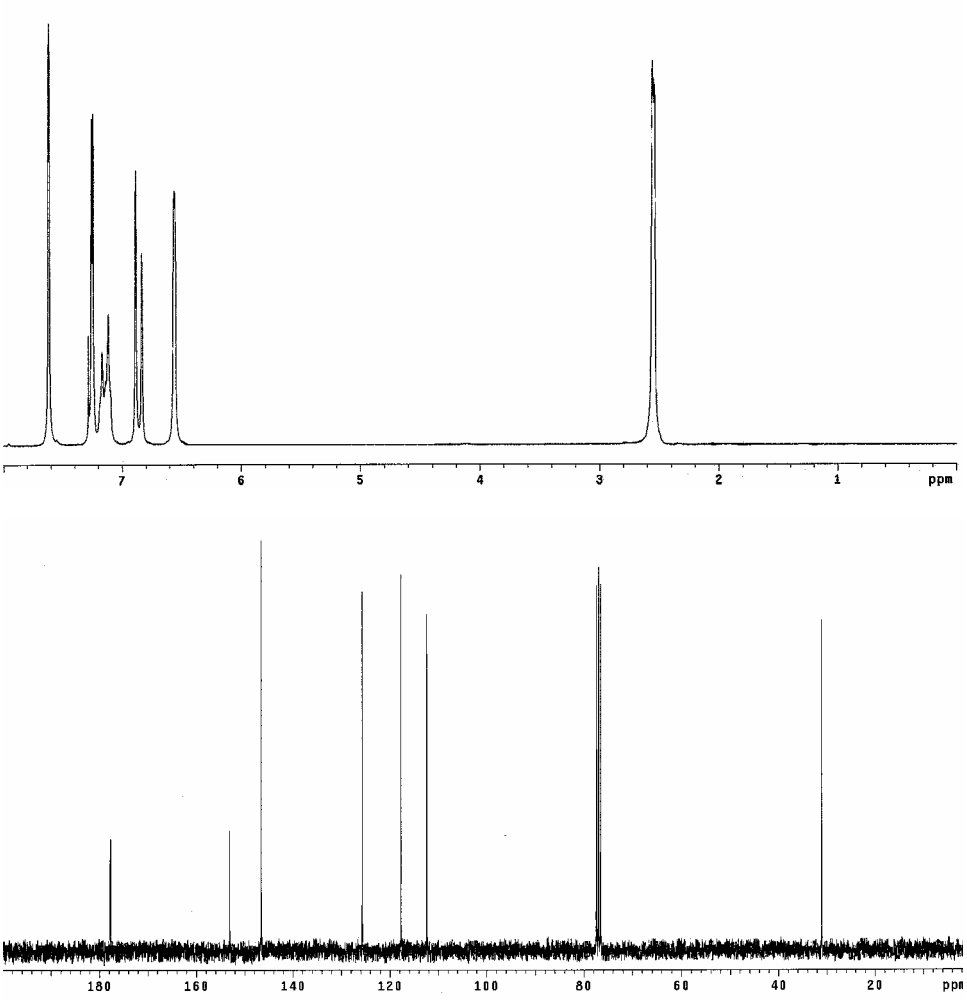
Substrate (100 mol%) was dissolved in the corresponding solvent (0.2 M) under argon and tributylphosphine (10-20 mol%) was added. The reaction was stirred at the indicated temperature until consumption of the starting material was observed. The solvent was removed under reduced pressure and the resulting oil was purified via flash chromatography (SiO_2 hexane:ethyl acetate) to provide cyclized products **4-2.1a – 4-2.18a** and **4-3.1a – 4-3.7a.**

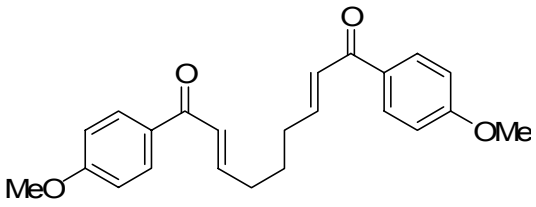
B. Spectroscopic Characterization Data



4-2.2

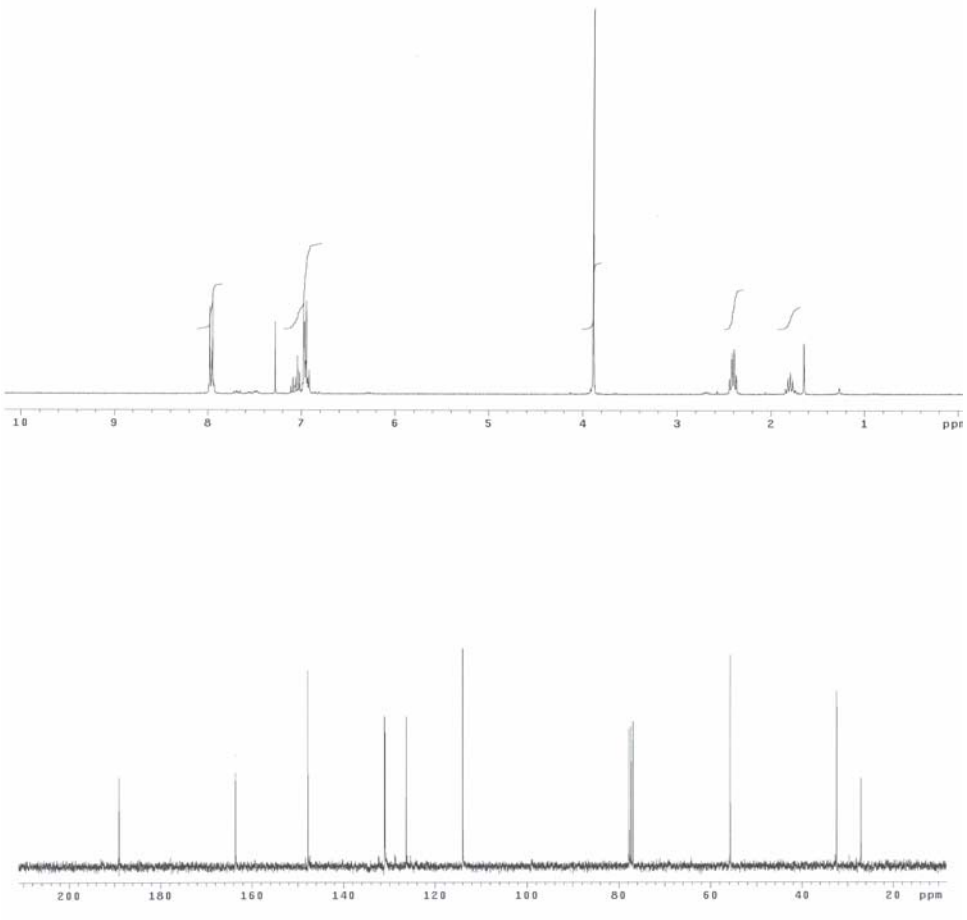
2-[2-(Furan-2-carbonyl)-cyclopentyl]-1-furan-2-yl-ethanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58 (s, 2H), 7.22 (m, 2H), 7.10 (m, 2H), 6.82 (dt, *J* = 1.5, 15.3 Hz, 2H), 6.52 (t, *J* = 15.0 Hz, 2H), 2.51 (d, *J* = 15.0 Hz, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 177.8, 153.1, 146.6, 146.5, 125.7, 117.7, 112.4, 31.0. FTIR (neat): 3016, 2969, 1737, 1726, 1663, 1464, 1365, 1227, 1010 cm^{-1}. HRMS: calcd for $C_{17}H_{16}O_4$ [M+1] 285.1126, found 285.1131.

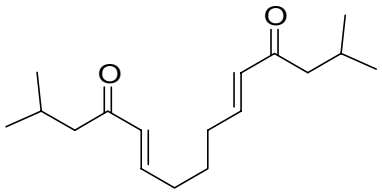




4-2.4

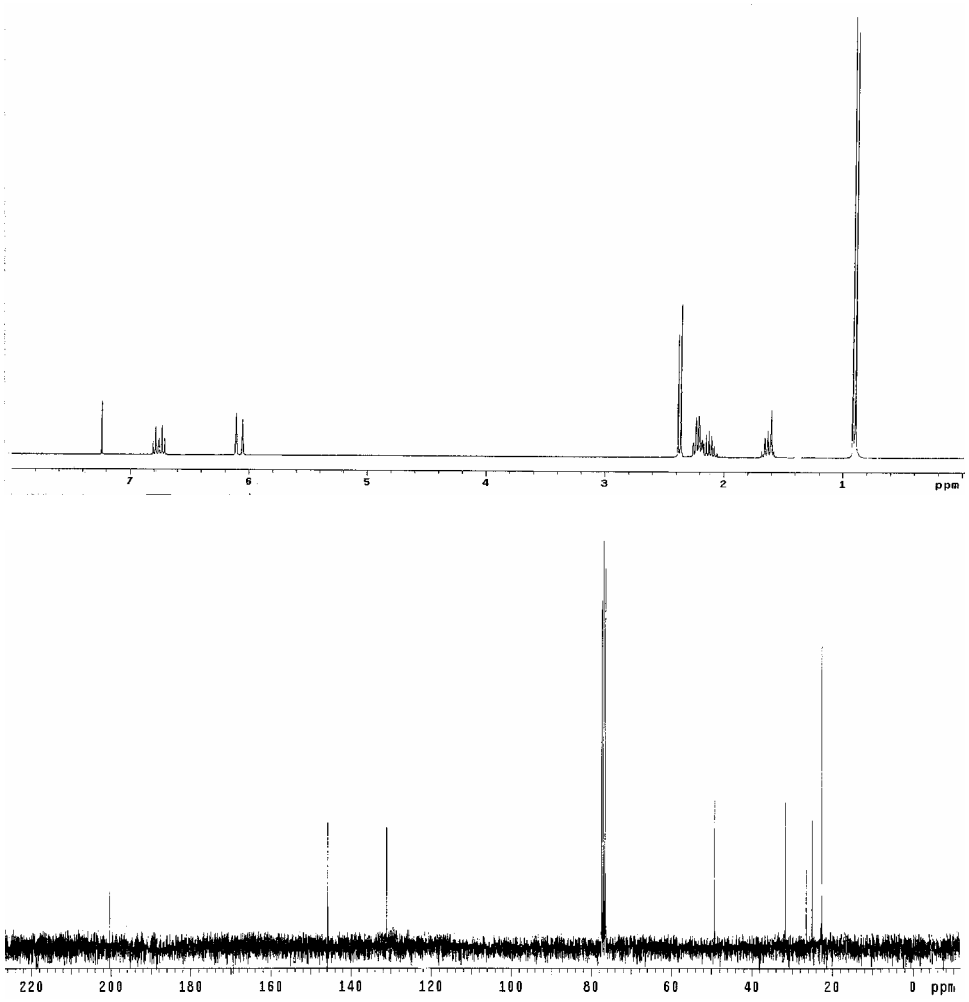
1,9-Bis -(4-methoxy-phenyl)-nona-2,7-diene-1,9-dione. ^{1}H NMR ($CDCl_3$, 300MHz): δ 7.94 (d, *J* = 7.2 Hz, 4H), 7.02 (m, 8H), 3.89 (s, 6H), 2.41 (dt, *J* = 7.2, 14.4 Hz, 4H), 1.80 (qt, *J* = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 189.1, 163.6, 147.8, 131.1, 130.9, 126.3, 114.0, 55.7, 32.3, 27.0. FTIR (neat): 2934, 2839, 1664, 1617, 1599, 1259, 1171 cm^{-1}. HRMS: Calcd for $C_{23}H_{24}O_4$ [M+1] 365.1753, found 365.1755. Mp = 77-78 ^{o}C.

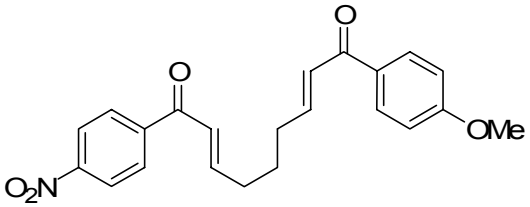




4-2.12

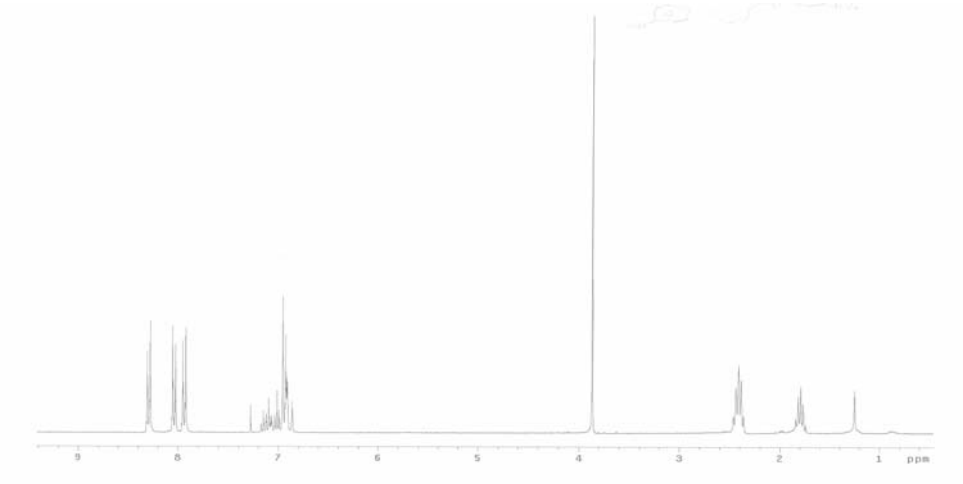
2,14-Dimethyl-pentadeca-5,10-diene-4,12-dione. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.76 (dt, J=15.9 Hz, 6.7 Hz, 2H), 6.08 (d, J=15.9 Hz, 2H), 2.38 (d, J=7.2 Hz, 4H), 2.22 (dt, J=6.9 Hz, 7.5 Hz, 4H), 2.13 (J=6.7 Hz, 2H), 1.63 (m, 2H), 0.91 (d, J=6.4 Hz, 12H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 200.7, 145.8, 131.1, 49.3, 31.7, 26.5, 25.1, 22.7. FTIR (neat): 3004, 2886, 1716, 1668, 1394, 1359, 1189 cm^{-1}. HRMS: calcd for $C_{17}H_{29}O_2$ (M+1): 265.2168, found: 265.2173.

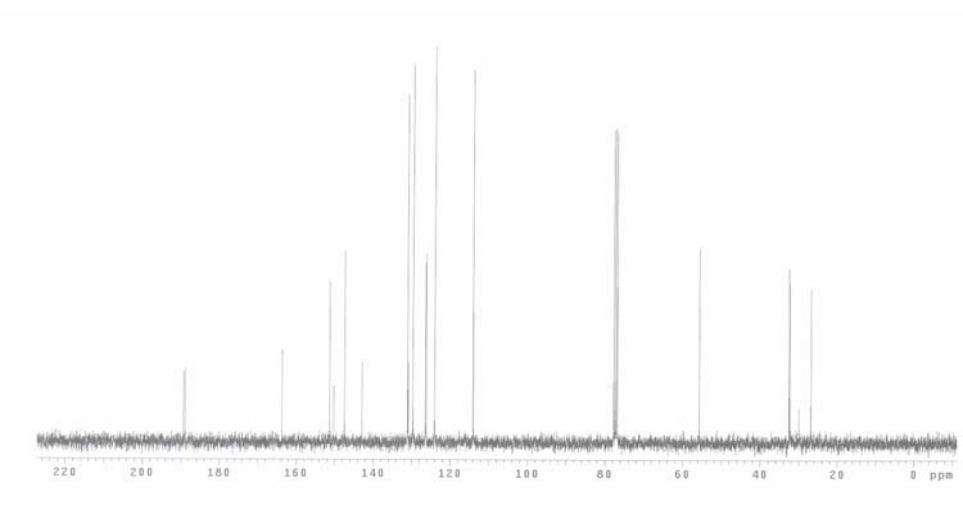


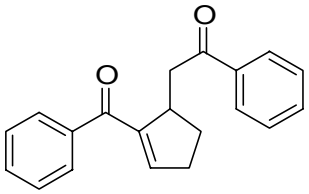


4-2.13

1-(4-Methoxy-phenyl)-9-(4-nitro-phenyl)-nona-2,7-diene-1,9-dione. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.30 (d, *J* = 9 Hz, 2H), 8.05 (d, *J* = 9 Hz, 2H), 7.95 (d, *J* = 9 Hz, 2H), 7.02 (m, 6H), 3.87 (s, 3H), 2.42 (m, 4H), 1.80 (qt, *J* = 7.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 189.32, 188.92, 163.67, 151.31, 150.25, 147.42, 142.89, 131.05, 130.83, 129.68, 126.44, 126.23, 124.03, 114.03, 55.73, 32.56, 32.36, 26.86. IR (neat) 2928, 2849, 1666, 1619, 1600, 1523, 1346, 1259, 1171 cm^{-1}. HRMS: calcd for $C_{22}H_{21}N_1O_5$ [M+1] 380.1498, found 380.1499. Mp = 96-97 ^{o}C.

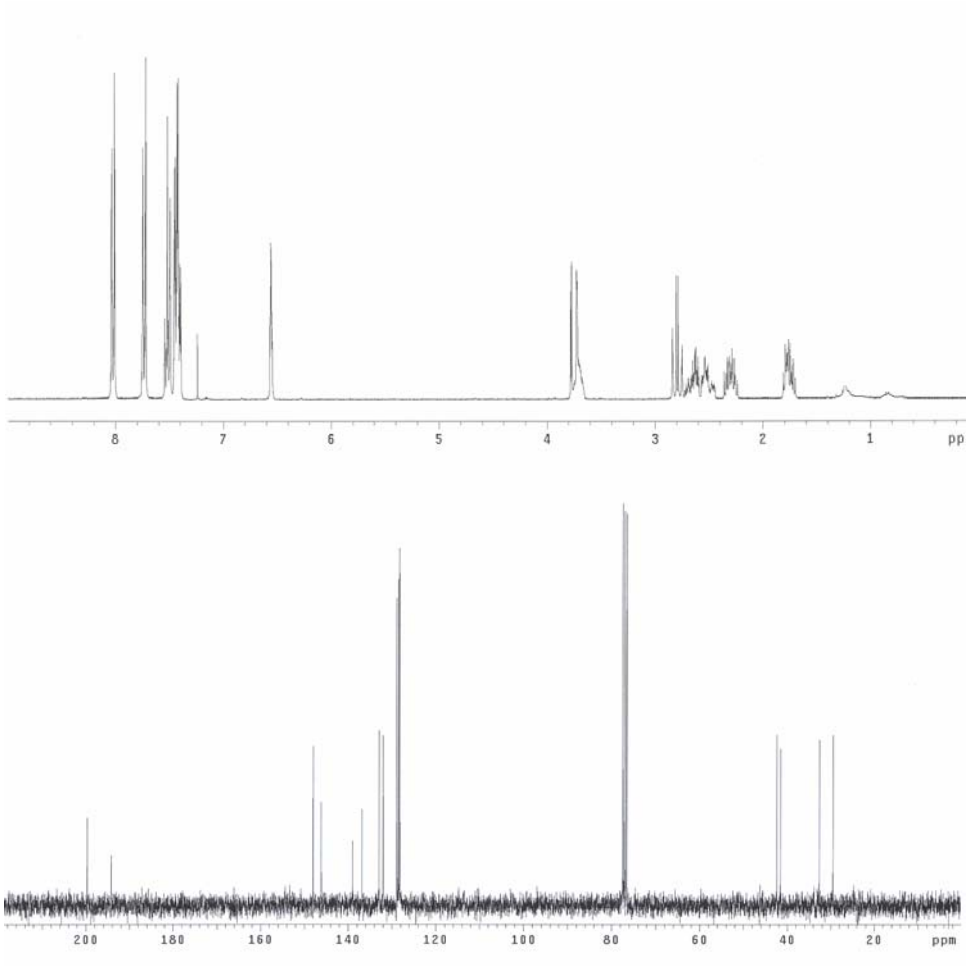


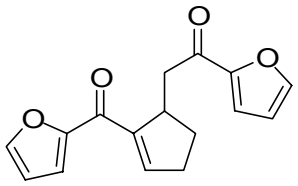




4-2.1a

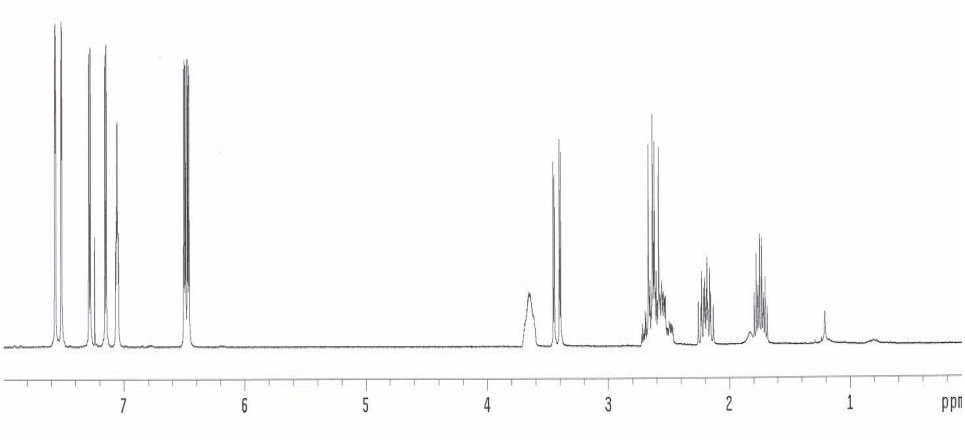
2-(2-Benzoyl-cyclopent-2-enyl)-1-phenyl-ethanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.04~8.01 (m, 2H), 7.75~7.72 (m, 2H), 7.55~7.43 (m, 6H), 6.56 (t, J = 3.15 Hz, 1H), 3.75 (dd, J = 2.7, 16.2 Hz, 1H), 3.74~3.66 (m, 1H), 2.79 (dd, J = 10.5, 16.2 Hz, 1H), 2.75~2.52 (m, 2H), 2.34~2.20 (m, 1H), 1.80~1.65 (m, 1H). ^{13}C NMR (75MHz, $CDCl_3$): δ 199.72, 194.20, 147.96, 146.11, 138.96, 136.82, 132.93, 132.00, 128.88, 128.55, 128.29, 128.21, 42.38, 41.58, 32.61, 24.99. FTIR (neat): 1681, 1638, 1276, 751cm^{-1}._HRMS: calcd for $C_{20}H_{19}O_2$ (M+1): 291.1385, found: 291.1383.

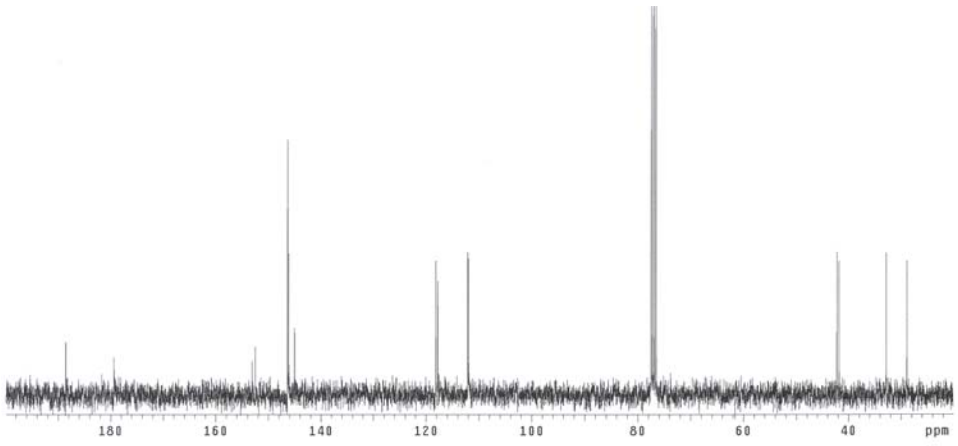


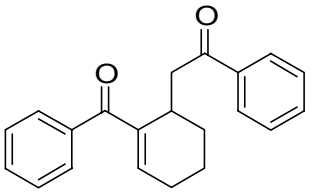


4-2.2a

2-[2-(Furan-2-carbonyl)-cyclopent-2-enyl]-1-furan-2-yl-ethanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58 (dd, J = 0.9, 1.8 Hz, 1H), 7.53 (dd, J = 0.6, 1.8 Hz, 1H), 7.31~7.24 (m, 1H), 7.17 (dd, 0.9, 3.6 Hz, 1H), 7.08~7.06 (m, 1H), 6.52~6.47 (m, 2H), 3.69~3.65 (m, 1H), 3.44 (dd, J = 3.3, 15.3 Hz, 1H), 2.68~2.50 (m, 3H), 2.24~2.17 (m, 1H), 1.80~1.72 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 188.57, 179.38, 153.09, 152.51, 146.36, 146.14, 145.02, 118.13, 117.26, 112.09, 111.98, 42.22, 41.83, 32.81, 28.86. FTIR (neat): 3005, 1664, 1620, 1468, 1275, 1261, 764, 750cm^{-1}. HRMS: calcd. for $C_{16}H_{15}O_4$ (M+1): 271.0970, found: 271.0974.

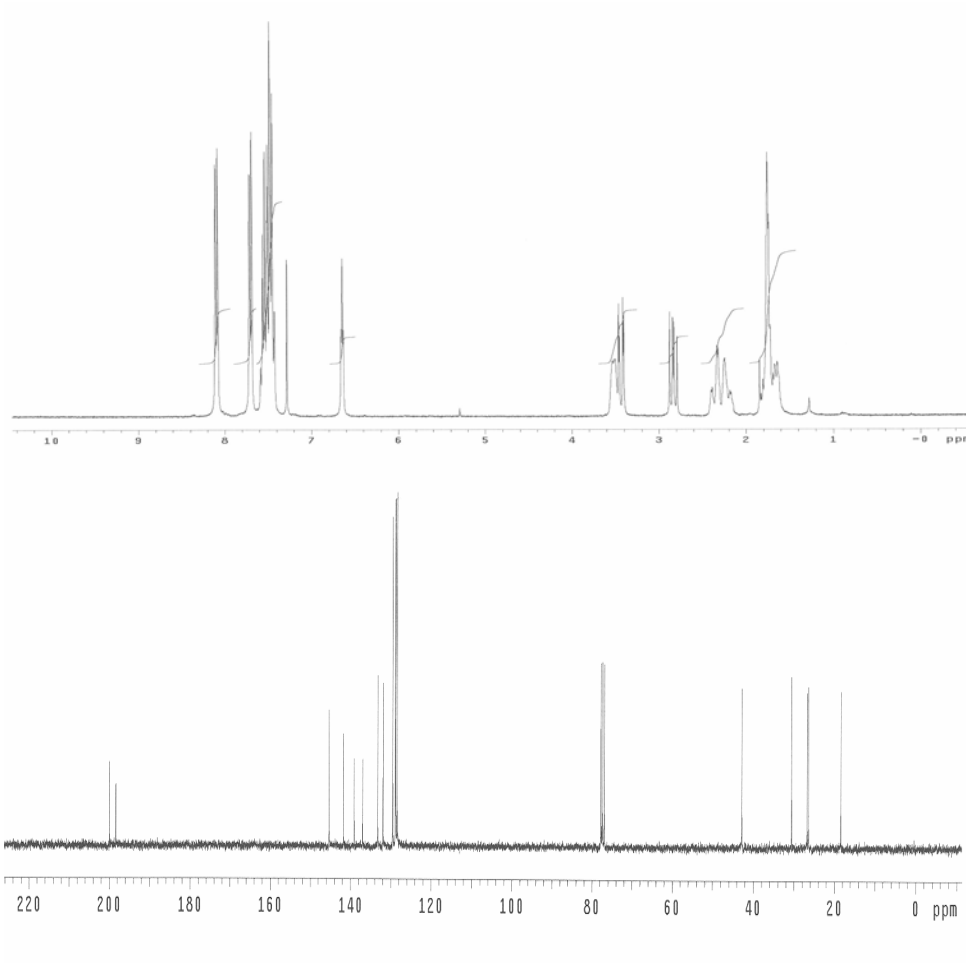


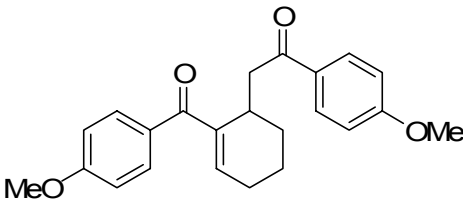




4-2.3a

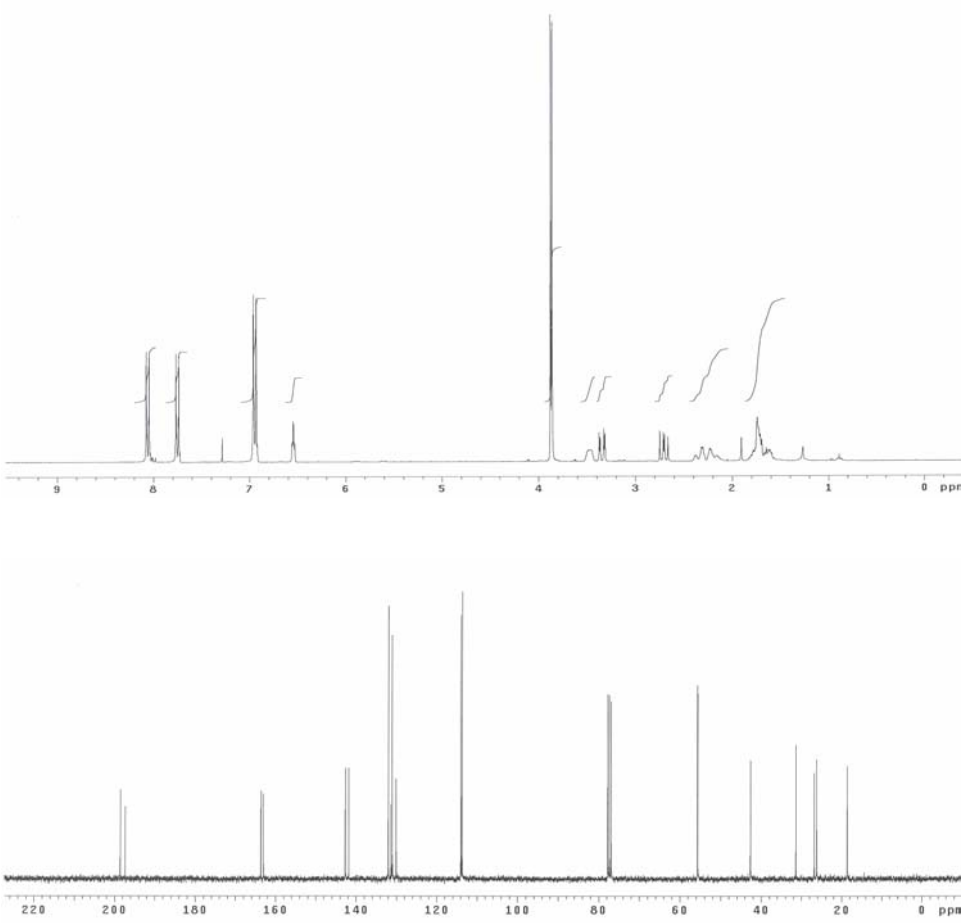
2-(2-Benzoyl-cyclohex-2-enyl)-1-phenyl-ethanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10 (d, J = 7.17 Hz, 2H), 7.70 (d, J = 7.17 Hz, 2H), 7.58~7.42 (m, 6H), 6.65 (t, J = 3.84 Hz, 1H), 3.53~3.50 (m, 1H), 3.43 (dd, J = 3.07, 14.86 Hz, 1H), 2.84 (dd, J = 10.50, 14.86 Hz, 1H), 2.40~2.17 (m, 2H), 1.83~1.64 (m, 4H). ^{13}C NMR (75MHz, $CDCl_3$): δ 199.93, 198.36, 145.32, 141.74, 139.05, 136.99, 133.26, 131.91, 129.51, 128.86, 128.74, 128.41, 42.75, 30.61, 26.74, 26.42, 18.35. FTIR (neat): 3013, 2936, 1678, 1642, 1597, 1448, 1271, 754cm^{-1}. HRMS: calcd for $C_{21}H_{21}O_2$ (M+1): 305.1542, found: 305.1538.

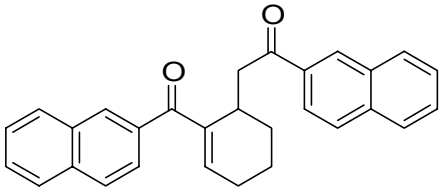




4-2.4a

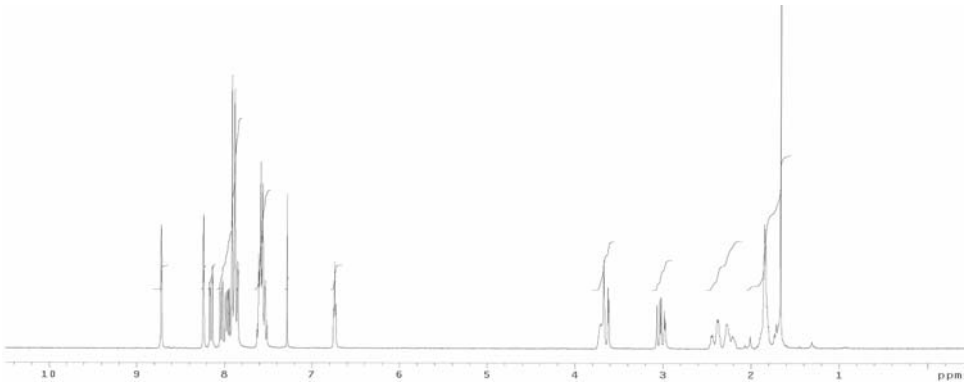
2-[2-(4-Methoxy-benzoyl)-cyclohex-2-enyl]-1-(4-methoxy-phenyl)-ethanone. ^{1}HNMR (300 MHz, $CDCl_3$): δ 8.07~8.03 (m, 2H), 7.76~7.73 (m, 2H), 6.96~6.92 (m, 4H), 6.55 (dt, J = 1.29, 3.84 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.48~3.46 (m, 1H), 3.34 (dd, J = 3.07, 14.34 Hz, 1H), 2.70 (dd, J = 10.76, 14.34 Hz, 1H), 2.32~2.15 (m, 2H), 1.81~1.59 (m, 4H). ^{13}CNMR (75MHz, $CDCl_3$): δ 198.58, 197.35, 163.63, 163.00, 142.67, 141.82, 131.98, 131.39, 131.07, 130.06, 113.96, 113.67, 55.70, 55.67, 42.63, 31.38, 26.83, 26.23, 18.62. HRMS calcd. for $C_{23}H_{25}O_4$ (M+1): 365.1753, found: 365.1759. FTIR (neat): 3054, 2936, 1671, 1634, 1600, 1259, 1171, 1029, 738cm^{-1}.

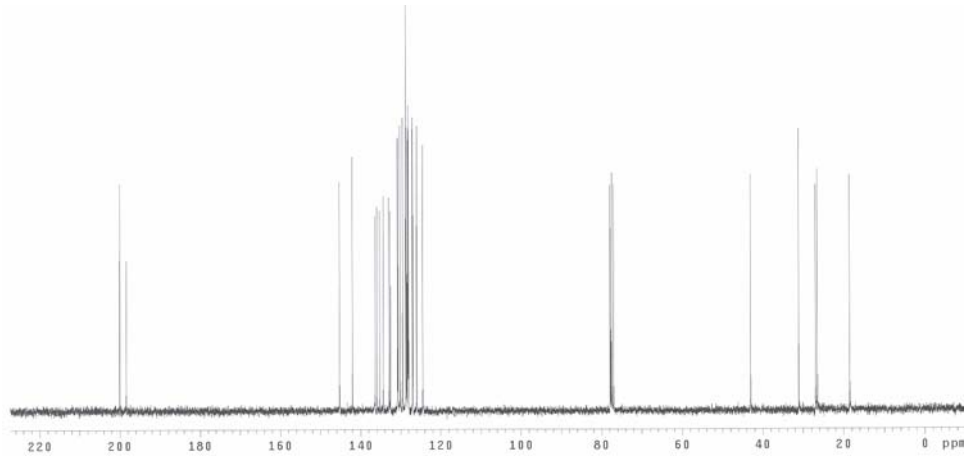


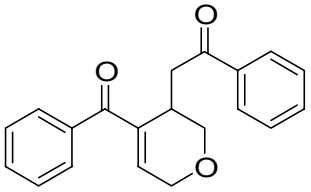


4-2.5a

2-[2-(Naphthalene-2-carbonyl)-cyclohex-2-enyl]-1-naphthalen-2-yl-ethanone. ^{1}HNMR (300 MHz, $CDCl_3$): δ 8.72 (s, 1H), 8.24 (s, 1H), 8.17~8.14 (m, 1H), 8.05~7.84 (m,7H), 7.61~7.54 (m, 4H), 6.74 (t, J = 3.59 Hz, 1H), 3.72~3.61 (m, 2H), 3.03 (dd, J = 10.24, 14.34 Hz, 1H), 2.45~2.19 (m, 2H), 1.85~1.66 (m, 4H). ^{13}CNMR (75MHz, $CDCl_3$): δ 199.97, 198.33, 145.22, 142.01, 136.32, 135.84, 135.19, 134.31, 132.91, 132.57, 130.76, 130.63, 130.08, 129.48, 128.67, 128.44, 128.18, 128.08, 127.97, 127.00, 126.90, 125.92, 124.42, 43.01, 31.10, 26.92, 26.51, 18.51. HRMS calcd. for $C_{29}H_{25}O_2$ (M+1): 405.1855, found: 405.1853. FTIR (neat): 3058, 2935, 1674, 1627, 1596, 1468, 1230, 909cm^{-1}.

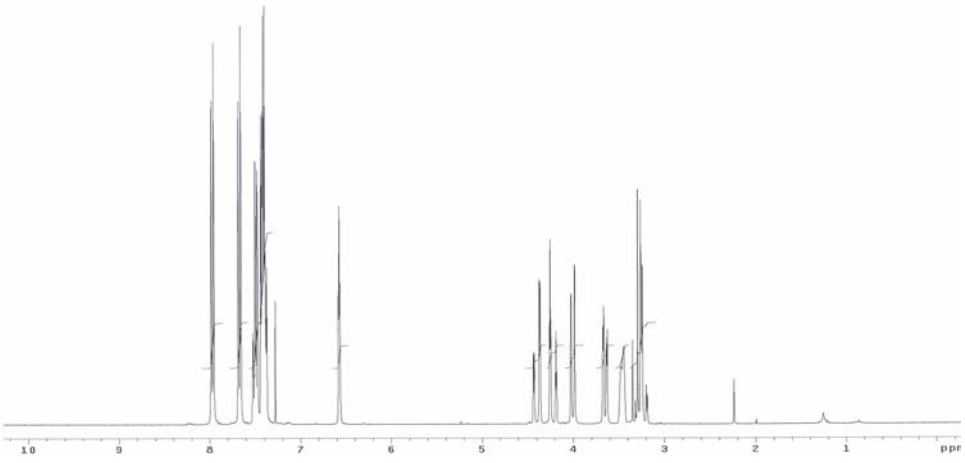


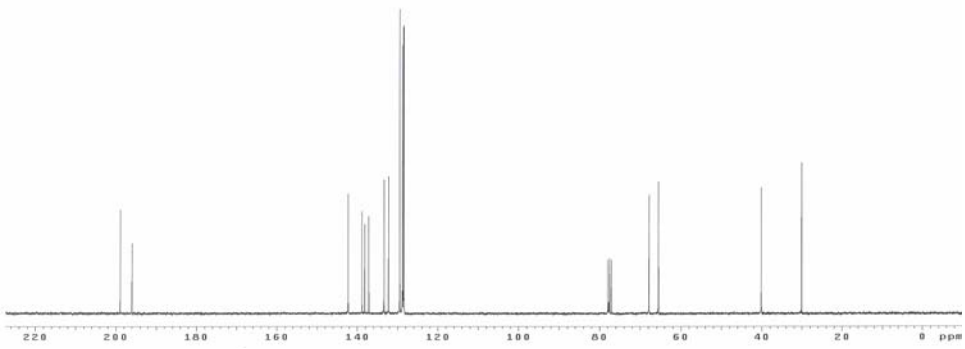


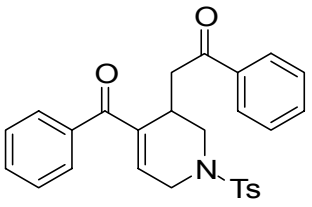


4-2.6a

2-(4-Benzoyl-3,6-dihydro-2H-pyran-3-yl)-1-phenyl-ethanone. ^{1}HNMR (300 MHz, $CDCl_3$): δ 7.98~7.95 (m, 2H), 7.68~7.65 (m, 2H), 7.52~7.47 (m, 2H), 7.44~7.37 (m, 4H), 6.57 (t, J = 2.82 Hz, 1H), 4.40 (dd, J = 3.33, 19.21 Hz, 1H), 4.22 (dt, J = 2.31, 19.21 Hz, 1H), 4.00 (dd, J = 1.54, 11.53 Hz, 1H), 3.65 (dd, J = 2.82, 11.53 Hz, 1H), 3.48~3.44 (m, 1H), 3.35~3.18 (m, 2H). ^{13}CNMR (75 MHz, $CDCl_3$): δ 198.90, 196.00, 142.23, 138.81, 138.14, 137.10, 133.34, 132.22, 129.43, 128.80, 128.55, 128.40, 67.81, 65.48, 40.12, 30.11. HRMS: calcd. for $C_{20}H_{19}O_3$ (M+1): 307.1334, found: 307.1334. FTIR (neat): 2982, 1732, 1685, 1647, 1598, 1448, 1373, 1046, 699cm^{-1}.

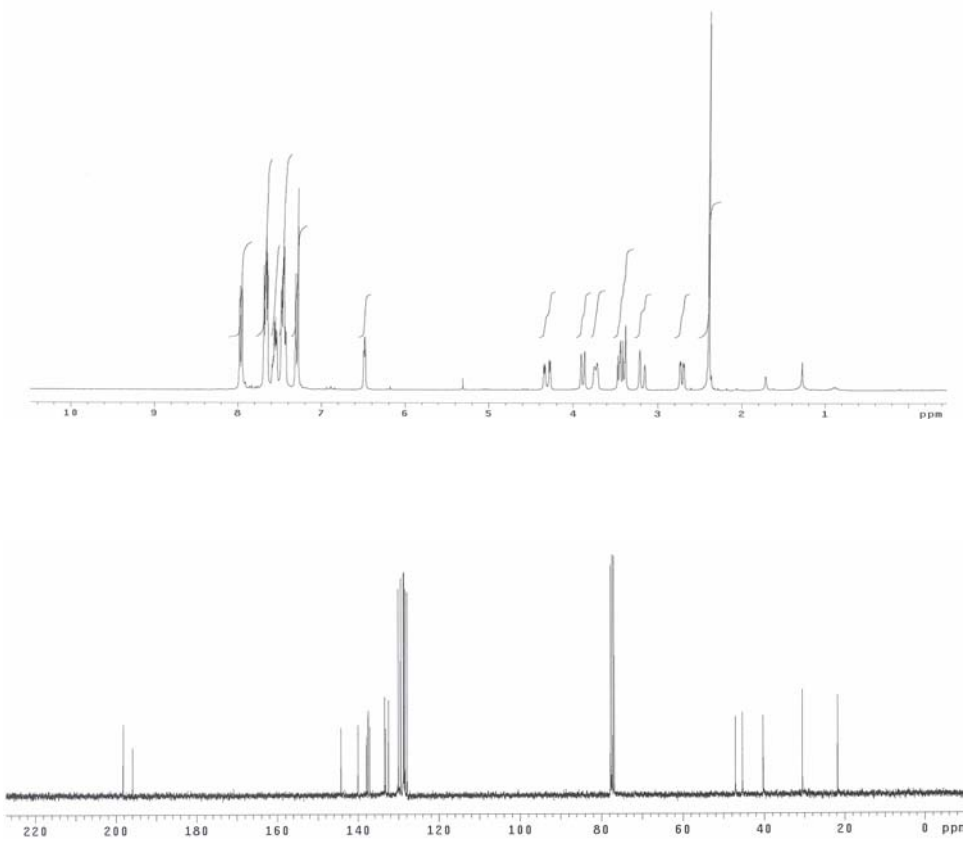


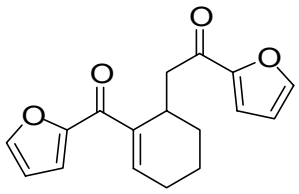




4-2.7a

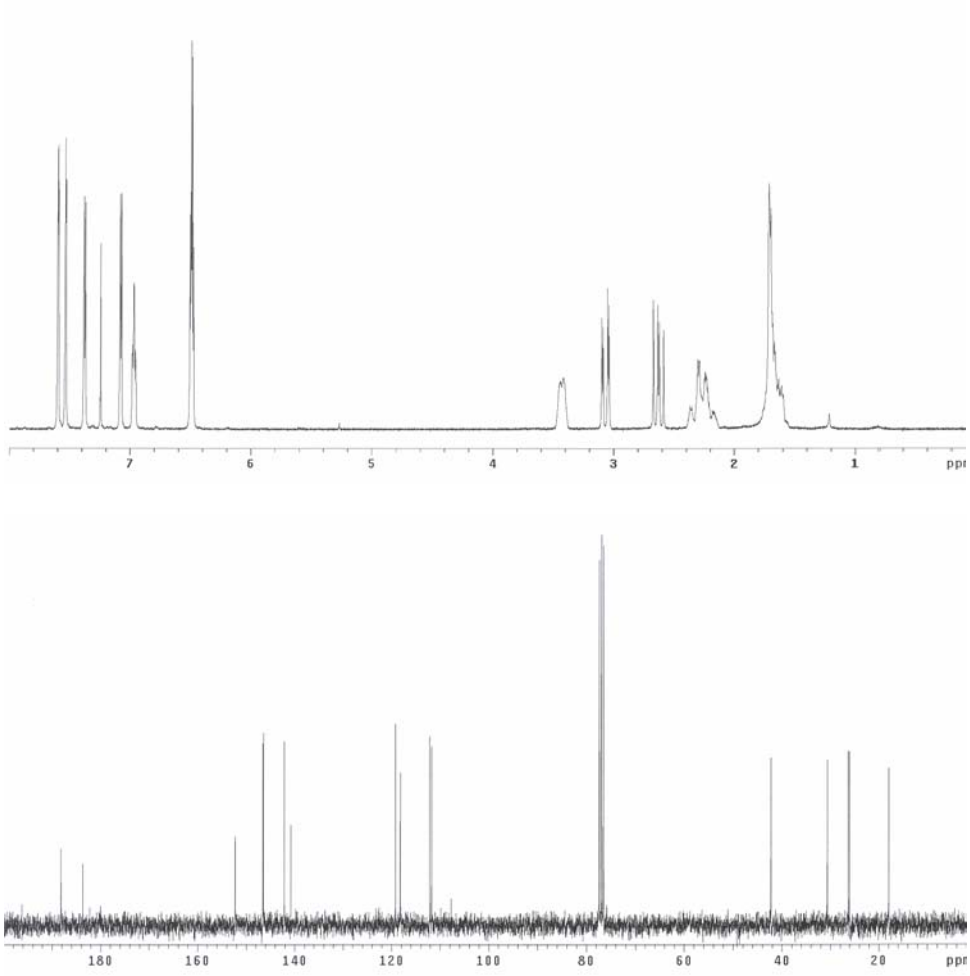
2-[4-Benzoyl-1-(toluene-4-sulfonyl)-1,2,3,6-tetrahydro-pyridin-3-yl]-1-phenyl-ethanone. ^{1}HNMR (300 MHz, $CDCl_3$): δ 7.98~7.95 (m, 2H), 7.69~7.65 (m,4H), 7.59~7.53 (m, 2H), 7.48~7.42 (m, 4H), 7.31~7.28 (m, 2H), 6.49~6.47 (m, 1H), 4.31 (dd, J = 4.35, 18.70 Hz, 1H), 3.89 (d, J = 12.04 Hz, 1H), 3.75~3.71 (m, 1H), 3.47~3.38 (m, 2H), 3.18 (d, J = 18.70 Hz, 1H), 2.71 (dd, J = 2.31, 12.04 Hz, 1H), 2.39 (s, 3H). ^{13}CNMR (75 MHz, $CDCl_3$): δ 198.26, 195.88, 144.22, 139.99, 137.90, 137.50, 137.04, 133.40, 133.16, 132.16, 132.47, 130.07, 129.48, 128.78, 128.62, 128.37, 127.90, 47.07, 45.37, 40.25, 30.55, 21.77. HRMS: calcd. for $C_{27}H_{26}NO_4S$ (M+1): 460.1583, found: 460.1590. FTIR (neat): 3022, 1684, 1648, 1598, 1448, 1215, 1165, 907cm^{-1}.

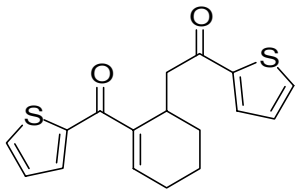




4-2.8a

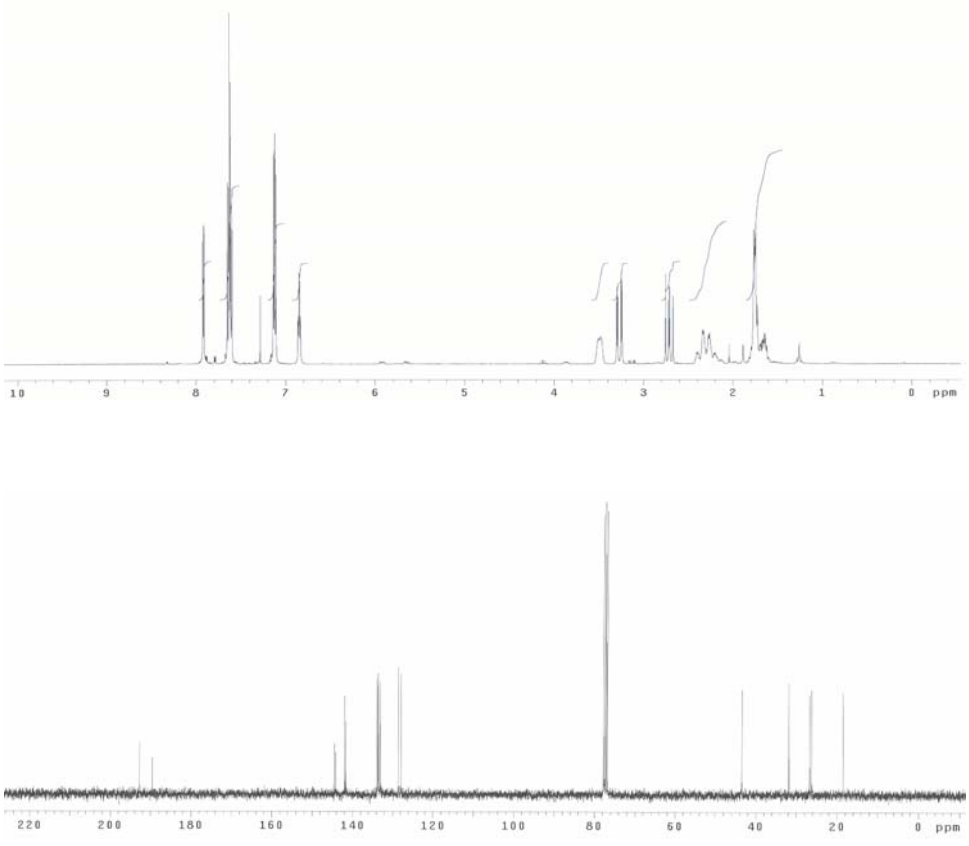
2-[2-Furan-2-carbonyl)-cyclohex-2-enyl]-1-furan-2-yl-ethanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59~7.53 (m, 2H), 7.37 (d, J = 3.6 Hz, 1H), 7.07 (d, J = 3.6 Hz, 1H), 6.97~6.95 (m, 1H), 6.50~6.47 (m, 2H), 3.43~3.41 (m, 1H), 3.06 (dd, J = 3.3, 14.7 Hz, 1H), 2.63 (dd, J = 10.80, 14.7 Hz, 1H), 2.30~2.18 (m, 2H), 1.76~1.60 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 188.18, 183.65, 152.29, 152.25, 146.54, 146.44, 142.15, 140.79, 119.19, 118.19, 112.13, 111.74, 42.25, 30.59, 26.30, 26.04, 17.91. FTIR (neat): 3005, 1661, 1619, 1464, 1275, 1260, 764cm^{-1}. HRMS: calcd. for $C_{17}H_{17}O_4$(M+1): 285.1127, found: 285.1133.

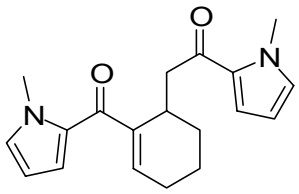




4-2.9a

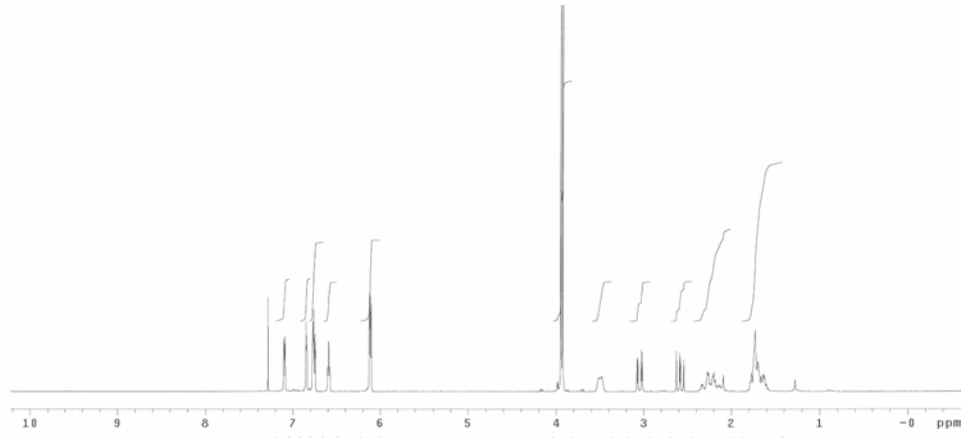
2-[2-(Thiophene-2-carbonyl)-cyclohex-2-enyl]-1-thiophen-2-yl-ethanone. ^{1}HNMR (300 MHz, $CDCl_3$): δ 7.92 (dd, J = 1.28, 3.84Hz, 1H), 7.65~7.60 (m, 3H), 7.13 (dd, J = 1.54, 3.84 Hz, 2H), 6.85 (dd, J = 1.28, 3.85 Hz, 1H), 3.51~3.48 (m, 1H), 3.27 (dd, J = 3.07, 14.34 Hz, 1H), 2.73 (dd, J = 10.76, 14.34 Hz, 1H), 2.34~2.26 (m, 2H), 1.80~1.62 (m, 4H). ^{13}CNMR (75 MHz, $CDCl_3$): δ 192.74, 189.56, 144.52, 144.17, 141.98, 141.71, 133.91, 133.61, 133.53, 133.13, 128.56, 127.92, 43.44, 31.82, 26.72, 26.25, 18.49. HRMS: calcd. for $C_{17}H_{17}O_2S_2$ (M+1): 317.0670, found: 317.0671. FTIR (neat): 3090, 2933, 1655, 1618, 1515, 1414, 723cm^{-1}.

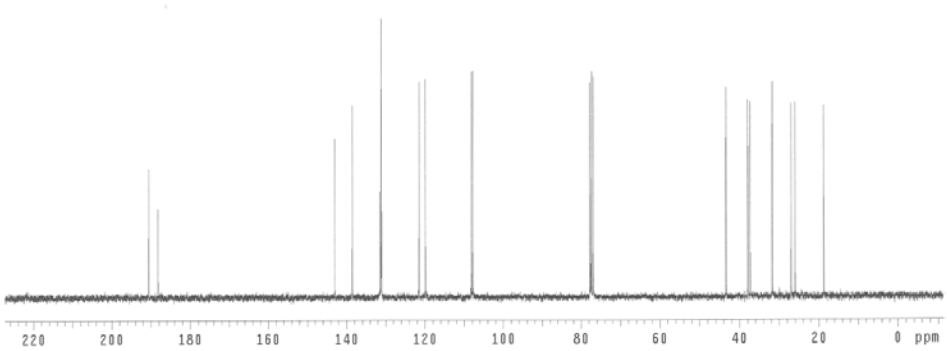


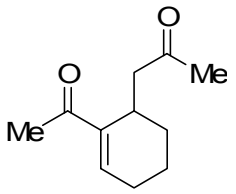


4-2.10a

2-[2-(1-Methyl-1H-pyrrole-2-carbonyl)-cyclohex-2-enyl]-1-(1-methyl-1H-pyrrol-2-yl)-ethanone. ^{1}HNMR (300 MHz, $CDCl_3$): δ 7.11~7.09 (m, 1H), 6.85~6.84 (m, 1H), 6.78~6.74 (m, 2H), 6.59 (t, J = 3.84 Hz, 1H), 6.12~6.10 (m, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 3.51~3.47 (m, 1H), 3.05 (dd, J = 3.33, 14.34 Hz, 1H), 2.58 (dd, J = 11.01, 14.34 Hz, 1H), 2.32~2.18 (m, 2H), 1.78~1.60 (m, 4H). ^{13}CNMR (75 MHz, $CDCl_3$): δ 190.58, 188.17, 142.95, 138.53, 131.47, 131.17, 131.04, 121.47, 119.87, 108.15, 107.78, 43.38, 37.88, 37.34, 31.73, 27.02, 26.02, 18.71. HRMS: calcd. for $C_{19}H_{23}N_2O_2$, (M+1): 311.1760, found: 311.1758. FTIR (neat): 3006, 2937, 1644, 1613, 1525, 1406, 1060cm^{-1}.

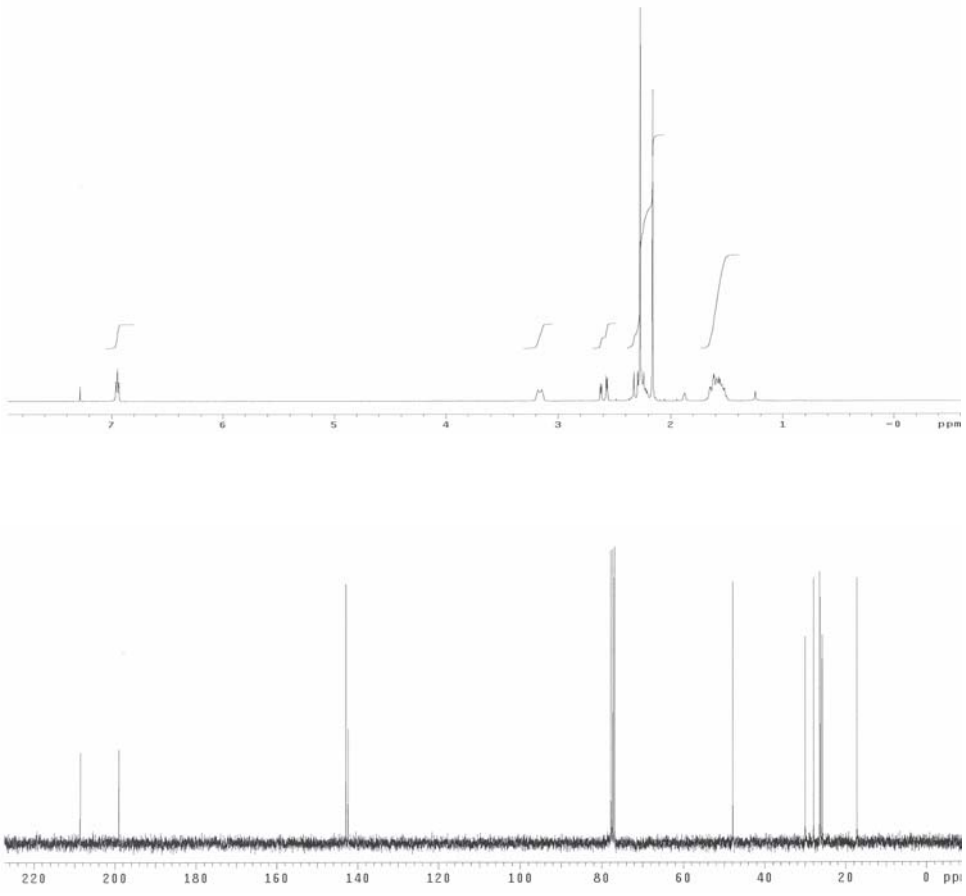


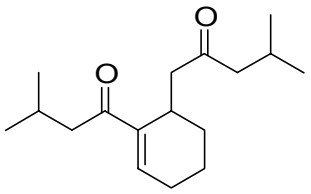




4-2.11a

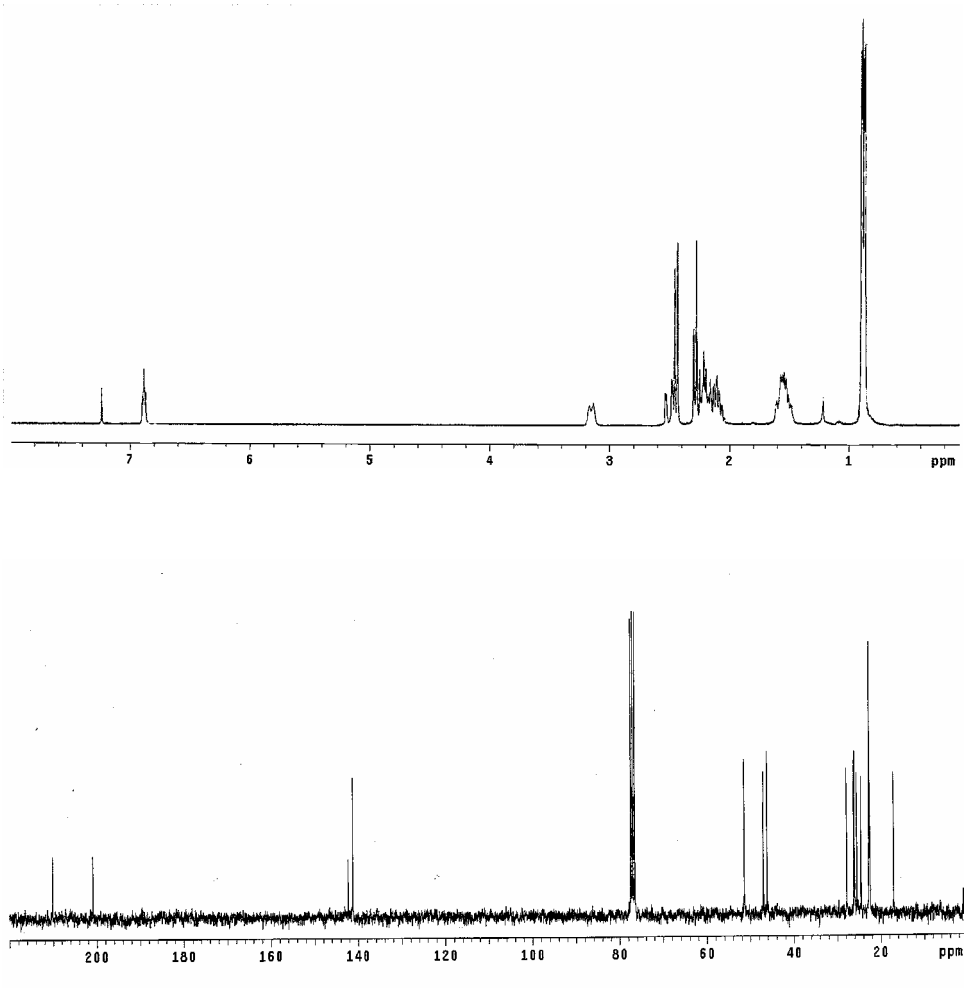
1-(2-Acetyl-cyclohex-2-enyl)-propan-2-one. ^{1}HNMR (300 MHz, $CDCl_3$): δ 6.95 (t, J = 3.84 Hz, 1H), 3.18~3.14 (m, 1H), 2.59 (dd, J = 3.07, 5.63 Hz, 1H), 2.32~2.21 (m, 3H), 2.27 (s, 3H), 2.16 (s, 3H), 1.65~1.52 (m, 4H). ^{13}CNMR (75 MHz, $CDCl_3$): δ 208.61, 199.08, 142.90, 142.34, 47.82, 29.99, 27.96, 26.44, 26.31, 25.82, 17.21. HRMS: calcd. for $C_{11}H_{17}O_2$ (M+1): 181.1229, found: 181.1226. FTIR (neat): 2932, 2864, 1714, 1663, 1633, 1617, 1272, 1238, 734cm^{-1}.

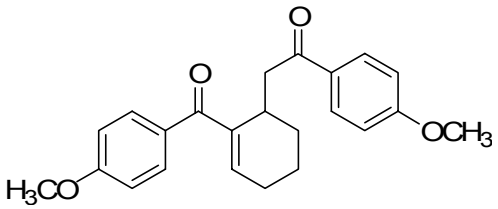




4-2.12a

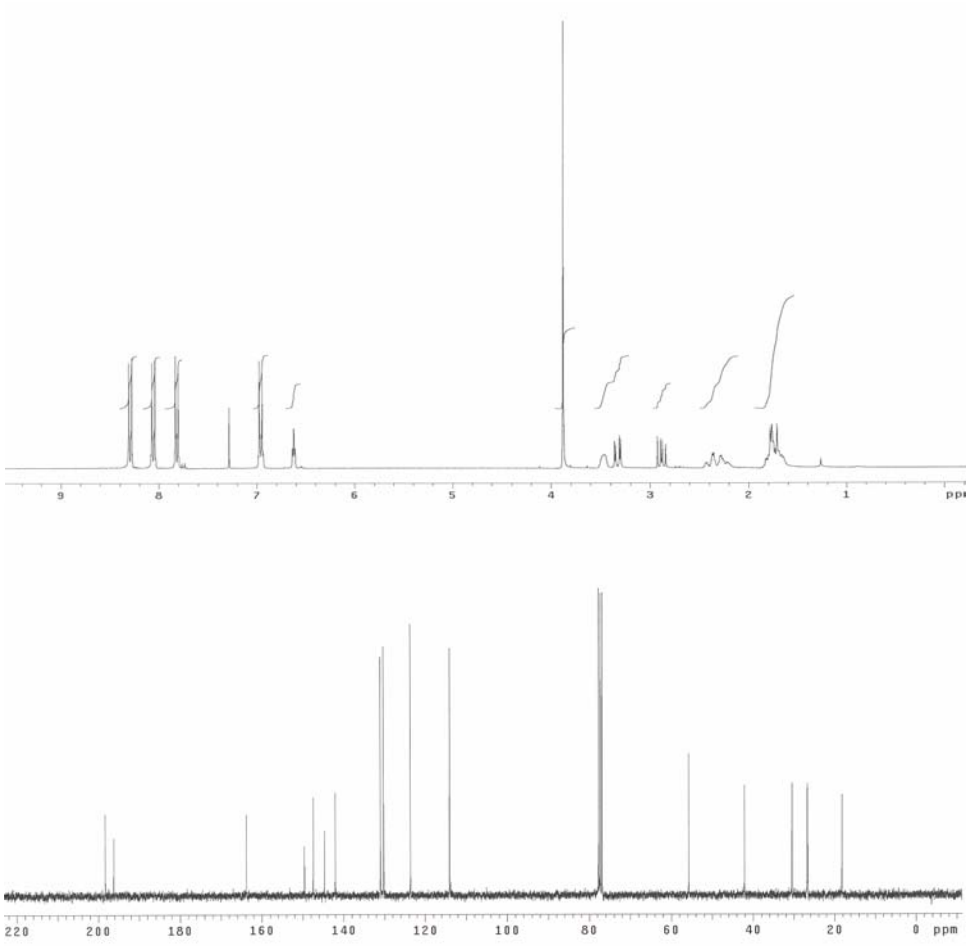
4-Methyl-1-[2-(3-methylbutyryl)-cyclohex-2-enyl]-pentan-2-one. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.09 (t, J = 3.97 Hz, 1H), 3.17~3.13 (m, 1H), 2.54~2.43 (m, 3H), 2.30~2.06 (m, 7H), 1.60~1.48 (m, 4H), 0.90~0.86 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 210.14, 200.94, 142.32, 141.22, 51.44, 47.03, 46.15, 27.80, 26.15, 26.04, 25.51, 24.57, 22.78, 522.65, 22.51, 17.07. FTIR (neat): 2955, 2870, 1710, 1660, 1399, 1366, 1195cm^{-1}. HRMS: calcd. for $C_{17}H_{29}O_2$ (M+1): 265.2168, found: 265.2173.

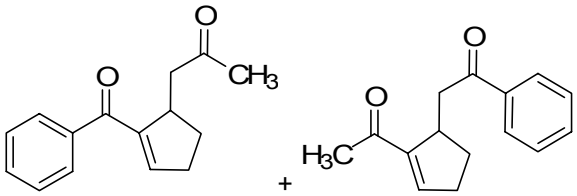




4-2.13a

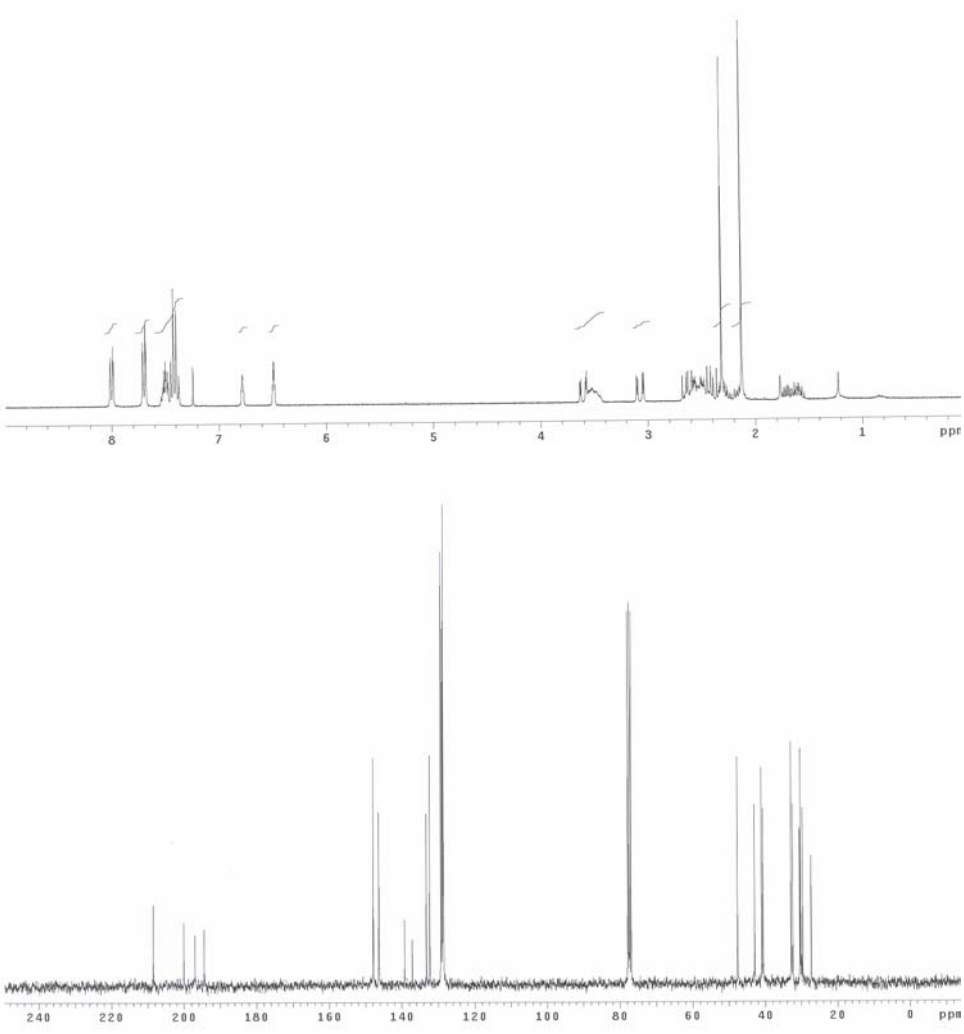
2-[2-(4-Methoxy-benzoyl)-cyclohex-2-enyl]-1-(4-methoxy-phenyl)-ethanone. ^{1}HNMR (300 MHz, $CDCl_3$): δ 8.31~8.27 (m, 2H), 8.08~8.03 (m, 2H), 7.84~7.80 (m, 2H), 6.99~6.94 (m, 2H), 6.62 (t, J = 3.33 Hz, 1H), 3.88 (s, 3H), 3.48~3.42 (m, 2H), 3.33 (dd, J = 3.59, 14.60 Hz, 1H), 2.88 (dd, J = 9.73, 14.60 Hz, 1H), 2.47~2.26 (m, 2H), 1.83~1.65 (m, 4H). ^{13}CNMR (75 MHz, $CDCl^3$): δ 198.29, 196.24, 163.76, 149.56, 147.42, 144.66, 142.01, 130.96, 130.23, 130.15, 123.61, 114.02, 55.72, 42.12, 30.50, 26.74, 26.64, 18.19. HRMS: calcd. for $C_{22}H_{22}NO_5$, (M+1): 389.1498, found: 380.1487. FTIR (neat): 2936, 1670, 1648, 1600, 1260, 1171cm^{-1}.

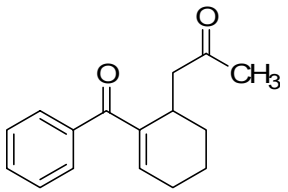




4-2.14a + 4-2.14b

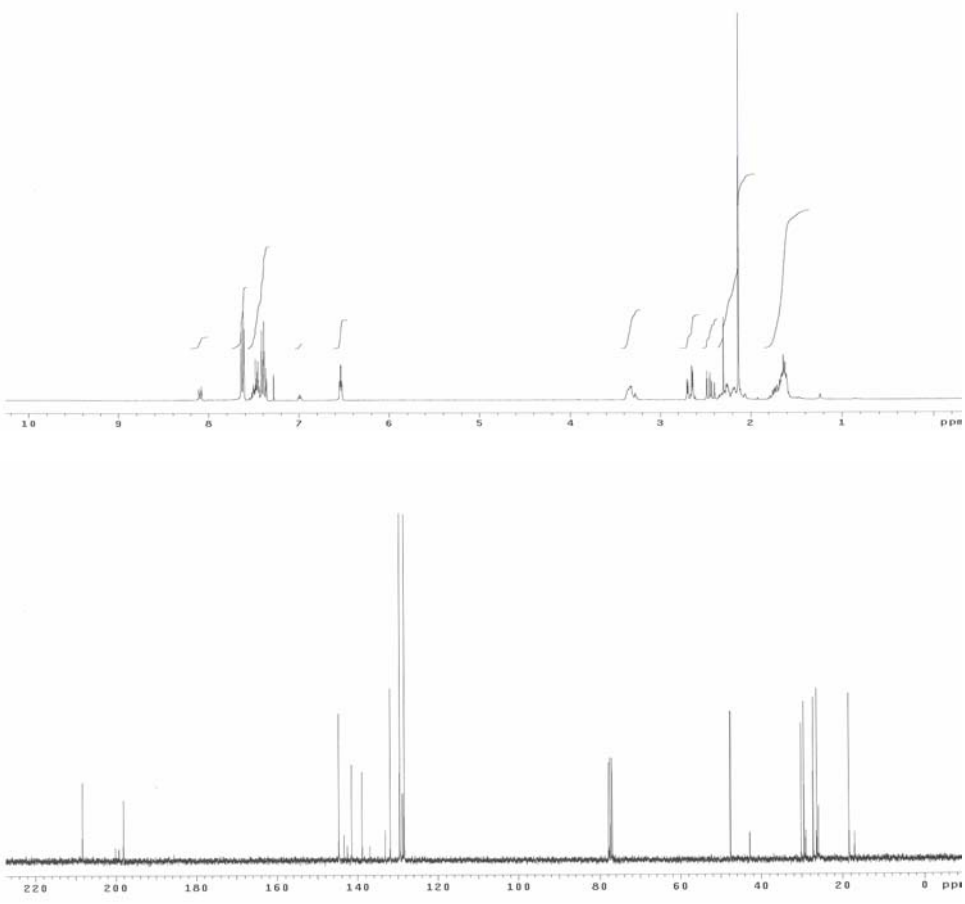
1-(2-Benzoyl-cyclopentyl)-propan-2-one (4-2.14a) and 2-(2-Acetyl-cyclopentyl)-1-phenyl-ethanone (4-2.14b.
HRMS: calcd. for $C_{15}H_{17}O_2$ (M+1): 229.1229, found: 229.1227.
FTIR (neat): 1712, 1681, 1661, 1640, 1279, 1260, 751cm^{-1}.

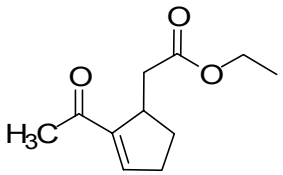




4-2.15a

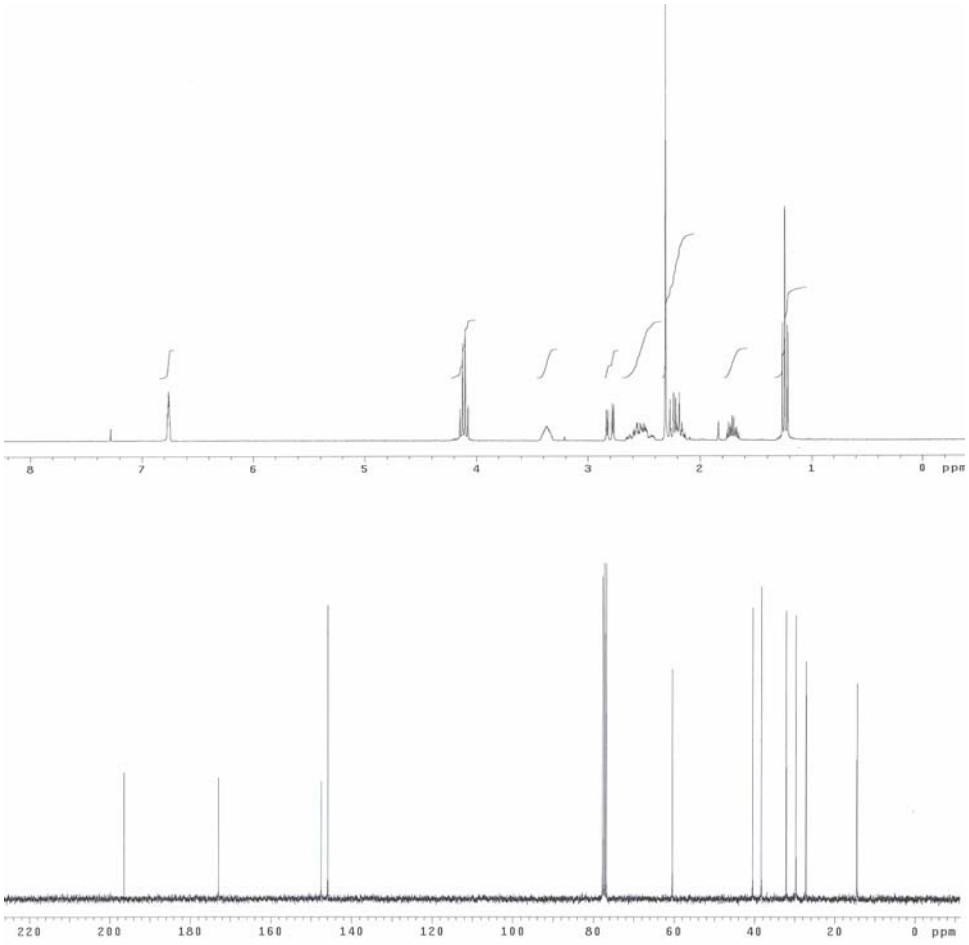
1-(2-Benzoyl-cyclohex-2-enyl)-propan-2-one. ^{1}HNMR (300 MHz, $CDCl_3$): δ 7.65~7.61 (m, 2H), 7.52~7.36 (m, 3H), 6.54 (dt, J = 1.28, 3.84 Hz, 1H), 3.38~3.27 (m, 1H), 2.67 (dd, J = 3.84, 15.88 Hz, 1H), 2.44 (dd, J = 9.73, 15.88 Hz, 1H), 2.31~2.06 (m, 2H), 2.14 (s, 3H), 1.76~1.58 (m, 4H). ^{13}CNMR (75 MHz, $CDCl_3$): δ 208.29, 198.09, 144.68, 141.50, 138.89, 131.87, 129.48, 128.33, 47.60, 30.17, 29.48, 27.20, 26.26, 18.40. HRMS: calcd. for $C_{16}H_{19}O_2$ (M+1): 243.1385, found: 243.1388. FTIR (neat): 2929, 2860, 1714, 1658, 1633, 1445, 1268, 1249, 697cm^{-1}.

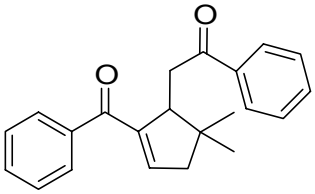




4-2.16a

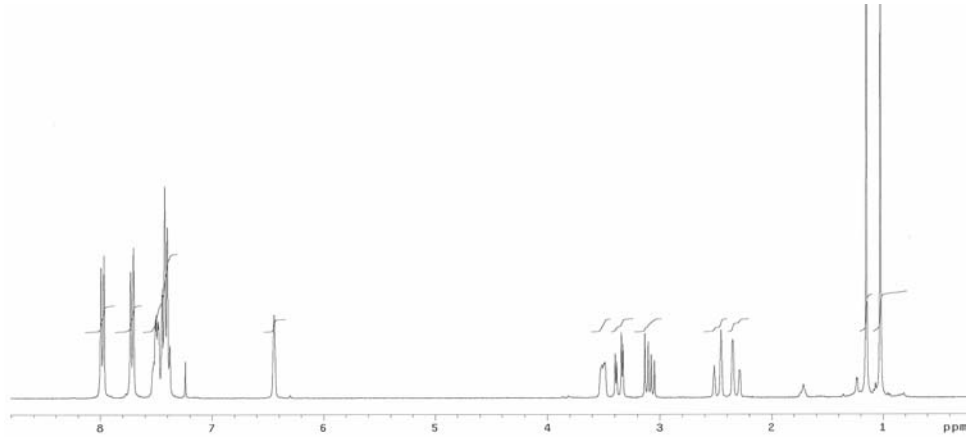
(2-Acetyl-cyclopent-2-enyl)-acetic acid ethyl ester. ^{1}HNMR (300 MHz, $CDCl_3$): δ 6.76 (dt, J = 1.28, 2.56 Hz, 1H), 4.11 (q, J = 7.17 Hz, 2H), 3.41~3.33 (m, 1H), 2.80 (dd, J = 3.84, 15.37 Hz, 1H), 2.63~2.42 (m, 2H), 2.30 (s, 3H), 2.27~2.13 (m, 2H), 1.76~1.65 (m, 1H), 1.24 (t, J = 7.17Hz, 3H). ^{13}CNMR (75 MHz, $CDCl_3$): δ 196.63, 172.98, 147.49, 145.86, 60.40, 40.50, 38.32, 32.14, 29.72, 27.20, 14.48. HRMS: calcd. for $C_{11}H_{17}O_3$ (M+1): 197.1178, found: 197.1178. FTIR (neat): 2980, 1731, 1666, 1613, 1434, 1256, 1174, 1029cm^{-1}.

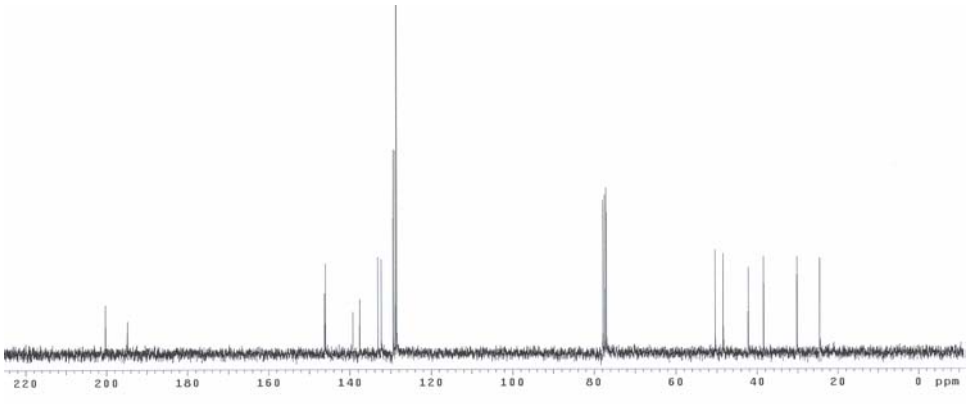


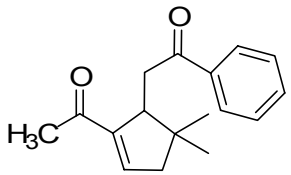


4-2.17a

2-(2-Benzoyl-5,5-dimethyl-cyclopent-2-enyl)-1-phenyl-ethanone. ^{1}HNMR (300 MHz, $CDCl_3$): δ 7.98 (d, J = 7.43 Hz, 2H), 7.72 (d, J = 7.17 Hz, 2H), 7.53~7.38 (m, 6H), 6.44 (s, 1H), 3.51~3.48 (m, 1H), 3.39~3.32 (dd, J = 4.10, 16.65 Hz, 1H), 3.13~3.05 (dd, J = 8.71, 16.39 Hz, 1H), 2.48 (d, J = 18.44 Hz, 1H), 2.32 (d, J = 18.44 Hz, 1H), 1.15 (s, 1H), 1.02 (s, 1H). ^{13}CNMR (75MHz, $CDCl_3$): δ 200.247, 194.82, 146.23, 146.01, 139.29, 137.61, 133.12, 132.31, 129.35, 128.89, 128.54, 50.32, 48.37, 42.20, 38.40, 30.14, 24.51. HRMS calcd. for $C_{22}H_{23}O_2$ (M+1): 319.1698, found: 319.1698. FTIR (neat): 3006, 1679, 1634, 1597, 1260, 689cm^{-1}. Mp = 90~92 ^{o}C.

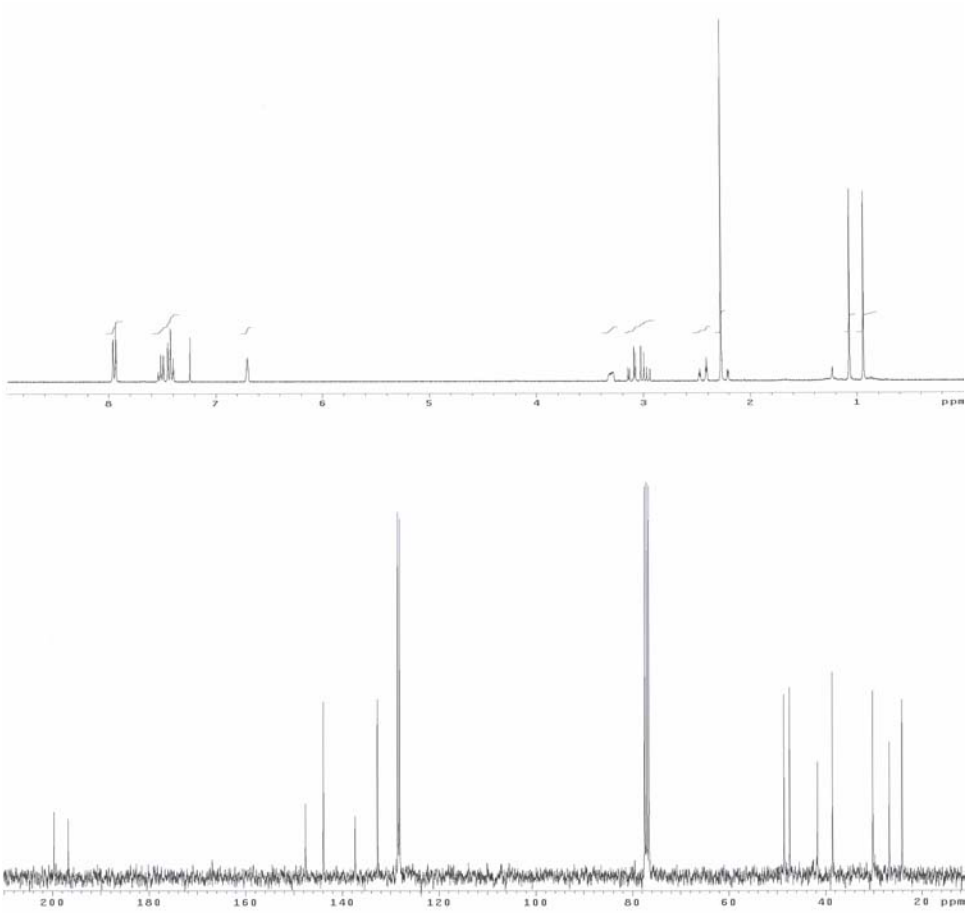


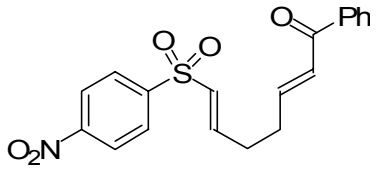




4-2.18a

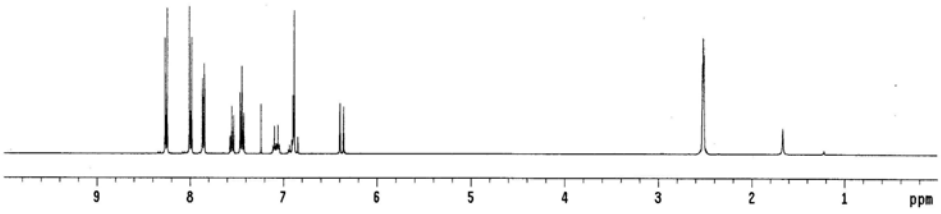
2-(2-Acetyl-5,5-dimethyl-cyclopent-2-enyl)-1-phenyl-ethanone. ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.96~7.93 (m, 2H), 7.54~7.39 (m, 3H), 6.75 (t, J = 2.75 Hz, H), 3.30~3.28 (m, 1H), 3.14~3.07 (dd, J = 4.27, 16.77Hz, 1H), 3.02~2.94 (dd, J = 8.69, 16.77Hz, 1H), 2.48~2.40, 1H), 2.27 (s, 3H), 2.26~2.20 (m, 1H), 1.23 (s, 3H), 1.07 (s, 3H). ^{13}CNMR (75MHz, $CDCl_3$): δ 199.67, 196.74, 147.54, 143.85, 137.31, 132.64, 128.44, 128.05, 48.53, 47.37, 41.63, 38.50, 30.10, 26.66, 24.04. HRMS calcd. for $C_{17}H_{21}O_2$ (M+1): 257.1542, found: 157.1544. FTIR (neat): 2955, 1677. 1654, 1207. 690cm^{-1}. Mp = 100~102 ^{o}C.

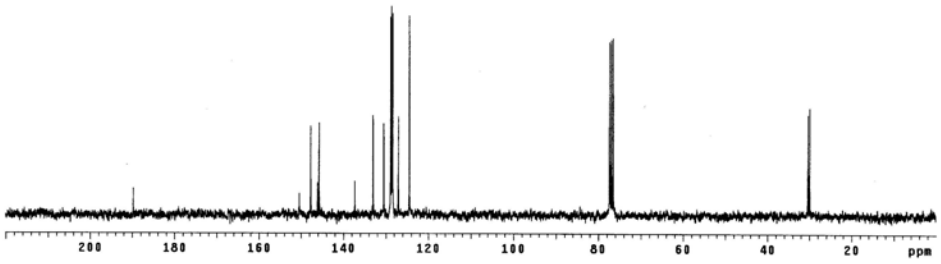


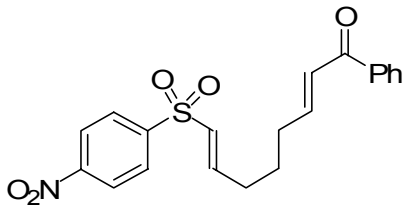


4-3.1

7-(4-Nitro-benzenesulfonyl)-1-phenyl-hepta-2,6-dien-1-one. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.25 (d, *J*=8.89 Hz, 2H), 8.00 (d, *J*=8.89 Hz, 2H), 7.86 (d, *J*=8.21 Hz, 2H), 7.55 (dt, *J*=7.35, 1.37 Hz, 1H), 7.44 (t, *J*=7.52 Hz, 2H), 7.08 (m, 1H), 6.87 (m, 2H), 6.38 (d, *J*= 15.0 Hz, 1H), 2.52 (t, *J*= 2.74 Hz, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 189.8, 150.4, 147.8, 146.1, 145.8, 137.3, 133.0, 130.5, 128.9, 128.6, 128.4, 127.0, 124.5, 30.4, 30.0. HRMS: calcd for $C_{19}H_{18}NO_5S$ [M+1] 372.0904, found 372.0906. FTIR (film): 3054, 2987, 2685, 2305, 1686, 1606, 1535, 1421, 1350, 1266, 1149, 1086, 1013, 896. Mp = 60-61ºC

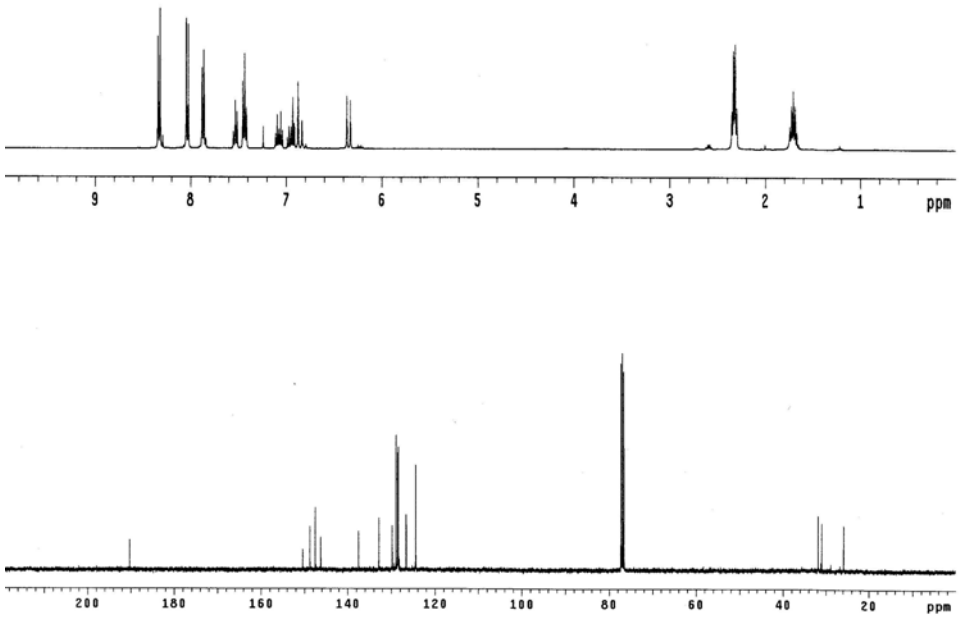


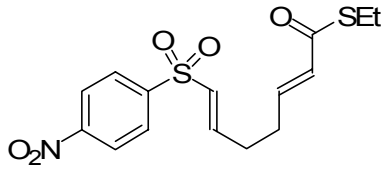




4-3.2

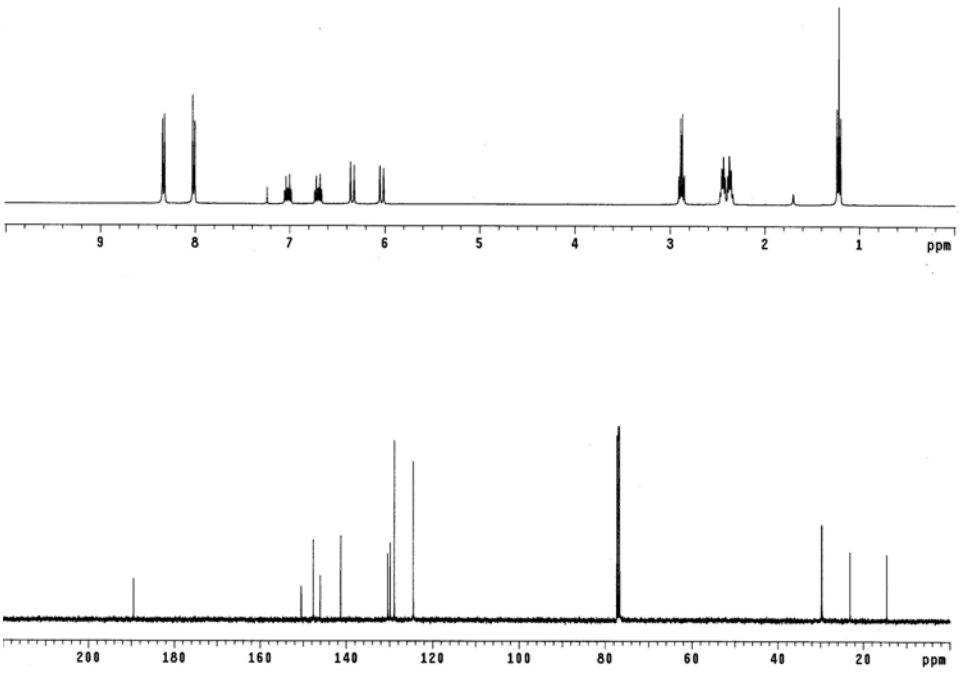
8-(4-Nitro-benzenesulfonyl)-1-phenyl-octa-2,7-dien-1-one. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.33 (d, *J*=8.89 Hz, 2H), 8.04 (d, *J*=8.89 Hz, 2H), 7.87 (d, *J*=7 *J*=.87 Hz, 2H), 7.53 (dt, *J*=7.35, 1.20 Hz, 1H), 7.43 (t, *J*=7.52 Hz, 2H), 7.08 (dt, *J*=15.0, 6.84 Hz, 1H), 6.95 (dt, *J*=15.4, 6.67 Hz, 1H), 6.86 (d, *J*=15.4 Hz, 1H), 6.35 (m, 1H), 2.33 (q, *J*=6.84 Hz, 4H), 1.70 (qt, *J*=7.44 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.3, 150.4, 148.7, 147.5, 146.2, 137.5, 132.8, 129.8, 128.9, 128.5, 128.4, 126.6, 124.4, 124.4, 31.8, 30.9, 25.9. HRMS: calcd for $C_{20}H_{20}NO_5S$ [M+1] 386.1068, found 386.1062. FTIR (film): 3054, 2987, 2685, 2305, 1686, 1606, 1535, 1421, 1350, 1266, 1149, 1086, 1013, 896. Mp = 63-65ºC.

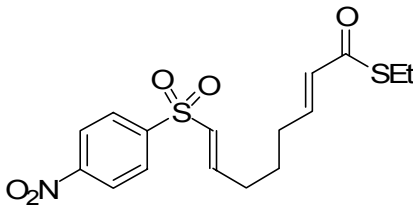




4-3.3

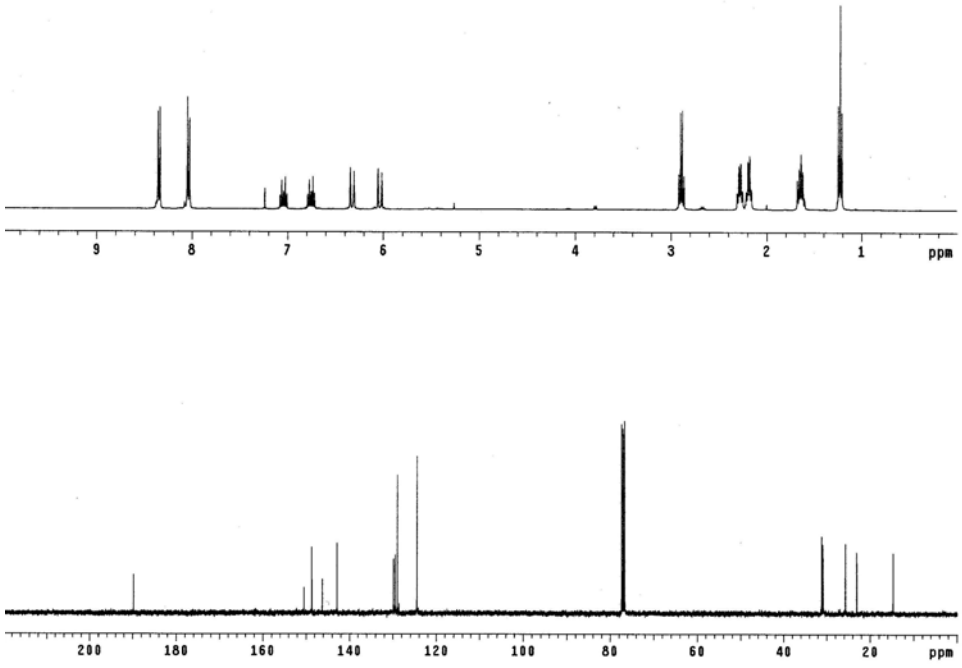
7-(4-Nitro-benzenesulfonyl)-hepta-2,6-dienethioic acid S-ethyl ester. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.33 (d, *J*=9.23 Hz, 2H), 8.01 (d, *J*=8.55 Hz, 2H), 7.02 (dt, *J*=15.0, 6.67 Hz, 1H), 6.70 (dt, *J*=15.7, 6.67 Hz, 1H), 6.34 (d, *J*=15.4 Hz, 1H), 6.03 (d, *J*=15.4 Hz, 1H), 2.88 (q, *J*=7.52 Hz, 2H), 2.45 (q, *J*=6.95 Hz, 2H), 2.37 (q, *J*=6.95 Hz, 2H), 1.22 (t, *J*=7.52 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 189.4, 150.4, 147.6, 146.1, 141.3, 130.4, 129.8, 128.9, 124.5, 29.7, 29.6, 23.1, 14.6. HRMS: calcd for $C_{14}H_{16}NO_5S$ [M+1] 356.0633, found 356.0626. FTIR (film): 3055, 2987, 2685, 2305, 1667, 1631, 1535, 1422, 1350, 1265, 1149, 1086, 972, 896. Mp = 78-79ºC.

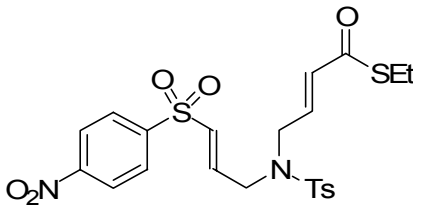




4-3.4

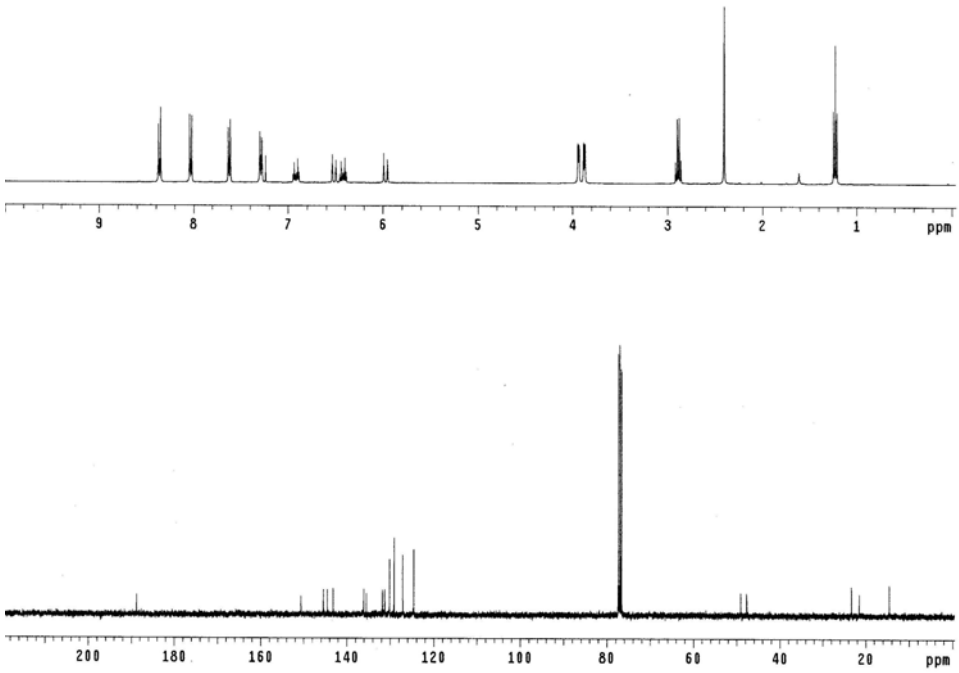
8-(4-Nitro-benzenesulfonyl)-octa-2,7-dienethioic acid S-ethyl ester. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.35 (d, *J*=8.55 Hz, 2H), 8.04 (d, *J*=8.89 Hz, 2H), 7.04 (dt, *J*=15.0, 6.75 Hz, 1H), 6.75 (dt, *J*=15.7, 7.01 Hz, 1H), 6.32 (d, *J*=15.0 Hz, 1H), 6.03 (d, *J*=15.7 Hz, 1H), 2.89 (q, *J*=7.41 Hz, 2H), 2.28 (q, *J*=6.84 Hz, 2H), 2.19 (q, *J*=7.18 Hz, 2H), 1.64 (qt, *J*=7.61 Hz, 2H), 1.23 (t, *J*=7.35 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 189.7, 150.4, 148.6, 146.2, 142.8, 129.8, 129.5, 128.9, 124.5, 31.1, 30.8, 25.7, 23.1, 14.7. HRMS: calcd for $C_{15}H_{18}NO_5S$ [M+1] 370.0781, found 370.0783. FTIR (film): 3055, 2987, 2685, 2305, 1667, 1631, 1535, 1422, 1350, 1265, 1149, 1086, 972, 896. Mp = 81-82ºC.

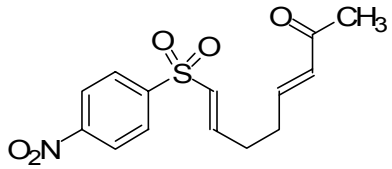




4-3.5

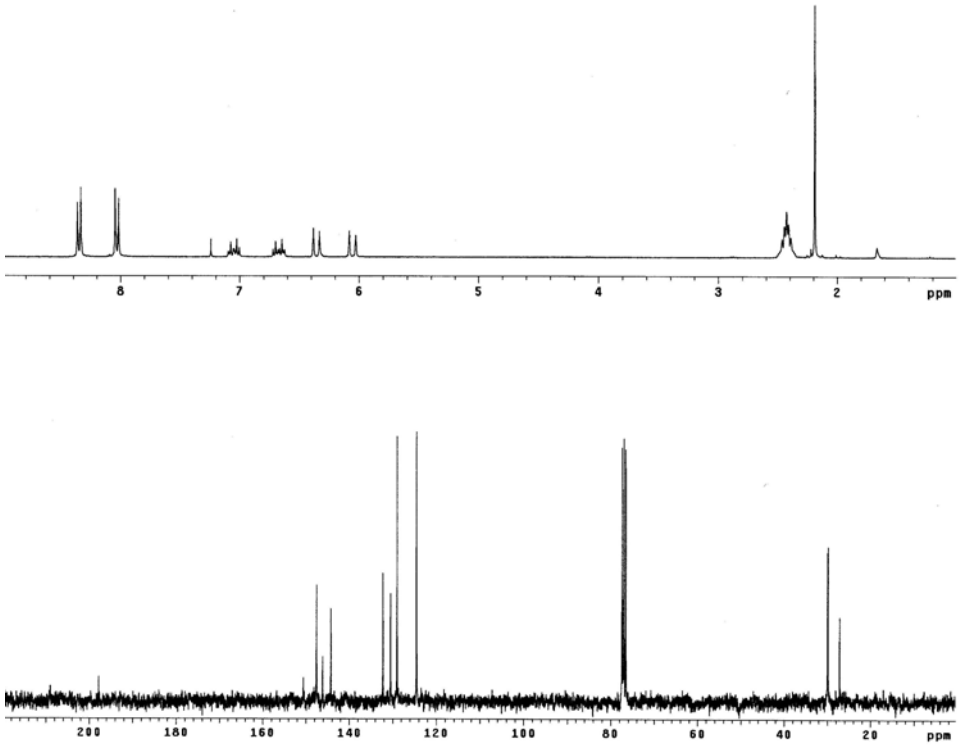
4-[[3-(4-Nitro-benzenesulfonyl)-allyl]-(toluene-4-sulfonyl)-amino]-but-2-enethioic acid S-ethyl ester. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.37 (d, *J*=8.89 Hz, 2H), 8.03 (d, *J*=8.89 Hz, 2H), 7.62 (d, *J*=8.21 Hz, 2H), 7.29 (d, *J*=7.87 Hz, 2H), 6.92 (dt, *J*=15.0, 4.96 Hz, 1H), 6.52 (d, *J*=15.0 Hz, 1H), 6.42 (dt, *J*=15.4, 5.98 Hz, 1H), 5.97 (d, *J*=15.4 Hz, 1H), 3.94 (d, *J*=4.79 Hz, 2H), 3.88 (d, *J*=6.16 Hz, 2H), 2.89 (q, *J*=7.41 Hz, 2H), 1.23 (t, *J*=7.35 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 188.8, 150.6, 145.4, 144.5, 143.2, 136.1, 135.5, 131.8, 131.2, 130.1, 129.1, 127.1, 124.6, 49.1, 47.7, 23.3, 21.5, 14.5. HRMS: calcd for $C_{22}H_{25}N_2O_7S_3$ [M+1] 525.0836, found 525.0824. FTIR (film): 3055, 2987, 2685, 2305, 1670, 1631, 1536, 1422, 1350, 1265, 1163, 1152, 1086, 972, 896. Mp = 134-136ºC.

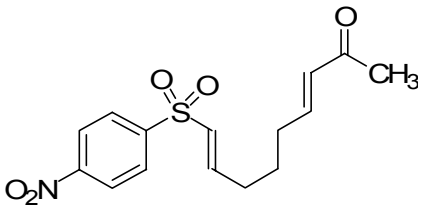




4-3.6

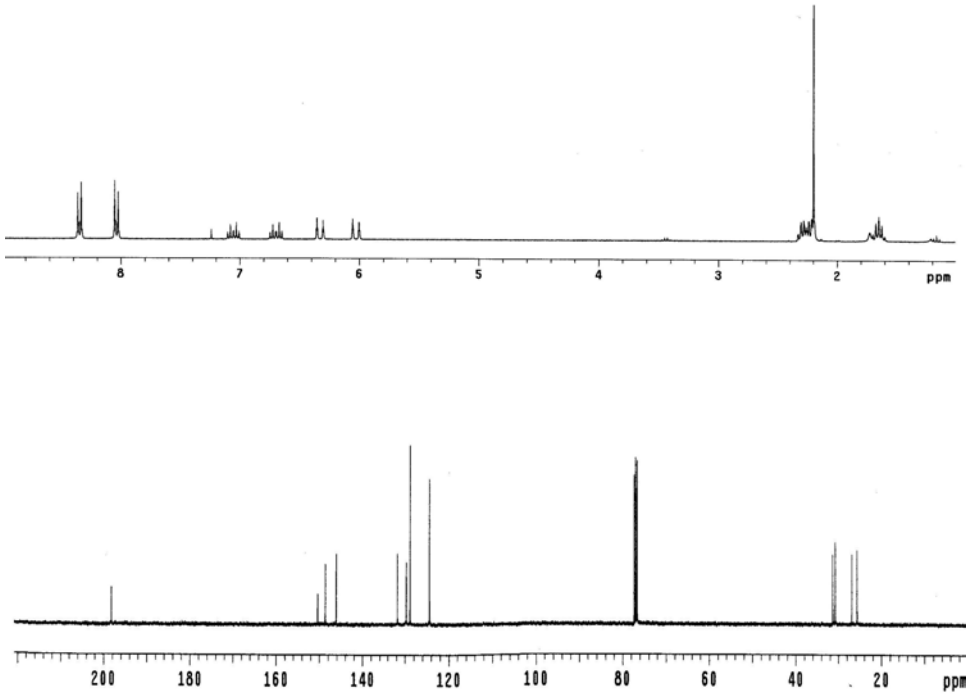
8-(4-Nitro-benzenesulfonyl)-octa-3,7-dien-2-one. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.35 (d, *J*=7.93 Hz, 2H), 8.03 (d, *J*=7.85 Hz, 2H), 7.05 (dt, *J*=14.9, 6.29 Hz, 1H), 6.67 (dt, *J*=15.9, 6.44 Hz, 1H), 6.36 (d, *J*=15.1 Hz, 1H), 6.06 (d, *J*=15.9 Hz, 1H), 2.43 (qt, *J*=5.60 Hz, 4H), 2.19 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 197.8, 150.6, 147.5, 146.1, 144.2, 132.2, 130.5, 129.0, 124.5, 30.0, 29.9, 27.2. HRMS: calcd for $C_{14}H_{16}NO_5S$ [M+1] 310.0747, found 310.0749. FTIR (film): 3054, 2987, 2685, 2305, 1675, 1628, 1535, 1422, 1351, 1265, 1149, 1086, 979, 896. Mp = 78-79ºC.

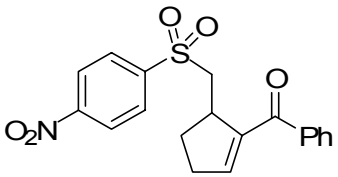




4-3.7

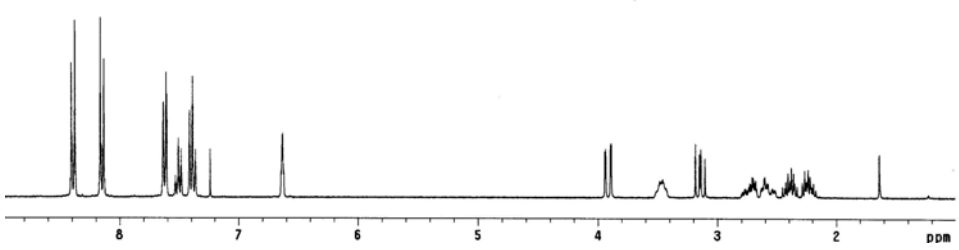
9-(4-Nitro-benzenesulfonyl)-nona-3,8-dien-2-one. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.32 (d, *J*=8.89 Hz, 2H), 8.02 (d, *J*=8.89 Hz, 2H), 7.03 (dt, *J*=15.0, 7.03 Hz, 1H), 6.68 (dt, *J*=16.1, 6.68 Hz, 1H), 6.32 (d, *J*=15.0 Hz, 1H), 6.0 (d, *J*=16.1 Hz, 1H), 2.24 (m, 7H), 1.65 (qt, *J*=7.52 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 198.2, 150.4, 148.6, 146.1, 146.1, 131.8, 129.7, 128.9, 124.4, 31.4, 30.8, 26.9, 25.7. HRMS: calcd for $C_{15}H_{18}NO_5S$ [M+1] 324.0906, found 324.0906. FTIR (film): 3054, 2987, 2685, 2305, 1675, 1628, 1535, 1422, 1351, 1265, 1149, 1086, 979, 896. Mp = 81-82ºC.

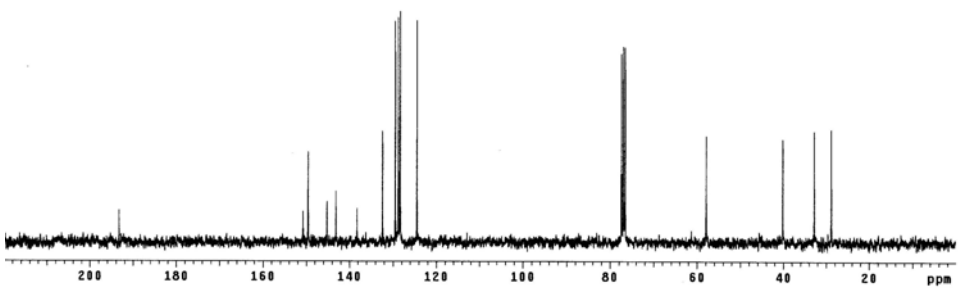


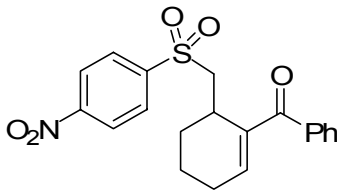


4-3.1a

[5-(4-Nitro-benzenesulfonylmethyl)-cyclopent-1-enyl]-phenyl-methanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.39 (d, *J*=9.00 Hz, 2H), 8.15 (d, *J*=8.89 Hz, 2H), 7.62 (d, *J*=7.47 Hz, 1H), 7.51 (t, *J*=7.39 Hz, 1H), 7.39 (t, *J*=7.42 Hz, 1H), 6.64 (q, *J*=2.29 Hz, 1H), 3.91 (dd, *J*=13.9, 2.37 Hz, 1H), 3.46 (m, 1H), 3.14 (m, 1H), 2.72, (m, 1H), 2.58 (m, 1H), 2.39 (m, 1H), 2.24 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.3, 150.8, 149.6, 145.2, 143.1, 138.2, 132.4, 129.5, 128.7, 128.3, 57.9, 40.2, 32.8, 28.8. HRMS: calcd for $C_{19}H_{18}NO_5S$ [M+1] 372.0907, found 372.0906. FTIR (film): 3054, 2987, 2685, 2305, 1686, 1606, 1535, 1421, 1350, 1266, 1149, 1086, 1013, 896. Mp = 105-106ºC.

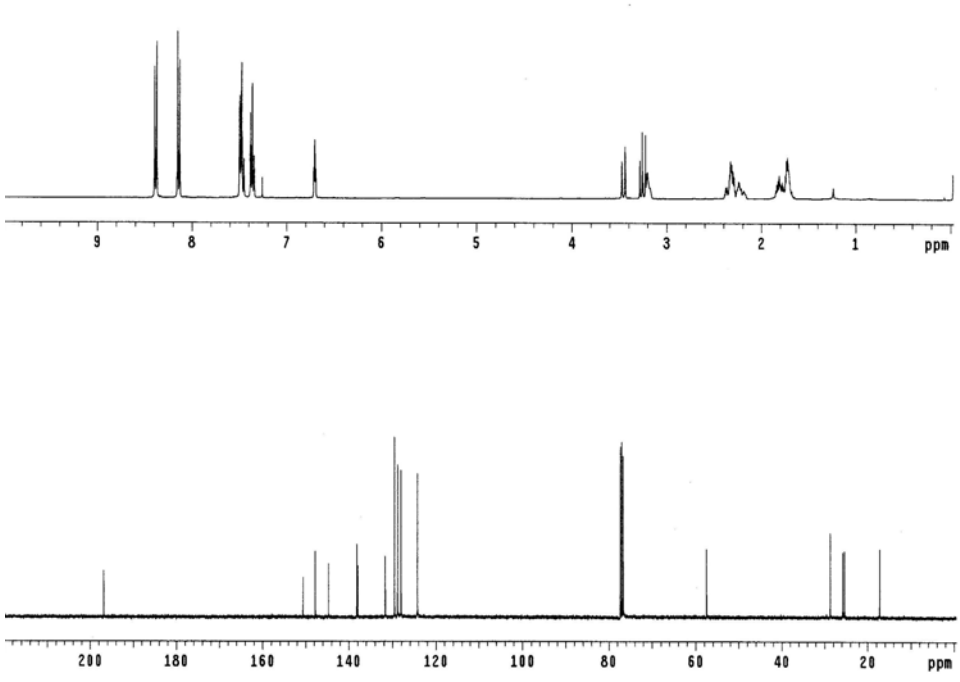


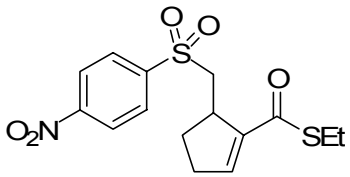




4-3.2a

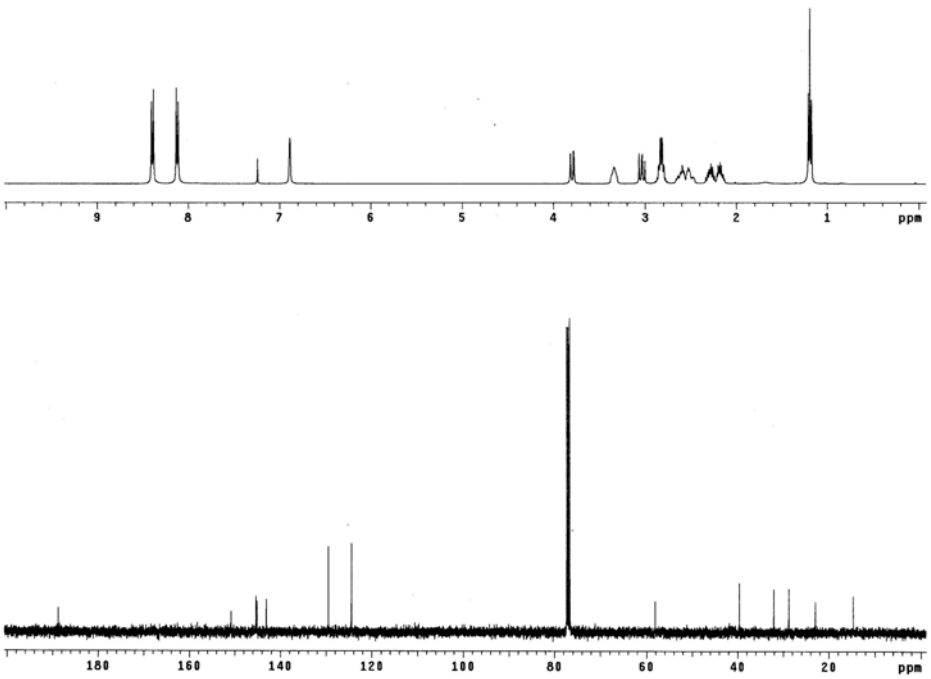
[6-(4-Nitro-benzenesulfonylmethyl)-cyclohex-1-enyl]-phenyl-methanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.39 (d, *J*=8.89 Hz, 2H), 8.14 (d, *J*=8.89 Hz, 2H), 7.47 (m, 3H), 7.36 (m, 2H), 6.70 (t, *J*=3.59 Hz, 1H), 3.46 (d, *J*=13.3 Hz, 1H), 3.23 (m, 2H), 2.33 (m, 2H), 2.22 (m, 1H), 1.76 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 196.9, 150.6, 147.8, 144.7, 138.2, 137.9, 131.7, 129.6, 128.9, 128.1, 124.3, 57.5, 28.7, 25.8, 25.4, 17.2. HRMS: calcd for $C_{20}H_{20}NO_5S$ [M+1] 386.1060, found 386.1062. FTIR (film): 3054, 2987, 2685, 2305, 1686, 1606, 1535, 1421, 1350, 1266, 1149, 1086, 1013, 896. Mp = 127-128ºC.

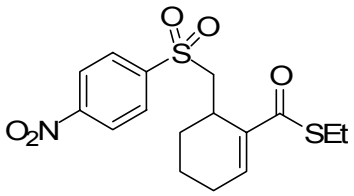




4-3.3a

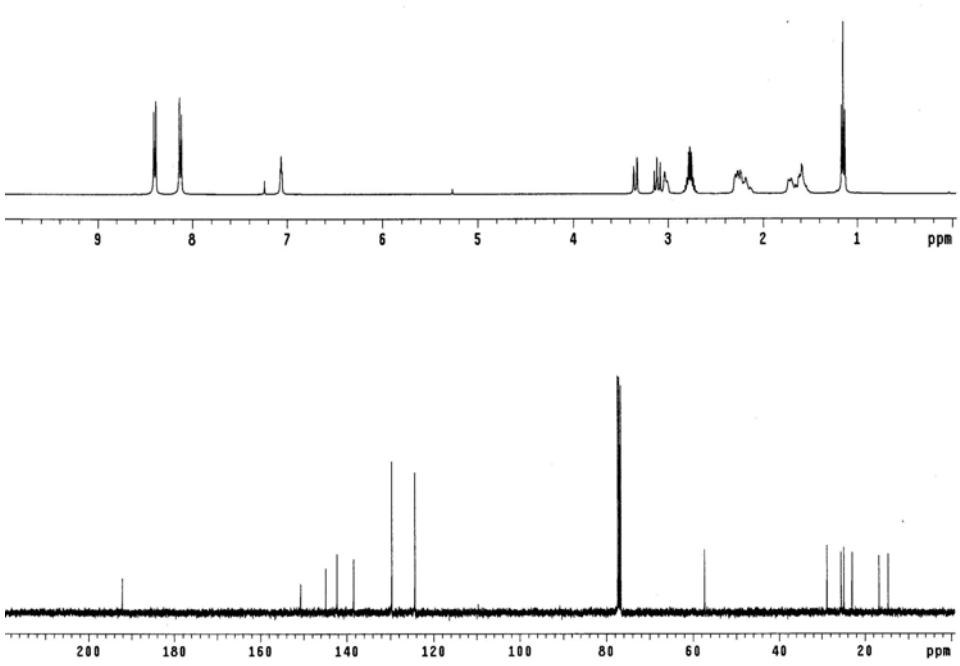
5-(4-Nitro-benzenesulfonylmethyl)-cyclopent-1-enecarbothioic acid S-ethyl ester. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.39 (d, *J*=8.89 Hz, 2H), 8.12 (m, *J*=8.55 Hz, 2H), 6.89 (d, *J*=1.71 Hz, 1H), 3.79 (dd, *J*=14.36, 1.88 Hz, 1H), 3.24 (m, 1H), 3.03 (dd, *J*=14.02, 10.94 Hz, 1H), 2.82 (m, 2H), 2.55 (m, 2H), 2.23 (m, 2H), 1.18 (t, 7.52 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 188.7, 150.8, 145.3, 145.1, 145.1, 143.1, 129.5, 124.4, 58.1, 39.6, 32.1, 28.8, 23.0, 14.6. HRMS: calcd for $C_{14}H_{16}NO_5S$ [M+1] 356.0626, found 356.0631. FTIR (film): 3054, 2987, 2685, 2410, 2305, 1650, 1609, 1536, 1422, 1351, 1265, 1151, 1087, 896. Mp = 102-103ºC.

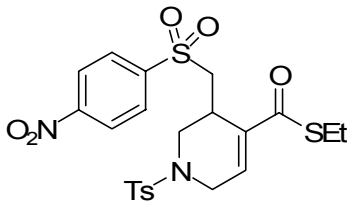




4-3.4a

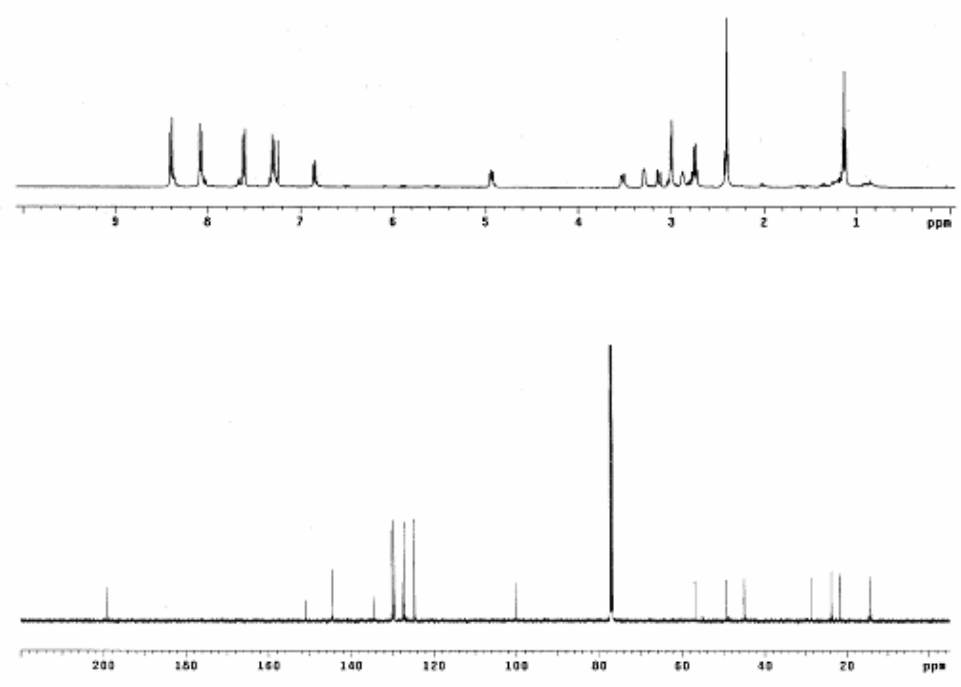
6-(4-Nitro-benzenesulfonylmethyl)-cyclohex-1-enecarbothioic acid S-ethyl ester. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.40 (d, *J*=8.55 Hz, 2H), 8.12 (d, *J*=8.55 Hz, 2H), 7.06 (t, *J*=3.42 Hz, 1H), 3.34 (d, *J*=3.76 Hz, 1H), 3.07 (m, 2H), 2.76 (m, 2H), 2.21 (m, 3H), 1.63 (m, 3H), 1.14 (t, *J*=7.52 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.1, 150.7, 144.7, 142.2, 138.4, 129.6, 124.3, 57.3, 28.8, 25.5, 24.9, 23.0, 16.7, 14.6. HRMS: calcd for $C_{15}H_{18}NO_5S$ [M+1] 384.0943, found 384.0939. FTIR (film): 3054, 2987, 2685, 2410, 2305, 1650, 1609, 1536, 1422, 1351, 1265, 1151, 1087, 896. Mp = 104-105ºC.

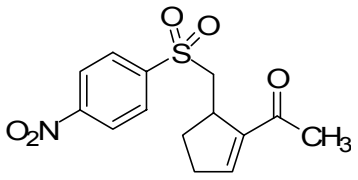




4-3.5a

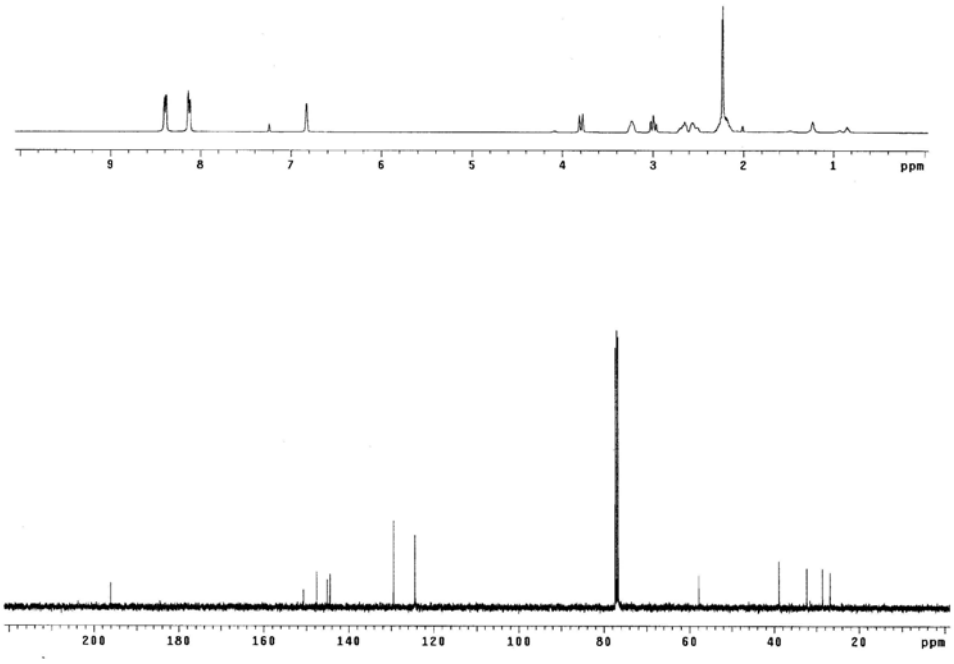
3-(4-Nitro-benzenesulfonylmethyl)-1-(toluene-4-sulfonyl)-1,2,3,6-tetrahydro-pyridine-4-carbothioic acid S-ethyl ester. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.36 (d, *J*=8.89 Hz, 2H), 8.03 (d, *J*=8.89 Hz, 2H), 7.62 (d, *J*=8.20 Hz, 2H), 7.29 (d, *J*= 7.86 Hz, 2H), 6.92 (dt, *J*=15.05, 4.96 Hz, 1H), 6.52 (d, *J*=5.98 Hz, 1H), 6.42 (dt, *J*=15.39, 5.98 Hz, 1H), 5.97 (d, *J*=15.39 Hz, 1H), 3.94 (d, *J*=4.787 Hz, 2H), 3.88 (d, *J*=6.156 Hz, 2H), 2.87 (q, *J*=7.41 Hz,, 2H), 2.40 (s, 3H), 1.23 (t, *J*=7.35 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.2, 151.0, 144.5, 134.4, 130.0, 129.6, 127.6, 127.1, 124.6, 100.2, 56.9, 49.5, 44.9, 28.5, 23.6, 21.6, 14.3. HRMS: calcd for $C_{22}H_{25}N_2O_7S_3$ [M+1] 525.0836, found 525.0824. FTIR (film): 3055, 2987, 2933, 2688, 2411, 2305, 1676, 1607, 1536, 1421, 1350, 1308, 1265, 1170, 1087, 1014, 956, 896.

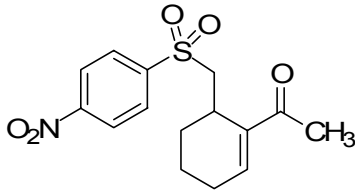




4-3.6a

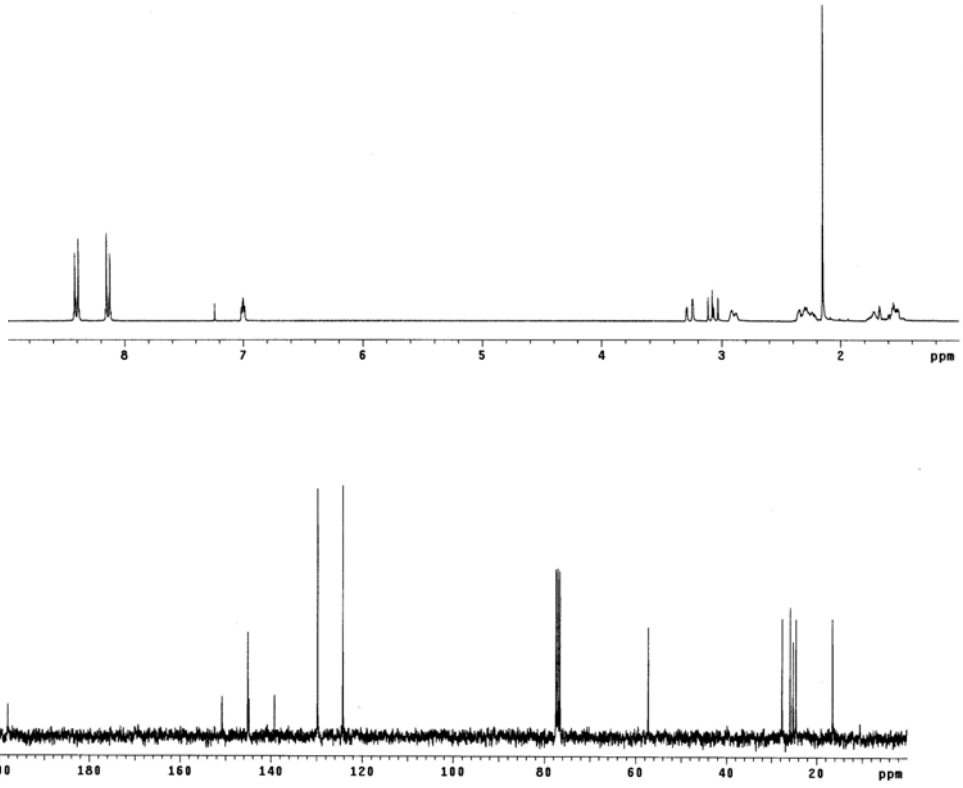
1-[5-(4-Nitro-benzenesulfonylmethyl)-cyclopent-1-enyl]-ethanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.39 (d, *J*=7.86 Hz, 2H), 8.13 (d, *J*=8.55 Hz, 2H), 6.83 (t, *J*=1.03 Hz, 1H), 3.79 (d, *J*=14.02 Hz, 1H), 3.24 (m, 1H), 2.99 (t, *J*=12.31 Hz, 1H), 2.60 (m, 2H), 2.23 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 196.0, 150.7, 147.6, 145.1, 144.5, 129.5, 124.4, 57.9, 39.0, 32.3, 28.6, 26.8. HRMS: calcd for $C_{14}H_{16}NO_5S$ [M+1] 310.0752, found 310.0749. FTIR (film): 3054, 2987, 2935, 2870, 2305, 1661, 1606, 1533, 1422, 1351, 1302, 1265, 1152, 1086, 896. Mp = 100-101ºC.





4-3.7a

1-[6-(4-Nitro-benzenesulfonylmethyl)-cyclohex-1-enyl]-ethanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.40 (d, *J*=8.69 Hz, 2H), 8.14 (d, *J*=8.69 Hz, 2H), 7.00 (t, *J*=3.97 Hz, 1H), 3.27 (d, *J*=14.0 Hz, 1H), 3.07 (m, 1H), 2.90 (d, *J*=10.4 Hz, 1H), 2.29 (m, 2H), 2.15 (s, 3H), 1.70 (m, 2H), 1.56 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 198.1, 150.7, 145.1, 144.8, 139.2, 129.8, 124.2, 57.2, 27.6, 25.8, 25.2, 24.6, 16.5. HRMS: calcd for $C_{15}H_{18}NO_5S$ [M+1] 324.0895, found 324.0906. FTIR (film): 3054, 2987, 2935, 2870, 2305, 1661, 1606, 1533, 1422, 1351, 1302, 1265, 1152, 1086, 896. Mp = 126-127ºC.



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VITA

Ana Liza Luis was born in Eagle Pass, Texas on September 4, 1976, the daughter of Carolina Trevino de Luis and Hipolito Luis Pena. After completing her work at Oliver Wendell Holmes High School, San Antonio, Texas in 1994, she pursued a chemistry degree at The University of Texas at San Antonio. Upon earning her B.S. degree in Chemistry in May 1999, she entered The Graduate School at The University of Texas at Austin under the supervision of Dr. Michael J. Krische. She received her M.A. in Organic Chemistry in August 2002 and continued work toward her Ph.D.

Permanent Address: 7543 Pipers Creek Street
San Antonio, TX 78251

This dissertation was typed by the author.