

DESIGNER BENZIMIDAZOLES:
SYNTHESIS, CHARACTERIZATION, AND APPLICATIONS

Steven Tai-hsiang Chao

*in Partial Fulfillment of the Requirements
for the Degrees of
Bachelor of Science & Bachelor of Arts*

Dean's Scholars Honors & Plan II Honors Programs

The University of Texas at Austin
Austin, Texas

Spring 2008

Christopher W. Bielawski, Ph.D.
Department of Chemistry and Biochemistry
Supervising Professor

Abstract

Author: Steven Tai-hsiang Chao

Title: Designer Benzimidazoles: Synthesis, Characterization, and Applications

Supervising Professor: Christopher W. Bielawski, Ph.D.

The research presented in this thesis is centered on the design and synthesis of molecules which are derived from benzimidazoles and their applications.

The first chapter provides an introduction to benzimidazoles and *N*-heterocyclic carbenes, a unique class of molecules derived from benzimidazoles.

The second chapter describes the use of benzobis(imidazolium) salts in the design and development of a new class of fluorescent materials demonstrated to be robust with strong photoluminescent properties as well as tunable electronic and physical characteristics. These materials have potential application as fluorophores, sensory materials, and models for photophysical studies.

The final chapter describes the development of a mechanically-activated catalyst system with applications to stress-responsive and self-healing materials.

Acknowledgments

I would not be in the place I am today if it were not for my family and the endless support and encouragement they have showered on me over the years. They have been there every step of the way, fighting with me and being incredibly patient and accommodating. My parents have encouraged me to study and pursue whatever I wanted ever since I was a kid; one of my most favorite pictures is of my 4- or 5-year old self sitting on the couch with a volume of the encyclopedia propped open. Their never-ending faith and confidence has certainly helped me become better.

I have also been extremely fortunate to have been a student of some excellent teachers. My thanks go particularly to my first high school chemistry teacher Ms. C. Delbar for her infectious enthusiasm for chemistry (and pyrotechnics!) which I have yet to see matched, and Ms. M. Acker, my IB HL Chemistry teacher who tolerated our class of four and all our ineptitudes as we attempted to learn organic chemistry.

Ms. Delbar was also the one who encouraged me to apply for the Welch Summer Scholar Program in 2003 where my love for basic research was kindled. Many thanks go to Professor Guigen Li of Texas Tech University for taking me as a Welch Summer Scholar and making my first dip into research a comfortable and painless one (I know now that this is not always the case).

I must also thank Dr. Ming-hsi 'Mitch' Chiang of the Institute of Chemistry at the Academia Sinica in Taipei, Taiwan for taking me as a summer intern in 2006; it was an unforgettable experience in which I was allowed great freedom and encouraged to explore and learn like I never had before. Truly, this is the point where I knew I could not stay away from research for long, if ever, again. My gratitude also goes to Professor Joe Ready of UT Southwestern Medical Center for accepting me as a summer research fellow in 2007. I think it was in his lab that I began to appreciate not only what a life in research was like but also the ubiquity of chemistry in this world

Perhaps most important of all, my thanks go to my advisor Professor Chris Bielawski for taking me into his lab and giving me an unforgettable research experience these past two years. Had it not been so exciting and challenging, I do not think that I would be continuing on

to graduate school. I think I have had the chance to really see what good, solid research is all about and been well-prepared for whatever I tackle next.

And to all the graduate students with whom I have worked, (now Dr.) David Chen, Robb Debergh, (now Dr.) A.J. Boydston, and Brent Norris, I thank for their patience and their endless help and advice; I would have been incredibly lost without you guys.

The sum of all my past experiences and the help and support I have received has truly made me who I am today and given me a deep appreciation and passion for the fascinating subject I study.

Thanks to all for helping me find my way.

Table of Contents

Abstract	i
Acknowledgments	ii
I. Introduction to Benzimidazoles and <i>N</i>-Heterocyclic Carbenes	1
References	6
II. Benzobis(imidazolium) Salt-based Fluorophores	
Abstract	7
Introduction	8
Results and Discussion	9
Conclusion	11
References and Notes	12
III. A Mechanically-Activated Catalyst System	
Abstract	13
Introduction	14
Results and Discussion	16
Experimental	16
References and Notes	18

List of Figures

I.:	Figure 1. Benzimidazole skeleton	1
	Figure 2. Purines, structural relatives of benzimidazoles	1
	Figure 3. Bioactive benzimidazoles	2
	Figure 4. Benzimidazole ring numbering and carbene center orbitals	3
	Figure 5. Wanzlick and Arduengo imidazole-2-ylidenes	4
II.	Figure 1. Applications of conjugated organic salts	8
III.	Figure 1. Mechanophore-linked polymer system	15

List of Schemes

I.:	Scheme 1. First stable crystalline carbene	2
	Scheme 2. Benzimidazole to <i>N</i> -heterocyclic carbene	3
II.	Scheme 1. General BBI synthesis route	10
III.	Scheme 1. Synthesis of 3,3-diphenylcyclopropene	16

List of Tables

II.	Table 1. Photoluminescent Benzobis(imidazolium) Salts and their Physical and Photophysical Properties	9
------------	---	---

I. Introduction to Benzimidazoles and *N*-Heterocyclic Carbenes

Benzimidazoles are a class of heterocyclic, aromatic chemical compounds which share a fundamental structural characteristic of six-membered benzene fused to five-membered imidazole (Figure 1).

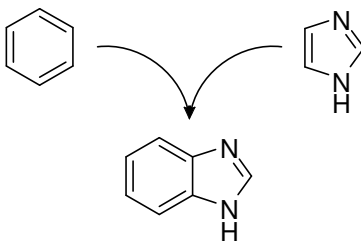


Figure 1. The benzimidazole skeleton is the fusion of benzene (top left) and imidazole (top right).

This basic ‘6+5’ heterocyclic structure is shared by another class of chemical compounds, the purines (Figure 2). Among the members of this group are several very well-known and important biomolecules, such as adenine and guanine, two of the four nucleic acid bases, uric acid, and caffeine.¹

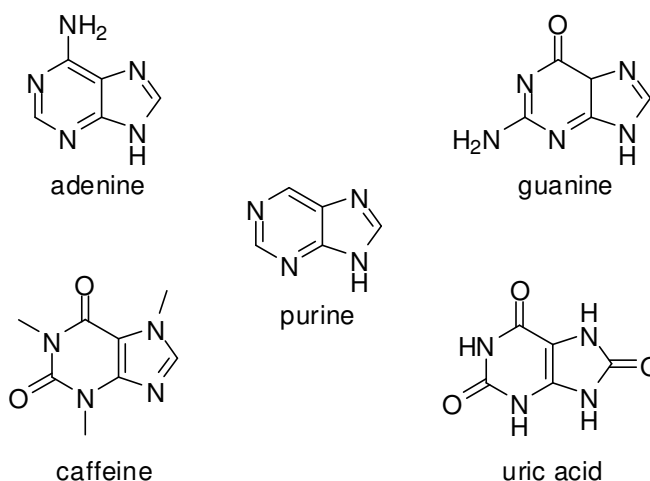


Figure 2. Purines, which include some of the most well-known biomolecules, share the ‘6+5’ heterocyclic structure with benzimidazoles.

From this fundamental structural similarity, it is not too surprising that benzimidazole-containing molecules and benzimidazole derivatives have been found to be biologically active

small molecules, such as vitamin B₁₂ and a variety of antimicrobial, antiparasitic, and even antitumor agents (Figure 3).^{1,2}

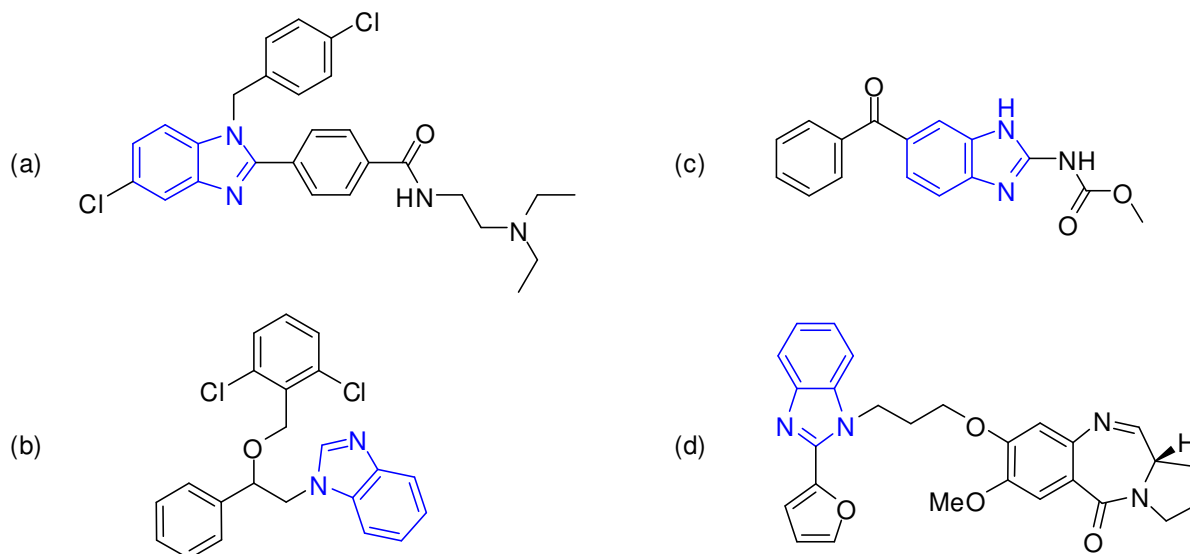
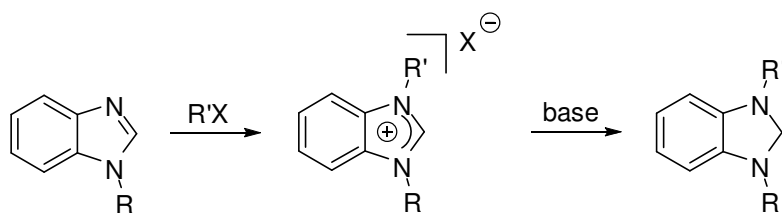


Figure 3. Examples of: (a,b) antimicrobial; (c) antiparasitic; and (d) antitumor agents containing the benzimidazole moiety (colored blue).

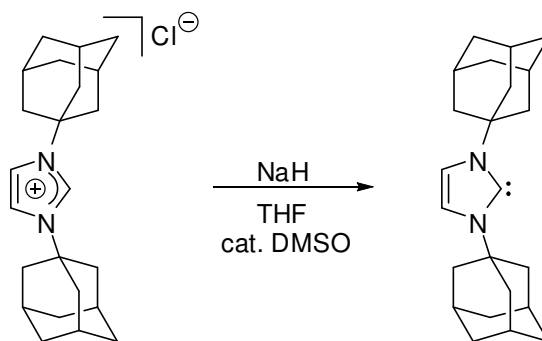
Aside from their place in biomedical research, benzimidazoles also have a prominent place in organocatalysis, organometallic³, and materials chemistry⁴ for two reasons stemming from their molecular architecture: the imidazole is a precursor to *N*-heterocyclic carbenes; and the benzene ring provides a convenient scaffold to which additional functionality may be easily added to modify the spatial and electronic characteristics of a benzimidazole derivative. This combination of a reactive carbene center with a modifiable backbone is without a doubt one of the reasons for the recent rise in study and use of benzimidazoles and their *N*-heterocyclic carbene derivatives (Scheme 1).



Scheme 1. Reaction of *N*-substituted benzimidazole with an alkyl- or arylhalide yields a benzimidazolium salt that, when treated with strong base (e.g. KO^tBu or NaH) yields *N*-heterocyclic carbenes.

N-heterocyclic carbenes, or NHCs, are a unique class of the carbene family. Carbenes, well known to be extremely reactive species due to their electron deficiency, are divalent carbon atoms with two nonbonding electrons that are covalently bonded to two adjacent groups.⁵ Typically carbenes exist for short periods of time and are not isolable. Long recognized to be important reaction intermediates, for some time they have, though, been employed in both synthetic organic and organometallic chemistry.⁶ However, it was not until relatively recently that carbenes could be stored and studied.

Interest in isolable carbenes extends as far back as the early part of the 1800s.⁷ However, it would not be until 1991 that Arduengo et al. would do so by isolating an NHC, 1,3-di-1-adamantyl-imidazol-2-ylidene (Scheme 2).⁸



Scheme 2. Arduengo et al. isolated the first stable crystalline carbene, 1,3-di-1-adamantyl-imidazol-2-ylidene

Several important revelations had been made previously, though, concerning NHCs. During the 1960s, several studies by Wanzlick with the saturated imidazoline ring allowed him to recognize that NHCs would be stable and isolable due to the carbene center, located at the 2-position of the imidazole ring, being stabilized by the electron-donating effects of the neighboring nitrogen atoms (Figure 4).^{3a,9}

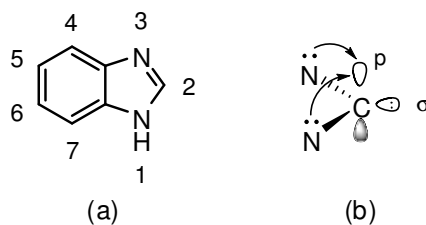


Figure 4. (a) The numbering scheme for benzimidazoles; the 2-position carbon becomes the NHC carbene center. (b) The singlet ground state has a vacant p orbital into which neighboring substituents may donate electrons to stabilize the carbene center.

This, of course, has been shown true; exceptionally stable, NHCs are able to be stored for long periods of time under standard dry box conditions or even on the benchtop.¹⁰

Initial studies by Wanzlick et al. with *N*-aryl-substituted imidazole-2-ylidenes **1** and **2** suggested that electronic stabilization alone is not significant enough to allow for isolation of NHCs and that steric contributions from bulky *N*-substituents are needed as well; certainly, steric bulk should contribute to the carbene center's kinetic stability by blocking access to the reactive carbene center.^{7,11} However, three decades later Arduengo not only isolated *N*-aryl-substituted imidazole-2-ylidenes **5** and **6** but also *N*-methyl-substituted imidazole-2-ylidenes **3** and **4**, effectively showing that electronic effects alone are enough to stabilize the carbene center.^{11b} However, without bulky substituents groups NHCs will slowly form dimers.

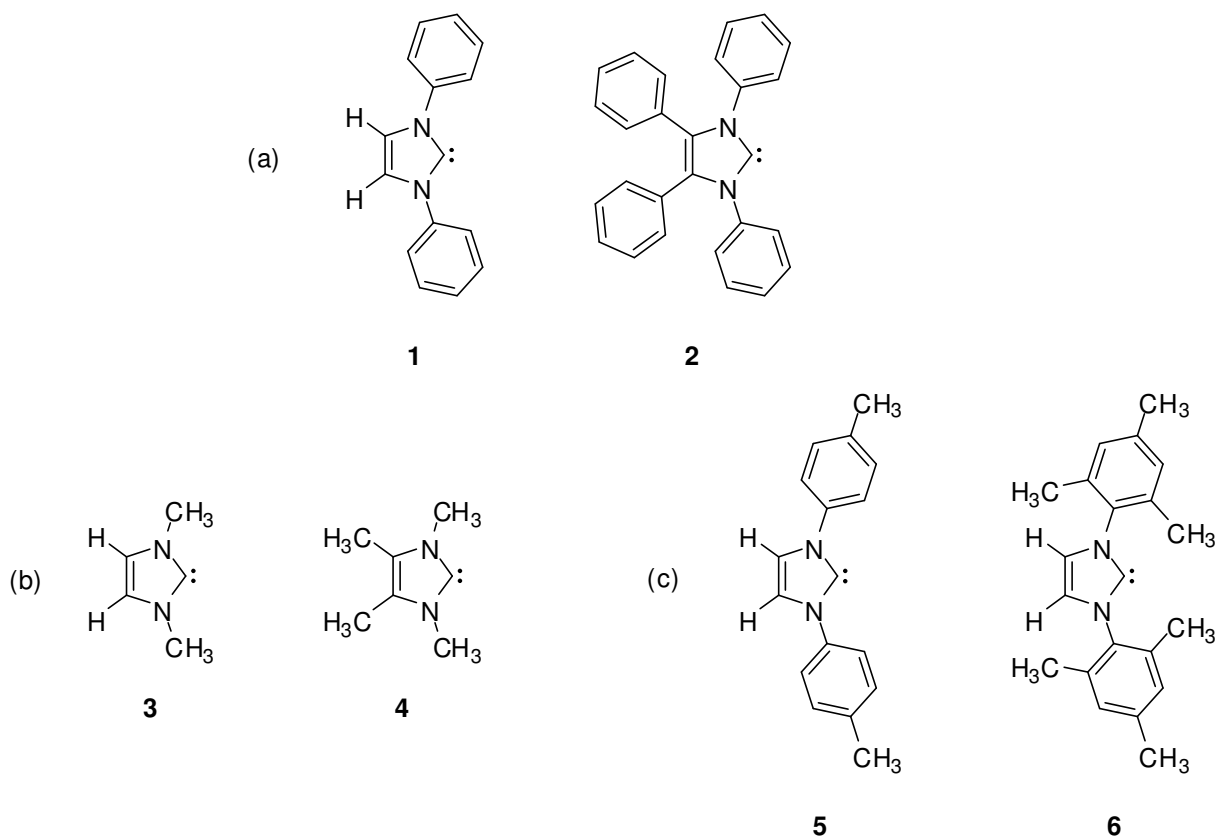


Figure 5. Wanzlick was unable to isolate (a) *N*-aryl-substituted imidazole-2-ylidenes; Arduengo, however, isolated both (b) *N*-methyl and (c) *N*-aryl-substituted imidazole-2-ylidenes as well.

NHCs are singlet carbenes, meaning that in the ground state the electrons are paired and occupy the in-plane σ orbital.^{6a,12} This leaves a *p* orbital vacant, into which neighboring

substituents may donate electrons and stabilize the carbene center (Figure 4). In NHCs, this electron-donation effect is so strong, in fact, that NHCs are nucleophilic rather than electrophilic as most carbenes are.

NHCs are excellent σ -donators with little backbonding character, and as such they have been widely used as ligands for organometallic catalyst complexes.^{3a} Often this is in place of less strongly-donating organophosphanes and resulting in improved catalyst reactivity and tolerance of functional groups.^{12b,13} Thus far NHCs have found use in a number of varied reactions, including polymerization, hydrogenation, hydroformylation, and allylic substitution.¹⁴

Benzimidazoles and their NHC derivatives are clearly powerful chemical species with a wide range of application and also great untapped potential; combining reactivity and modularity, the possibilities for these unique compounds seem endless.

References

- (1) Kamal, A.; Kumar, P.P.; Sreekanth, K.; Seshadri, B.N.; Ramulu, P. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 2594.
- (2) (a) Göker, H.; Kuş, C.; Boykin, D.W.; Yildiz, S.; Altanlar, N. *Bioorg. Med. Chem.* **2002**, *10*, 2589. (b) Güven, Ö.Ö.; Erdoğan, T.; Göker, H.; Yildiz, S. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 2233. (c) Nobilis, M.; Jira, T.; Lísa, M.; Holčápek, M.; Szotáková, B.; Lamka, J.; Skálová, L. *J. Chromatogr. A.* **2007**, *1149*, 112. (d) Denny, W.A.; Rewcastle, G.W.; Baguley, B.C. *J. Med. Chem.* **1990**, *33*, 814.
- (3) (a) Nair, V.; Bindu, S.; Sreekumar, V. *Angew. Chem. Int. Ed.* **2004**, *43*, 5130. (b) Enders, D.; Balensiefer, T. *Acc. Chem. Res.* **2004**, *37*, 534.
- (4) Boydston, A.J.; Williams, K.A.; Bielawski, C.W. *J. Am. Chem. Soc.* **2005**, *127*, 12496.
- (5) Kirmse, W. *Carbene Chemistry*, Academic Press: New York, 1964.
- (6) (a) Bourissou, D.; Guerret, O.; Gabbai, F.P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39. (b) Doering, W.v.E.; Hoffmann, A.K. *J. Am. Chem. Soc.* **1954**, *76*, 6162. (c) Fischer, E.O.; Maasböl, A. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 580.
- (7) Arduengo, A.J., III; Harlow, R.L.; Kline, M. *J. Am. Chem. Soc.* **1991**, *113*, 363.
- (8) Arduengo, A.J. *Acc. Chem. Res.* **1999**, *32*, 913.
- (9) Wanzlick, H.-W. *Angew. Chem.* **1962**, *74*, 128.
- (10) Arduengo, A.J., III; Davidson, F.; Dias, H.V.R.; Harlow, R.L.; Kline, M.K. *J. Am. Chem. Soc.* **1997**, *119*, 12742.
- (11) (a) Lachmann, B.; Steinmaus, H.; Wanzlick, W.-W. *Tetrahedron.* **1971**, *27*, 4085. (b) Arduengo, A.J. III; Dias, H.V.R.; Harlow, R.L.; Kline, M. *J. Am. Chem. Soc.* **1992**, *114*, 5530.
- (12) (a) Arduengo, A.J., III; Rasika Dias, H.V.; Dixon, D.A.; Harlow, R.L.; Klooster, W.T.; Koetzle, T.F. *J. Am. Chem. Soc.* **1994**, *116*, 6812. (b) Kirmse, W. *Angew. Chem. Int. Ed.* **2004**, *43*, 1767.
- (13) Herrmann, W.A. *Angew. Chem. Int. Ed.* **2002**, *41*, 1290.
- (14) Crudden, C.M.; Allen, D.P. *Coord. Chem. Rev.* **2004**, *248*, 2248.

II. Benzobis(imidazolium) Salt-based Fluorophores[†]

Abstract

The design and synthesis of a new series of fluorophores based on benzobis(imidazolium) salts with tunable electronic and physical characteristics is described. With systematic modification of the N-substituent groups and counterions, a set of robust materials with glass transition temperatures spanning from below 0 to above 100°C was synthesized that was capable of maintaining its emissive properties across phases. In addition, with the synthesis of thermotropic liquid-crystalline fluorescent benzobis(imidazolium) salts further phase-tuning capability was demonstrated .

Introduction

The development of conjugated organic salts for a broad range of applications, including organic light-emitting diodes (OLEDs), ionic liquids, ionic liquid crystals, and task-specific functions, has recently received considerable interest (Figure 1).¹

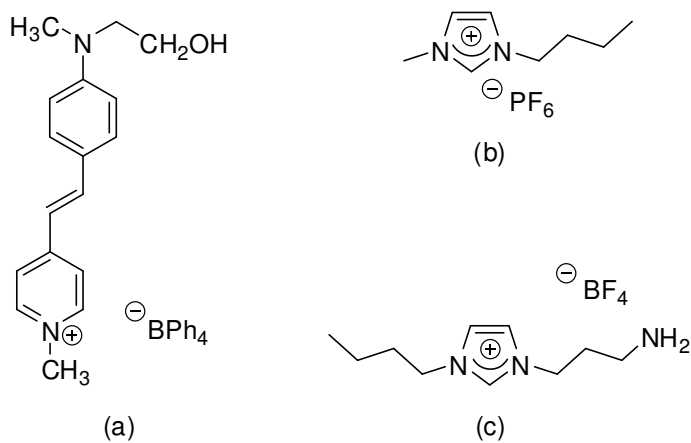


Figure 1. Conjugated organic salts as (a) OLED; (b) ionic liquid; and (c) task-specific ionic liquid for CO₂ capture.

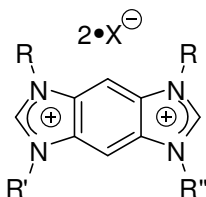
Many of these studies have been performed with traditional imidazolium-based ionic liquids, in part for their photoluminescent qualities; however, they exhibit extremely low emission intensities in the visible region, hence complicating analytical analyses and limiting their utility overall.² Thus, to improve the applicability of this class of materials, a means of enhancing their photoluminescent properties was set as the primary objective, as improving these properties for low melting organic salts could potentially allow for significant advances to be made in each of the aforementioned fields of research.

Benzobis(imidazolium) (BBI) salts have several important features which make them ideal candidates as fluorescent conjugated organic salts with tunable electronic and physical characteristics: they contain imidazolium moieties that provide high thermal stability and phase control; a fluorogenic, heteroaromatic core capable of efficient photoluminescence; and easily modified N-substituents with which liquid crystalline phase properties may be modified. Together, these characteristics should allow for satisfaction of the need for increased photoemission compared to traditional imidazolium-based ionic liquids while also allowing for phase tunability.

Results and Discussion

Photophysical studies with *N*-alkyl and *N*-aryl-substituted BBIs **1** and **2** (Table 1), respectively, had been previously initiated.³ High quantum efficiencies, Φ_f , for both BBIs were observed but with vastly different maximum emission wavelength values. This was a strong indication that modification of the *N*-substituents would serve as a general means to tuning the electronic characteristics of BBIs. Tuning of the phase characteristics of BBIs by structural modification also became an area of focus after it was found that **1** and **2** decomposed prior to observation of a phase transition by differential scanning calorimetry (DSC).

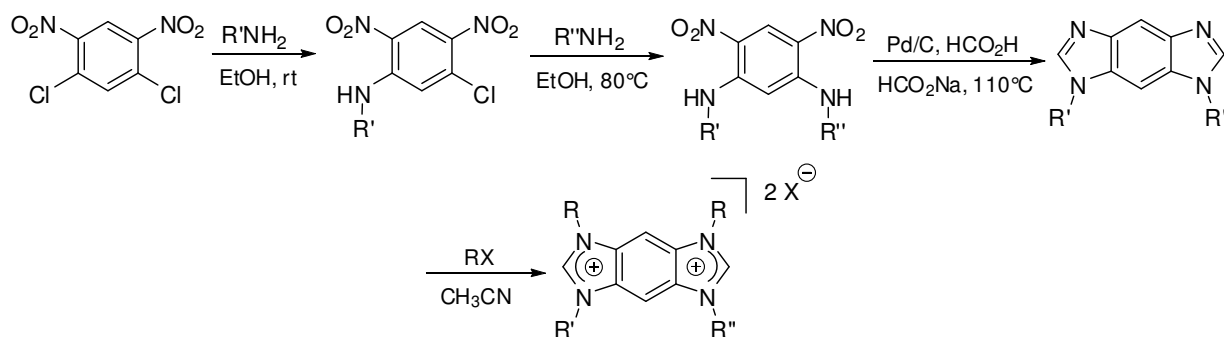
Table 1. Photoluminescent Benzobis(imidazolium) Salts and their Physical and Photophysical Properties



BBI	R	R'	R''	X	yield (%) ^a	T_g^b (°C)	T_d^c (°C)	λ_{abs}^d (nm)	λ_{em}^d (nm)	Φ_f^e
1	Bu	Bu	Bu	Br	93	<i>f</i>	271 (265)	288 (4.29)	330	0.64
2	Ph	Ph	Ph	Cl	48	<i>f</i>	325 (314)	352 (3.94)	474	0.41
3	Me	Ph	Ph	MeSO ₄	86	89	267 (263)	345 (3.31)	447	0.91
4•MeSO₄	Me	<i>i</i> -Bu	4-BuPh	MeSO ₄	89	43	273 (276)	287 (4.04)	410	0.53
4•BF₄	Me	<i>i</i> -Bu	4-BuPh	BF ₄	85	84	338 (335)	288 (4.27)	408	0.51
4•I	Me	<i>i</i> -Bu	4-BuPh	I	88	113	218 (215)	288 (4.20)	408	0.47
5	Me	<i>i</i> -Bu	3-MePh	MeSO ₄	90	35	270 (262)	286 (4.19)	402	0.52
6	Et	Me	3-MePh	MeSO ₄	91	0.8	272 (269)	289 (4.01)	403	0.63
7	Et	Me	4-OctPh	MeSO ₄	89	-0.3	274 (270)	289 (4.13)	408	0.57
8a	C ₁₂ H ₂₅	C ₁₂ H ₂₅	C ₁₂ H ₂₅	BF ₄	99	<i>g</i>	338 (314)	291 (4.14)	332	0.85
8b	Me	4-OctPh	4-OctPh	BF ₄	78	<i>g</i>	341 (335)	348 (4.03)	451	0.72

^a Overall yield from commercially available starting material. ^b Glass transition temperature from second heating run using DSC under N₂, rate = 5°C/min. ^c Decomposition temperature is temperature at which 10% weight loss occurred as determined by TGA under N₂ with high-resolution analysis; parenthetical values obtained under air. ^d In MeOH under ambient conditions; log (ϵ) values in parentheses. ^e Reported quantum efficiencies relative to *E*-stilbene or anthracene. ^f No transition observed by DSC up to decomposition. ^g Mesomorphic.

With knowledge of related ionic liquids previously reported^{1f} and X-ray crystallographic analysis of select BBIs, systematic optimization of the BBI structure (Scheme 1) was performed that resulted in the synthesis of BBIs **3-7** with relatively low T_g values (cf. **1** and **2**).



Scheme 1. General BBI synthesis route via S_NAr -reductive cyclization-alkylation sequence.⁴

This was a consequence of not only reducing molecular symmetry by using dissimilar N-substituents to discourage molecular stacking and disrupting the π - π^* facial interactions of the polycyclic core structures, but also of the use of non-coordinating counterions, with $MeSO_4$ being identified as ideal for lowering the T_g value of these BBI salts. For BBIs **4-7** the molecular symmetry was even further reduced, a consequence of dissimilar imidazolium ring substituents, and for **5-7** N-substituents which imparted π -facial asymmetry were incorporated. One particularly notable result of this systematic optimization process was the synthesis of a BBI which exhibited a T_g below $0^\circ C$ (**7**).

The robustness of these compounds was demonstrated by the observation of high decomposition temperatures, usually greater than $270^\circ C$, for each of the BBIs.

The key objective for this study was the attainment of desirable photoluminescence properties. Absorption and emission properties of BBIs **3-7** in MeOH were first studied, and it was found that the absorption and emission spectra of **4-7** were rather consistent. This indicated that the physical properties of BBIs could be selectively altered while control over the electronic characteristics could still be maintained. Also, as was the case with the BBIs first investigated, high Φ_f values were observed for each of the BBIs, a feature demonstrative of the viability of these BBIs as solution-based fluorophores.

In addition to photoluminescence in solution, it was important for the BBI chromophore to demonstrate an ability to avoid self-quenching mechanisms and maintain its intense emission properties in condensed phases. For each BBI **3-7** heated to a temperature at or around their respective T_g values to give a flowing liquid, photoluminescence was qualitatively observed. An annealed thin film of **4**·MeSO₄ was also found to fluoresce. Together, these results demonstrated that BBI salt-based ionic liquid fluorophores could maintain their photoemissive properties in solution, as flowing liquids, and in solid state.

Following this, the synthesis of liquid crystalline, mesomorphic fluorophores based on BBIs was pursued out of knowledge that liquid crystalline behavior in neutral organic fluorophores greatly improved their performance in electronic applications.⁵ Also, a BBI-based liquid crystal would introduce a unique structural class of ionic liquid crystals with rigid, polycyclic cationic cores similar to dye-based chromonic liquid crystals but naturally photoluminescent.⁶ Hence, BBI-based mesogens **8a** and **8b** were synthesized and analyzed. By variable-temperature power X-ray diffraction, they were found to be in smectic and thermotropic cubic liquid crystalline phases, respectively.

Conclusion

A new series of phase-tunable fluorophores based upon BBI salts with tunable electronic and physical properties has been synthesized and characterized. Careful N-substituent and counterion selection for these robust and highly fluorescent materials allowed for demonstration of high thermal stability but also fluidic behavior below 0°C. Through the synthesis of two BBI-based mesogens, a new route to fluorescent ionic liquid crystals has also been introduced. In summary, BBI salts have been demonstrated to be a robust yet flexible class of materials with potential application as fluorophores, sensory materials, and models for basic photophysical studies.

References and Notes

† This chapter encompasses research previously reported, see: Boydston, A.J.; Pecinovsky, C.S.; Chao, S.T.; Bielawski, C.W. *J. Am. Chem. Soc.* **2007**, *129*, 14550.

- (1) (a) Xu, H.; Meng, R.; Xu, C.; Zhang, J.; He, G.; Cui, Y. *Appl. Phys. Lett.* **2003**, *83*, 1020. (b) Chondroudou, K.; Mitzi, D.B. *Appl. Phys. Lett.* **2000**, *76*, 58. (c) Bates, E.D.; Mayton, R.D.; Ntai, I.; Davis, J.H., Jr. *J. Am. Chem. Soc.* **2002**, *124*, 926. (d) Binnemans, K. *Chem. Rev.* **2005**, *105*, 4148. (e) Welton, T. *Chem. Rev.* **1999**, *99*, 2071. (f) López-Marín, I.; Burello, E.; Davey, P.N.; Seddon, K.R.; Rothenberg, G. *ChemPhysChem* **2007**, *8*, 690. (g) Kato, T. *Science* **2002**, *295*, 2414.
- (2) (a) Paul, A.; Mandal, P.K.; Samanta, A. *J. Phys. Chem. B* **2005**, *109*, 9148. (b) Paul, A.; Mandal, P.K.; Samanta, A. *Chem. Phys. Lett.* **2005**, *402*, 375.
- (3) (a) Boydston, A.J.; Williams, K.A.; Bielawski, C.W. *J. Am. Chem. Soc.* **2005**, *127*, 12496. (b) Boydston, A.J.; Khramov, D.M.; Bielawski, C.W. *Tetrahedron Lett.* **2006**, *47*, 5123.
- (4) Applies to BBIs **4-7** and **8b**; synthesis of **1** and **2** previously reported³; synthesis of **3** combined both S_NAr steps into one; synthesis of **8a** performed by alkylation of benzobis(imidazole); where applicable, anion metathesis performed per literature protocol, see: Vu, P.D.; Boydston, A.J.; Bielawski, C.W. *Green Chem.* **2007**, *9*, 1158.
- (5) (a) O'Neill, M.; Kelly, S.M. *Adv. Mater.* **2003**, *15*, 1135. (b) Levitsky, I.A.; Kishikawa, K.; Eichhorn, S.H.; Swager, T.M. *J. Am. Chem. Soc.* **2000**, *122*, 2474.
- (6) (a) Lydon, J. *Curr. Opin. Colloid Interface Sci.* **2004**, *8*, 480. (b) Tortora, L.; Park, J.-S.; Antion, K.; Finotello, D.; Lavrentovich, O.D. *Proc. SPIE* **2007**, *6487*, 648701-1. (c) Tam-Chang, S.-K.; Helbley, J.; Carson, T.D.; Seo, W.; Iverson, I.K. *Chem. Commun.* **2006**, 503.

III. A Mechanically-Activated Catalyst System

Abstract

The theory and precedent for the design and synthesis of a mechanically activated ruthenium alkylidene ROMP catalyst is detailed. Progress in its synthesis is also reported.

Introduction

Perhaps the most direct and efficient manner in which a chemical reaction may be encouraged in the forward direction is through the input of external energy. In all reactions, there is an energy barrier which must be crossed by reactants in order for their conversion into products to occur. Most often heat, pressure, electricity, or light are used to provide the necessary impetus to accelerate reactions by either: 1) changing the distribution of reactants in the lowest energy, ground-state configuration; or 2) exciting reactants into a higher-energy, excited-state configuration to ease movement over the energy barrier.¹

It is also possible to use mechanical force to supply the requisite activation energy. Relative to the other methods available, though, examples of mechanochemical activation are few; two of the more notable examples are carbon radical formation via stress-induced cleavage of polystyrene and the activation of magnesium turnings for Grignard reactions via constant hammering.^{1a,2a,3}

The use of force to cause mechanical deformation and thereby provide potential energy is by far the least common option for chemical activation because in the majority of chemical systems the application of mechanical energy is an inefficient means of activation as the greater part of the energy input into the system is easily lost as heat or work used in bulk deformation processes; little energy then remains to be applied as chemical potential.² Yet, its use has been long established in material science, solid-state and polymer chemistry because these types of systems are capable of storing free-energy upon stress-induced deformation and sustaining that energy for a period of time in excess of that requisite for a chemical reaction to occur.^{1c,2}

At present mechanochemistry and its unique mode of action is generating interest in stress-responsive materials.⁴ Stress-responsive materials are widely applicable precisely because the energy requirements of the system may be met by application of external force which, compared to heat, pressure, electricity and light, is more easily controlled and delivered.

One potential application is in self-healing materials; envisioned is the eventual development of materials embedded with other materials capable of performing repair functions in the event of the formation of structural defects in the bulk material.

Proposed is a mechanophore-linked polymer system, specifically a centrally placed Grubbs-type ring-opening metathesis polymerization (ROMP) catalyst⁵ bis-coordinated by two NHC-functionalized atom-transfer radical polymerization (ATRP) initiators off which polymer

chains may be grown⁶, whereby upon application of mechanical force the catalyst will be activated (Figure 1).

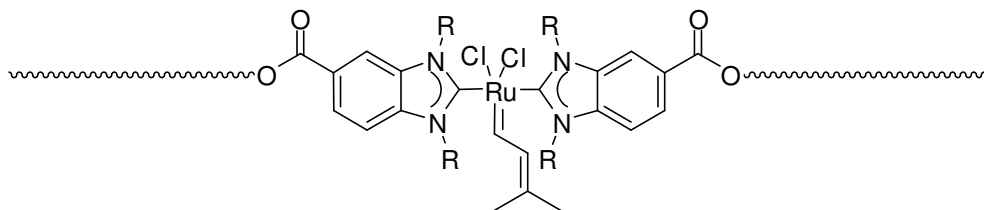


Figure 1. Proposed mechanophore-linked polymer system.

This design incorporates, quite literally, molecular handles into the architecture of the system that may, with applied force, be pulled upon; the polymer chains serve as functionalities with which energy from mechanical force may be transferred to the targeted bond and cause bond scission and activate the catalyst as desired.

It is possible for bond scission to occur in one of two fashions. In solution and under exposure to ultrasound, cavitation events induce bond cleavage in polymers.⁷ Acoustic cavitation produces vapor filled vacuoles which rapidly grow and implode, resulting in the generation of ‘hot spots’ with immense amounts of heat and energy for a very short period of time.⁸

In solid-state, though, when mechanical force is applied and stress is introduced to a macromolecular system, deformation occurs in order for the total free-energy of the system to be minimized. Typically when the force is small, so-called ‘soft’ deformational modes are adopted, resulting in the events such as bond rotation or disruption of weak interactions such as Van der Waals forces. In polymers, chain extension allows for this storage of this applied external energy; how it is translated into chemical potential, though, is yet unknown.²

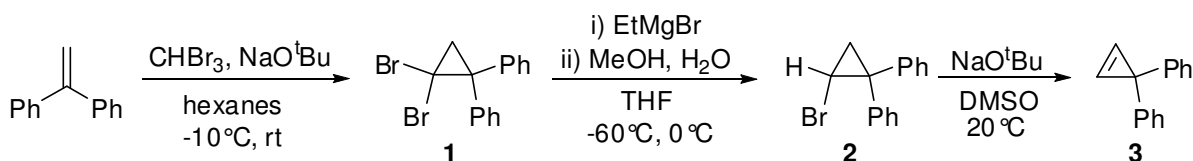
Regardless of how force is introduced to the system, the weakest bond thermodynamically is the bond most likely to break in the polymer chain; in this case, one of the Ru-carbene bonds serves as the labile connection which will allow for activation of the catalyst.

Results and Discussion

The synthesis of 3,3-diphenylcyclopropene was first pursued. Considerable difficulty was encountered when attempting a reported preparation of 1-bromo-2,2-diphenylcyclopropane utilizing a tin radical species.⁹ Fortunately, an alternative preparation via electrophilic trapping of an ethyl Grignard analogue was found¹⁰ and allowed for synthesis to proceed onwards to the desired product, though in low yields.

Remaining synthetic steps are now in progress.

Experimental



Scheme 1. 3,3-diphenylcyclopropene synthesis sequence.

Synthesis of 1,1-dibromo-2,2-diphenylcyclopropane (1)

In the dry box, sodium t-butoxide (2.02 g, 21.0 mmol) was placed into a 50 mL round bottom flask with a magnetic stirbar which was then charged with dry hexanes (25 mL) and then sealed and removed from the glove box and placed on a Schlenk line. The solution was then cooled to -10°C , after which 1,1-diphenylethylene (3.00 mL, 16.9 mmol) was added dropwise over 10 minutes. Bromoform (3.9 mL, 45.0 mmol) in dry hexanes (2 mL) was then added to the reaction mixture over 4 hours via syringe pump, during which the solution turned into slurry as precipitation of tan-colored solids was observed. The reaction mixture was then allowed to warm to room temperature overnight under continued stirring. The mixture was then poured into a beaker of water and chloroform and the organic layer then recovered via separatory funnel and the aqueous layer extracted three times. The combined organic portions were then dried over magnesium sulfate and filtered. Solvent was then removed via rotary evaporation to yield wet, tan solids which were then washed with 75 mL cold hexanes, 75 mL cold 5% EtOAc/hexanes, and 75 mL cold hexanes again. The resulting off-white powder was then collected and dried in vacuo, yielding 3.39 g (57%) of the desired product. ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 7.58-7.55 (m, 4H), 7.33-7.30 (m, 4H), 7.24-7.19 (m, 2H), 2.55 (s, 2H).

Synthesis of 1-bromo-2,2-diphenylcyclopropane (2)

In the dry box, a 100 mL round bottom flask was charged a magnetic stirbar and dry THF (15 mL), then sealed and removed and placed on a Schlenk line. Magnesium turnings (0.387 g, 15.9 mmol) were then added to the flask, followed by 1-bromoethane (1.19 mL, 15.9 mmol). The solution was then vigorously stirred until warm and the magnesium had dissolved to form ethylmagnesium bromide. In the dry box a second round bottom flask was charged with 1,1-dibromo-2,2-diphenylcyclopropane (1.40 g, 3.98 mmol), a magnetic stirbar, and dry THF (35 mL), then sealed and removed and placed on the Schlenk line. After the solution was cooled to -70°C, the EtMgBr solution was added via cannula and the reaction mixture stirred vigorously for 45 minutes. Methanol (2 mL) was then slowly added. The reaction mixture was then warmed to 0°C, then water (1.5 mL) added. The solution was diluted with 25 mL ether and the solvent removed via rotary evaporation to yield an off-white solid that was then washed with 100 mL water. The resulting solid was then collected and dried in vacuo, yielding 0.80 g (74%) of the desired product. ¹H NMR (400 MHz, DMSO-*d*₆): δ 7.39-7.32 (m, 4H), 7.28-7.24 (m, 4H), 7.21-7.14 (m, 2H), 3.96-3.90 (m, 1H), 1.89-1.77 (m, 2H).

Synthesis of 3,3-diphenylcyclopropene (3)

In the dry box a 25 mL round bottom flask was charged with a magnetic stirbar, 1-bromo-2,2-diphenylcyclopropane (0.122 g, 0.45 mmol), and dry DMSO (5 mL), then sealed and removed and placed on a Schlenk line and cooled to 20°C. To a second flask in the dry box was charged a magnetic stirbar, sodium t-butoxide (0.047 g, 0.49 mmol), and dry DMSO (3 mL), then sealed and removed and vigorously stirred till dissolved, at which point the solution was transferred to a syringe. The NaO^tBu solution was then added over 2.5 hours via syringe pump. The reaction mixture was allowed to slowly warm to room temperature, then poured into ice water, then a 2:1 hexanes/ether mixture. The layers were separated and the aqueous layer extracted twice with 2:1 hexanes:ether mixture. The combined organic layers were then washed with brine and dried over magnesium sulfate and filtered. The filtrate was then concentrated via rotary evaporation. The resulting liquid was purified via column chromatography, eluting with hexanes. Fractions containing product were collected and concentrated by rotary evaporation to yield a yellowish liquid. ¹H NMR (400 MHz, DMSO-*d*₆): δ 7.91 (br s, 1H), 7.28-7.23 (m, 4H), 7.19-7.13 (m, 2H), 7.12-7.08 (m, 4H).

References and Notes

- (1) (a) Rosen, B.M.; Percec, V. *Nature* **2007**, *446*, 381. (b) Hickenboth, C.R.; Moore, J.S.; White, S.R.; Sottos, N.R.; Baudry, J.; Wilson, S.R. *Nature* **2007**, *446*, 423. (c) Beyer, M.K.; Clausen-Schaumann, H. *Chem. Rev.* **2005**, *105*, 2921.
- (2) (a) Nguyen, T.Q.; Kausch, H.-H. *Adv. Polym. Sci.* **1992**, *100*, 73-182. (b) Casale, A.; Porter, R.S. *Polymer Stress Reactions*, vol. 1, New York: Academic Press, 1978.
- (3) Many chemical processes previously thought to proceed via mechanochemical activation have been found to, in actuality, be thermal in nature with activation occurring as a result of heat generated by viscous friction; see: Sacher, E.; Engel, P.A.; Bayer, R.G. *J. Appl. Polym. Sci.* **1979**, *24*, 1503.
- (4) (a) Potisek, S.L.; Davis, D.A.; Sottos, N.R.; White, S.R.; Moore, J.S. *J. Am. Chem. Soc.* **2007**, *129*, 13808. (b) Paulusse, J.M.J.; Huijbers, J.P.J.; Sijbesma, R.P. *Chem. Eur. J.* **2006**, *12*, 4928. (c) Cravotto, G.; Cintas, P. *Angew. Chem. Int. Ed.* **2007**, *46*, 5476. (d) Isozaki, K.; Takaya, H.; Naota, T. *Angew. Chem. Int. Ed.* **2007**, *46*, 2855. (e) Paulusse, J.M.J.; Sijbesma, R.P. *Angew. Chem. Int. Ed.* **2004**, *43*, 4459. (f) Paulusse, J.M.J.; Sijbesma, R.P. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 5445. (g) Kersey, F.R.; Yount, W.C.; Craig, S.L. *J. Am. Chem. Soc.* **2006**, *128*, 3886. (h) Naota, T.; Koori, H. *J. Am. Chem. Soc.* **2005**, *127*, 9324. (i) Paulusse, J.M.J.; van Beek, D.J.M.; Sijbesma, R.P. *J. Am. Chem. Soc.* **2007**, *129*, 2392. (j) Yount, W.C.; Loveless, D.M.; Craig, S.L. *J. Am. Chem. Soc.* **2005**, *127*, 14488.
- (5) Ruthenium alkylidene complexes with NHC ligands, such as the Grubbs 1st and 2nd generation catalysts, have been shown to be excellent catalysts for ring-opening olefin metathesis polymerizations (ROMP); see: (a) Crudden, C.M.; Allen, D.P. *Coord. Chem. Rev.* **2004**, *248*, 2247-2273. (b) Odian, G. *Principles of Polymerization*, 4th ed., New York: Wiley-Interscience, 2004. (c) Nguyen, S.T.; Johnson, L.K.; Grubbs, R.H.; Ziller, J.W. *J. Am. Chem. Soc.* **1992**, *114*, 3974. (d) Nguyen, S.T.; Grubbs, R.H.; Ziller, J.W. *J. Am. Chem. Soc.* **1993**, *115*, 9858.
- (6) Use of a bisinitiator structural unit for simultaneous growth of two linked polymer chains has been reported, see: Boffa, L.S.; Novak, B.M. *Macromolecules* **1997**, *30*, 3494.

- (7) Berkowski, K.L.; Potisek, S.L.; Hickenboth, C.R.; Moore, J.S. *Macromolecules* **2005**, *38*, 8975. Sonication has also been used for radical chain polymerization initiation, see: Odian, G. *Principles of Polymerization*, 4th ed., New York: Wiley-Interscience, 2004.
- (8) Suslick, K.S.; Goodale, J.W.; Schubert, P.F.; Wang, H.H. *J. Am. Chem. Soc.* **1983**, *105*, 5781.
- (9) Baird, M.S.; Nizovtsev, A.V.; Bolesov, I.G. *Tetrahedron*. **2002**, *58*, 1581.
- (10) Huang, J.-H.; Lee, T.-Y.; Swenson, D.C.; Messerle, L. *Inorg. Chim. Acta.* **2003**, *345*, 209.

Biography

Steven Tai-hsiang Chao was born in Dallas, TX on January 10, 1987 and lived in neighboring Plano until the age of 6 when he moved with his family to Austin, TX where they have resided since. He entered the University of Texas at Austin in 2004 to pursue a degree in Chemistry and enrolled in both the Dean's Scholars Honors program in the College of Natural Sciences and the Plan II Honors program in the College of Liberal Arts. He will attend the California Institute of Technology in Pasadena, CA starting the fall of 2008 in pursuit of a Ph.D. in Chemistry.