

Optical Effects of S-Oxidation and M^{n+} Binding in *meso*-Thienyl Dipyrin Systems and of Stepwise Bromination of 4,4-Difluoro-8-(2,5-dibromo-3-thienyl)-4-bora-3a,4a-diaza-s-indacene

Shin Hei Choi,[†] Kibong Kim,[†] June Jeon,[†] Bhupal Meka,^{†,‡} Daniela Bucella,[§] Keliang Pang,[§] Snehadrinarayan Khatua,[†] Junseong Lee,[†] and David G. Churchill^{*,†}

Molecular Logic Gate Laboratory, Department of Chemistry and School of Molecular Science -BK 21, Korea Advanced Institute of Science and Technology (KAIST), 373-1 Guseong-dong, Yuseong-gu, Daejeon, 305-701, Republic of Korea, and Department of Chemistry, Columbia University, 3000 Broadway, New York, New York 10027

Received July 19, 2008

We report 16 novel species and 8 molecular structures in studying how *meso*-thienyl-substituted dipyrrole oxidation, bromination, and metal ion binding impart optical changes, as monitored by UV–vis absorption/emission spectroscopy. Treatment of 4,4-difluoro-8-(3-benzothieryl)-4-bora-3a,4a-diaza-s-indacene ($\phi_F = 0.19$) with *m*-CPBA gives selective S-dioxidation ($\phi_F = 0.006$). Results of titrations of transition metal- and “scorpionate”-like dipyrin species varied under room temperature treatment of *m*-CPBA. Ni-(thienyl-dipyrin)_{*n*} (*n* = 2) degraded significantly in the presence of *m*-CPBA, whereas related species (M = Cu, Fe, Co; *n* = 2, 3) were inert. *meso*-Thienyl group properties were revealed through the use of 3,4,4-triphenyl-8-(thienyl)-4-bora-3a,4a-diaza-s-indacene; Cu²⁺ addition resulted in smooth absorption decreases which were modeled to support 1:1 substrate:M²⁺ binding; for Hg²⁺ 1:2 substrate:M²⁺ binding was found. Treatment of 4,4-difluoro-8-(2,5-dibromo-3-thienyl)-4-bora-3a,4a-diaza-s-indacene with Br₂ gave red-shifted UV–vis absorption band features that grow with increasing dipyrin bromination. Structures of the di- and tetra-substituted bromination products were obtained.

Introduction

Well-defined, novel small molecules that cleanly switch optical properties as they interact with external stimuli are of interest in emergent sensing technologies.^{1,2} New discrete systems are being investigated to expand the basis and understanding of small molecule switching,³ especially compounds whose mechanisms can be linked to applications in industry or the environment, such as (i) fossil fuel desulfurization pathways or (ii) selective metal ion sensing.

There is a continued and growing interest in boron-, and more specifically, difluoroboryl-dipyrin chemistry,⁴ as encouraged by the significant literature contributions of Lindsey et al.,⁵ Burgess et al.,⁴ and Ziessel et al.,⁶ which readily serve as a basis for further studies. Convenient preparation of 5-aryl-substituted dipyrromethanes which are well-known precursors to dipyrins have been reported in the 1990s by Lindsey et al.,^{7,8} oxidation of these species was first reported by Dolphin et al.,⁹ and the formation of BF₂ dipyrin species involving BF₃ first appeared in an early report by Treibs and Kreuzer.¹⁰ Many reports relate to 8-aryl-substituted boradiazaindacene derivatives and to sensing and molecular probing.^{4,6,11,12} Various dipyrri-nato complexes¹³ of the transition metals, for example, Fe(I-II),^{14–16} Co(III),^{14,17} Ni(II),^{18,9} and Cu(II),^{19–21} are also known (Figure 1).

* To whom correspondence should be addressed. Telephone: +82-42-350-2845. Fax: +82-42-350-2810. E-mail: dchurchill@kaist.ac.kr.

[†] Korea Advanced Institute of Science and Technology (KAIST).

[‡] Former BK-21 Postdoctoral researcher in the D.G. Churchill laboratory. Current appointment: Research and development scientist at Suven Life Sciences Ltd., Hyderabad, India 500-034.

[§] Columbia University.

- (1) de Silva, A. P.; Uchiyama, S. *Nat. Nanotechnol.* **2007**, *2*, 399–410.
- (2) de Silva, A. P.; Leydet, Y.; Lincheneau, C.; McClenaghan, N. D. *J. Phys.: Condens. Matter* **2006**, *18*, S1847–S1872.
- (3) Ambroise, A.; Wagner, R. W.; Rao, P. D.; Riggs, J. A.; Hascoat, P.; Diers, J. R.; Seth, J.; Lammi, R. K.; Bocian, D. F.; Holten, D.; Lindsey, J. S. *Chem. Mater.* **2001**, *13*, 1023–1034.

(4) Loudet, A.; Burgess, K. *Chem. Rev.* **2007**, *107*, 4891–4932.

(5) Kee, H. L.; Kirmaier, C.; Yu, L. H.; Thamyongkit, P.; Youngblood, W. J.; Calder, M. E.; Ramos, L.; Noll, B. C.; Bocian, D. F.; Scheidt, W. R.; Birge, R. R.; Lindsey, J. S.; Holten, D. *J. Phys. Chem. B* **2005**, *109*, 20433–20443.

Kind of Substrate and Type of Reactivity Under Investigation

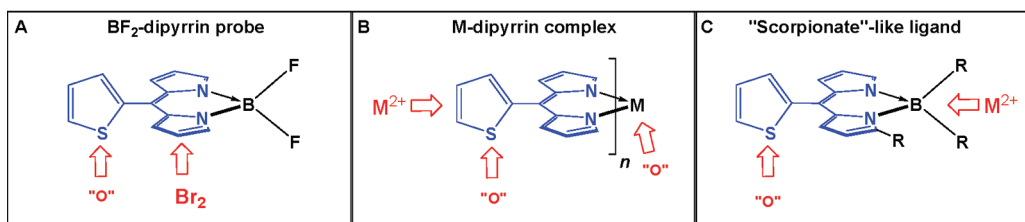


Figure 1. Generalized formulations of the dipyrrolic species presented herein. $n = 2$ or 3 , $R =$ thienyl or phenyl. A. Research questions: (i) Is clean sulfur oxidation achievable? (ii) Is stepwise dipyrrolic bromination observable? B. (iii) Can *meso*-thienyl mediate metal ion recognition, and (iv) does sulfur oxidation precede metal oxidation? C. Question (i) and (v) can aryl groups devoid of heteroatoms mediate metal ion recognition?

There is a growing number of reports that feature thienyl polypyrrole substrates as light absorbing materials and ligand frameworks. Aside from an initial report on the photochemical preparation of 2-thienyl-dipyrromethane by D'auria and co-workers,²² this laboratory has reported on 5-thienyl dipyrromethanes^{23,24} and -dipyrrolics.^{11,25} In addition to the efforts of this laboratory, there is a growing number of reports on *meso*-tetrathienyl polypyrrole porphyrins from many different laboratories as well,^{26–36} underscoring the growing interest in substrates with this substitution.

The Zissel research group has reported the synthesis and photophysical properties of boron-dipyrromethane species bearing aryl substituents at boron.³⁷ This inspired our interest in preparing boron *thienyl*-substituted analogues.²⁴ In our

systems, a third thiophene becomes incorporated at the 3-position, leading to “scorpionate”-like derivatives bearing [SSS] binding sites.

Our general design parameters involve (i) having *meso*-aryl groups whose sterics are modifiable and affect fluorescence⁵ and (ii) substituting F's with heterocycles that selectively revive latent fluorescence upon M^{n+} binding.²⁴ We are now seeking to test our thienyl-dipyrrolic systems for notable changes with neutral, yet reactive, small molecules. Herein, we study three different *meso*-thienyl species with three types of external stimulants (*m*-CPBA, Br_2 , and M^{2+}) with five questions in mind (Figure 1).

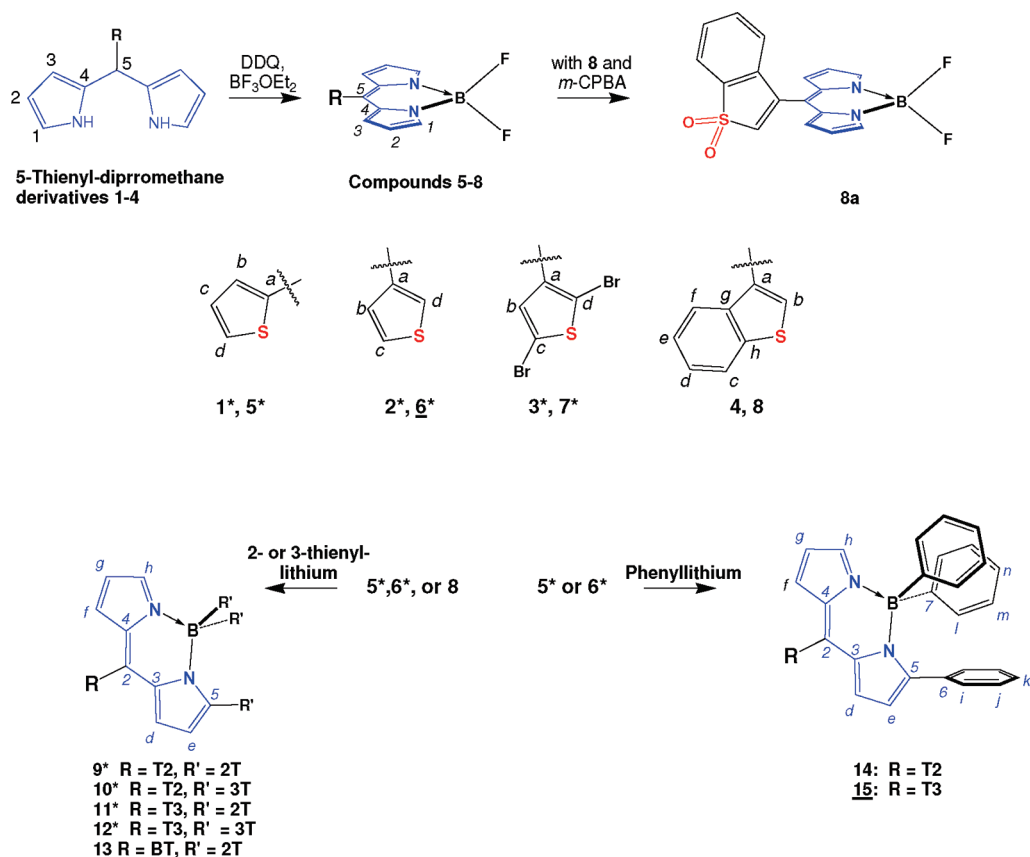
(i) Sulfoxidations are an important class of oxidative transformations that occur in chemistry and biology. Thus, a substrate that can gauge the extent of such thienyl oxidation would be of great interest to the molecular probes community. Fluorogenic derivatives containing thiophenes which give rise to distinct photophysical changes upon oxidizing may be suitable as metal and element-based catalytic or biological probes alike. Specifically, these probes may be considered for instance, in oxidative sulfur removal which continues to be an essential and central theme in researching means to achieve cleaner fossil fuels.^{38,39}

(ii) While the 8-position and boron substituents may contain an oxidizable sulfur, we were also interested at the same time in exploring oxidative modifications to the dipyrrolic moieties. One way is to treat the substrate with bromine. Bromination

- (6) Ulrich, G.; Zissel, R.; Harriman, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 1184–1201.
- (7) Lee, C. H.; Lindsey, J. S. *Tetrahedron* **1994**, *50*, 11427–11440.
- (8) Littler, B. J.; Miller, M. A.; Hung, C. H.; Wagner, R. W.; O'Shea, D. F.; Boyle, P. D.; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 1391–1396.
- (9) Brückner, C.; Karunaratne, V.; Rettig, S. J.; Dolphin, D. *Can. J. Chem.* **1996**, *74*, 2182–2193.
- (10) Treibs, A.; Kreuzer, F. H. *Justus Liebigs Ann. Chem.* **1968**, *718*, 208–223.
- (11) Choi, S. H.; Kim, K.; Lee, J.; Do, Y.; Churchill, D. G. *J. Chem. Crystallogr.* **2007**, *37*, 315–331.
- (12) Haugland, R. P. *Handbook of Fluorescent Probes and Research Chemicals*, 9th ed.; Molecular Probes, Inc.: Eugene, OR, 2002.
- (13) Maiti, N.; Lee, J.; Kwon, S. J.; Kwak, J.; Do, Y.; Churchill, D. G. *Polyhedron* **2006**, *25*, 1519–1530.
- (14) Halper, S. R.; Cohen, S. M. *Inorg. Chem.* **2005**, *44*, 486–488.
- (15) Halper, S. R.; Cohen, S. M. *Chem. Eur. J.* **2003**, *9*, 4661–4669.
- (16) Cohen, S. M.; Halper, S. R. *Inorg. Chim. Acta* **2002**, *341*, 12–16.
- (17) Halper, S. R.; Stork, J. R.; Cohen, S. M. *Dalton Trans.* **2007**, 1067–1074.
- (18) Thamyongkit, P.; Bhise, A. D.; Taniguchi, M.; Lindsey, J. S. *J. Org. Chem.* **2006**, *71*, 903–910.
- (19) Kulikov, O. V.; Schmidt, I.; Muresan, A. Z.; Lee, M. A. P.; Bocian, D. F.; Lindsey, J. S. *J. Porphyrins Phthalocyanines* **2007**, *11*, 699–712.
- (20) Muthukumar, K.; Zaidi, S. H. H.; Yu, L. H.; Thamyongkit, P.; Calder, M. E.; Sharada, D. S.; Lindsey, J. S. *J. Porphyrins Phthalocyanines* **2005**, *9*, 745–759.
- (21) Yu, L. H.; Muthukumar, K.; Sazanovich, I. V.; Kirmaier, C.; Hindin, E.; Diers, J. R.; Boyle, P. D.; Bocian, D. F.; Holten, D.; Lindsey, J. S. *Inorg. Chem.* **2003**, *42*, 6629–6647.
- (22) D'auria, M.; DeLuca, E.; Esposito, V.; Mauriello, G.; Racioppi, R. *Tetrahedron* **1997**, *53*, 1157–1166.
- (23) Maiti, N.; Lee, J.; Do, Y.; Shin, H. S.; Churchill, D. G. *J. Chem. Crystallogr.* **2005**, *35*, 949–955.
- (24) Churchill, D. G.; Maiti, N.; Choi, S. H. Repub. Korean Kongkae Taehoe Kongbo (patent written in Korean). KR 2007049466 A, 2007; CAN 147:475473, AN 2007:1191159, CODEN: KRXXA7.
- (25) (a) Choi, S. H.; Pang, K.; Kim, K.; Churchill, D. G. *Inorg. Chem.* **2007**, *46*, 10564–10577. (b) Churchill, D. G.; Choi, S. H.; Kim, K.; Pang, K. *Abs. Pap., 234th ACS Nat. Mtg.* **2007**, INOR-119. (c) Churchill, D. G.; Choi, S. H.; Pang, K.; Kim, K. *Abs. Pap., 235th ACS Nat. Mtg.* **2008**, INOR-431.

- (26) Paul-Roth, C. O.; Letessier, J.; Juillard, S.; Simonneaux, G.; Roisnel, T.; Rault-Berthelot, J. *J. Mol. Struct.* **2008**, *872*, 105–112.
- (27) Li, X. X.; Guo, Y. J.; Wang, J. W.; Kong, L. H.; Pan, J. H. *Supramol. Chem.* **2008**, *20*, 243–248.
- (28) Li, X. X.; Wang, J. W.; Guo, Y. J.; Kong, L. H.; Pan, J. H. *J. Inclusion Phenom. Macrocyclic Chem.* **2007**, *58*, 307–315.
- (29) Gupta, I.; Ravikanth, M. *J. Photochem. Photobiol., A* **2006**, *177*, 156–163.
- (30) Bhyrappa, P.; Sankar, M.; Varghese, B.; Bhavana, P. *J. Chem. Sci.* **2006**, *118*, 393–397.
- (31) Yuasa, M.; Oyaizu, K.; Yamaguchi, A.; Ishikawa, M.; Eguchi, K.; Kobayashi, T.; Toyoda, Y.; Tsutsui, S. *Polym. Adv. Technol.* **2005**, *16*, 616–621.
- (32) Sun, X. D.; Zhang, J. L.; He, B. *J. Photochem. Photobiol., A* **2005**, *172*, 283–288.
- (33) Li, Z. F.; Wang, S. W.; Song, W. S.; Deng, H. N.; Wang, Y. Q.; Wang, Y. X. *Chin. J. Org. Chem.* **2003**, *23*, 588–594.
- (34) Purushothaman, B.; Varghese, B.; Bhyrappa, P. *Acta Crystallogr., C* **2001**, *57*, 252–253.
- (35) Diskin-Posner, Y.; Balasubramanian, S.; Patra, G. K.; Goldberg, I. *Acta Crystallogr., E* **2001**, *57*, M346–M348.
- (36) Bhyrappa, P.; Bhavana, P. *Chem. Phys. Lett.* **2001**, *349*, 399–404.
- (37) Goze, C.; Ulrich, G.; Mallon, L. J.; Allen, B. D.; Harriman, A.; Zissel, R. *J. Am. Chem. Soc.* **2006**, *128*, 10231–10239.

Scheme 1. Reaction Scope for This Contribution Showing *meso*-Thienyl Dipyrin Derivatization (Our Atom Numbering), Stemming from 5-Thienyl-dipyrromethane and Oxidative Transformations^a



^a T = thienyl; * = known compound; species crystallographically characterized herein are noted with underlining.

may impart the heavy atom effect which will change the nature of intersystem crossing. Thus we studied the mild oxidative effect of Br_2 addition onto aryl C–H moieties (Figure 1). Since bromine can easily add indiscriminantly to C–H bonds, we selected to choose a derivative bearing bromines at the *meso*-group position so that this group is unreactive.

(iii, iv) How a transition metal complex, bearing a pendant thienyl group, undergoes oxidation through the use of *m*-CPBA has not been studied before to the best of our knowledge. Thus we can directly probe changes in the spectra of various complexes to investigate patterns of metal or sulfur oxidation.

(v) In a previous report we have used thienyl groups in selective Cu^{2+} recognition. Now we want to explore if these binding atoms are necessary; we will use phenyl groups at the B-substituent, but the *meso*-thienyl substituent will be retained. Through experimental studies that focus on these five points, it will become clear that derivatives of *meso*-thienyl dipyrin core are readily accessible to yield an array of robust products.²⁵

Results and Discussion

Synthesis and Spectroscopic Characterization of *meso*-Thienyl Dipyrin Systems. In this section we will describe all synthetic procedures and some aspects of

NMR spectroscopic characterization that were useful in describing structural aspects (all synthetic details are provided in the Supporting Information for additional data). The dipyrromethane molecules with a variety of thienyl-*meso* groups were prepared by the Lindsey method^{7,8} and used in forming the difluoroboryl species (Scheme 1). Dipyrromethanes **1**, **2**, and **3** have been reported previously.¹¹ The conversion by DDQ/ BF_3OEt_2 afforded the BODIPY-type species **5**, **6**, and **7**.¹¹ The benzothiophene-containing species (compounds **4** and **8**) are reported for the first time and were prepared analogously. Upon treatment of compound **8** with *m*-CPBA, a clean oxidation product (**8a**) is formed. This species (i) possesses significantly different polarity, based on simple selective 8-position⁵ oxidation as observed by a TLC assay (see Supporting Information), and (ii) displays different optical characteristics ($\lambda_{\text{abs, max}} = 511 \text{ nm}$, $\phi_{\text{F}} = 0.006$, Stokes' shift = 38 nm, CH_2Cl_2) from those of **8** ($\lambda_{\text{abs, max}} = 502 \text{ (nm)}$, $\phi_{\text{F}} = 0.192$, Stokes' shift = 14 nm, CH_2Cl_2). Moreover, the IR spectrum of **8a** reveals new bands assignable to the S=O groups (see Supporting Information). The ^1H NMR spectra of **8** and **8a** bear the same number of signals with some minor, but important, differences. The H_b residue shifts from δ 6.95 in **8** to δ 7.73 in **8a**; the H_f residue is also brought from δ 7.81 to δ 7.33, whereas that for H_e moves from δ 7.92 to δ 7.82.

(38) Zhang, Q.; Tong, M. Y.; Li, Y. S.; Gao, H. J.; Fang, X. C. *Biotechnol. Lett.* **2007**, *29*, 123–127.

(39) Li, F. L.; Zhang, Z. Z.; Feng, J. H.; Cai, X. F.; Xu, P. *J. Biotechnol.* **2007**, *127*, 222–228.

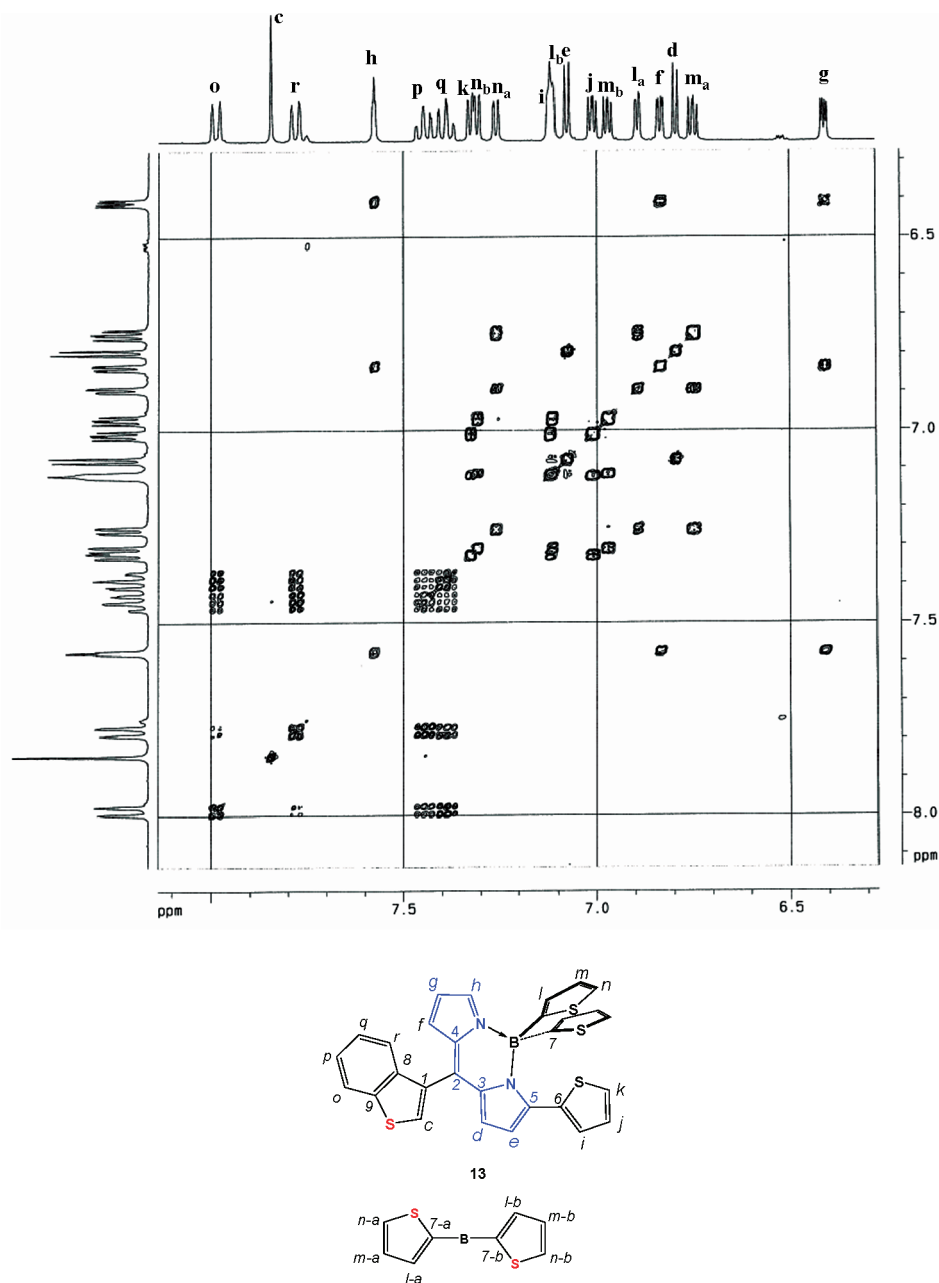


Figure 2. ^1H - ^1H COSY NMR spectrum for **13** accompanied by a diagram of **13** with atomic labels. The B-thienyl groups are inequivalent due to the hindered rotation of the sterically bulky benzothieryl group on the NMR time scale (room temperature).

H_f and H_e are positioned proximal to the Bodipy moiety opposite the sulfur group. All of these changes can be clearly seen in the ^1H - ^1H NOESY NMR spectra (Supporting Information). We then investigated many other species possessing the *meso*-thienyl group, but these oxidations led to products that were not nearly as isolable by chromatographic methods as compound **8a** was. Various thienyl-*meso* derivatives were, however, titrated with *m*-CPBA as discussed below.

Reactions with bromine (Br_2) involved exclusively the 4,4-difluoro-8-(2,5-dibromo-3-thienyl)-4-bora-3*a*,4*a*-diaz*a-s*-indacene compound (**7**). **7** was treated with Br_2 to give isolable products of tetra-(**7b**) and hexa-bromination (**7c**). As with thienyl di-oxidation, bromination is also by twos; pairs of Br's add to dipyrrole carbons 1, 2, and 3 (Figure 3). Specifically, with a ratio of 1:38, boron-dipyrrin: Br_2 , the

tetra-bromination product (**7b**) was favored; with a ratio of 1:800, boron-dipyrrin: Br_2 , the hexa-bromination product (**7c**), was favored. The elusive compound **7a**, likened to 3,5-dichloro-8-(phenyl)-4-bora-3*a*,4*a*-diaz*a-s*-indacene,⁴⁰ could not be obtained cleanly via synthetic methods.⁴¹ Intermediate products of bromination must occur but were neither isolated nor characterized herein. Other halogenation reactions have been for the BF_2 species, such as the selective Bodipy 2,6-iodination of 1,3,5,7-tetramethyl-4-bora-3*a*,4*a*-diaz*a-s*-indacene.⁴² While we were able to purify two individual bromination products, we can go further and study **7** in

(40) The halogenation was performed before the formation of the Bodipy derivative was present; this species was made by chlorinating the dipyrromethane before $\text{BF}_3 \cdot \text{OEt}_2$ addition.

(41) A crude product was obtained, however, and tentatively assigned as the 3,5-dibromo-4,4-difluoro-8-(2,5-dibromo-3-thienyl)-4-bora-3*a*,4*a*-diaz*a-s*-indacene derivative.

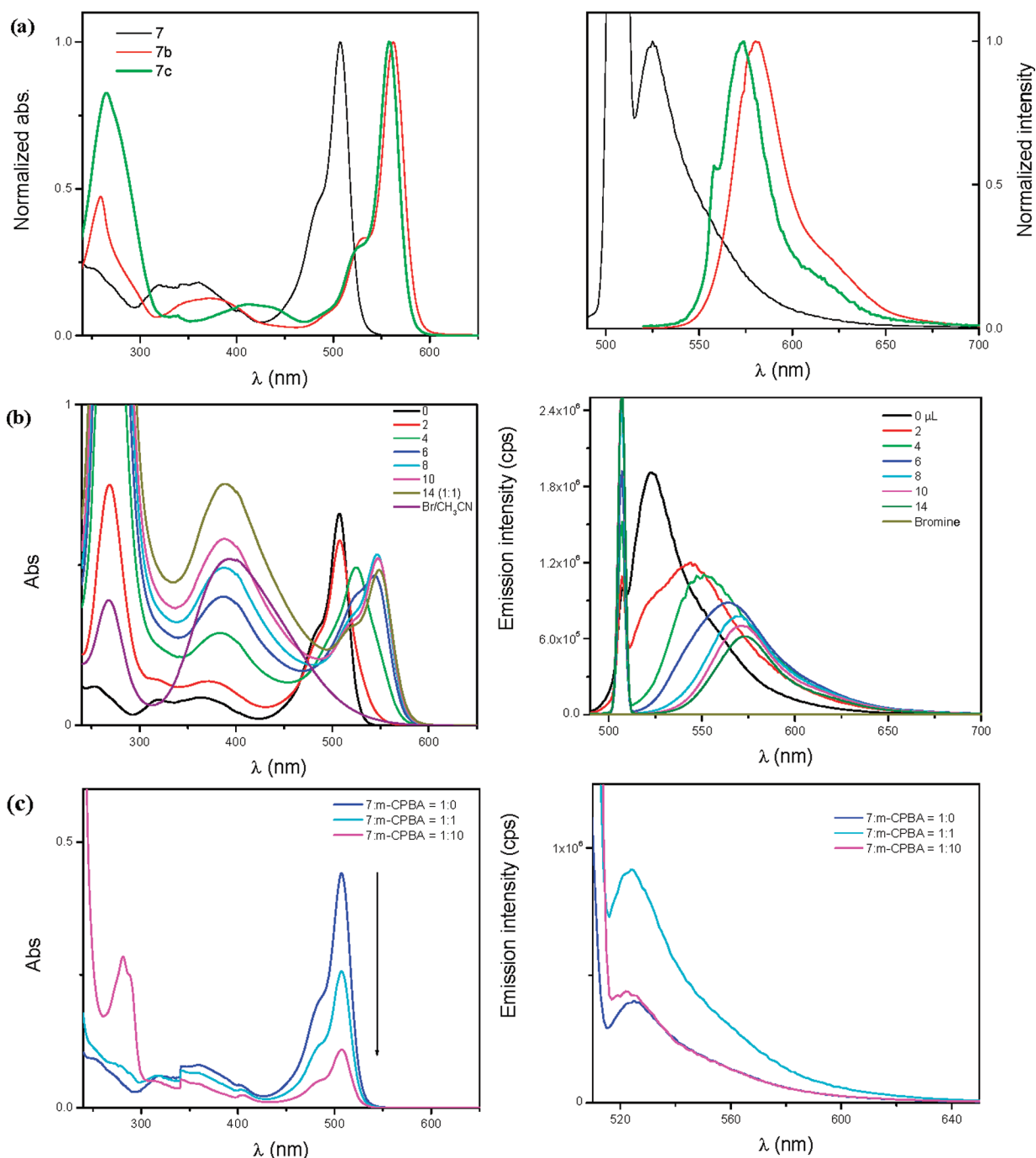
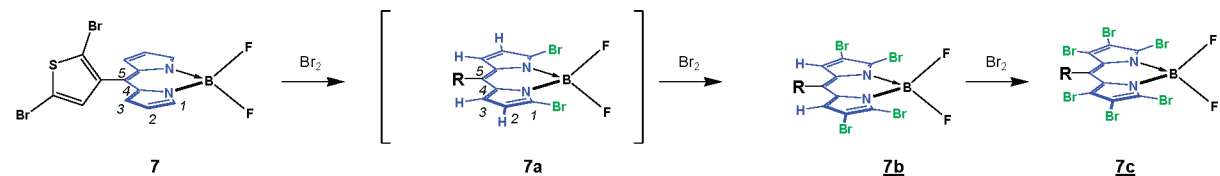


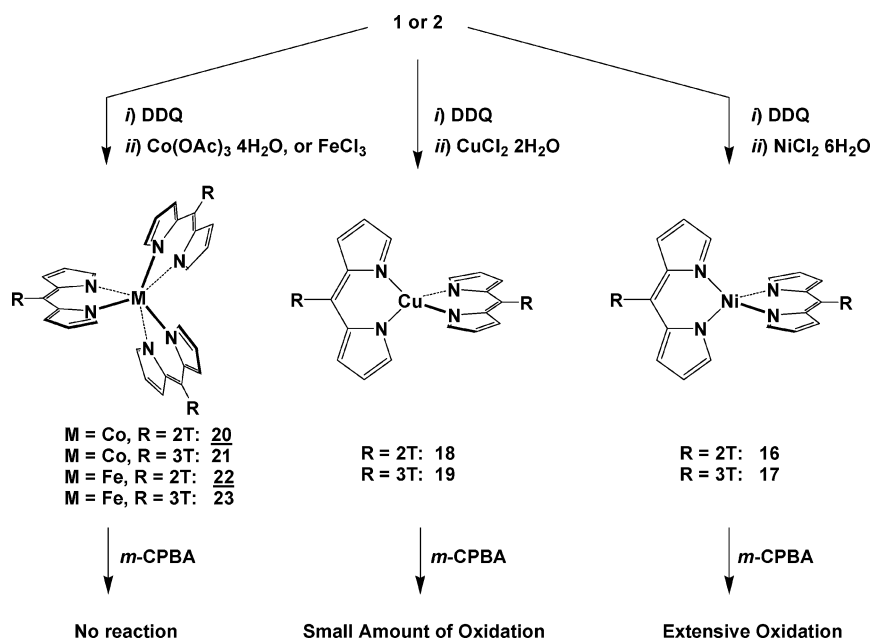
Figure 3. (top) Scheme of stepwise bromination. (a) Absorption and emission spectra of **7** (1.4×10^{-5} M), **7b** (5.9×10^{-5} M), **7c** (8.0×10^{-5} M). (b) Absorption and emission spectra for the titration of **7** (1.4×10^{-5} M) with bromine (1.0×10^{-3} M) in CH_3CN . (c): **7** with *m*-CPBA (absorption and emission). For emission spectra, excitation was at 507 nm.

bromination titration studies involving the addition of increasing amounts of Br_2 in the reaction mixture that is monitored optically (see Supporting Information).

Boron dipyrins having multiple peripheral thienyl sites can also be prepared. Compounds **9–12** have previously been synthesized and reported. Treatment of compound **8** with

2-thienyl lithium affords **13**. Compound **13** exhibits interesting 8-position ring rotation that is slow on the NMR time scale giving rise to two sets (*a*'s and *b*'s) of signals assigned to atoms H_7 , H_I , H_n , and H_m (Figure 2). In the case of **9–13**, three inequivalent thienyl positions create a complicated situation for monitoring stepwise thiophene-S-oxidation,

Scheme 2. Preparation and Oxidation of the Neutral bis-Species and Retention of Oxidation by the Neutral tris-Species upon Treatment with *m*-CPBA in DMF^a



^a R = thienyl. M = Fe, Co.

however. To circumvent this problem we also synthesized the “scorpionate”-like derivatives (**14** and **15**) in which only the 8-position substituent bears an oxidizable sulfur site. The new triphenyl compounds (**14** and **15**) possess the same 8-position group as in our previous report.²⁴ These compounds and their titrations with strong oxidant are presented and discussed below.

We have also prepared related transition metal dipyrinato complexes of copper(II), nickel(II), cobalt(III), and iron(III) (Scheme 2). NMR spectroscopy was used where possible (Supporting Information) but is less useful in characterization for some of these species: (i) it may not account for the number of bidentate ligands bearing chemically shift-equivalent protons; furthermore, (ii) spectral peak shifts and widths may be greatly affected by a paramagnetic metal center. As seen in Table 1, these metallo-species possess virtually no fluorescence. However, they are still chromophoric and possess an absorption (444–494 nm) that can be usefully monitored in oxidation trials.

Optical Changes upon Titration of Thienyl Dipyrin Substrates with Strong Oxidant. We will now qualitatively determine the degree of selective oxidation of various substrates through titration of *m*-CPBA, in organic solvent at room temperature after various delay times. (For all oxidation titration spectra, please see the Supporting Information.) For compound **8** with *m*-CPBA, we can see absorption diminution and fluorescent enhancement at a substrate:oxidant ratio of 1:100 after 10 min. An analogous pattern is seen when **8** is treated with portions of H₂O₂ (30%,

Table 1. Optical Properties for Boron–Dipyrin and Transition Metal Thienyl–Dipyrin Derivatives^a

compound	$\lambda_{\text{abs,max}}$ (nm)	ϵ (M ⁻¹ cm ⁻¹)	$\lambda_{\text{em,max}}$ (nm)	Stokes' shift ^b (nm)	ϕ_{F} ^c
7	506	31,000	524	18	0.098
7b	563	5,300	580	17	0.12
7c	559	11,300	574	15	0.006
8	502	15,000	516	14	0.19
8a	511	17,900	549	38	0.006
13	557	33,800	577	20	0.072
14	518	18,800	548	30	0.004
15	509	17,100	546	37	0.008
16	469	37,300	511	18	0.0012
17	461	33,300	499	38	0.0012
18	502	40,800	519	17	0.0008
19	494	56,200	503	9	0.0005
20	476	27,200	551	75	0.0007
21	469	56,800	544	75	0.0004
22	449	51,000	518	69	0.0005
23	444	44,000	510	66	0.0006

^a Spectral properties in CH₃CN at RT. ^b Stokes' shifts were calculated from respective absorption and emission wavelengths. ^c Quantum yields (taken to two significant figures or four decimal places) were referenced using fluorescein⁴³ dissolved in 0.1 N NaOH as a reference ($\phi_{\text{F}} = 0.93$). Values for ϵ (M⁻¹cm⁻¹) are rounded to the hundreds place.

aqueous solution), demonstrating oxidant insensitivity and the possibility to apply our probe to realistic biological environments. In the UV–vis absorption spectrum for compound **8** at 1:500 probe:oxidant equivalency, there was a ~28% reduction (at 502 nm); for compound **13**, there was a ~65% reduction (at 557 nm). As a means of comparison, in the emission spectra, there was a ~20% reduction for **8** (at 515 nm) and a ~30% reduction for **13** (at 576 nm).

Notably, in the oxidation of compound **13**, there occurs a more thorough band diminution than that is seen for species **9** and **11**. This greater decrease suggests that the *meso*-benzothienyl group is being oxidized more in compound **13** than the 2-thienyl group is in compound **9** or that the 3-thienyl group is in compound **11**. For the pairs of species

(42) Yogo, T.; Urano, Y.; Ishitsuka, Y.; Maniwa, F.; Nagano, T. *J. Am. Chem. Soc.* **2005**, *127*, 12162–12163.

(43) Pretsch, E.; Clerc, T.; Seibl, J.; Simon, W. *Tables of Spectral Data for Structure Determination of Organic Compounds*, 2nd ed.; Springer-Verlag: New York, 1989.

in which the 3- and 4-position thienyl groups are the same (**9** and **11**; **10** and **12**), there exist similar patterns of decrease in the absorption band.

The 3,4,4-triphenyl derivative bearing one sulfur atom reveals an absorption spectrum whose peak diminishes only partially. When considering a 1:500 probe:oxidant equivalency, derivatives **14** and **15** give $\sim 10\%$ and $\sim 12\%$ absorbance decreases, respectively, whereas **9** and **11** gave $\sim 55\%$ and $\sim 40\%$ diminutions, respectively. Lastly, compounds **10**, **12**, and **13** afford larger respective signal losses: $\sim 80\%$, $\sim 80\%$, and 65% . Thus, the *meso*-thienyl effect in **14** and **15** is minimal under these conditions.

In terms of fluorescence characteristics, sulfur-oxidation turns *off* substrate emission (generally) with species **9–12**; this is interesting in light of previous results that clearly show that Cu^{2+} complexation turns *on* emission.²⁴ However, derivatives **10** and **12** (bearing a *tri*-3-thienyl pocket) give a fluorescence increase at a probe:oxidant ratio of 1:100; this enhancement decreases upon further oxidant addition and is suggested to be an effect of oxidation on the groups on or proximal to the boron, since **10** and **12** contain different *meso*-substituents and **9** and **11** do not have similar responses. The initial increase for **10** and **12** is ascribed to heightened emissive properties of transient mono-oxidation products which are expected to be isolated and identified through future studies. Lastly, we can now determine the effect of oxidation of thienyl groups attached to or proximal to the boron by comparing **14** with **9** or **10** and **15** with **11** or **12**.

Next, we wanted to investigate oxidative titrations of transition metal–dipyrrin derivatives to explore optical patterns arising from the presence of a substrate bearing a metal center (i.e., compounds **18–23**) instead of a boron center. Notably, the nickel(II) species degrades when compared to those of copper(II), which nearly completely resist oxidation. The cobalt(III) and iron(III) species are not affected by these titrations of oxidant at concentrations used herein. In the case of the nickel(II) species, whether the 2- or 3-thienyl *meso*-substituent is present, appears not to matter. At this oxidation concentration, the *metal center* appears to be the target of oxidation, different from the boron centered derivatives that resist boron attack.

The isolation and characterization of **8a** suggest that any Bodipy oxidation will begin with sulfur oxidation and lead to dioxidation, prior to attack at other possible sites (e.g., the nitrogen, to give *n*-oxides, and boron to give boron oxides). Focusing on sulfur oxidation for now, such oxidation will remove lone pairs of sulfur in bonding, allowing for the frontier orbitals to change their nature, leading to changes in electronic transition energies (see computation discussion in the Supporting Information). Some confusion arises since, if a bulky group is proximal to the fluorophore, there could be *greater* fluorescence characteristics⁵ or *depleted* photo-physical characteristics.⁴⁴ For **8**, however, effects on 8-aryl group rotation are negligible due to the distally positioned sulfur; to address this effect of S-oxidation, simple thiophene-S-dioxide formation derivatives are also investigated theoretically (Supporting Information). An important consideration is that slow addition of oxidant may give rise to longer-

lived S–O intermediates which may allow for facile decomposition.^{45,46} Careful characterization of the behavior of **8a** allows it to be considered as a potential oxidative desulfurization probe; its clean conversion is attributed to system rigidity and 8-(3-benzothienyl) orthogonality.

Titration of 4,4-Difluoro-(2,5-dibromo-3-thienyl)-8-4-bora-3a,4a-diaza-s-indacene with Molecular Bromine.

Next, we wanted to explore the effect of Br_2 addition to a thienyl–dipyrrin species to examine whether there are stepwise optical effects that relate to stepwise optical changes in the pyrrolyl moieties (Figure 3). We focused on compound **7**, because the *meso* group in 4,4-difluoro-(2,5-dibromo-3-thienyl)-8-4-bora-3a,4a-diaza-s-indacene will resist further bromination, allowing for selective bromination of the Bodipy periphery. Since greater amounts of Br_2 allow for the formation of greater amounts of more highly Br-substituted products, titrations will allow for stepwise product formation. To simplify this analysis, we prepared and characterized compounds **7b** and **7c**, products of tetra- and hexa-bromination (Scheme 1); the product of dibromination, compound **7a**, was elusive. The spectra of **7b** and **7c** clearly show a progression of increasingly bathochromically shifted spectral signals. In the titrations there is this same trend; the spectral progression is devoid of isosbestic points, strongly indicating the involvement of many transient intermediate products of uneven bromination with finite lifetimes (Figure 3). The large bathochromic shift in the main absorption and emission band for **7b** and **7c** upon bromination can be cleanly interpreted as sequential bromination: $7 \rightarrow 7a \rightarrow 7b \rightarrow 7c$.

Titration of Substrates with M^{n+} . In this section we discuss metal ions which are a third and last form of external chemical stimulant described herein. First, we present spectra of species **14** and **15** upon addition of various metal ions (Figures 4 and 5). Noticeable responses for Cu^{2+} and Hg^{2+} , as observed previously for compounds **9–12** (Scheme 1), led to our interest in the inspection of Cu^{2+} and Hg^{2+} addition again here.²⁴ In compounds **14** and **15**, there is a decrease in the S_0 – S_2 band at 385 nm (**14**) and 360 nm (**15**) upon treatment with Cu^{2+} (Figures 4 and 5). The progress in these spectra is very smooth indicating that the conversions are markedly cleaner than those for **9–12**. This observation is in line with the notion that various conformations necessary to engage [SSS] tridentate binding for **9–12** are not required or possible for **14** and **15**.²⁴ Importantly, Cu^{2+} sulfur binding appears not to be mandatory in producing a marked signal change in these systems. Clear isosbestic points are present at 352, 412, and 480 nm for **14**– Cu^{2+} , at 405 nm for **14**– Hg^{2+} , at 335, 382, and 465 nm for **15**– Cu^{2+} , and at 378 nm for **15**– Hg^{2+} . These features support direct metal ion binding into what we propose is an “ansa-metalloocene-type” pocket created by the [Ph-B-Ph] moiety. For **14**, upon titration with

(44) Sun, Z.-N.; Liu, F.-Q.; Chen, Y.; Tam, P. K. H.; Yang, D. *Org. Lett.* **2008**, *10*, 2171–2174.

(45) Arima, K.; Ohira, D.; Watanabe, M.; Miura, A.; Mataka, S.; Thiemann, T.; Valcarcel, J. I.; Walton, D. J. *Photochem. Photobiol. Sci.* **2005**, *4*, 808–816.

(46) Thiemann, T.; Ohira, D.; Arima, K.; Sawada, T.; Mataka, S.; Marken, F.; Compton, R. G.; Bull, S. D.; Davies, S. G. *J. Phys. Org. Chem.* **2000**, *13*, 648–653.

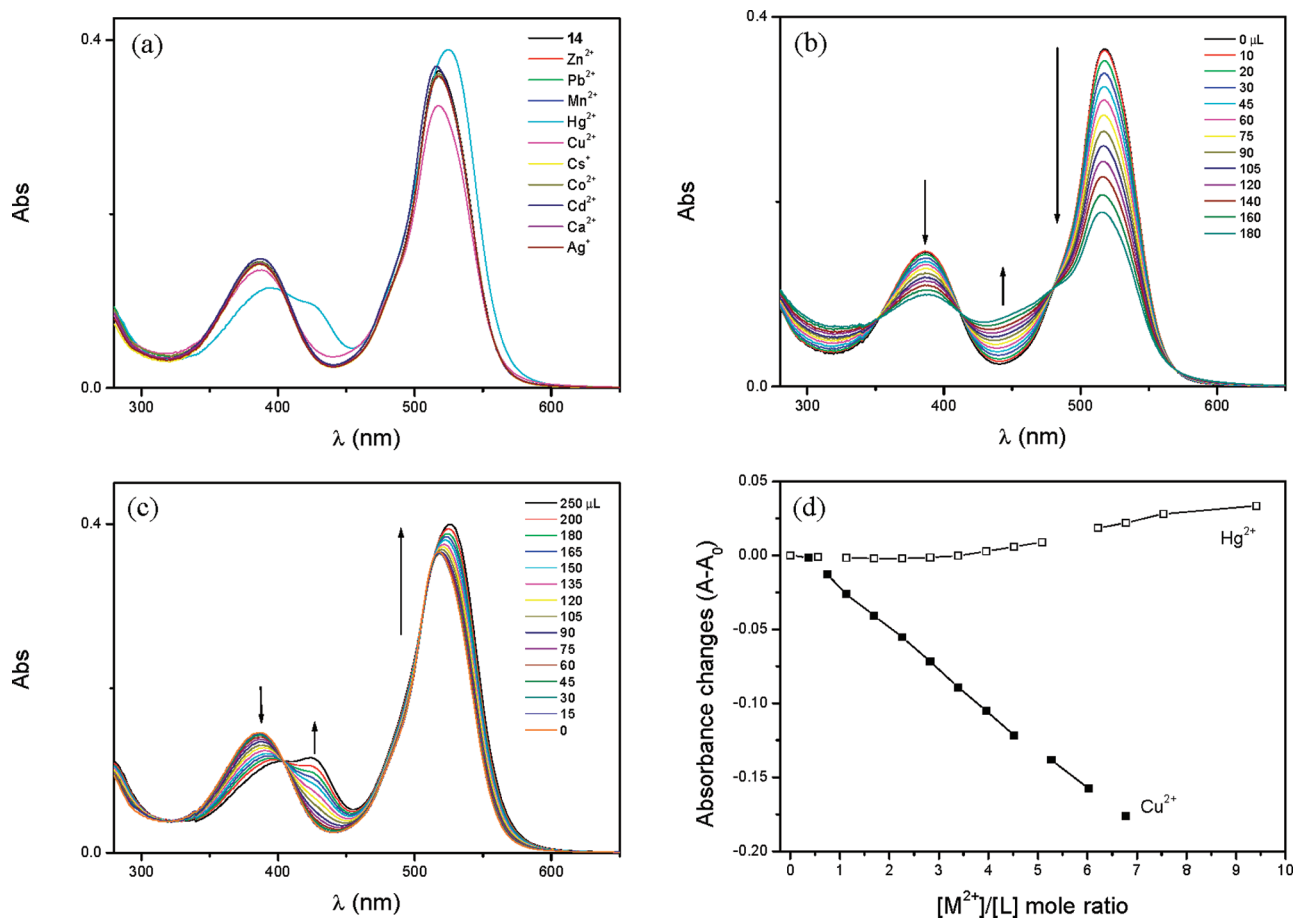


Figure 4. Titration of **14** (1.54×10^{-5} M) with (a) a variety of metal ions, (b) Cu^{2+} , and (c) Hg^{2+} . (d) Plot of absorbance changes of **14** with addition of Hg^{2+} , Cu^{2+} : 1.0×10^{-3} M.

Hg^{2+} , a new shoulder appears at 426 nm; for **15** one appears at 402 nm. Upon modeling this M^{2+} binding using the Benesi-Hildebrand method, we obtain a 1:1 ligand-to-metal binding model for Cu^{2+} but a 1:2 ligand-to-metal binding for Hg^{2+} . This 1:2 binding ratio is at odds with the presence of clean spectral isosbestic points. Thus, determining how multiple binding is accommodated in these systems will require further study.

After looking at Hg^{2+} and Cu^{2+} independently, we then investigated if one bound metal ion could be displaced by a free metal ion. Upon treatment of **14**- Cu^{2+} with an excess of Hg^{2+} , the original band profile prior to Cu^{2+} addition is recovered (Figure 6). This smooth and excellent reversibility allows **14** and **15** to be investigated in terms of reversible molecular sensing when considering either the $\text{S}_0\text{-S}_1$ or $\text{S}_0\text{-S}_2$ absorption bands.

In terms of M^{n+} invoked responses, the “scorpionate” systems have shown distinct changes. We then wanted to see if responses from M^{2+} could be considered from the dipyrro-nato-M in which there is no cavity but just substitutions. Thus we titrated **16** and **17** with Hg^{2+} and Cu^{2+} because they were the most sensitive species of this type upon exposure to strong oxidation (Supporting Information). We again used the perchlorate salts⁴⁷ of Hg^{2+} and Cu^{2+} in separately titrating **16** and **17** in DMF to invoke optical signal

changes (Figure 7). In the four titrations generally, the major band assigned as the $\text{S}_0\text{-S}_1$ absorption upon interaction with M^{2+} gives a sharpened band of increased intensity at ~ 499 nm for **16** (with Cu^{2+}), ~ 489 nm for **17** (with Cu^{2+}), ~ 493 nm for **16** (with Hg^{2+}), and ~ 485 nm for **17** (with Hg^{2+}). These optical signal changes suggest weak M^{n+} complexation to the *meso*-thienyl group with binding constants (K_a) for **14**: Cu^{2+} 1:1 = $2.1 \times 10^3 \text{ M}^{-1}$; **15**: Cu^{2+} 1:1 = $1.0 \times 10^3 \text{ M}^{-1}$; **14**: Hg^{2+} 1:2 = $7.3 \times 10^7 \text{ M}^{-1}$; and **15**: Hg^{2+} 1:2 = $8.6 \times 10^6 \text{ M}^{-1}$. Thus, sensing through the use of these *meso*-groups due to this weak binding is selective but not sensitive.

Structural Characterization. In this section we will present and discuss eight molecular structures. First, we discuss the molecular structures of 4,4-difluoro-8-(3-thienyl)-**(6)** and 4,4-difluoro-8-(3-benzothienyl)-4-bora-3*a*,4*a*-diazas-indacene (**8**). The benzothienyl compound **8**, when compared to **6**, formally bears an additional $[\text{C}_4\text{H}_2]$ unit and adopts a space group of $P2_1/c$ (Figure 8). The 2,3,5,6-tetrabromo-4,4-difluoro-8-(2,5-dibromo-3-thienyl)-4-bora-3*a*,4*a*-diazas-indacene species (**7b**) is a direct derivative of **7**. In both **7b** and **7c**, the $[\text{BF}_2]$ unit is refined sensibly by least-squares methods. Compound **7b** involves four Br atoms that occupy sites on carbons 2, 3, 5, 6 (Figure 9). Compound **7c** (1,2,3,5,6,7-hexabromo-4,4-difluoro-8-(2,5-dibromo-3-thienyl)-4-bora-3*a*,4*a*-diazas-indacene) has two more bromines than **7b** does; these new substituents are at the two

(47) Churchill, D. G. *J. Chem. Educ.* **2006**, *83*, 1798–1803.

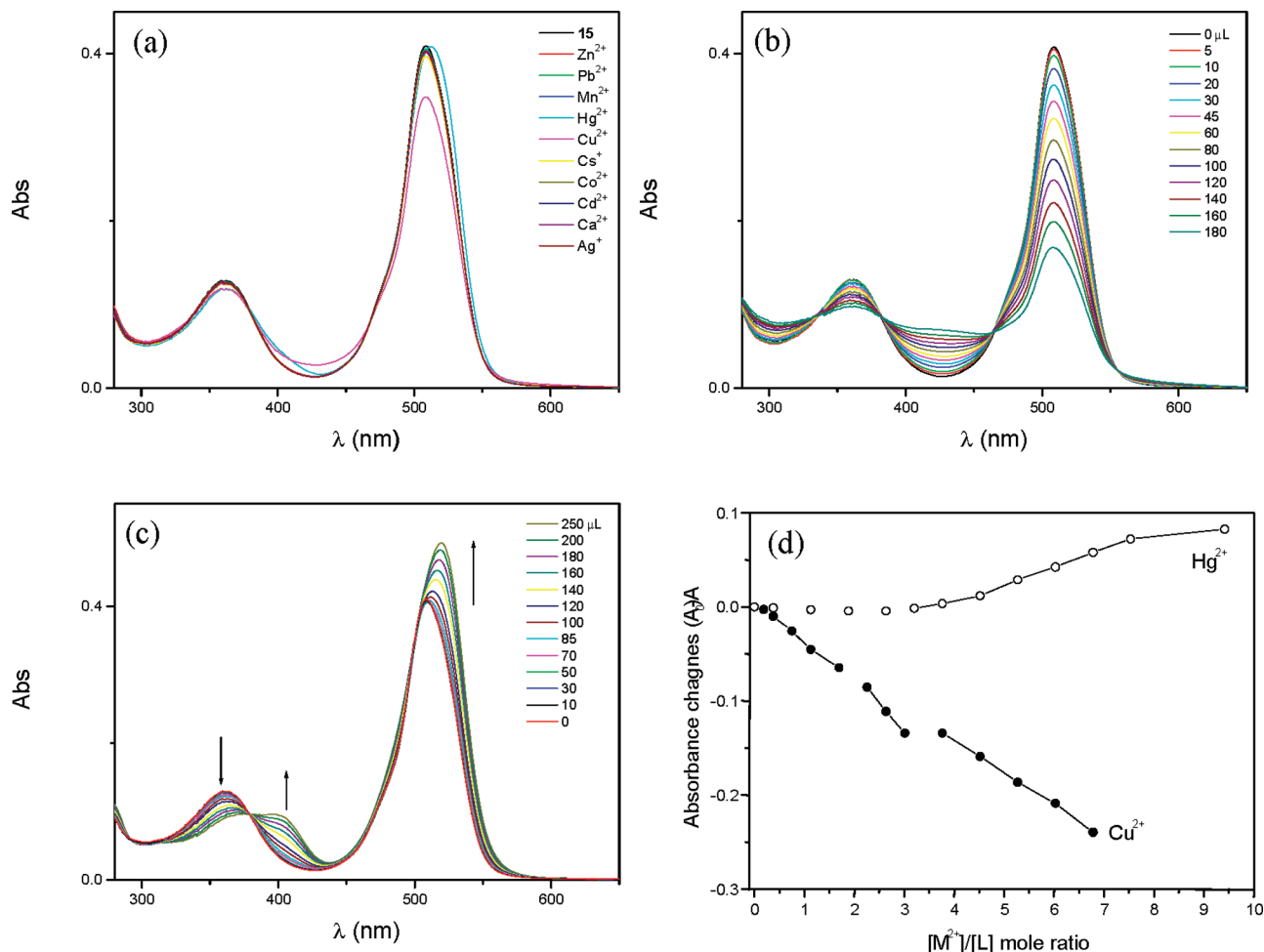


Figure 5. Titration of (a) **15** (1.54×10^{-5} M) with a variety of metal ions, (b) Cu^{2+} titration, and (c) Hg^{2+} titration. (d) Plot of absorbance changes of **15** with addition of Hg^{2+} , Cu^{2+} : 1.0×10^{-3} M.

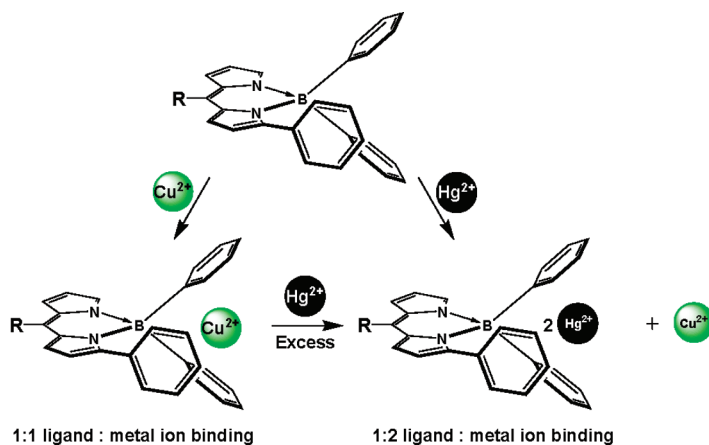
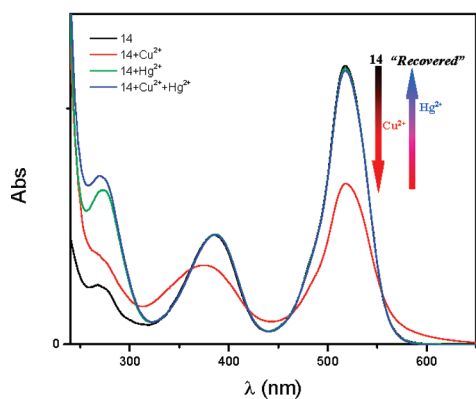


Figure 6. Four samples were prepared. Compound **14** (2.58×10^{-5} M) when treated with Cu^{2+} and Hg^{2+} ion (500 μL , 1.0×10^{-3} M) after ~ 1 h after preparation.

remaining diazaindacene [C–H] sites leaving only one hydrogen (H_b , Scheme 1). No molecular symmetry is lost via sequential bromine substitutive addition.

The availability of molecular structures for **6**, **7b**, **7c**, and **8** allow us to consider a trend in crystallographic density as bromines replace hydrogens on the dipyrin or as the thienyl group is formally extended (Figure 10). Significantly, the density for **6**, as determined crystallographically, is 1.483

g/mL with a formal increase to 2.613 g/mL upon hexabromination (i.e., **7b**). A fuller correlation of density by the number of remaining hydrogen atoms would be later interesting to prepare: i.e., H9 (**6**), H7 (**7**), H5 (**7a**), H3 (**7b**), and H1 (**7c**).

The nonplanarity of the 8-thienyl moiety is likely a result of increased steric bulk. The dihedral angle between mean planes 2 and 7 (Figure 10) increases from **6** to **8** as the greater

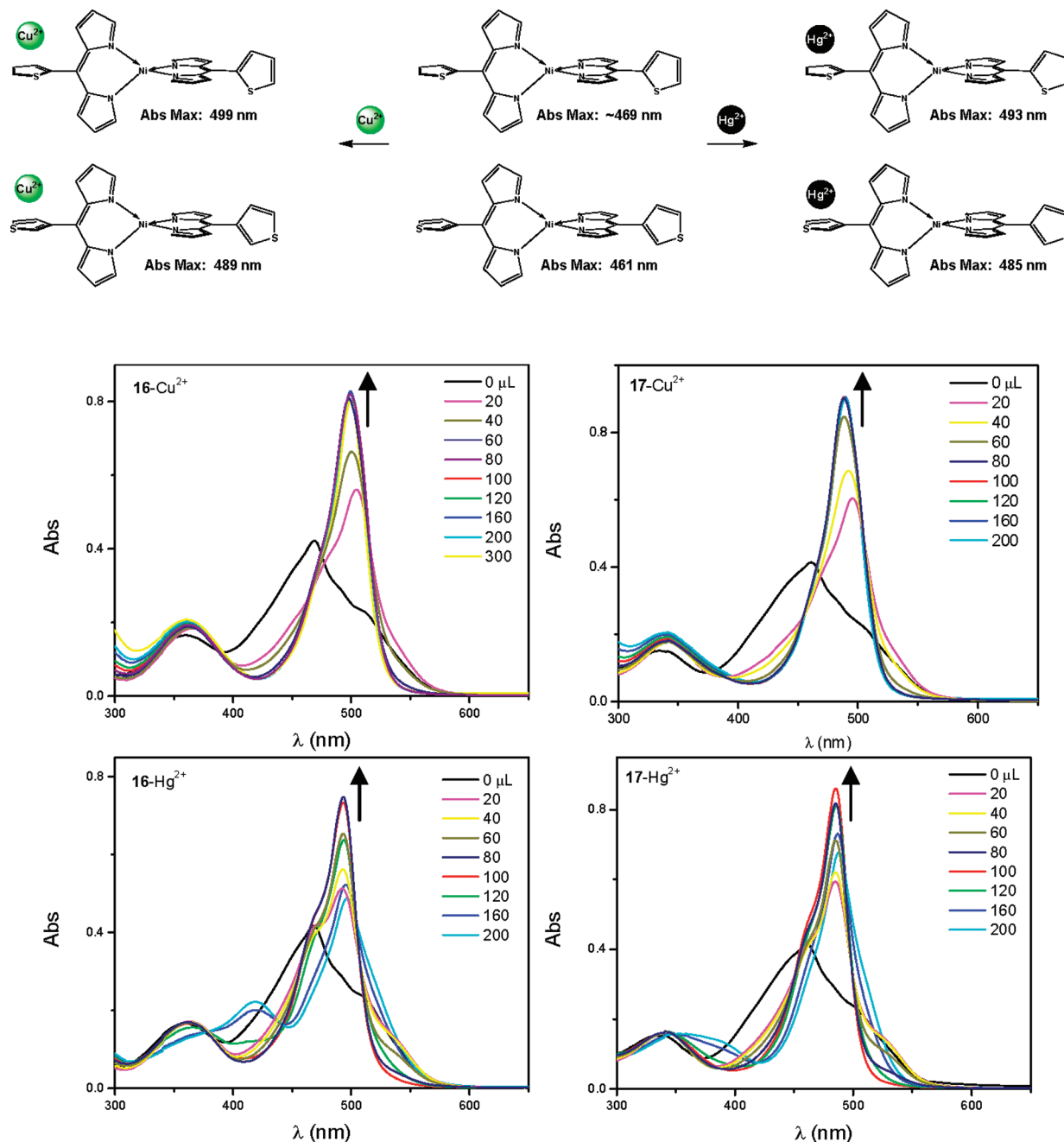


Figure 7. Treatment of **16** and **17** with Hg^{2+} and Cu^{2+} and the values of the absorption band maxima. Separate titration solutions (DMF) of **16** (left) and **17** (right) with ligand 1.0×10^{-5} M, metal ion (Cu^{2+} or Hg^{2+}) perchlorate titrant: 1.0×10^{-3} M.

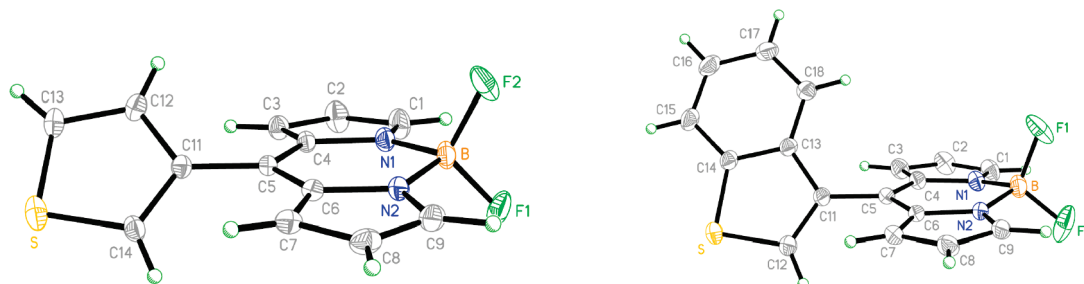


Figure 8. Molecular structures of **6** and **8**.

8-position benzothienyl group is present at, or as bromines are formally added on to, the *meso*-substituent (compound **6** \rightarrow **7b**) or as the 1 and 7 boradiazaindacene ring positions become

brominated (compound **7b** \rightarrow **7c**). The atoms in mean plane 2 are usually puckered, as shown by a small but distinct hinge angle, between mean plane 1 and the [N–B–N] plane. This

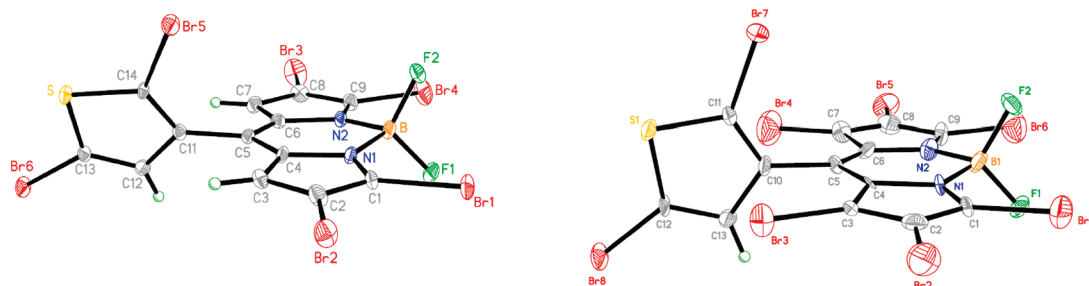


Figure 9. Molecular structures of **7b** and **7c**. For **7b** the solvent of crystallization is omitted for clarity.

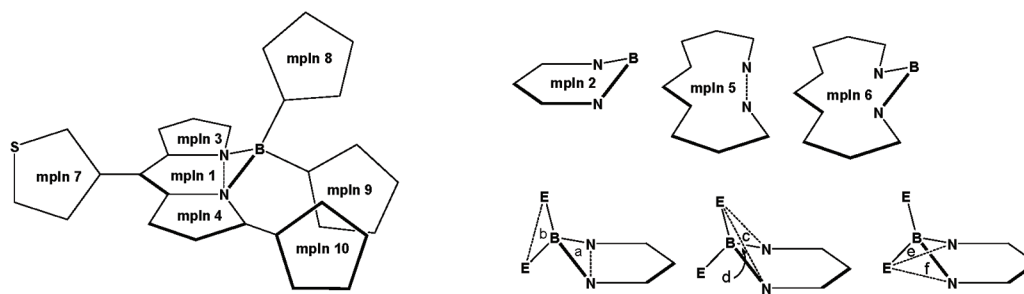
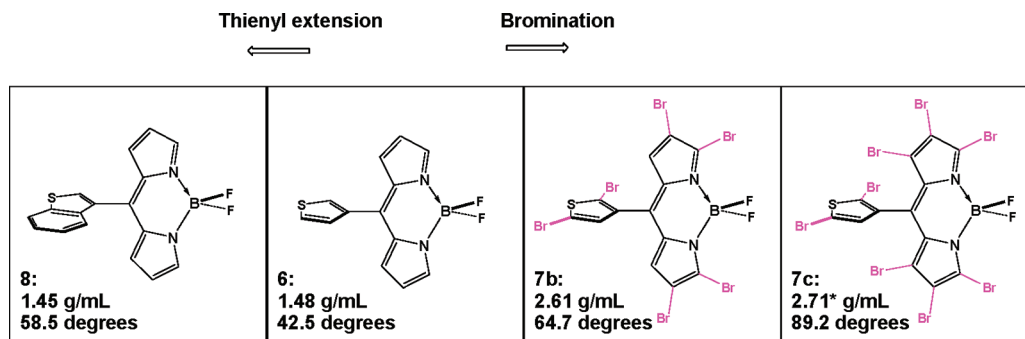


Figure 10. (top) The density and the dihedral angle between mean planes 2 and 7 for the brominated and nonbrominated derivatives **6**, **7b**, **7c**, and **8**. * = solvent of crystallization is present. (bottom) The various mean planes (mplns) for the dipyrin species. Substituents are represented as pentagons but may also be present as hexagons, that is, in the case of the triphenyl species **14** and **15**.

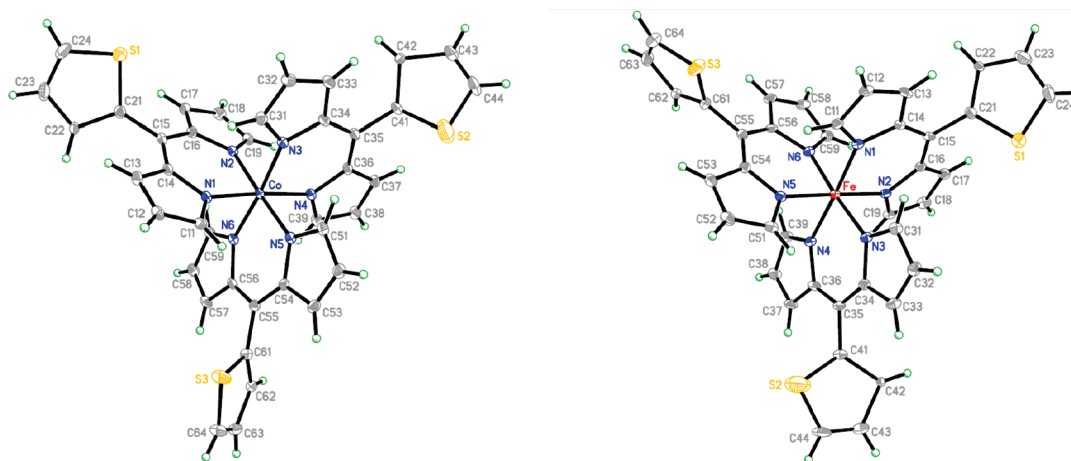


Figure 11. Molecular structures of **22** and **20**.

gives rise to mean planar (mpln 2) deviations of 0.028 Å (**8**), 0.052 Å (**6**), 0.038 Å (**7b**), and 0.036 Å (**7c**).

Next, the geometries of *tris*-5-(2-thienyl)dipyrinato) M (III) (M = cobalt, **20**; iron, **22**; Figure 11) are presented. These species are simple neutral coordination complexes involving

an octahedral M^{3+} center. As expected, they are nearly cocrystalline in the $P2_1/c$ space group with similar cell parameters. **20**: 14.6499(6) Å, 14.3707(6) Å, 16.9666(7) Å, 113.7130(10)°. **22**: 14.6785(11) Å, 14.3529(11) Å, 16.9461(12) Å, 113.556(2)°.

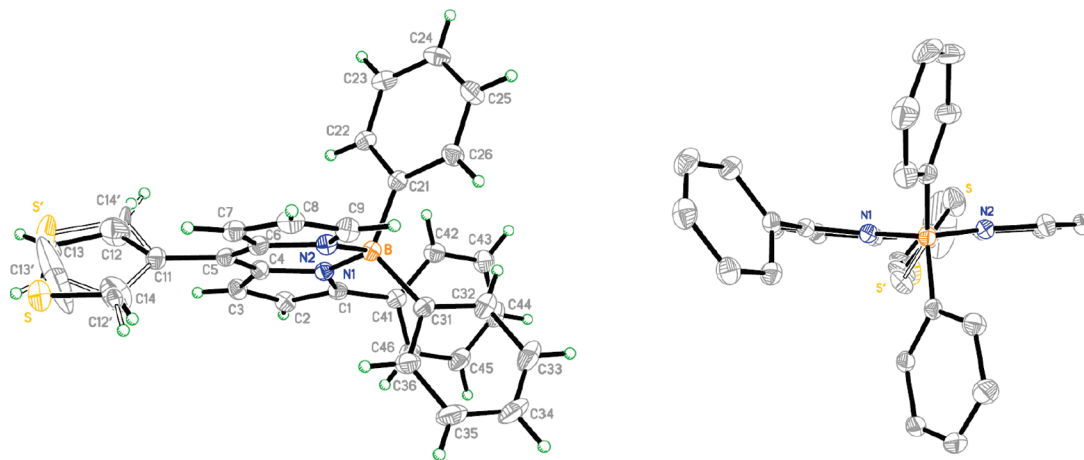


Figure 12. Front and side view of molecular structure of **15**.

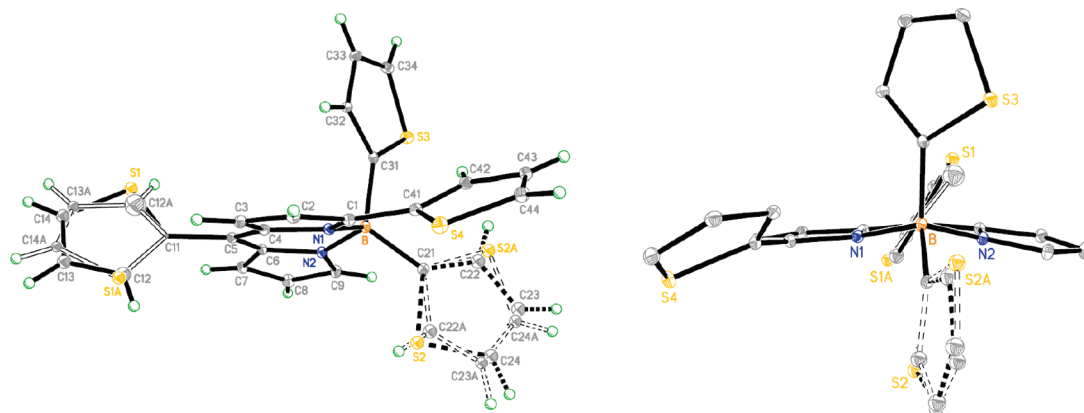


Figure 13. Front and side view of molecular structure of **9**.

Finally, we provide the structure of 3,4,4-(phenyl)-8-(3-thienyl)-4-bora-3*a*,4*a*-diaz*a*-*s*-indacene (**15**). This geometry confirms the presence of three phenyl moieties attached as expected at the 3- and 4-positions (Figure 12). We also obtained the structure of **9** (Figure 13) which allows for a better understanding of the structural imposition on the thienyl substituents by the “scorpionate”-like frame.²⁴

Conclusion

In this paper we have presented the synthesis, characterization, reactivity, and photophysical properties of various *meso*-thienyl dipyrin species. In trying to explore how selective oxidation using simple chemical inputs can lead to interesting and useful optical outputs in this submission, we have centered on the five questions listed in the caption of Figure 1. (i) A product of clean sulfur dioxide oxidation (**8a**) was achieved for compound **8** but not for other closely related systems, thought to be due in part to the rigidity of the benzothienyl group. *m*-CPBA was titrated into solutions of various related species to give various levels of oxidation as monitored by UV–vis spectroscopy. We also demonstrated that the 3,4,4-triphenyl-(thienyl)-8-4-bora-3*a*,4*a*-diaz*a*-*s*-indacene species (**14** and **15**) partially degraded in *m*-CPBA. Generally, thiophene-*S*-dioxide formation quenches fluorescence and bathochromically shifts the strong absorption band assigned to the S_0 – S_1 transition. (ii) Stepwise dipyrin bromination was observable. Elemental bromine was

used to treat 4,4-difluoro-(2,5-dibromo-3-thienyl)-8-4-bora-3*a*,4*a*-diaz*a*-*s*-indacene to afford two derivatives stepwise. The UV–vis bands in these bromine species are red-shifted and their photophysical properties were obtained. (iii, iv) *M*-dipyrins also exhibit interesting differences in which the Ni(II) species degraded significantly in *m*-CPBA, whereas that for Cu(II) is only very slightly degraded; the other two did not, regardless of whether it is a 2- or 3-thienyl substituent. In the case of Ni(II), the 8-position substituent effect is minor when changing between 2- and 3-thienyl substitution; in other words no sulfur oxidation occurred prior to Ni(II) oxidation. (v) Aryl groups devoid of heteroatoms *can* mediate metal ion recognition. Binding studies of Cu^{2+} with compounds **14**–**17** gave adequate responses; experiments involving Hg^{2+} showed minor responses. There is also a possibility to measure the exchange of Cu^{2+} with Hg^{2+} . In the future, these probe precursors might be studied in the context of fluorescent oxidative desulfurization which could be used in lieu of mass spectral or chromatographic techniques^{38,39} for direct monitoring of chemical or biological media alike.

Acknowledgment. D.G.C. acknowledges support from (i) the Korea Research Foundation Grant KRF-2005-003-C00100, funded by the Korean Government (MOEHRD, Basic Research Promotion Fund), (ii) the Korea Science and Engineering Foundation (KOSEF) grant (No. R01-2008-000-

12388-0), funded by the Korean Government (MOST), (iii) KAIST (Grant Nos. GK02100 and G10K080), (iv) the BK 21 Project, and (v) the Korea Science Academy (Pusan, South Korea) (Grants NN4880M, NC4066U). Dr. Sang Hyun Park (Rad. Appl. Research Div., KAERI, Jeongeup-si, Rep. of Korea.) helped establish additional funding (Grant NN49810). Prof. Gerard Parkin (Dept. of Chem., Columbia University) facilitated X-ray diffraction studies. K.B.K. acknowledges Prof. Charles Lake (Dept. of Chemistry, Indiana University of Pennsylvania) for coordinating the 2007 ACA Summer course (Pittsburgh, PA, U.S.A.) during which the structure of **9** was obtained. Hack Soo Shin is gratefully acknowledged for his help in acquiring NMR data. Professor Youngkyu Do (KAIST) facilitated the X-ray diffraction study of **7c**. Professor Hong-ku Shim is acknowledged for the use of his photoluminescence spectrometer. MALDI-TOF were gratefully obtained with the help of the KAIST research supporting team. Teresa Lindstead (Cam-

bridge, U.K.) is thanked for her assistance in filing crystallographic structures CCDC 684992, 684993, 684995-684997, 685000, 685001, and 688080.

Supporting Information Available: (i) All experimental data; (ii) reproductions of 1-D ¹H and ¹³C NMR spectra and 2-D COSY, NOESY, HMQC, and HMBC spectra; (iii) ¹¹B NMR spectra; (iv) UV-vis absorption and emission spectra; (v) high resolution MALDI-TOF mass spectra; (vi) details of X-ray studies. CIF files for the eight crystallographic determinations. This material is available free of charge via the Internet at <http://pubs.acs.org>. The CIF files were also deposited with the Cambridge Crystallographic Data center (CCDC), and codes CCDC 684992, 684993, 684995-684997, 685000, 685001, and 688080 were allocated. These data are available without cost at www.ccdc.cam.ac.uk/conts/retrieving.html or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, United Kingdom; fax: +44(0)1223-336033; e-mail: deposit@ccdc.cam.ac.kr.

IC801354Y