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Synthesis of a BF_2 complex of indol-2-yl-isoindol-1-ylidene-amine: a fully conjugated azadipyrromethene

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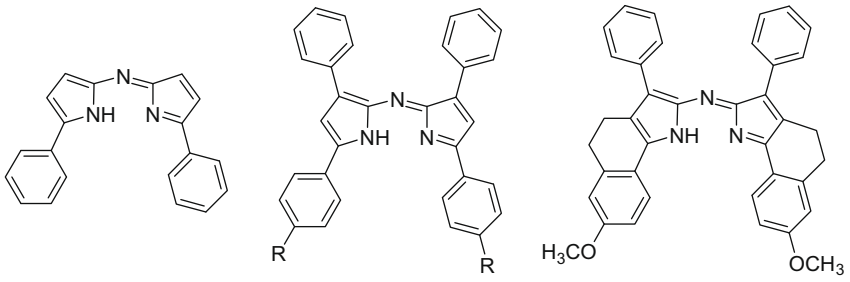
ABSTRACT

Starting from commercially available 3-methylindole and 1,3-diiminoisoindoline, the BF_2 complex of indol-2-yl-isoindol-1-ylidene-amine (**7**) has been prepared in three steps; its wavelength of maximum visible absorption is similar to that of a tetra-phenyl-conjugated azadipyrromethene (**4**).

Azadipyrromethenes are the bridged nitrogen analogues of dipyrromethenes and have longer wavelengths of maximum visible absorption. Although azadipyrromethene itself is unknown, various azadipyrromethenes with extended or expanded π-conjugation have been synthesized,[1,2] and some of their BF_2 complexes have shown potential applications in photodynamic therapy and as biological probes.[1d,f,h]

The known π-conjugation-extended azadipyrromethenes are diarylazadipyrromethenes and tetraarylazadipyrromethenes and their typical structures were shown in Figure 1. 5,5′-Diphenylazadipyrromethene (**1**) has a maximum visible absorption at 595 nm in ethanol.[1c] While the additional phenyl groups at 3 and 3′ positions in 3,3′,5,5′-tetraphenylazadipyrromethene (**2a**) slightly blue-shift the maximum visible absorption to 587 nm,[3] the electron-donating substituents on 5,5′-diphenyl groups in the BF_2 complexes of **2** give rise to a red-shift of the maximum visible absorption from 650 (R = H),[1d] 688 (R = OMe)[1d] to 799 ($R = NMe_2$)[1h] nm in chloroform. Differences were also seen in the X-ray



1

2a R = H
2b R = OCH_3
2c R = $N(CH_3)_2$

3

Figure 1. Typical structures of π-conjugation-extended azadipyrromethenes.

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crystallographic structures. As shown in Figure 2,[4] the four phenyl groups in the BF_2 complex of **2a** are not effectively conjugated with the core plane, the dihedral angles between the phenyl planes C3–C8, C12–C17, C18–C23, and C27–C32 and the core plane B1N1C9C10C11C1N2C2C26C25C24 N3 are 45.32°, 3.79°, 53.22°, and 39.93°, respectively. With dimethylamino substituents, the 5,5′-diaryl groups in the BF_2 complex of **2c** become fully coplanar with the core plane.[1h] When the 5,5′-diaryl groups have restricted conformations, the maximum visible absorption of the BF_2 complex of **3** can reach to 740 nm.[1f]

Relatively, the π-conjugation-expanded azadipyrromethenes have received less attention. Among their possible structures (Fig. 3), the BF_2 complex of di(benz[*c*,*d*]indol) azamethene (**4**) has been reported.[2b] Diisoindolazamethene (**5**) and pyrrolisoindolazamethene (**6**) are subunits of phthalocyanines, which have been suggested as photosensitizers for clinical photodynamic therapy.[5] But the known complexes of diisoindolazamethenes (**5**)[2a,d] and pyrrolisoindolazamethenes (**6**)[2c] also have extended conjugation through two phenyl substituents. Our attempts to prepare diindolazamethene (**8**) failed when 1-Boc-2-nitrosoindole was condensed with indole[6] or when 2-bromoindole[7] was reacted with sodium azide.[8] 1-Boc-2-nitrosoindole was prepared in situ by lithiation[9] of 1-Boc-indole followed by the reaction with isoamylnitrite, but its condensation product with indole, identified by mass spectroscopy, was di(indol-2-yl)amine, which could not be oxidized to the desired diindolazamethene. We describe here the design and synthesis of the BF_2 complex of (3-dipropylamino-isoindol-1-ylidene)-(3-methyl-indol-2-yl)-amine (**12**), which is an analogue of indolisoindolazamethene (**7**) (Scheme 1).

The starting materials were commercially available 3-methylindole and 1,3-diiminoisoindoline. 3-Methylindole was chlorinated at the 2-position using NCS and then nucleophilically substituted, in situ, with the amino form of 1,3-diiminoisoindoline to give (3-amino-isoindol-1-ylidene)-(3-methyl-indol-2-yl)-amine **10**.[10] This method was developed from the reaction of 2-chloroindole with aniline leading to 2-arylaminoindole.[11] Tautomers **10a–c** are the most likely structures for compound **10**. While **10a** and **10c** should exhibit three N–*H* signals in the ^1H NMR, only two such signals, with a ratio of 1:2, were observed at 11.23 and 8.68 ppm, suggesting that the amino form (**10b**) is the predominant tautomer. According to the literature,[12] 1,3-diimineisoindoline can undergo replacement of the exocylic imino group by amines along with the evolution of ammonia. In our case, when indolisoindolazamethene **10** was dissolved in dipropylamine under argon and refluxed for 10 hours, **10** was converted into (3-dipropylamino-isoindol-1-ylidene)-(3-methyl-indol-2-yl)-amine (**11**) in moderate yield. The ^1H NMR of **11** contains only one N–*H* signal at 11.75 ppm; the proton signals of dipropylamino group appear at 3.79, 2.58, and 1.93 ppm, with integrations for four, four, and six protons, respectively.[13] The desired product **12** was readily obtained by refluxing indolisoindolazamethene **11** with boron trifluoride etherate for 1 h in the presence of diisopropylethylamine under argon.[14] Complex **12** has been characterized by ^1H and ^{13}B NMR and HR-MS. The N–*H* proton signal disappears; the ^{13}B signal is a triplet due to coupling with the neighboring fluorines and appears at 1.74 ppm (referenced to $BF_3{\cdot}OEt_2$), whereas the ^{13}B signal of the BF_2 complex of **2a** appears at 0.94 ppm.[3]

As shown in Figure 4, indolisoindolazamethenes **10** and **11** exhibit maximum visible absorptions at 465 nm and 484 nm, respectively. The minor absorption peaks appearing as shoulders on the blue and red sides belong to tautomers. The BF_2 complex **12** has its maximum visible absorption at 528 nm with a half band width

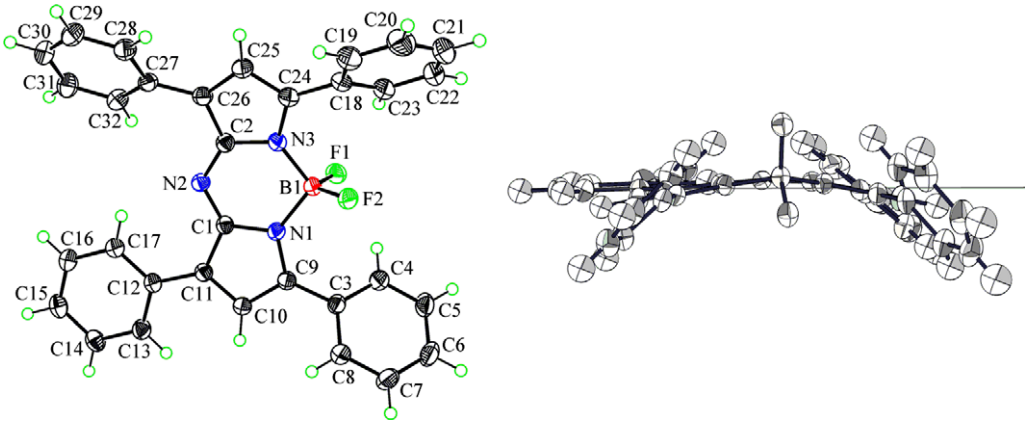


Figure 2. ORTEP view and side view of the BF_2 complex of **2a** and selected bond distances (Å) and angles (°): B1–N1: 1.561(2). B1–N3: 1.553(2). N2–C1: 1.320(2). N2–C2: 1.328(2). N1–B1–N3: 105.3(1). C1–N2–C2: 119.7(1).

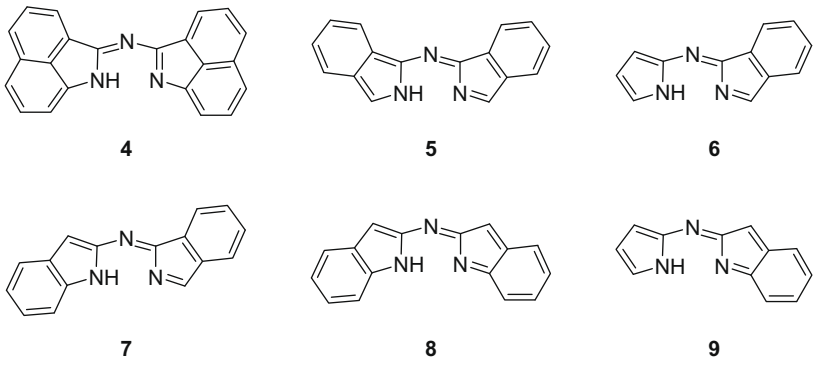
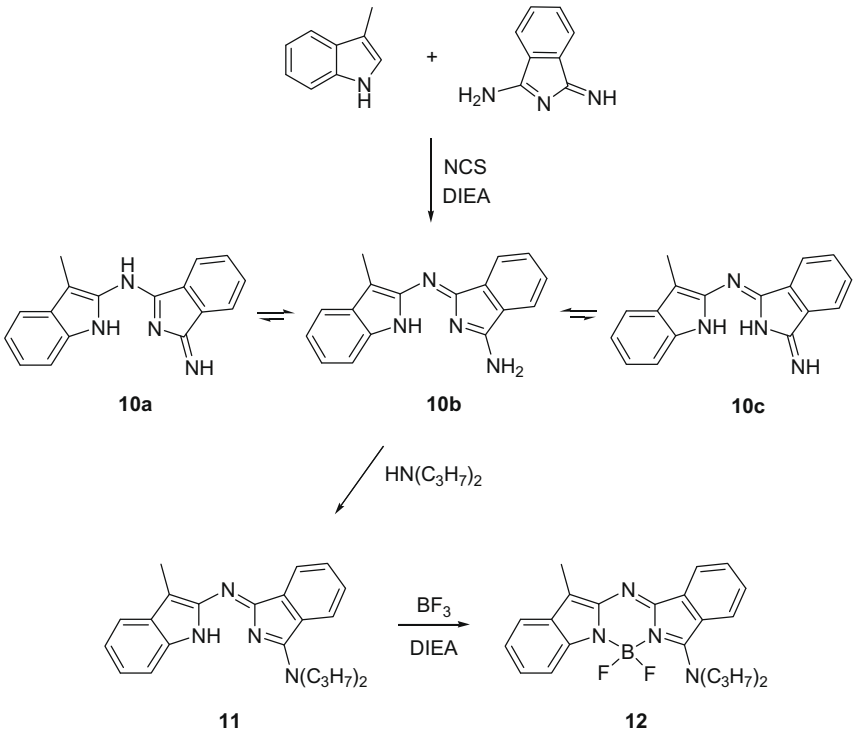


Figure 3. Some possible structures of π-conjugation-expanded azadipyrromethenes.



Scheme 1. Synthesis of indolisoindolazamethene–BF_2 complex.

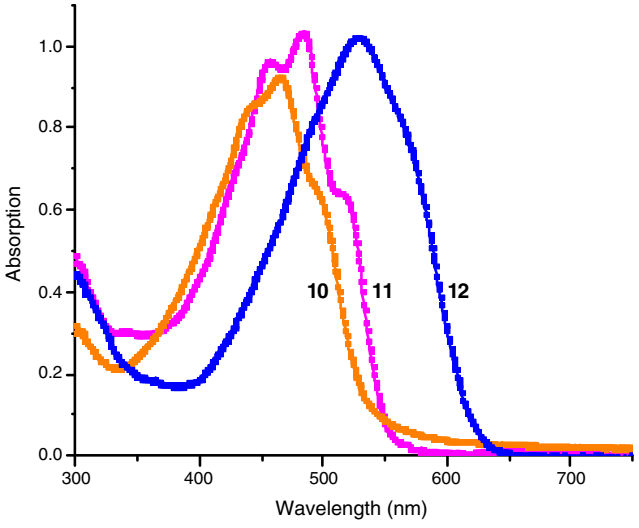


Figure 4. The UV–vis absorption spectra of **10** (—), **11** (—) and **12** (—).

of 132 nm, which is in the same wavelength range as that of tetraphenyl-conjugated azadipyrromethene (**4**), whereas the BF_2 complex of **4** has two distinct absorptions at 502 and 537 nm.[2b]

In conclusion, we report the facile synthesis and spectral characteristic of a novel BF_2 complex of indol-2-yl-isoindol-1-ylideneamine as a new π-conjugation-expanded azadipyrromethene. Further investigation into the variation of the indole ring substituents and their effect on maximum absorption as well as their photophysical properties are in progress.

Acknowledgments

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3. *3,3′,5,5′-Tetraphenylazadipyrromethene* (**2a**) and its BF_2 complex were prepared according to the literature.[1a] Diffraction-quality crystal of the BF_2 complex of **2a** was grown by the slow evaporation of solutions in dichloromethane and hexane at 5 °C.
4. *Crystal data* for the BF_2 complex of **2a** ($C_{32}H_{22}BF_2N_3$): $M = 497.34$, monoclinic, $P2_1/c$, $a = 14.0667(9)$, $b = 7.6528(4)$, $c = 23.049(1)$ Å, $\beta = 94.272(2)°$, $V = 2474.3(2)$ Å^3, $T = -100.0 \pm 0.1$ °C, $Z = 4$, $D_{calcd} = 1.335$ g/cm^3, 53028 reflections collected, 5896 unique ($R_{int} = 0.032$); $wR_2 = 0.097$, CCDC 727264.
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10. *(3-Amino-isoindol-1-ylidene)-(3-methyl-indol-2-yl)-amine* (**10b**): To a solution of 3-methylindole (2.04 mmol, 0.268 g) in dichloromethane (40 mL) were added diisopropylethylamine (2.25 mmol, 0.39 mL) and NCS (2.25 mmol, 0.300 g) under argon. The mixture was stirred at 0 °C for 2 h and then a solution of trifluoroacetic acid (0.5 mmol, 0.04 mL) and 1,3-diiminoisoindoline (3.06 mmol, 0.445 g) in dichloromethane (100 mL) was added. After stirring at room temperature overnight, the resulting mixture was evaporated under vacuum to dryness. The residue was purified by column chromatography (silica gel) eluting with a mixture of ethyl acetate and hexane (1:1) to provide

the orange product **10**. Yield: 77%. mp: 223–224 °C. Anal. Calcd for $C_{17}H_{14}N_4 \cdot 1/10CH_2Cl_2 \cdot 1/10C_6H_{14}$ (solvent of crystallization determined by NMR): C, 72.95; H, 5.40; N, 19.22. Found: C, 72.53; H, 5.01; N, 18.82. ^{1}H NMR ($CDCl_3$): δ 11.23 (s, 1H), 8.68 (b, 2H), 7.92 (d, 1H, J = 7.00), 7.83 (d, 1H, J = 7.07), 7.58–7.48 (m, 2H), 7.41 (d, 1H, J = 7.77), 7.24 (d, 1H, J = 7.99), 7.07–7.01 (dt, 1H, J = 7.16, 1.06), 6.96–6.90 (dt, 1H, J = 7.84, 0.79), 2.38 (s, 3H). ^{13}C NMR ($CDCl_3$): 168.0, 141.2, 140.6, 135.4, 132.5, 131.2, 129.8, 129.3, 128.5, 125.8, 123.5, 122.7, 119.5, 119.2, 119.0, 111.0, 8.8. UV–vis (2.50×10^{-5} M, CH_2Cl_2): λ_{max} (log ε) 440 (sh. 4.38), 464 (4.40), 494 (sh. 4.22). EI MS: m/z (%) = 273 (100) $[M]^+$, 249 (5). HR-EI MS: m/z calcd for $C_{17}H_{14}N_4$: 274.1222; found: 274.1218.

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13. *(3-Dipropylamino-isoindol-1-ylidene)-(3-methyl-indol-2-yl)-amine* (**11**): To the dipropylamine (20 mL) was added indolisoindolazamethene **10** (0.30 mmol, 0.083 g). The mixture was refluxed under argon for 10 h and then evaporated under vacuum to recycle unreacted dipropylamine. The residue was purified by column chromatography eluting with a mixture of ethyl acetate and hexane (1:10) to give product **11**. Yield: 23%. mp: 187–188 °C. ^{1}H NMR ($CDCl_3$): δ 11.75 (s, 1H), 8.10 (d, 1H, J = 7.42), 7.55 (t, 2H, J = 7.40), 7.50 (d, 1H, J = 7.40), 7.42 (t, 1H, J = 7.40), 7.17 (d, 1H, J = 7.44), 7.16 (t, 1H, J = 7.44), 7.06 (t, 1H, J = 7.44), 3.79 (t, 4H, J = 7.94), 2.58 (s, 3H), 1.97–1.88 (m, 4H), 1.15–1.07 (m, 6H). ^{13}C NMR: ($CDCl_3$): 167.2, 143.2, 141.9, 136.6, 134.7, 132.4, 130.3, 129.3, 129.0, 128.7, 123.1, 122.9, 122.6, 119.2, 118.8, 110.6, 52.4, 29.9, 21.8, 8.8. UV–vis (0.94×10^{-5} M, CH_2Cl_2): λ_{max} (log ε) 458 (4.34), 483 (4.38), 515 (sh, 4.18). EI MS: m/z (%) = 358 (100) $[M]^+$, 315 (16), 258 (14). HR-EI MS: m/z calcd for $C_{23}H_{26}N_4$: 358.2158; found: 358.2161.
14. *BF_2 complex of (3-dipropylamino-isoindol-1-ylidene)-(3-methyl-indol-2-yl)-amine* (**12**): To a solution of indolisoindolazamethene **11** (0.05 mmol, 0.018 g) in benzene (10 mL) were added diisopropylethylamine (0.20 mmol, 34 μL) and boron trifluoride diethyletherate (0.06 mmol, 6.8 μL) under argon. The resulting mixture was refluxed for 1 h and then evaporated under vacuum to dryness. The residue was purified by column chromatography eluting with a mixture of dichloromethane and hexane (1:1) to provide the desired product **12**. Yield: 59%. Mp: 204–205 °C. ^{1}H NMR ($CDCl_3$): δ 8.19 (d, 1H, J = 7.59), 7.73 (d, 1H, J = 8.17), 7.69–7.43 (m, 4H), 7.19 (dt, 1H, J = 8.15, 1.09), 7.02 (dt, 1H, J = 7.02, 0.80), 4.15 (t, 4H, J = 7.61), 2.52 (s, 3H), 1.95–1.85 (m, 4H), 1.05 (t, 6H, J = 7.22). ^{13}B NMR: δ 1.74 (t). UV–vis (4.05×10^{-5} M, CH_2Cl_2): λ_{max} (log ε) 528 (4.40). EI MS: m/z (%) = 406 (48) $[M]^+$, 358 (100), 315 (30), 258 (40). HR-EI MS: m/z calcd for $C_{23}H_{25}N_4BF_2$: 406.2140; found: 406.2153.