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Synthesis of 8-heteroatom-substituted 4,4-difluoro-4-bora-3a, 4a-diaza-*s*-indacene dyes (BODIPY)

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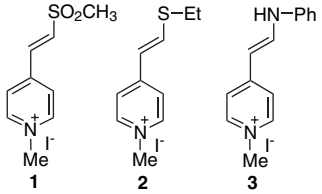
Abstract—Thioketones, bis-(5-R-1*H*-pyrrol-2-yl)-methanethiones (R=H, Me, Et), **4** react with methyl iodide or isopropyl triflate to give the pyrrolium salts, which are treated with tertiary amine and boron trifluoride to produce the 8-(thiomethyl/thioisopropyl) 4,4-difluoro-3,5-di-R-4-bora-3a,4a-diaza-*s*-indacenes **6a**–**6c** and **8a**–**8c**. The reaction of the methyl thioether group of **6a** and **6b** with aniline gives the substitution products whose structure corresponds to formula **10**. The structures of the thioethers **6a**–**6c** and compound **10a** were determined by X-ray diffraction. The thiomethyl groups in **6a**–**6c** are close to be coplanar to the flat ring system, the strain due to the interaction of methyl with the hydrogen at C1 is released by shifting of the sulfur atom away from carbon C1 and opening of the angle C8–*S*-methyl. This coplanarity of the thiomethyl group with ring system agrees with the preference of the *syn* conformation of methyl vinyl thioether. In the structures of the aniline compound **10a** the length of the nitrogen to C8 is close to that of N=C double bond. Thioethers **6a**–**6c** show high wavelength absorption at 523–530 nm and fluorescence with a Stokes shift of 12–24 nm and with a quantum yield of 0.15–0.37. In contrast the aniline substituted compounds **10a** and **10b** showed absorption at 410 and 430 nm, respectively, with no fluorescence. According to their spectral properties they are better described by structure **10** than **7**.

1. Introduction

In recent years, the search for selective and sensitive fluorescent probes for metal ions has tremendously gained an importance. The development of functional group molecules capable of performing chemically and/or physically controlled actions and reporting on or transducing these through luminescence signal has attracted considerable attention. Examples of functional supramolecular systems communicating through the luminescence include molecular scale sensors,[1] switches,[2] motors and machines,[3] wires or arrays,[4] cascades and cassettes that operate through energy or electron transfer process. Herein, we report the synthesis of sulfur containing BODIPY (4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene) compounds under mild reaction conditions in good to reasonable yield. The high wavelength absorption at 523–530 nm and the fluorescence with a Stokes shift of 12–24 nm compounds are well described. BODIPY dyes are used for their physical properties in biotechnological applications.[5]

Earlier we described a thiol reagent sulfone **1**. The reaction of this sulfone **1** with thiol gave thioether **2** whose long wavelength absorption appears on the reaction.[6] But this vinylic thioether **2** is not fluorescent. So we planned synthesis of thioether with the 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (BODIPY) group. BODIPY dyes are prepared by reaction of pyrroles with acid chlorides (or aldehydes) to the dipyrrolomethenes (or dipyrrolomethanes oxidized to former). The dipyrrolomethenes are then condensed to 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene by action of a tertiary base and boron trifluoride. A limited range of functional groups are compatible with these reaction conditions. In order to avoid further condensation, the pyrroles have to be substituted at C-2. In view of the interest of the spectral properties of this system, there is a need of preparation methods under milder reaction conditions compatible with most functional groups. We report herein such a reaction for the synthesis of sulfur containing BODIPY.



1 **2** **3**

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The reaction of thiophosgene with pyrrole and substituted pyrroles is fast and provides thioketones **4** in rather mild conditions. Even pyrrole itself gives the thioketone **4a** in a good yield.[7] The reaction is specially interesting because no further condensation products have been detected. This may be due to the reduced reactivity of the intermediate and of the thioketone **4**. We prepared the thioketones **4a**–**4c** by the reaction of thiophosgene with pyrrole, 2-methyl- and 2-ethyl-pyrrole in yields close to the published ones.[7]

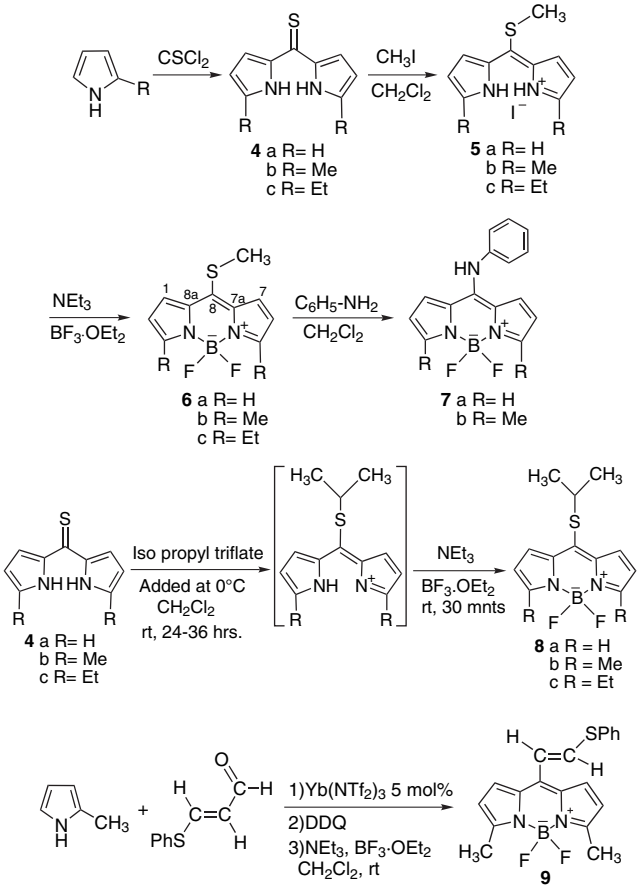
2. Results and discussion

The reaction of thioketones with electrophilic reagents tends to occur at the sulfur. With thiopyridone, for instance, one obtains the pyridinyl thioether.[8] So, we explored the reaction of the thioketones **4a**–**4c** with methyl iodide and isopropyl triflate. The reaction of thioketones **4a**–**4c** with methyl iodide gives the dipyrrolomethene probably as hydroiodides **5a**–**5c** as brown gummy solids. These compounds are not too stable and were characterized as crude products. Their purity seems to be high and they showed a high absorption in the range of 458–480 nm. Their NMR spectra indicate that they are present as single isomer or that the interconvertion of the (*E*) and (*Z*) isomers is rapid. The chemical shifts of the ring protons of pyrrolomethenes **5a**–**5c** are shifted to lower fields when compared to the pyrrolomethenes taken as base in CS_2.[9] So, we favor the presence of the pyrrolomethenes **5a**–**5c** as hydroiodides.

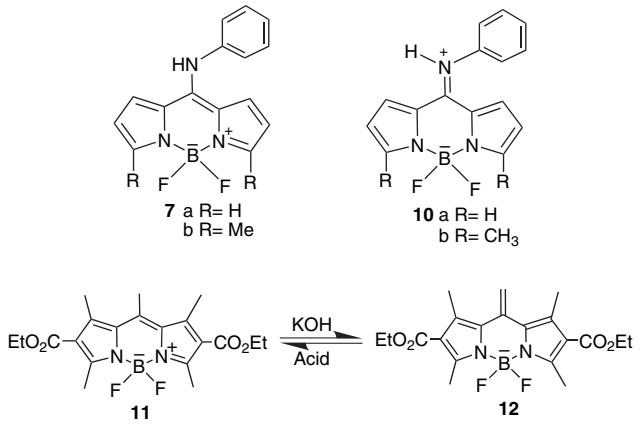
Reaction of pyrrolomethenes **5a**–**5c** with boron trifluoride etherate in presence of triethylamine gave the red colored 8-(thiomethyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacenes **6a**–**6c**. The thiomethyl group of **6a** and **6b** is displaced by aniline to give 8-(anilino) compounds, which initially we presented as **7a** and **7b**. But their spectral properties are in better agreement with structures **10a** and **10b**. In future discussion we use the structures **10a** and **10b**. The substitution reaction is similar to the one observed with *N*-methyl 4-thiomethylvinylic pyridinium salt.[10] The reaction of indacene **6c** with aniline was very slow and was not studied.

The same reaction sequence of thioketones **4a**–**4c** first with isopropyl triflate and later with boron trifluoride gave the isopropyl thioethers **8a**–**8c**. These compounds **8a**–**8c** were obtained as amorphous material and failed to crystallize in our hands.

In order to compare the spectral properties of vinylic thioether, we prepared 8-(2-thiophenylethene) 4,4-difluoro-3,5-dimethyl-4-bora-3a,4a-diaza-*s*-indacene **9** (Scheme 1). The condensation of 2-methylpyrrole with 3-(phenylthio)-propenal in presence of ytterbium (III) trifluoromethane sulfonamide in catalytic amount gave the nonisolated dipyrrolomethane, which was oxidized by DDQ to the pyrrolomethene. By reaction of boron trifluoride etherate in presence of triethylamine, the indacene **9** was obtained in low yield. But the spectral properties of the vinylic thioether **9** were not what we had expected so that we did only limited attempts in preparing compound **9** and the related ones.



Scheme 1.



3. Structure

Structures of the three indacenes **6a**–**6c** were determined by X-ray diffraction study. As the indacene **6a** (Fig. 1) crystallized with two different molecules in the asymmetric unit, we have four structures. The general features of these four structures will be presented here. The indacene atoms except the fluorine atoms are close to be in one plane. The methyl group of the thiomethyl group is close to the plane of the indacene system (torsion angle CH_3–S–C8–C7a of 0.00°; 2.21°; 2.39°; 4.48°, respectively) and in close contact with the hydrogen at C7 (C of methyl group–H (at C7) 2.50–2.53 Å) whereas the van der Waals distance for hydrogen

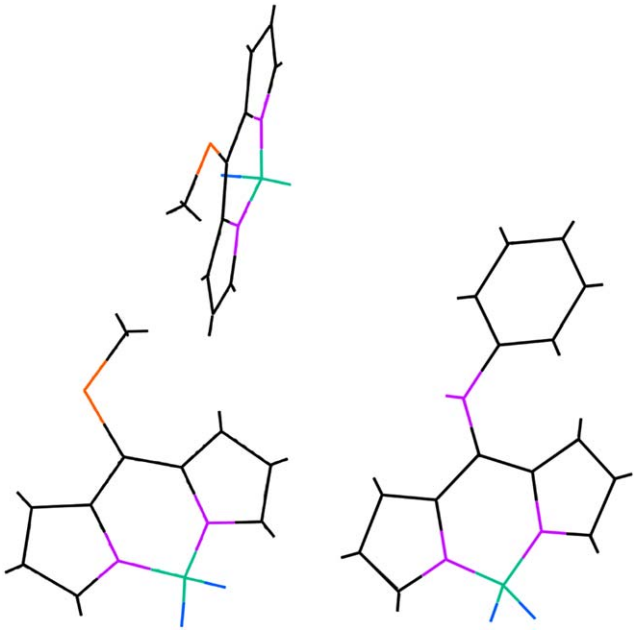


Figure 1. X-ray crystal structures of compounds **6a** (left) and **10a** (right). The carbon and hydrogen atoms are in black, the boron atoms in green, the nitrogen is magenta, and sulfur in yellow. The two molecules of compound **6a** present in the asymmetric unit are presented.

to carbon is 2.9–3.0 Å.[10] The sulfur is displaced toward carbon C1 so that the angles at C8 are in the range of 127.2–127.8° for S–C8–C7a and of 111.8–112.2° for S–C8–C8a. The distance of the sulfur to the hydrogens at C7 and C1 are in the range of 2.77–2.83 Å and 3.31–3.33 Å so that the sulfur atom is shifted by 0.25 Å. The van der Waals distance for sulfur to H is 2.91 Å.[11] The bond angles CH_3–S–C8 in **4a**–**4c** are in the range 109.89–110.22° to be compared with 104° found in thioethers. So the strain was in part released by increasing the angles C7a–C8–S and CH_3–S–C8. The length of the S–CH_3 bond is 1.77–1.78 Å compared to 1.789 Å (σ=0.008) for such bond whereas the length of the C8–S bond is 1.77 Å in the range for such bond 1.773 Å (σ=0.009).[12] In solution no hindrance of the rotation could be detected by NMR spectroscopy and this is not unexpected, since the barrier calculated for the methyl vinyl thioether is low.[13] The systems in the crystals are devoid of symmetry so that the bond distances are different. The solid state NMR of products **6a** and **6b** showed that all the carbon atoms were different in the solid.

The strain induced by the interaction of the methyl group with the hydrogen at C7 must reflect a preference of the methyl group to be coplanar with the indacene system. Indeed the experimental evidence and calculations show a preference for the *syn* conformation of methyl vinyl thioether over the next *gauche* preferred conformation by about 6.92 kJ mol^{-1}.[13] The effect of a donor–acceptor substituent on the equilibrium *gauche*–*syn* of vinylic thioethers as present in **6a**–**6c** does not seem to have been evaluated. The structure of vinylic thioethers seems to have been scarcely determined. We had prepared the vinylic thioether **2**, had determined its structure by X-ray diffraction, and found the cis conformation in the crystalline state with the torsion angle Et–S–C–C of 2.23° and the distance of the sulfur to the *syn* hydrogen of 2.62 Å.[6] The number of aromatic methyl thioether structures Ar–S–CH_3 collected in the data bank at the date of writing is about 150, if the *ortho*-disubstituted are excluded. On closer examination one finds that 47% have a torsional angle in the range of 0–5°, 67% in 0–10°, 80% in 0–15°, and 85% in 0–20°. Such abundance could reflect a preference for the *syn* conformation in solution of such thioethers.

In order to have more information about the systems studied here, we prepared the isopropyl thioethers **8a**–**8c** with the idea that the isopropyl group would be out of the indacene plane. But in our hands these thioethers failed to crystallize.

In view of the unexpected spectral data of the aniline compounds, we determine the structure of the two allotropic forms of **10a**. One contains two molecules in a different arrangement in the lattice, so we have the data for three molecules. The ring system is close to be planar except the two fluorine atoms and the phenyl group. The phenyl group makes an angle of 83°, 88°, and 56° with the plane of the ring system (Fig. 1). The noticeable feature is the short nitrogen–C8 (1.23 Å, 1.33 Å, and 1.34 Å). This bond length is close to the one found for Car-C=N–C (1.28 Å).[12]

4. Spectral properties

The absorption maximum of the thioethers **6a**, **6b** (Fig. 2), and **6c** is shifted to higher wavelength 523–530 nm (MeOH) (Table 1). Indeed related systems such as 4,4-difluoro-5,7-dimethyl-4-bora-3a,4a-diaza-*s*-indacene-3-propanol show an absorption maximum at 505 nm in ethanol.[14] So the introduction of a thioether group at C8 induces a shift of 18–25 nm to be compared to the shift 22–40 nm on going from *N*-methyl pyridinium salt to *N*-methyl 4-thiomethyl pyridinium salt.[15] The absorption maximum of 1-methyl-4-ethenylpyridinium iodide is at 265 nm (15,000)[16] and that of 1-methyl-4-[2-ethylsulfanyl-1-ethenyl]pyridinium salt **2** at 362 nm. So a shift of about 100 nm is observed by introduction of a thioether group in this system. In the crystal structure the thiovinylic group forms a torsion angle of 6.7° with the pyridinium plane so that conjugation may be

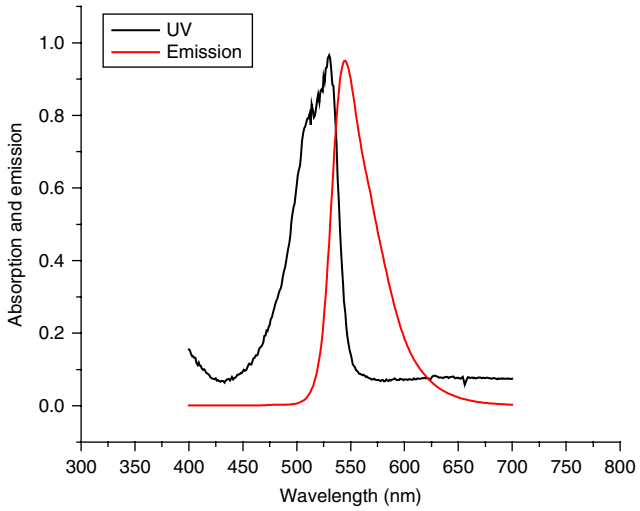


Figure 2. Absorption and fluorescence spectrum (excitation at 530 nm) of compound **6b** in methanol.

Table 1. Spectroscopic data for compounds **6a–c**, **8a–c**, **9** and **10a–b**

Compound	Absorption λ_{max} (nm)	ε (M^{-1} cm^{-1})	Emission λ_{max} (nm)	Stokes shift	Quantum yield
6a	527	40,000	539	12	0.15
6b	530	45,000	554	24	0.37
6c	523	35,000	544	21	0.27
8a	513	30,000	534		
8b	526	40,000	544		
8c	528	35,000	542		
9	528	20,000	580		
10a[a]	410	40,000			
10b[a]	430	20,000			

[a] Taken in MeOH except in CH_2Cl_2.

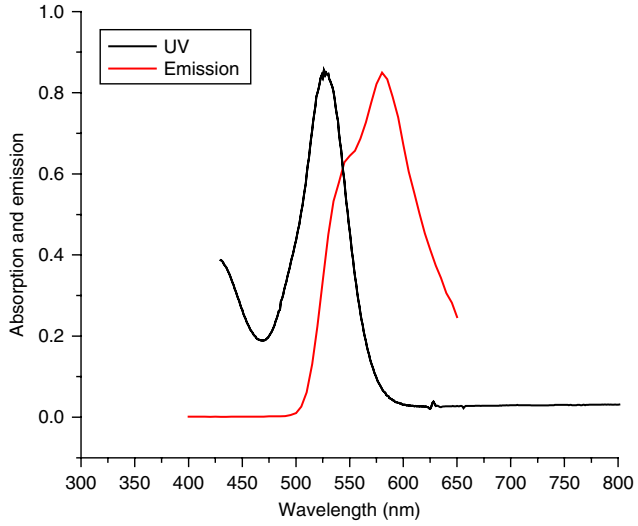


Figure 3. Absorption and fluorescence spectrum (excitation at 528 nm) of compound **9** in methanol.

achieved.[1] However, the introduction of the double bond as in **9** (Fig. 3) induces no shift, the absorption maximum is located at 528 nm in **9** compared to 523–530 nm for **6a–6c**. This can be attributed to the fact that the thiovinylic group of **9** is not coplanar with indacene plane due to the presence of the hydrogens at carbon C1 and C7. The torsion angle of the phenyl group at C8 in related indacene system (with hydrogens at C1 and C7) with the dipyrrolomethane is in the range of 51.5–87.8°.[17] So, for 8-phenyl substituted indacenes and product **9**, the conjugation between the aryl group and the thiovinylic group with the indacene system is low.[18]

In contrast the anilino substituted compounds **10a** and **10b** (Fig. 4) do not show any long wavelength absorption and any fluorescence. The analogous compound **3** shows absorption at 424 nm (ε 40,000).[10] This difference is unexpected. In the crystalline state of compound **10a**, the C8–N bond length (1.23–1.34 Å) is definitely shorter than a nitrogen bond to carbon of an aromatic ring (1.42 Å) and close to nitrogen–carbon double bond, so we propose that the structure of aniline substituted compounds is better described by structure **10** instead of structure **7**. In the NMR spectrum of these compounds one notices the upfield shift of about 1 ppm of the signals of indacene ring protons in agreement with the aromatic character of the structure **10**. The properties expected for structure **10** are close to the ones described by *Treibs* and *Kreuzer* about the compound **12** obtained by

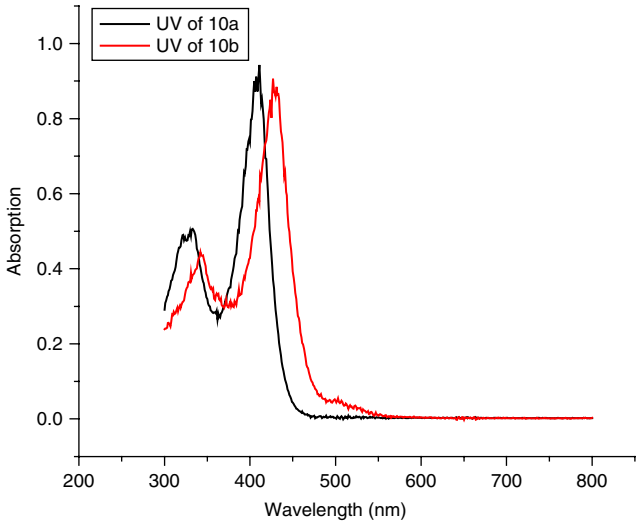


Figure 4. Absorption spectrum of compounds **10a** and **10b** in dichloromethane.

base treatment of 1,3,5,7,8-pentamethyl-2,6-carboethoxy derivative **11**. As found for the compounds **10a** and **10b**, compound **12** does not show any long wavelength absorption and fluorescence.[19] The related 3-phenyl imonomethyl indole hydrochloride has been described with an absorption maximum at 390 nm close to the maximum found for the compounds **10a** and **10b**.[20]

Compounds **6a**, **6b**, **6c**, **8a**, **8b**, **8c**, and **9** show fluorescence when excited at the wavelength of the absorption maximum. The emission spectrum of compound **9** shows an inflexion point at 550 nm.

5. Conclusion

The reaction of the electrophilic reagents occurs at the sulfur atom under mild conditions. This should allow the introduction of more functionalized groups. The vinylic thiother **9** does not show the spectral properties for a reporting group, so the preparation of the corresponding activated vinylic group was not undertaken. Also the thioethers directly attached to the ring as in **6** show some interesting properties, but we did not succeed in preparing any activated derivative, which would give rise to the thioethers **6** by substitution reaction.

6. Experimental

6.1. General procedure

All the reactions were carried out under an atmosphere of nitrogen. Melting points (mp) were taken on capillary tube apparatus and are uncorrected. UV and the fluorescent spectra were recorded in MeOH solution unless otherwise stated. The quantum yield was determined as in Ref. 21. FTIR spectra were recorded in CH_2Cl_2 solution. ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solution, chemical shifts were reported using TMS (0 ppm) and $CDCl_3$ (77.0 ppm) as internal standards. Purification by column chromatography was carried out with neutral silica gel 60

(70–230). MS spectra were determined on VG 70-250S spectrometer. HRMS spectra were collected on Autospec orthogonal acceleration-time of flight mass spectrometer with a resolution of 6000 (5%).

Caution: handling thiophosgene requires a fume hood and container has to be kept tightly closed for storage. Thiophosgene is highly toxic.

6.1.1. Bis-(5-methyl-1*H*-pyrrol-2-yl)-methanethione (4b). A solution of 2-methylpyrrole (0.81 g)[22] in dry ether (15 ml) was added dropwise to a vigorously stirred solution of thiophosgene (0.55 g) in dry toluene (13 ml) at 0 °C. After 10 min, aqueous methanol (10%) (12 ml) was added and the mixture stirred for further 30 min at room temperature (rt). The solvents were removed in vacuo and the residue, dissolved in toluene/chloroform (9:1), was chromatographed on neutral alumina. The pure compound fraction was collected, which, after removal of the solvents in vacuo, yielded the thioketone **4b** as a crystalline orange red solid (0.64 g; 65%), mp 106–108 °C. λ_{max}: 419 nm (ε 50,000), 293 (ε 3200). IR (CH_2Cl_2): 3405, 3360, 1280. ^{1}H NMR ($CDCl_3$): δ 2.78 (s, 6H), 6.10 (2H, d, J=6.0 Hz), 6.90 (2H, d, J=6.0 Hz), 9.58 (1H, br s). ^{13}C NMR ($CDCl_3$): δ 14.0 (CH_3), 111.7 (CH), 115.8 (CH), 137.4 (C), 139.5 (C), 187.2 (C). Mass spectrum (EI): m/z 204 (M^+); Anal. Calcd for $C_{11}H_{12}N_2S$: C, 64.67; H, 5.92; N, 13.71. Found: C, 64.62; H, 5.88; N, 13.67.

6.1.2. Bis-(5-ethyl-1*H*-pyrrol-2-yl)-methanethione (4c). A solution of 2-ethylpyrrole (0.81 g)[22] in dry ether (15 ml) was added dropwise to a vigorously stirred solution of thiophosgene (0.486 g) in dry toluene (10 ml) at 0 °C. After 10 min, aqueous methanol (10%) (12 ml) was added and the mixture stirred for further 30 min at rt. The solvents were removed in vacuo and the residue, dissolved in toluene/chloroform (9:1), was chromatographed on neutral alumina. The pure compound fraction was collected, which, after removal of the solvents in vacuo, yielded the thioketone **4c** as a crystalline orange red solid (0.62 g; 63%), mp 110–111 °C. λ_{max}: 416 nm (ε 50,000), 295 (ε 3100). IR (CH_2Cl_2): 3400, 3362, 1280. ^{1}H NMR ($CDCl_3$): δ 1.29 (6H, t, J=7.2 Hz), 2.66 (4H, q, J=7.2 Hz), 6.12–6.14 (m, 2H), 6.91–6.93 (m, 2H), 9.59 (1H, br s). ^{13}C NMR ($CDCl_3$): δ 12.8 (CH_3), 21.1 (CH_2), 110.1 (CH), 115.7 (CH), 137.0 (C), 145.4 (C), 188.4 (C). Mass spectrum (EI): m/z 232 (M^+); Anal. Calcd for $C_{13}H_{16}N_2S$: C, 67.20; H, 6.94; N, 12.06. Found: C, 67.15; H, 6.90; N, 12.02.

6.1.3. 2-[Methyl sulfanyl-(1*H*-pyrrol-2-yl)-methylene]-2*H*-pyrrolium iodide (5a). To a solution of compound bis-(1*H*-pyrrol-2-yl)-methanethione **4a** (0.30 g) (**1b**) in anhydrous dichloromethane (5 ml) was added methyl iodide (0.48 ml) at rt. The reaction mixture was stirred for 24 h for completion (TLC monitoring). Solvent was removed under reduced pressure to obtain brown colored gummy solid. The compound **5a** was used without further purification for the next reaction. ^{1}H NMR ($CDCl_3$): δ 2.89 (s, 3H), 6.63–6.64 (m, 2H), 7.23–7.24 (m, 2H), 7.87–7.88 (m, 2H), 12.0 (br s). ^{13}C NMR ($CDCl_3$): δ 21.5 (CH_3), 116.7 (CH), 128.6 (CH), 129.3 (CH), 138.4 (C), 162.2 (C). Mass spectrum (EI): m/z 190 (M^+); HRMS calcd for $C_{10}H_{11}N_2S$ 191.0637, found 191.0640.

6.1.4. 5-Methyl-2-[(5-methyl-1*H*-pyrrol-2-yl)-methylsulfanyl-methylene]-2*H*-pyrrolium iodide (5b). To a solution of compound bis-(5-methyl-1*H*-pyrrol-2-yl)-methanethione **4b** (0.30 g) in anhydrous dichloromethane (5 ml) was added methyl iodide (0.41 ml) at rt. The reaction mixture was stirred for 24 h for completion (TLC monitoring). Solvent was removed under reduced pressure to obtain brown colored gummy solid. The obtained compound **5b** is directly used for the next reaction. ^{1}H NMR ($CDCl_3$): δ 2.60 (s, 6H), 2.76 (s, 3H), 6.35 (2H, d, J=8.0 Hz), 7.02 (2H, d, J=8.0 Hz), 11.6 (br s). ^{13}C NMR ($CDCl_3$): δ 14.8 (CH_3), 21.9 (CH_3), 118.1 (CH), 129.4 (CH), 129.8 (C), 152.6 (C), 156.3 (C). Mass spectrum (EI): m/z 218 (M^+); HRMS calcd for $C_{12}H_{15}N_2S$ 219.0951, found 219.0956.

6.1.5. 5-Ethyl-2-[(5-ethyl-1*H*-pyrrol-2-yl)-methylsulfanyl-methylene]-2*H*-pyrrolium iodide (5c). To a solution of compound **4c** (0.30 g) in anhydrous dichloromethane (5 ml) was added methyl iodide (0.36 ml) at rt. The reaction mixture was stirred for 24 h for completion (TLC monitoring). Solvent was removed under reduced pressure to obtain brown colored gummy solid. The obtained compound **5c** is directly used for the next reaction. ^{1}H NMR ($CDCl_3$): δ 1.21(6H, t, J=7.0 Hz), 2.72 (4H, q, J=7.0 Hz), 2.93 (s, 3H), 6.34–6.35 (m), 6.93–6.94 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 12.8 (CH_3), 21.6 (CH_3), 116.0 (CH), 129.2 (CH), 129.7 (C), 156.7 (C), 158.1 (C). Mass spectrum (EI): m/z 247 (M^+); HRMS calcd for $C_{14}H_{19}N_2S$ 247.1268, found 247.1262.

6.1.6. 8-(Thiomethyl)4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (6a). To a solution of compound **5a** (0.30 g) in anhydrous dichloromethane (7 ml) under nitrogen atmosphere at rt was added triethylamine (0.22 ml). After stirring for 30 min $BF_3\cdot OEt_2$ (0.18 ml) was added. The mixture was stirred for 30 min at rt. After the evaporation of solvents under vacuum, the crude product was chromatographed on silica gel (70–230 mesh, using 15% EtOAc in hexane), yielded compound **6a** as a dark red solid (0.21 g; 60%), mp 88–90 °C. λ_{max}: 527 nm (ε 40,000). IR (CH_2Cl_2): 1489, 1264 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.88 (s, 3H), 6.50–6.51 (m, 2H), 7.39–7.40 (m, 2H), 7.77–7.78 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 20.0 (CH_3), 117.6 (CH), 127.3 (CH), 133.4 (C), 140.8 (C), 154.0 (C). ^{19}F (CCl_3F in $CDCl_3$): δ −145.6, −145.7, −145.8, −145.9. Mass spectrum (EI): m/z 238 (M^+); Anal. Calcd for $C_{10}H_9BF_2N_2S$: C, 50.45; H, 3.81; N, 11.77. Found: C, 50.38; H, 3.78; N, 11.67.

6.1.7. 8-(Thiomethyl) 4,4-difluoro-3,5-dimethyl-4-bora-3a,4a-diaza-*s*-indacene (6b). To a solution of compound **5b** (0.30 g) in anhydrous dichloromethane (7 ml) under nitrogen atmosphere at rt was added triethylamine (0.19 ml). After stirring for 30 min $BF_3\cdot OEt_2$ (0.16 ml) was added. The mixture was stirred for 30 min at rt. After the evaporation of solvents under vacuum, the crude product was chromatographed on silica gel (70–230 mesh, using 15% EtOAc in hexane), yielded compound **6b** as a dark red solid (0.23 g; 63%), mp 96–97 °C. λ_{max}: 515 (inflexion), 530 nm (ε 45,000). IR (CH_2Cl_2): 1558, 1264 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.57 (s, 6H), 2.68 (s, 3H), 6.24 (2H, d, J=5.2 Hz), 7.26 (2H, d, J=5.2 Hz). ^{13}C NMR ($CDCl_3$): δ 14.8 (CH_3), 21.5 (CH_3), 119.1 (CH), 128.2 (CH), 135.3 (C), 144.2 (C), 156.8 (C). Mass spectrum (EI): m/z 266 (M^+); Anal. Calcd for

$C_{12}H_{13}BF_2N_2S$: C, 54.16; H, 4.92; N, 10.53. Found: C, 54.10; H, 4.87; N, 10.50.

6.1.8. 8-(Thiomethyl) 4,4-difluoro-3,5-diethyl-4-bora-3a,4a-diaza-*s*-indacene (6c). To a solution of compound **5c** (0.30 g) in anhydrous dichloromethane (7 ml) under nitrogen atmosphere at rt was added triethylamine (0.17 ml). After stirring for 30 min $BF_3 \cdot OEt_2$ (0.14 ml) was added. The mixture was stirred for 30 min at rt. After the evaporation of solvents under vacuum, the crude product was chromatographed on silica gel (70–230 mesh, using 15% EtOAc in hexane), yielded compound **6c** as a dark red solid (0.21 g; 58%), mp 96–98 °C. λ_{max} (CH_2Cl_2): 523 nm (ε 35,000), 378 (ε 17,000). IR (CH_2Cl_2): 1546, 1262 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.31 (6H, t, J=6.2 Hz), 2.66 (s, 3H), 3.02 (4H, q, J=6.2 Hz), 6.32 (2H, d, J=3.2 Hz), 7.30 (2H, d, J=3.2 Hz). ^{13}C NMR ($CDCl_3$): δ 12.6 (CH_3), 21.5 (CH_3), 21.9 (CH_2), 117.0 (CH), 128.2 (CH), 135.0 (C), 144.5 (C), 162.7 (C). Mass spectrum (EI): m/z 294.16 (M^+); Anal. Calcd for $C_{14}H_{17}BF_2N_2S$: C, 57.16; H, 5.82; N, 9.52. Found: C, 57.10; H, 5.78; N, 9.47.

6.1.9. 8-(Thioisopropyl) 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (8a). To a dried 50 ml round-bottom flask was added compound **4a** (0.250 g) in anhydrous dichloromethane (10 ml) under nitrogen atmosphere at 0 °C and then isopropyl triflate (0.545 ml)[23] was added and the reaction mixture was stirred for 12–16 h at rt. To the reaction mixture triethylamine (0.161 ml, 1.14 mmol) was added. After stirring for 30 min $BF_3 \cdot OEt_2$ (0.13 ml) was added and the reaction mixture was stirred for another 30 min at rt. Solvents were evaporated in vacuo, the above crude product was chromatographed on silica gel (70–230 mesh, using 15% EtOAc in hexane), yielded compound **8a** (0.10 g: 34%) as a dark red gum. λ_{max}: 513 nm (ε 30,000), 388 (ε 3000). IR (CH_2Cl_2): 2932, 1552, 1264 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.37 (6H, d, J=6.8 Hz), 3.80–3.82 (sept, 1H), 6.49–6.50 (m, 2H), 7.44–7.45 (m, 2H), 7.81 (2H, d, J=2.0 Hz). ^{13}C NMR ($CDCl_3$): δ 23.7 (CH_3), 44.1 (CH), 118.2 (CH), 129.5 (CH), 137.0 (C), 143.3 (CH), 148.4 (C). Mass spectrum (EI): m/z 266 (M^+); HRMS calcd for $C_{12}H_{13}BF_2N_2S$ 266.0861, found 266.0864.

6.1.10. 8-(Thioisopropyl) 4,4-difluoro-3,5-dimethyl-4-bora-3a,4a-diaza-*s*-indacene (8b). To a dried 50 ml round-bottom flask was added compound **4b** (0.20 g) in anhydrous dichloromethane (10 ml) under nitrogen atmosphere at 0 °C and then isopropyl triflate (0.38 ml) was added and the reaction mixture was stirred for 12–16 h at rt. To the reaction mixture triethylamine (0.114 ml) was added. After stirring for 30 min $BF_3 \cdot OEt_2$ (0.95 ml) was added and the reaction mixture was stirred for another 30 min at rt. Solvents were evaporated in vacuo, the above crude product was chromatographed on silica gel (70–230 mesh, using 15% EtOAc in hexane), yielded compound **8b** (0.09 g: 38%) as a dark red gummy liquid. λ_{max}: 526 nm (ε 40,000). IR (CH_2Cl_2): 2937, 1550, 1270 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.29 (6H, d, J=6.8 Hz), 2.58 (s, 6H), 3.53–3.55 (sept, 1H), 6.24 (2H, d, J=4.0 Hz), 7.30 (2H, d, J=4.0 Hz). ^{13}C NMR ($CDCl_3$): δ 14.9 (CH_3), 23.7 (CH_3), 44.1 (CH), 119.4 (CH), 129.5 (CH), 137.9 (C), 151.0 (C), 158.0 (C). Mass spectrum (EI): m/z 294 (M^+); Anal. Calcd for $C_{14}H_{17}BF_2N_2S$: C, 57.16; H, 5.82; N, 9.52. Found: C, 57.10; H, 5.78; N, 9.47.

6.1.11. 8-(Thioisopropyl) 4,4-difluoro-3,5-diethyl-4-bora-3a,4a-diaza-*s*-indacene (8c). To a dried 50 ml round-bottom flask was added compound **4c** (0.20 g) in anhydrous dichloromethane (10 ml) under nitrogen atmosphere at 0 °C and then isopropyl triflate (0.33 ml) was added and the reaction mixture was stirred for 12–16 h at rt. To the reaction mixture triethylamine (0.102 ml) was added, after stirring for 30 min $BF_3 \cdot OEt_2$ (0.086 ml) was added and the reaction mixture was stirred for another 30 min at rt. Solvents were evaporated in vacuo, the above crude product was chromatographed on silica gel (70–230 mesh, using 15% EtOAc in hexane), yielded compound **8c** (0.085 g: 36%) as a dark red gummy liquid. λ_{max} 528 nm (ε 35,000). IR (CH_2Cl_2): 2937, 1548, 1266 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.28 (6H, d, J=6.8 Hz), 1.30 (6H, t, J=6.0 Hz), 3.01 (4H, q, J=6.0 Hz), 3.53–3.55 (sept, 1H), 6.32 (2H, d, J=4.4 Hz), 7.33 (2H, d, J=4.4 Hz). ^{13}C NMR ($CDCl_3$): δ 12.6 (CH_3), 22.0 (CH_2), 23.7 (CH_3), 44.2 (CH), 117.2 (CH), 129.6 (CH), 137.6 (C), 140.1 (C), 164.0 (C). Mass spectrum (EI): m/z 322 (M^+); HRMS calcd for $C_{16}H_{21}BF_2N_2S$ 322.1487, found 322.1489.

6.1.12. 8-(2-Thiophenylethene) 4,4-difluoro-3,5-dimethyl-4-bora-3a,4a-diaza-*s*-indacene (9). To a solution of 2-methylpyrrole (162 mg) and 3-(phenylthio) propenal (164 mg)[24] in N_2-flushed dichloromethane (20 ml) was added ytterbium (III) trifluoromethane sulfonimide (50 mg) at once at rt. After 20 min TLC (silica–hexane/ethylacetate 9:1) showed that the propenal had been consumed. Then DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) (0.25 g) was added at once and the reaction mixture was stirred at rt under nitrogen atmosphere. After stirring for 10 min, triethylamine (1 ml) and $BF_3 \cdot OEt_2$ (1.6 ml) were added and the mixture was stirred at rt for further 30 min. After evaporation of the solvent, the crude product was chromatographed on silica gel (70–230 mesh, 10% EtOAc in hexane) to give compound **9** (7 mg) as red gummy solid. λ_{max}: 528 nm (ε 20,000). ^1H NMR ($CDCl_3$): δ 2.58 (s, 6H), 6.22 (2H, d, J=4 Hz), 6.64 (1H, d, J=15 Hz), 6.98 (2H, d, J=4 Hz), 7.35–7.49 (m, 6H). ^{13}C NMR ($CDCl_3$): δ 14.9 (CH_3), 118.7 (CH), 120.0 (CH), 127.0 (CH), 128.9 (CH), 129.8 (CH), 131.0 (C), 132.0 (CH), 132.9 (C), 137.6 (C), 142.1 (CH), 156.3 (C); ^{19}F (CCl_3F in $CDCl_3$): δ −147.9, −148.0, −148.1, −148.2. FABMS (*m*-NBA) m/z 354.0 $(M)^+$; HRMS calcd for $C_{19}H_{17}BF_2N_2S$ 354.1174, found 354.1179.

6.1.13. Compound 10a. To a dried 50 ml round-bottom flask was added compound **6a** (0.20 g) in anhydrous dichloromethane (5 ml) under nitrogen atmosphere at rt and then aniline (0.078 ml) was added. The reaction mixture was stirred for 12 h at rt. Solvent was evaporated in vacuo, the crude product was chromatographed on silica gel (70–230 mesh, using 20% EtOAc in hexane), yielded compound **10a** as a light red crystals from hexane/chloroform (0.130 g; 55%). Two allotropic forms were obtained: the first from hexane/chloroform and the second from chloroform: mp 191–193 °C; 199–201 °C. λ_{max} (CH_2Cl_2): 410 nm (ε 40,000), 332 (ε 21,000). IR (CH_2Cl_2): 3300, 1699, 1272 cm^{-1}. ^1H NMR ($CDCl_3$): δ 6.25 (2H, t, J=2.0, 1.6 Hz), 6.31 (2H, d, J=1.6 Hz), 7.27 (2H, d, J=2.0 Hz), 7.46–7.47 (m, 5H), 8.33 (br s). ^{13}C NMR ($CDCl_3$): δ 114.3 (CH), 120.5 (C), 123.9 (C), 126.4 (CH), 129.0 (CH), 130.0 (CH), 134.2 (CH), 137.4 (C), 147.7 (C). ^{19}F (CCl_3F in

$CDCl_3$): δ −144.8, −144.9, −145.0, −145.1. Mass spectrum (EI): *m/z* 283 (M^+); Anal. Calcd for $C_{15}H_{12}BF_2N_3$: C, 63.64; H, 4.27; N, 14.84. Found: C, 63.60; H, 4.20; N, 14.80.

6.1.14. Compound 10b. To a dried 50 ml round-bottom flask was added compound **6b** (0.20 g) in anhydrous dichloromethane (5 ml) under nitrogen atmosphere at rt and then aniline (0.07 ml) was added. The reaction mixture was stirred for further 12 h at rt. Solvent was evaporated in vacuo, the crude product was chromatographed on silica gel (70–230 mesh, using 20% EtOAc in hexane), yielded compound **10b** as a light yellow solid (0.04 g: 20%), mp 198–200 °C. λ_{max}(CH_2Cl_2): 430 nm (ε 20,000), 343 (ε 13,000). IR (CH_2Cl_2): 3310, 1692, 1270 cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.54 (s, 6H), 6.03 (2H, d, *J*=4.0 Hz), 6.40 (2H, d, *J*=4.0 Hz), 7.24 (s, 1H), 7.36 (2H, d, *J*=6.0 Hz), 7.45 (2H, d, *J*=6.0 Hz). ^{13}C NMR ($CDCl_3$): δ 14.2 (CH_3), 115.4 (CH), 120.3 (CH), 123.8 (C), 126.8 (CH), 128.7 (CH), 130.2 (CH), 138.5 (C), 149.0 (C). Mass spectrum (EI): *m/z* 311 (M^+); HRMS calcd for $C_{17}H_{16}BF_2N_3$ 311.1400, found 311.1388.

7. Crystal structure determination

Diffraction measurements were made on an Enraf-Nonius CAD-4 diffractometer by use of graphite-monochromatized Mo Kα radiation (λ=0.7107 Å). Unit cell parameters were obtained by least-squares fit to the automatically centered settings for 25 reflections. Intensity data were collected by use of ω–2θ scan mode. All intensity data were collected for Lorentz polarization and absorption (empirical ψ corrections).

7.1. Crystal data

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC 289285–289289.

7.1.1. 8-(Thiomethyl) 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 6a (CCDC 289286). $C_{10}H_9BF_2N_2S$, *M*=238.06 triclinic space group *P*-1, *a*=8.0683(14), *b*=9.0846(14), *c*=14.517(5) Å, α=98.89(2)°, β=92.70(2)°, γ=95.868(13)°, *V*=1043.6(4) $Å^3$, *T*=298(2) K, *Z*=4, μ (Mo Kα)=0.307 mm^{-1}, 3676 reflections measured (*R*(int)=0.0214), which were used in all calculations. The final $wR(F^2)$ was 1.010.

7.1.2. 8-(Thiomethyl) 4,4-difluoro-3,5-dimethyl-4-bora-3a,4a-diaza-*s*-indacene 6b (CCDC 289285). $C_{12}H_{13}BF_2N_2S$, *M*=266.11 orthorhombic space group *Pnma*, *a*=15.994(3), *b*=7.053(4), *c*=10.856(3) Å, *V*=1224.6(9) $Å^3$, *T*=298(2) K, *Z*=4, μ(Mo Kα)=0.270 mm^{-1}, 1168 reflections measured (*R*(int)=0.0000), which were used in all calculations. The final $wR(F^2)$ was 1.041.

7.1.3. 8-(Thiomethyl) 4,4-difluoro-3,5-diethyl-4-bora-3a,4a-diaza-*s*-indacene 6c (CCDC 289287). $C_{14}H_{17}BF_2N_2S$, *M*=294.17 monoclinic space group *P*2(1)/*c*, *a*=7.4558(3), *b*=18.5780(5), *c*=10.6193(3) Å, α=90°, β=108.188(2)°, γ=90°, *V*=1397.43(8) $Å^3$, *T*=293(2) K, *Z*=4, μ (Mo Kα)=0.244 mm^{-1}, 2455 reflections measured (*R*(int)=0.0305), which were used in all calculations. The final $wR(F^2)$ was 1.048.

7.1.4. Compound 10a (CCDC 289288–289289). $C_{15}H_{12}BF_2N_3$, *M*=283.09

- Triclinic space group *P*-1, *a*=9.7381(2), *b*=11.7125(2), *c*=12.1698(3) Å, α=97.0980(10)°, β=105.3670(10)°, γ=96.0900(10)°, *V*=1314.12 $Å^3$, *T*=100(1) K, *Z*=4, μ (Mo Kα)=0.106 mm^{-1}, 4634 reflections measured (*R*(int)=0.0176), which were used in all calculations. The final $wR(F^2)$ was 1.051.
- Triclinic space group *P*-1, *a*=7.3696(3), *b*=9.6925(3), *c*=9.9641(4) Å, α=109.2870(10)°, β=101.8620(10)°, γ=100.4640°, *V*=633.00(4) $Å^3$, *T*=100(1) K, *Z*=2, μ (Mo Kα)=0.110 mm^{-1}, 2222 reflections measured (*R*(int)=0.0194), which were used in all calculations. The final $wR(F^2)$ was 1.040.

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