Organic & Biomolecular Chemistry

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View Journal

3,5-Bis(acetaldehyde) substituted BODIPY†

Cite this: DOI: 10.1039/c2ob27004h

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Received 15th October 2012,
Accepted 13th November 2012

DOI: 10.1039/c2ob27004h

www.rsc.org/obc

Two versions of a facile and efficient synthetic approach to 3,5-bis(acetaldehyde) substituted BODIPY have been developed and this compound has been used to obtain, in high yields, a variety of 3,5-divinyl BODIPY derivatives (vinylacetates, enamines, vinyl chlorides, and some multiple-functionalized products). As shown, vinyl substituents have an additive effect on the position of the BODIPY absorption maximum. The dyes synthesized are quite stable and exhibit intense absorption and fluorescence with wavelengths longer than 600 nm.

Introduction

Boron-dipyrromethene dyes (4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene, BODIPY, BDP) have found numerous applications, especially in biochemistry and molecular biology, owing to their excellent thermal, chemical and photochemical stability, high molar absorptivity, high fluorescence quantum yield, and low sensitivity to both solvent polarity and pH.[1] For the dyes to be used as fluorescent indicators for pH, metal ions, anions, or biomolecules, they need to be appropriately functionalized (with the carboxyl, amino, azido groups, *etc.*).[2] Since functionalization presents one of the main challenges in the boron-dipyrromethene chemistry, the methods have been developed to substitute the nucleus concerned at all possible positions. Substituted BODIPYs can be obtained from correspondingly functionalized pyrrole precursors as well as by functionalizing intermediate dipyrromethanes or directly the BODIPY nucleus.

Electrophilic substitution reactions such as nitration,[3] sulfonation,[3,4] formylation,[5] or palladium-catalyzed C–H functionalization[6] are known to proceed at positions 2 and 6 (β-positions) of the BODIPY core (Fig. 1). Halogenation occurs first at the same positions,[3,7] but can further involve other unsubstituted carbon atoms as well.[8] Halogen atoms at positions 3 or 5 (α-positions)[9] and at 1 or 7[10] of the BODIPY nucleus can be nucleophilically substituted. The methylthio group at *meso*-position is likewise substitutable.[11] Alkylthio-substituted BODIPYs also enter into the Liebeskind–Srogl cross-coupling,[12] whereas their halogen-containing analogues undergo palladium-catalyzed reactions like Suzuki, Heck, or Sonogashira.[13] With free α-positions, oxidative[14a,b] or vicarious nucleophilic substitution of hydrogen[14c] can occur.

α-Methyl groups on the BODIPY ring appear especially promising in the context of chemical modification, first of all because they readily enter into the Knoevenagel condensation.[15] Therefore, this method was employed to obtain a great variety of derivatives including combinatorial series.[15f] Very importantly, the Knoevenagel condensation leads not only to the structural variations of the parent BODIPY system but also to a significant red shift both in absorption and emission of the reaction products. Methyl groups at the 1-, 7-,[16] and *meso*-positions[17] can be reacted likewise affording nontrivial structures with specific spectral properties. Further, the α-methyl can be oxidized to an aldehyde group[18] or brominated followed by nucleophilic substitution.[19]

We have recently found another use of the α-methyl group in BODIPY functionalization: it produces a formylmethyl group in the reaction with DMF acetal (conversion **1** → **3** in Scheme 1).[20] Thus obtained acetaldehyde **3** shows great synthetic promise since it gives rise to a wide variety of derivatives (including some rather unusual structures) with intense long-wavelength absorption and fluorescence. The tempting potentialities of this approach have also motivated us to develop it further in the present work which addresses the synthesis of 3,5-bis(acetaldehyde) substituted BODIPY **8** and its derivatives.

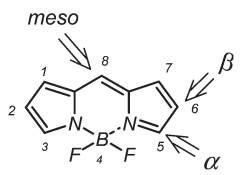

Fig. 1 Numbering of positions in BODIPY nucleus.

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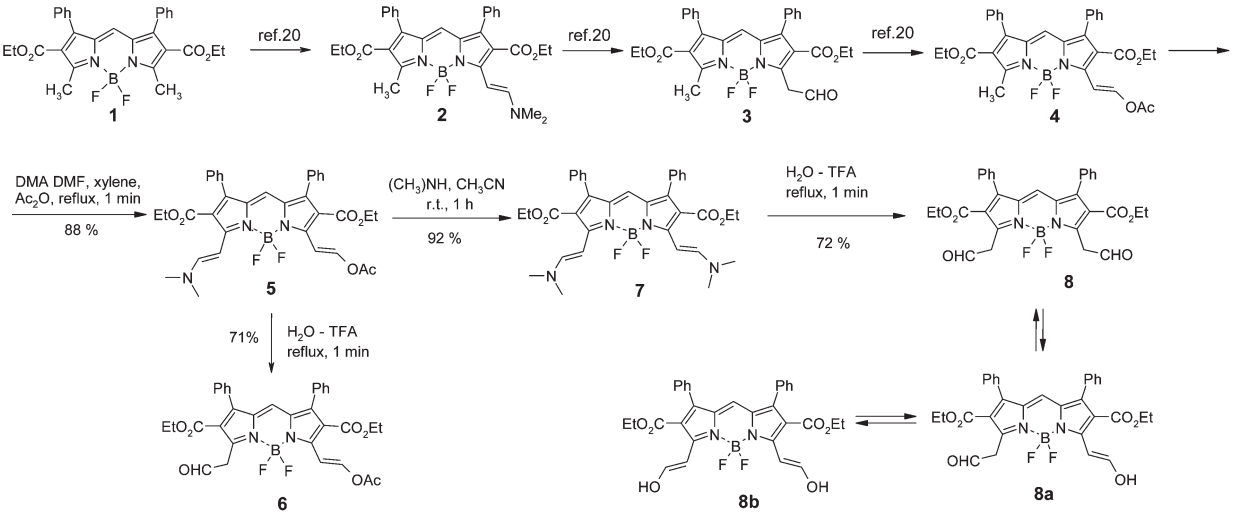
†Electronic supplementary information (ESI) available: These data include copies of ^{1}H and ^{13}C NMR spectra for all compounds. See DOI: 10.1039/c2ob27004h

Results and discussion

Compound **1** (Scheme 1) contains β-ethoxycarbonyl groups which activate α-methyl groups in electrophilic substitution



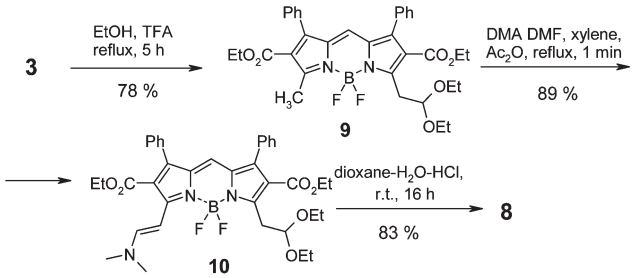
Scheme 1 Synthesis of dialdehyde **8** *via* enole acetate **4**.

reactions. This activation is sufficient to obtain enamine **2** by the reaction with DMF dimethyl acetal (but insufficient to run the Vilsmeier reaction). However, aldehyde **3** became inconvenient for some further manipulations due to the additional activation of methylene group in its molecule, as it is easily involved in side reactions. Thus, the corresponding enamine cannot be obtained directly from **3** by the reaction with DMF dimethyl acetal; instead, a complex mixture of products is formed.[20] To circumvent the problem, enolacetate **4** was used as a starting compound and it indeed produced desired product **5** readily and in high yield. Under the conditions of acid hydrolysis, only an amine molecule is eliminated from this substance to give aldehyde **6**. To obtain free dialdehyde **8**, we had to additionally synthesize dienamine **7**, which was then easily hydrolyzed by acid.

Like its mono analogue **3**, dialdehyde **8** undergoes keto–enol tautomerism. The ^{1}H NMR spectrum recorded in $CDCl_3$ indicates the presence of dialdehyde in the form of **8** solely, whereas all three forms exist in DMSO-d_6. As evidenced by the intensity ratio 0.2 : 1 : 0.1 for the respective *meso*-proton signals at 7.07 (**8**), 6.7 (**8a**), and 6.62 ppm (**8b**), the monoenol form accounts for 77%, the dialdehyde for 15%, and the dienol for 8% of the total amount of compound **8** in DMSO-d_6. It should be noted that the same tautomerism was observed for α-phenacyl substituted BODIPY.[14a]

Further studies resulted in another, one step shorter and more facile, synthetic route to compound **8**. It has been found that diethyl acetal **9**, if heated for a short time in xylene with DMF dimethyl acetal in the presence of acetic anhydride, affords compound **10** in high yield (89%) as shown in Scheme 2. According to ^{1}H NMR data, the condensation occurs just at the methyl rather than methylene group of the acetal moiety. Compound **10** is efficiently hydrolyzed (in 83% yield) in a mixture of dioxane and hydrochloric acid to produce dialdehyde **8**.

The ability of acetaldehyde fragments of product **8** to exist in enol forms allows for very easy formation of some its divinyl



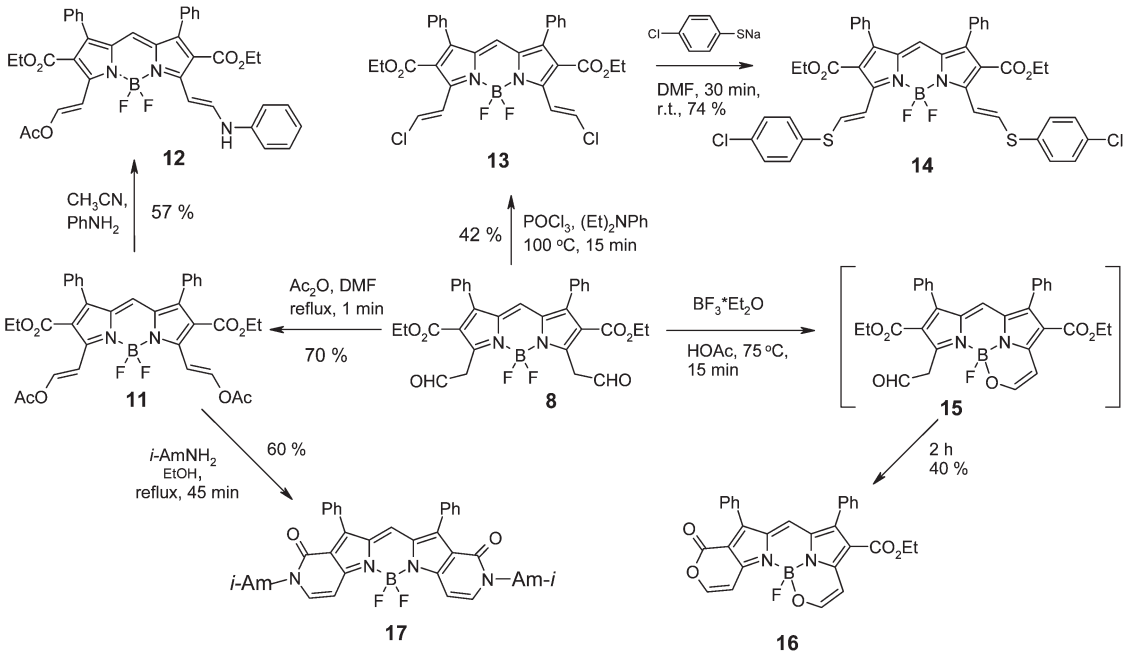
Scheme 2 Synthesis of dialdehyde **8** *via* acetal **9**.

derivatives. For instance, acetylation with acetic anhydride in the presence of DMF leads to dienol acetate **11** (Scheme 3). On treating the product with aniline, one acetyl group is substituted with ease to provide dye **12**. However, an attempted substitution of the other acetyl group does not give the expected di(anilinovinyl) derivative but only a complex mixture of inseparable products.

Short heating of compound **8** with phosphorus oxychloride produces di(chlorovinyl) derivative **13** which can be converted to disulfide **14** by the reaction with sodium *p*-chlorothiophenolate. On heating **8** in acetic acid in the presence of boron trifluoride etherate for 15 min, a compound results which has λ_{max} = 579 nm in dichloromethane; the same absorption maximum is characteristic of the *peri*-condensed cyclic dye with the bridgehead boron atom obtained from the corresponding monoaldehyde under similar conditions.[20] This dye, though not isolated, is supposed with good reason to have structure **15**.

Indeed, further heating causes the cyclization of the second aldehyde moiety, this time at the carboxyl group rather than the boron atom, so that pyranone system **16** is formed.

Similar to monoaldehyde **3**, dialdehyde **8** also reacts with aliphatic amines to form dye **17** but this conversion proceeds more smoothly with dienol acetate **11**. Since compounds of this kind have low solubility, the reaction was performed with isoamylamine.



Scheme 3 Chemical transformations of dialdehyde **8**.

Table 1 Phothophysical properties of dyes **5–18** in dichloromethane

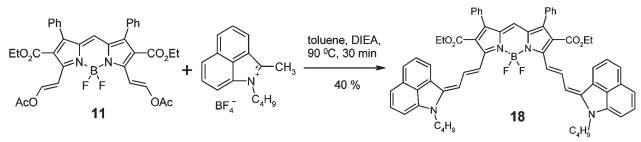
Dye	λ_{abs}, nm($\varepsilon \times 10^{-3}$, M^{-1} cm^{-1})	fwhm, cm^{-1}	λ_{em}, nm (φ)
5	643 (49)	2619	684 (0.001)
6	552 (104)	926	567 (0.91)
7	728 (79)	1236	—
8	519 (95)	820	535 (0.95)
9	522 (105)	774	536 (0.98)
10	622 (65)	2417	658 (0.001)
11	585 (114)	987	601 (0.71)
12	655 (75)	2010	695 (0.16)
13	578 (90)	1094	596 (0.81)
14	648 (81)	1638	680 (0.60)
16	609 (82)	1235	638 (0.45)
17	658 (134)	767	683 (0.74)
18	960 (47)	—	—

The spectral characteristics of the dyes synthesized are listed in Table 1. In the symmetrically substituted compounds, vinyl groups have an additive effect on the position of absorption maximum, so that the first and second substituents cause the same red shift. For example, the bathochromic effect of one chlorovinyl group is 28 nm, whereas two such groups increase the absorption wavelength by 59 nm; the red shifts caused by one and two *p*-chlorophenylthiovinyl groups are 65 and 129 nm, respectively; the corresponding values for one and two dimethylaminovinyl groups are 102 and 209 nm (from here on, all data for monosubstituted dyes are taken from ref. 20 and bathochromic effects are estimated with reference to parent dye **1**).

The additivity of substituent spectral effects is retained for unsymmetrically substituted dyes provided the substituents do not differ strongly in their electron-donor properties. For instance, the cyclization of the enol moiety at the boron atom shifts dye absorption to longer wavelengths by 60 nm and the pyranone cyclization by 34 nm. The combined effect of two cyclic moieties in compound **16** amounts to 90 nm (much the same as 94 nm, the sum of individual red shifts). As another example of quasi-additivity, an acetoxyvinyl and anilinovinyl moieties induce respective bathochromic shifts of 33 and 107 nm, whereas their combined effect for compound **12** is found to be 136 nm. A more electron-unsymmetric structure, *e.g.*, compound **5** containing the aminovinyl and acetoxyvinyl groups, exhibits more pronounced deviations from additivity: the sum of individual bathochromic effects of the two substituents is 135 nm whereas a real red shift is 124 nm. It is thus possible to predict, with good accuracy, the absorption maximum position for a divinyl-substituted BODIPY based on the individual spectral effects of the corresponding substituents.

Unsymmetrical dyes containing an aminovinyl moiety are characterized by the broadest absorption bands, with fwhm values of 2400 to 2600 cm^{-1} (Table 1). A much narrower (with fwhm of 1236 cm^{-1}) and, accordingly, more intense absorption band is observed for symmetrically substituted dienamine **7**. The absorption intensity is enhanced the most if the BODIPY structure is symmetrically annelated with pyridone rings. The thus diannelated dye **17** has the molar absorptivity of 134 000 M^{-1} cm^{-1} (*cf.* to the corresponding value of its monoannelated counterpart,[20] 95 000 M^{-1} cm^{-1}).

All the synthesized vinyl-substituted BODIPYs exhibit high fluorescence quantum yields (φ = 0.45–0.95) except amino derivatives in which the enamine moiety so drastically reduces emission that it could not even be detected for dienamine **7**. The above observation is in good agreement with the previously reported view of boron-dipyrromethene optical properties, as free conjugated terminal amino groups most often lead to fluorescence quenching.[21] At the same time, φ = 0.16



Scheme 4 Synthesis of dye **18**.

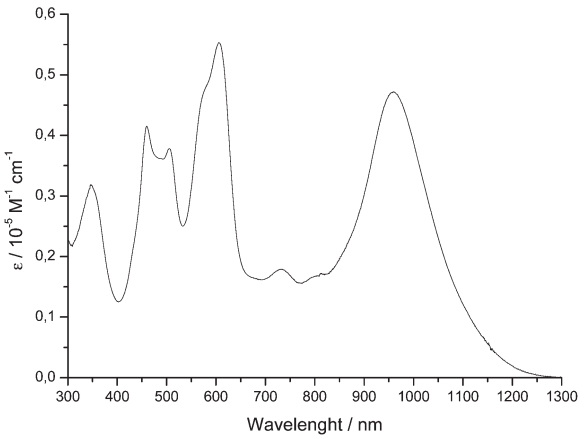


Fig. 2 Absorption spectra of dye **18** in CH_2Cl_2.

for aminovinyl derivative **12** and φ = 0.17 for its monosubstituted analogue[20] represent few cases when relatively strong fluorescence persists in spite of the mentioned quenching effect.[9a,b,22]

As already noted, dienol acetate **11** appears to be a better reagent than free dialdehyde **8** thus offering new synthetic opportunities as, for instance, condensations with CH acids. We have recently obtained a number of peculiar polymethine dyes which contain the BODIPY nucleus as a central moiety of the conjugated chromophore.[23] The most interesting of these compounds are those containing a terminal groups of low electron-donor ability. However, the method employed by us for dye synthesis, *viz.*, the reaction between hemicyanines and compound **1**, was not always successful. In particular, we could not thus obtain dye **18** containing the benz[*c*,*d*]indolium nucleus. The reaction presented in Scheme 4 also fails to provide the desired product, if performed with dialdehyde **8** which is prone to self-condensation under basic conditions; in contrast, compound **11** is smoothly converted to dye **18**.

The absorption spectra of this dye (Fig. 2) and its analogues (previously analyzed in detail[23]) are qualitatively similar. Among the compounds of this series, dye **18** is noted for its most red-shifted first absorption band (λ_{abs} = 960 nm in CH_2Cl_2) and for the most intense multicomponent short-wavelength absorption. In addition, it proved to be quite stable on storage and fairly photostable. At the typical spectroscopic concentration, its solution in dichloromethane remained unchanged on standing in diffuse light for three months. This behaviour of dye **18** is consistent with the previously established fact that the stability of α-borondipyrromethenecyanine dyes increases with decreasing electron-donor ability of terminal heterocyclic nuclei.[23] Indeed, the 2-benz[*c*,*d*]indolium residue is one of the least electron-donor groups applied in the conventional cyanine chemistry.[24]

Conclusions

In summary, we have developed two versions of the facile and efficient method to obtain dialdehyde **8** which appears to be a useful synthon in the preparation of various 3,5-divinyl BODIPY derivatives. Many of these compounds are characterized by intense absorption and fluorescence in the wavelength region longer than 600 nm, *i.e.*, in the so-called "phototherapeutic window" (about from 600 to 900 nm) which is of particular biological significance. Importantly, these dyes are quite stable substances. As also shown, dialdehyde **8** in its dienol acetate form **11** is readily condensed with CH acids; for instance, it reacts with 2-methylbenz[*c*,*d*]indolium salt to produce previously inaccessible NIR dye **18** having peculiar spectral properties. The above-described reactions illustrate well that dialdehyde **8** has much synthetic potential in further functionalization of the BODIPY nucleus.

Experimental section

Absorption spectra were recorded on a Shimadzu UV-3100 spectrophotometer. ^{1}H NMR (300 MHz, 25 °C, TMS as internal standard) and ^{13}C NMR (75 MHz, $CDCl_3$ as internal standard) spectra were obtained on a Varian VXR-300 instrument. Fluorescence spectra were recorded on a Solar CM 2203 fluorescence spectrophotometer. The relative fluorescent quantum yields (φ) were determined using Rhodamine 6G (φ = 0.95, EtOH) and indodicarbocyanine iodide (φ = 0.25, EtOH) as the references. Column chromatography was performed using Fluka Silica Gel 100 (0.063–0.200 mm).

3-(2-Acetoxyethen-1-yl)-5-(2-dimethylaminoethen-1-yl)-1,7-diphenyl-2,6-dicarbethoxy-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (5)

A solution of compound **4** (4.9 g, 8.4 mmol), of DMF dimethyl acetal (4.97 g, 41.8 mmol), of acetic anhydride (8.53 g, 83.6 mmol) of in *o*-xylene (20 mL) was refluxed for 1 min. After cooling, the mixture was evaporated to dryness under reduced pressure, the residue was washed with *i*-PrOH and filtered. Yield: 4.71 g (88%). M.p. 174–175 °C. ^{1}H NMR ($CDCl_3$): δ = 0.91 (t, J = 6.6 Hz, 3 H, CH_3), 0.99 (t, J = 6.6 Hz, 3 H, CH_3), 2.22 (s, 3 H, $COCH_3$), 3.10 (s, 3 H, NCH_3), 3.33 (s, 3 H, NCH_3), 4.01–4.13 (m, 4 H, CH_2), 6.21 (d, J = 13.2 Hz, 1 H, CH), 6.42 (s, 1 H, *meso*-H), 7.14–7.36 (m, 11 H, 10 Ar-H, CH), 8.54 (d, J = 13.2 Hz, 1 H, CH), 8.62 (d, J = 12.9 Hz, 1 H, CH) ppm. Anal. calcd for $C_{35}H_{34}BF_2N_3O_6$: C, 65.52; H, 5.30; N, 6.55. Found: C, 65.65; H, 5.19; N, 6.71.

3-(2-Acetoxyethen-1-yl)-5-(2-formylmethyl)-1,7-diphenyl-2,6-dicarbethoxy-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (6)

A mixture of compound **5** (0.25 g, 0.4 mmol), water (2 mL) and trifluoroacetic acid (0.5 mL) was boiled for 1 min. After cooling

to room temperature, the precipitate was filtered and recrystallized from the mixture of *i*-PrOH and hexane. Yield: 0.16 g (71%). M.p. 150–152 °C. ^{1}H NMR ($CDCl_3$): δ = 1.01–1.08 (m, 6 H, CH_3), 2.26 (s, 3 H, $COCH_3$), 4.11–4.13 (m, 4 H, CH_2), 4.52 (s, 2 H, CH_2CHO), 6.97 (s, 1 H, *meso*-H), 7.06 (d, J = 12.9 Hz, 1 H, CH), 8.69 (d, J = 12.9 Hz, 1 H, CH), 9.82 (s, 1 H, CHO) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.6, 13.8, 20.6, 43.5, 60.5, 61.3, 104.9, 127.8, 127.9, 128.3, 129.0, 129.3, 129.6, 130.3, 131.3, 131.6, 133.9, 135.5, 146.4, 147.8, 148.7, 153.1, 153.6, 163.2, 164.0, 166.9, 195.3 ppm. Anal. calcd for $C_{33}H_{29}BF_2N_2O_7$: C, 64.49; H, 4.72; N, 4.56. Found: C, 64.59; H, 5.01; N, 4.71.

3,5-Bis(2-dimethylaminoethen-1-yl)-1,7-diphenyl-2,6-dicarbethoxy-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (7)

To a solution of compound **5** (4 g, 6.2 mmol) in of acetonitrile (30 mL) of 30% aqueous dimethylamine (1.80 g, 12 mmol) was added. After 1 h, 10 ml of water was added, the precipitate was filtered and washed with *i*-PrOH. Yield: 3.6 g (92%). M.p. 216–218 °C. ^{1}H NMR ($CDCl_3$): δ = 0.89 (t, J = 7.2 Hz, 6 H, CH_3), 3.05 (s, 12 H, NCH_3), 3.97 (q, J = 7.2 Hz, 4 H, CH_2), 6.11 (d, J = 13.5 Hz, 2 H, CH), 6.34 (s, 1 H, *meso*-H), 7.20–7.30 (m, 10 H, Ar-H), 8.12 (d, J = 13.5 Hz, 1 H, CH) ppm. ^{13}C NMR (DMSO-d_6): δ = 14.0, 60.46, 87.8, 114.6, 118.2, 128.4, 129.8, 133.3, 133.5, 142.7, 151.0, 153.1, 165.5 ppm. Anal. calcd for $C_{35}H_{37}BF_2N_4O_4$: C, 67.09; H, 5.91; N, 8.94. Found: C, 67.33; H, 6.07; N, 9.05.

3,5-Bis(2-formylmethyl)-1,7-diphenyl-2,6-dicarbethoxy-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (8)

A mixture of compound **10** (2.58 g, 4 mmol), of dioxane (25 ml), of water (6 mL) and of concentrated hydrochloric acid (2.85 g) was stirred at room temperature for 18 h. After that, the mixture was washed with water, the precipitate was filtered and recrystallized from the mixture of benzene and hexane. Yield: 1.8 g (83%). M.p. 185–186 °C. ^{1}H NMR ($CDCl_3$): δ = 1.1 (t, J = 6.5 Hz, 6 H, CH_3), 4.14 (q, J = 6.5 Hz, 4 H, CH_2CH_3), 4.53 (s, 4 H, CH_2), 7.08 (s, 1 H, *meso*-CH), 7.31–7.42 (m, 10 H, Ar-H), 9.81 (s, 2 H, CHO) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.8, 43.5, 60.7, 121.3, 127.9, 128.4, 129.3, 130.3, 131.2, 132.0, 134.6, 148.7, 155.4, 162.9, 194.7 ppm. Anal. calcd for $C_{31}H_{27}BF_2N_2O_6$: C, 65.03; H, 4.72; N, 4.89. Found: C, 65.13; H, 5.05; N, 5.12.

3-(2,2-Diethoxyethyl)-5-methyl-1,7-diphenyl-2,6-dicarbethoxy-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (9)

A suspension of compound **3** (2.25 g, 4.1 mmol) in of anhydrous EtOH (30 mL) and of trifluoroacetic acid (0.7 g, 6.14 mmol) was refluxed for 5 h. After cooling, the precipitate was filtered and washed with EtOH. Yield: 1.88 g (78%). M.p. 148–150 °C. ^{1}H NMR (DMSO-d_6): δ = 1.06–1.09 (m, 12 H, CH_3), 2.84 (s, 3 H, CH_3), 3.41 (t, J = 7 Hz, 2 H, CH_2), 3.57–3.64 (m, 4 H, CH_2CH_3), 4.13 (q, J = 7 Hz, 4 H, CH_2CH_3), 4.81 (t, J = 7.2 Hz, 1 H, CH), 7.01 (s, 1 H, *meso*-CH), 7.45 (m, 10 H, Ar-H) ppm. ^{13}C NMR (DMSO-d_6): δ = 14.1, 15.0, 15.5, 33.1, 60.6, 60.7, 62.5, 102.1, 120.8, 123.4, 128.4, 128.7, 129.6, 130.4, 130.6, 130.8, 131.4, 131.6, 133.1, 133.5, 146.1, 147.7, 157.3, 160.3, 163.2, 163.6 ppm. Anal. calcd for $C_{34}H_{37}BF_2N_2O_6$: C, 66.01; H, 5.99; N, 4.52. Found: C, 66.13; H, 6.27; N, 4.65.

3-(2,2-Diethoxyethyl)-5-(2-dimethylaminoethen-1-yl)-1,7-diphenyl-2,6-dicarbethoxy-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (10)

A mixture of compound **9** (2.95 g, 5 mmol), of DMF dimethyl acetal (2.98 g, 25 mmol) and of acetic anhydride (5.1 g, 50 mmol) in *o*-xylene (20 mL) was boiled for 1 min. After cooling, solvent was evaporated under reduced pressure and the residue was refluxed in 15 mL of *i*-PrOH. A resulting precipitate was filtered and washed with *i*-PrOH. Yield: 2.89 g (89%). M.p. 165–167 °C. ^{1}H NMR (DMSO-d_6): δ = 0.94 (t, J = 8.5 Hz, 3 H, CH_3),1.03–1.08 (m, 9 H, CH_3), 3.09 (s, 3 H, NCH_3), 3.32 (s, 3 H, NCH_3), 3.36 (t, J = 7 Hz, 2 H, CH_2), 3.47–3.51 (m, 4 H, CH_2CH_3), 4.01–4.13 (m, 4 H, CH_2CH_3), 4.77 (t, J = 7.5 Hz, 1 H, CH), 6.03 (d, J = 16.5 Hz, 1 H, CH), 6.35 (s, 1 H, *meso*-CH), 7.25–7.45 (m, 10 H, Ar-H), 8.18 (d, J = 15 Hz, 1 H, CH) ppm. ^{13}C NMR (DMSO-d_6): δ = 13.9, 14.2, 15.6, 32.5, 59.8, 61.4, 62.2, 88.7, 102.6, 115.6, 119.3, 123.3, 127.8, 128.3, 128.7, 129.6, 130.3, 131.5, 133.7, 134.9, 137.5, 146.2, 148.6, 155.6, 157.8, 164.9 ppm. Anal. calcd for $C_{37}H_{42}BF_2N_3O_6$: C, 65.97; H, 6.24; N, 6.23. Found: C, 66.02; H, 6.54; N, 6.35.

3,5-Bis(2-acetoxyethen-1-yl)-1,7-diphenyl-2,6-dicarbethoxy-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (11)

A solution of compound **8** (0.28 g, 0.5 mmol) in acetic anhydride (2 mL) and DMF (0.25 mL) was boiled for 1 min. After cooling to room temperature, the mixture was diluted with 10 mL of diethyl ether and the precipitate was filtered. Yield: 0.23 g (70%). M.p. 238–240 °C. ^{1}H NMR (DMSO-d_6): δ = 0.96 (t, J = 7.5 Hz, 6 H, CH_3), 2.29 (s, 6 H, $COCH_3$), 4.08 (q, J = 7.2 Hz, 4 H, CH_2), 6.92–6.96 (m, 3 H, CH), 7.45 (m, 10 H, Ar-H), 8.60 (d, J = 13.2 Hz, 2 H, CH) ppm. ^{13}C NMR (DMSO-d_6): δ = 13.9, 60.5, 87.8, 114.6, 118.2, 128.4, 128.5, 129.8, 133.3, 133.5, 142.7, 151.0, 153.1, 165.5 ppm. Anal. calcd for $C_{35}H_{31}BF_2N_2O_8$: C, 63.94; H, 4.72; N, 4.26. Found: C, 64.09; H, 4.83; N, 4.39.

3-(2-Acetoxyethen-1-yl)-5-(2-phenylaminoethen-1-yl)-1,7-diphenyl-2,6-dicarbethoxy-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (12)

To a hot solution of compound **11** (0.2 g, 0.3 mmol) in acetonitrile (6 mL) was added of aniline (0.11 g, 1.2 mmol). After cooling to room temperature, the precipitate was filtered. Yield: 0.12 g (57%). M.p. 229–230 °C. ^{1}H NMR (DMSO-d_6): δ = 0.87–0.95 (m, 6 H, CH_3), 2.28 (s, 3 H, $COCH_3$), 3.99–4.13 (m, 4 H, CH_2), 6.44 (s, 1 H, *meso*-CH), 6.68 (d, J = 12.9 Hz, 1 H, CH), 7.01 (d, J = 12.6 Hz, 1 H, CH), 7.11–7.21 (m, 3 H, Ar-H), 7.30–7.46 (m, 12 H, Ar-H), 8.52 (d, J = 12.9 Hz, 1 H, CH), 8.88 (t, J = 12.6 Hz, 1 H, CH), 11.14 (d, J = 12.6 Hz, 1 H, NH) ppm. ^{13}C NMR (DMSO-d_6): δ = 13.8, 13.9, 21.0, 60.6, 61.5, 94.8, 105.6, 116.7, 117.4, 118.7, 123.7, 124.5, 128.5, 128.8, 129.7, 130.2, 130.5, 131.5, 132.1, 133.2, 137.7, 140.6, 142.3, 143.0, 147.0, 148.7, 164.9, 165.0, 168.0 ppm. Anal. calcd for $C_{39}H_{34}BF_2N_3O_6$: C, 67.82; H, 4.92; N, 6.09. Found: C, 68.01; H, 5.18; N, 6.23.

3,5-Bis(2-chloroethen-1-yl)-1,7-diphenyl-2,6-dicarbethoxy-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (13)

A mixture of compound **8** (2.0 g, 3.5 mmol), of *N*,*N*-diethylaniline (2.0 g, 14 mmol) and phosphorus oxychloride (10 mL) was heated at 100 °C for 15 min. After cooling, the mixture was poured into ice water, the precipitate was filtered, washed with water, *i*-PrOH and recrystallized from mixture of toluene and hexane. Yield: 0.90 g (42%). M.p. 224–226 °C. ^{1}H NMR ($CDCl_3$): δ = 1.03 (t, J = 6.5 Hz, 6 H, CH_3), 4.13 (q, J = 6.5 Hz, 4 H, CH_2), 6.99 (s, 1 H, *meso*-CH), 7.28–7.28 (d, J = 6 Hz, 4 H, Ar-H), 7.40–7.43 (m, 6 H, Ar-H), 7.55 (d, J = 13.5 Hz, 2 H, CH), 7.72 (d, J = 13.5 Hz, 2 H, CH) ppm. Anal. calcd for $C_{31}H_{25}BCl_2F_2N_2O_4$: C, 61.08; H, 4.10; N, 4.59. Found: C, 61.18; H, 4.41; N, 4.72.

3,5-Bis(2-(4-chlorophenylsulfanyl)ethen-1-yl)-1,7-diphenyl-2,6-dicarbethoxy-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (14)

To a solution of compound **13** (150 mg, 0.25 mmol) in DMF (2 mL) was added a solution of sodium *p*-chlorothiophenolate (from *p*-chlorothiophenol (92 mg, 0.64 mmol) and sodium hydroxide (26 mg, 0.65 mmol) in EtOH (1 mL). After 30 min, the mixture was diluted with 10% aqueous ammonium chloride, the precipitate was filtered and flesh-chromatographed on silica gel (eluent dichloromethane). Yield: 150 mg (74%). M.p 170–171 °C. ^{1}H NMR ($CDCl_3$): δ = 0.97 (t, J = 7 Hz, 6 H, CH_3), 4.07 (q, J = 7 Hz, 4 H, CH_2), 6.83 (s, 1 H, *meso*-CH), 7.25–7.29 (m, 6 H, 2 CH, 4 Ar-H), 7.37–7.41 (m, 10 H, Ar-H), 7.48 (d, J = 8.5 Hz, 4 H, Ar-H), 8.14 (d, J = 16 Hz, 2 H, CH) ppm. Anal. calcd for $C_{43}H_{33}BCl_2F_2N_2O_4S_2$: C, 62.54; H, 4.00; N, 3.39. Found: C, 62.65; H, 4.31; N, 3.53.

Compound 16

A solution of compound **7** (0.23 g, 0.4 mmol) and boron trifluoride etherate (1.14 g, 4 mmol) in acetic acid (15 mL) was heated at 75 °C for 2 h. After cooling, the reaction mixture was diluted with water and product was extracted with dichloromethane. The organic layer was dried over sodium sulfate, evaporated to dryness and the residue was chromatographed on silica gel (eluent hexane–ethylacetate, 3 : 1). Yield: 0.08 g (40%). M.p. 125–127 °C. ^{1}H NMR ($CDCl_3$): δ = 1.25 (t, J = 7.5 Hz, 3 H, CH_3), 4.26 (q, J = 7.5 Hz, 2 H, CH_2), 6.74 (d, J = 5.5 Hz, 1 H, CH), 7.10 (d, J = 6 Hz, 1 H, CH), 7.16 (s, 1 H, *meso*-H), 7.44–7.49 (m, 8 H, Ar-H), 7.54–7.56 (m, 3 H, 1 CH, 2 Ar-H), 7.62 (d, J = 6 Hz, 1 H, CH) ppm. ^{13}C NMR (DMSO-d_6): δ = 14.2, 61.2, 98.6, 99.3, 110.8, 119.0, 125.6, 127.0, 128.6, 128.7, 129.5, 129.7, 130.3, 130.5, 130.7, 130.8, 131.0, 135.5, 136.1, 139.5, 141.6, 147.9, 150.1, 150.8, 153.0, 154.2, 158.1, 161.3, 162.2 ppm. Anal. calcd for $C_{29}H_{20}BFN_2O_5$: C, 68.77; H, 3.95; N, 5.52. Found: C, 68.81; H, 4.16; N, 5.71.

Compound 17

A mixture of compound **11** (196 mg, 0.3 mmol) and isoamylamine (117 mg, 1.3 mmol) in EtOH (3 mL) was refluxed for 45 min. After cooling, the product was filtered. Yield: 100 mg (54%). M.p. 182–183 °C. ^{1}H NMR ($CDCl_3$): δ = 0.92 (d, J = 5.6 Hz, 12 H, CH_3), 1.59 (m, 6 H, 4 CH_2, 2 CH), 3.90 (t, J = 7.2 Hz, 4 H, NCH_2), 6.78 (d, J = 6.8 Hz, 1 H, CH), 7.32 (d, J = 6.8 Hz, 1 H, CH), 7.37 (s, 1 H, *meso*-H), 7.44 (m, 6 H, Ar-H), 7.58 (m, 4 H, Ar-H) ppm. Anal. calcd for $C_{37}H_{37}BF_2N_4O_2$: C, 71.84; H, 5.99; N, 9.06. Found: C, 71.78; H, 6.06; N, 8.97.

3,5-Bis(3-(1-butyl-1*H*-benz[*c*,*d*]indole-2-ylidene)propen-1-yl)-1,7-diphenyl-2,6-dicarbethoxy-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (18)

A mixture of dienole acetate **8** (0.2 g, 0.3 mmol), of 1-butyl-2-methylbenz[*c*,*d*]indolium tetrafluoroborate (0.25 g, 0.8 mmol), of DIEA (0.2 g, 1.55 mmol) in toluene (4 mL) was heated with stirring at 90 °C for 30 min. After cooling, a solution was filtered and evaporated to dryness under reduced pressure. The residue was boiled with acetonitrile, the product was filtered and recrystallized from the mixture of benzene and hexane. Yield: 0.12 g (40%). M.p. 218–220 °C. ^{1}H NMR ($CDCl_3$): δ = 0.99–1.04 (m, 12 H, CH_3), 1.54 (m, 4 H, CH_2), 1.86, (m, 4 H, CH_2), 3.93 (t, J = 6.8 Hz, 4 H, NCH_2), 4.17 (q, J = 7.2, 4 H, CH_2), 6.52 (d, J = 12 Hz, 2 H, CH), 6.70 (d, J = 6 Hz, 2 H, Ar-H), 6.78 (s, 1 H, *meso*-H), 6.90 (d, J = 8 Hz, 2 H, Ar-H), 7.09 (t, J = 7.2 Hz, 2 H, Ar-H), 7.17 (d, J = 8 Hz, Ar-H), 7.25 (m, 2 H, Ar-H), 7.61 (d, J = 6.4 Hz, 2 H, Ar-H), 7.70 (d, J = 15.2 Hz, 2 H, CH), 8.13 (t, J = 13.2 Hz, 2 H, CH) ppm. Anal. calcd for $C_{63}H_{57}BF_2N_4O_4$: C, 76.91; H, 5.80; N, 5.70. Found: C, 76.63; H, 6.07; N, 5.75.

Acknowledgements

This work was partially financially supported by the NATO "Science for Peace" program, project NUKR.SFPP 984189.

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