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4,8-DIHYDROPYRROL[3,4-*f*]ISOINDOLE AS A USEFUL BUILDING BLOCK FOR NEAR-INFRARED DYES

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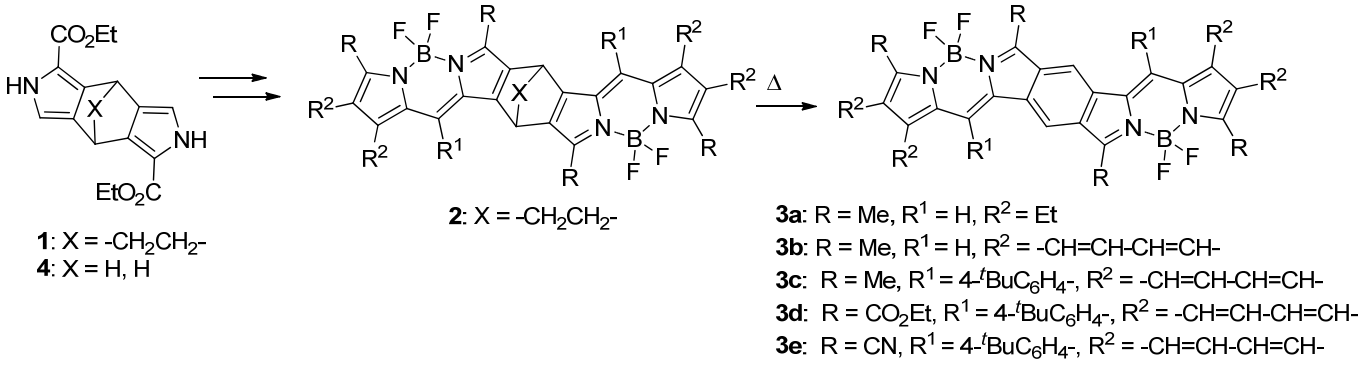
Dedicated to Prof. Dr. Isao Kuwajima on the occasion of his 77th birthday

Abstract – 4,8-Dihydropyrrol[3,4-*f*]isoindole was prepared from 4,7-dihydroisoindole based on the modified Barton-Zard reaction. Addition of phenylsulfenyl chloride followed by oxidation and dehydrochlorination gave phenylsulfonyldihydroisoindole, which underwent the smooth reaction with an isocyanoacetate under basic conditions to give 4,8-dihydropyrrol[3,4-*f*]isoindole-1,5- and 1,7-dicarboxylates in good yields. The pyrrolisoindole was successfully converted to the benzene-fused bisBODIPY, absorption maximum of which was 758 nm.

INTRODUCTION

Considerable interest has been paid for near-infrared (NIR) dyes due to a broad range of applications. They have been reported as promising dyes both for clinical use as NIR photosensitizers[1] in photo-dynamic therapy[2] and microscopic imaging agents[3] in diagnosis due to good transparency in living cells and for functional material use as NIR light emitting diode.[4] We have explored a new class of NIR-selective dyes based on the retro-Diels-Alder protocol for chromophore fusion:[5] bisBODIPYs **2** connected with a bicyclo[2.2.2]octadiene (BCOD) skeleton was thermally converted to benzene-fused bisBODIPYs **3** in the final step (Scheme 1).[6] The NIR dyes were proven to have an advantageous property for NIR-selective filters. They were almost transparent in the visible region although the dyes had very strong absorption maxima in the red to NIR region. This property is closely related to the fusion mode of the BODIPY chromophore.[6] 4,8-Ethano-4,8-dihydropyrrol[3,4-*f*]isoindole (**1**)[7] was the key

compound for the synthesis of the bisBODIPYs and the preparation of **1** was the bottle neck for the application of the dyes. The preparation must be started from rather expensive 1,3-cyclohexadiene. One of the alternative methods for the thermal conversion of BCOD to benzene is oxidation of 1,4-cyclohexadiene to benzene moieties.[8] Filatov *et al.* have explored the synthesis of π-expanded porphyrins based on the oxidation protocol using 4,7-dihydroisoindole as the key compound.[9] In this paper, we describe the synthesis of 4,8-dihydropyrrol[3,4-*f*]isoindole (**4**) and its application for the synthesis of NIR-selective bisBODIPY dye **3a**.

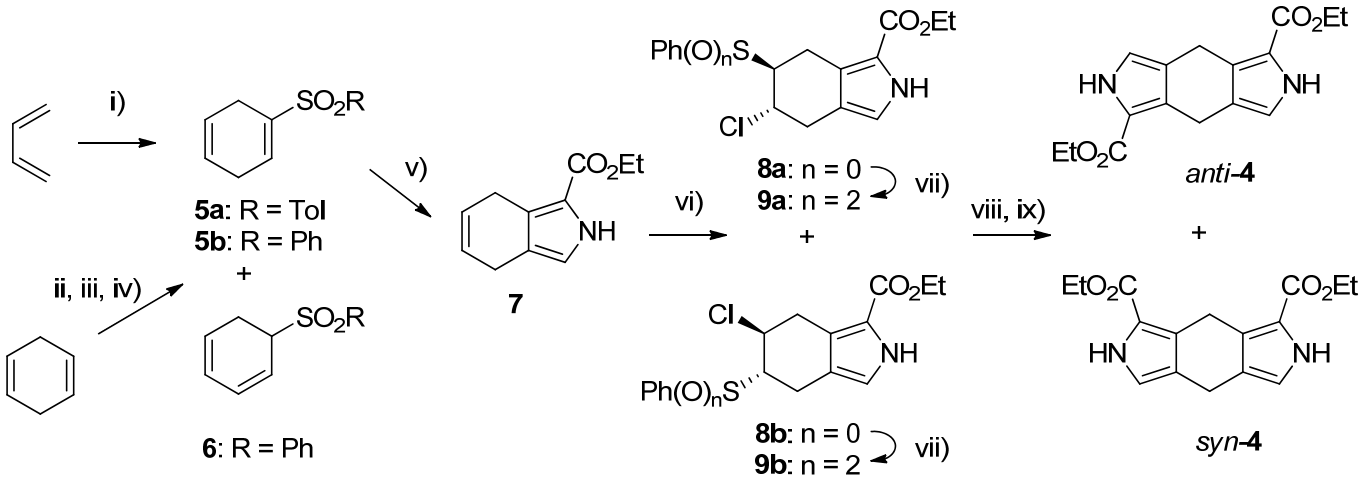


Scheme 1. Preparation of benzene-fused bisBODIPY

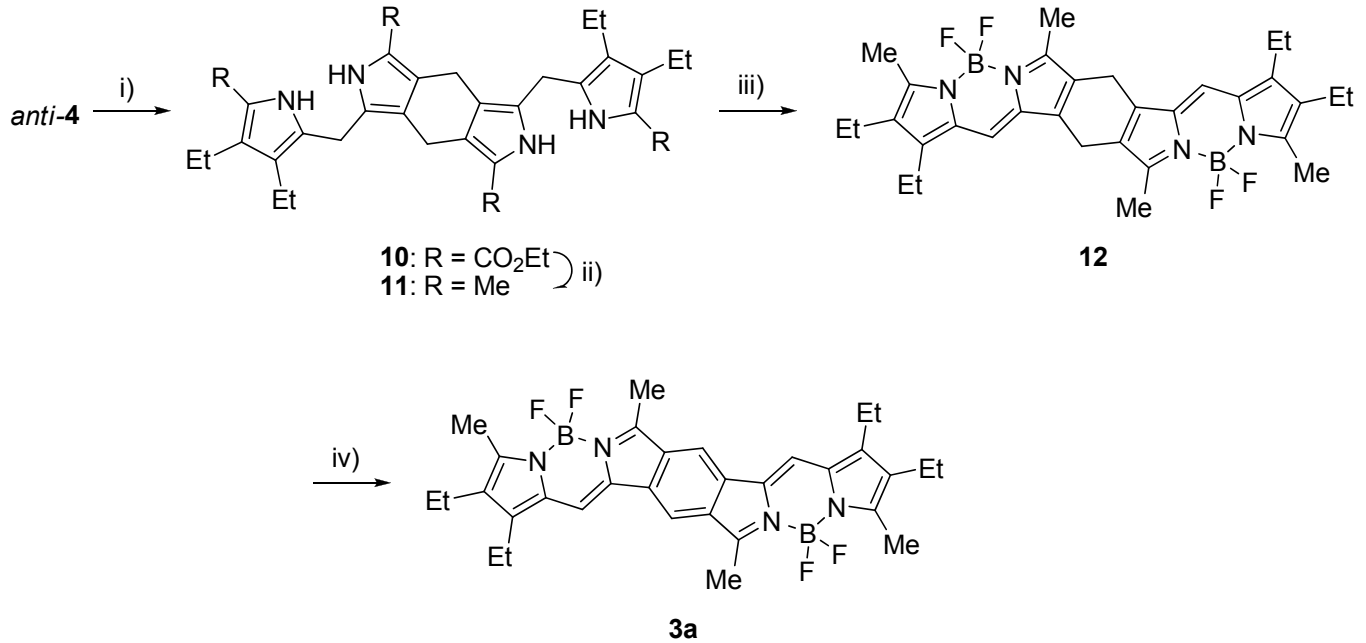
RESULTS AND DISCUSSION

In order to prepare 4,8-dihydropyrrol[3,4-*f*]isoindole (**4**), we planned to construct a pyrrole ring at the double bond of dihydroisoindole **7**, which was reported to be prepared from the modified Barton-Zard reaction of 1-tosyl-1,4-cyclohexadiene (**5a**) with ethyl isocyanoacetate by Filatov *et al* (Scheme 2).[9] The key 1,4-diene **5a** was prepared by the Diels-Alder reaction of 1,3-butadiene with tosylacetylene.[10] We prepared 1,4-diene **5b** starting from readily available 1,4-cyclohexadiene due to practically difficult treatment of 1,3-butadiene with high vapor pressure: addition of phenylsulfenyl chloride followed by oxidation with *m*-chloroperbenzoic acid (*m*CPBA) and then treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).[11] In this method, however, a mixture of aimed **5b** and **6** were obtained in a ratio of 2:1 and this mixture was used for the modified Barton-Zard reaction. Dihydroisoindole **7** was obtained in a total yield of 18% from 1,4-cyclohexadiene. Addition of phenylsulfenyl chloride to dihydroisoindole **7** gave a diastereomeric mixture (*ca*. 1:1) of β-chloro sulfides **8a** and **8b** in 84% yield. Oxidation of the sulfide mixture with *m*CPBA gave diastereomeric β-chloro sulfones **9a** and **9b** (*ca*. 1:1) in good yield. Dehydrochlorination of β-chloro sulfones **9a** and **9b** with potassium *tert*-butoxide gave regioisomeric α,β-unsaturated sulfones, which was then subjected to the modified Barton-Zard reaction with ethyl isocyanoacetate to give dipyrrole **4**. Chromatographic purification of the reaction mixture with ether gave an analytically pure sample of regioisomeric dipyrrole

4, ratio of which was determined to be *anti:syn* = 10:3 by ^{1}H NMR. Recrystallization of the sample from acetone/hexane gave pure *anti*-**4** in 11% yield.



Scheme 2. *Reagents, conditions, and yields*: i) tosylacetylene, rt, 48 h, pressure bottle; 95%; see ref 9; ii) PhSCl; CH_2Cl_2, −78 °C; 86%; iii) *m*CPBA; CH_2Cl_2, 0 °C; 64%; iv) DBU; CH_2Cl_2, rt; 62% (**5b**:**6** = 2:1); v) $CNCH_2CO_2Et$; KO^{t}Bu, THF, 0 °C; 53%; vi) PhSCl; CH_2Cl_2, −78 °C; 84%; vii) *m*CPBA; CH_2Cl_2, 0 °C; 99%; viii) KO^{t}Bu; THF, rt; 76%; ix) $CNCH_2CO_2$ Et; KO^{t}Bu, THF, 0 °C; 24% (*anti*-**4**:*syn*-**4** = 10:3).



Scheme 3. *Reagents, conditions, and yields*: i) ethyl 5-acetoxymethyl-3,4-diethylpyrrole-2-carboxylate, AcOH, *p*-TsOH, rt; 50%; ii) $LiAlH_4$, THF, reflux; iii) chloranil, CH_2Cl_2, rt; Et(*i*-Pr)$_2$N, $BF_3 \cdot OEt_2$; 56%; iv) chloranil, CH_2Cl_2, rt; quant.

As the reactivity of dipyrrole **4** was thought be similar to a simple pyrrole-2-carboxylate ester, the conversion of *anti*-**4** to a bisdipyrromethane derivative was achieved under the similar conditions as those of BCOD-fused dipyrroles.[6] Dihydropyrrolisoindole *anti*-**4** was alkylated with ethyl 2-acetoxymethyl-3,4-diethylpyrrole-1-carboxylate under acid-catalyzed conditions with *p*-toluenesulfonic acid to afford bisdipyrromethane **10** in 50% yield. After the ester groups of **10** were reduced to methyl groups with $LiAlH_4$ in refluxing THF, double BODIPY formation was performed. The resulting tetramethyl derivative **11** was oxidized with chloranil and then reacted with $BF_3{\cdot}OEt_2$ in the presence of ethyldiisopropylamine to give cyclohexadiene-connected bisBODIPY **12** contaminated with further oxidized bisBODIPY **3a** in 56% yield. Dehydrogenation of bisBODIPY **12** with chloranil gave fully conjugated bisBODIPY **3a**, UV-vis spectrum of which was the same as that of reported one (Figure 1).[6]

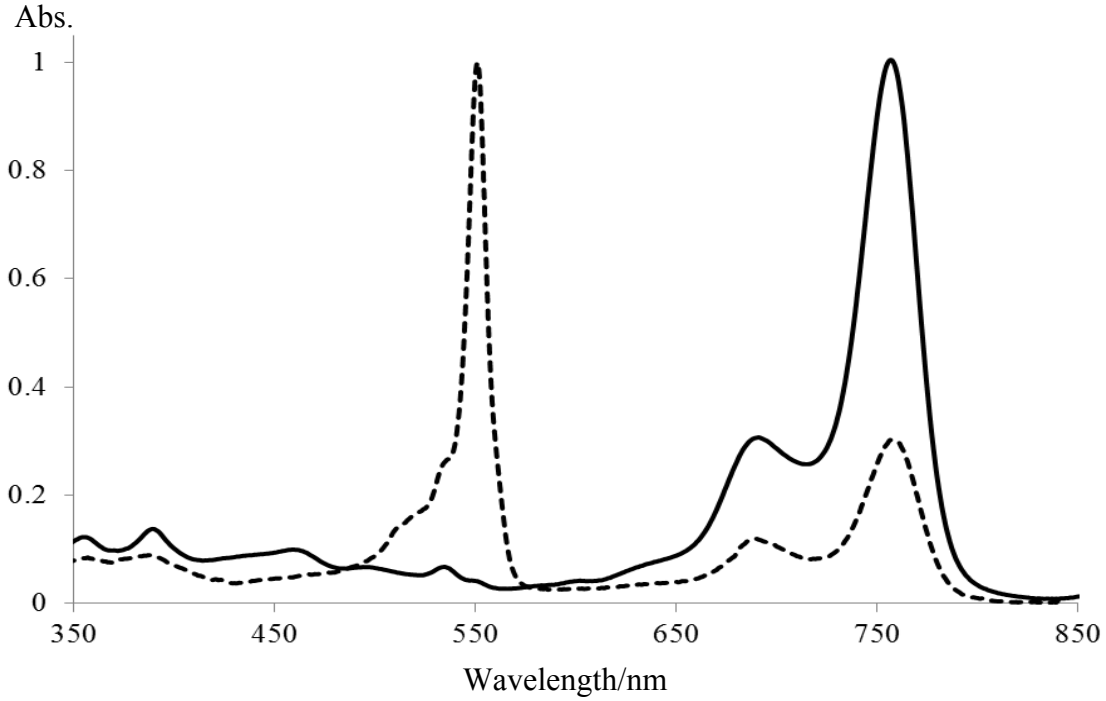


Figure 1. UV-vis-NIR spectra of **12** (dotted line, contaminated with **3a**) and **3a** (solid line)

In conclusion, we succeeded in the exploitation of an alternative route for the synthesis of bisBODIPY, chromophores of which were fully conjugated by the benzene moiety. The route is based on the dehydrogenation of cyclohexadiene to benzene moieties.

EXPERIMENTAL

General: Melting points were measured on a Yanagimoto micro-melting point apparatus and are uncorrected. NMR spectra were obtained with a JEOL AL-400 spectrometer at the ambient temperature by using $CDCl_3$ as a solvent and tetramethylsilane as an internal standard for ^1H and ^{13}C. IR spectra were obtained by a Thermo Scientific Nicolet iS5 FT-IR spectrometer with an iD5 ATR diamond plate. Mass

spectra (EI, 70 eV; FAB^+, *p*-nitrobenzyl alcohol, MALDI-TOF) were measured with a JEOL JMS-700 or a Voyager DE Pro instrument. Elemental analyses were performed with a Yanaco MT-5 elemental analyzer at Integrated Center for Sciences. Dehydrated tetrahydrofuran and dichloromethane were purchased from Kanto Chemical Co. (Tokyo Japan) and used without further purification. Potassium *tert*-butoxide was sublimed at 200 °C under a reduced pressure (*ca*. 13 Pa) and dissolved in dry THF (1.0 $mol \cdot L^{-1}$). DBU was distilled from CaH_2 under a reduced pressure and stored on molecular sieves 13X. Other commercially available materials were used without further purification.

Ethyl 4,7-dihydroisoindole-1-carboxylate (**7**):[11] To a stirred solution of 1,4-cyclohexadiene (5.0 mL, 53 mmol) in dry CH_2Cl_2 (50 mL) was slowly added phenylsulfenyl chloride (6.0 mL, 53 mmol) at −78 °C. After the addition, the reaction mixture was allowed to warm up to room temperature and stirred for 1 h. The reaction mixture was sequentially washed with a saturated aqueous solution of $NaHCO_3$, water, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to leave 10.26 g (86%) of (4*R**,5*R**)-4-chloro-5-phenylsulfanylcyclohexene as colorless viscous oil, which was proven to be analytically pure: ^{1}H NMR δ 7.45 (m, 2H), 7.31 (m, 3H), 5.67 (m, 1H, H^{2}*), 5.60 (m, 1H, H^{1}*), 4.19 (q, *J* 4.5 Hz, 1H, H^5), 3.59 (q, *J* 4.5 Hz, 1H, H^4), 2.97 (br d, *J* 18.3 Hz, 1H, $H^{3eq\dagger}$), 2.84 (m, 1H, $H^{6eq\dagger}$), 2.25 (br d, *J* 18.3 Hz, 1H, $H^{3ax\ddagger}$), 2.38 (br d, *J* 18.6 Hz, 1H, $H^{6ax\ddagger}$) (asterisks, daggers, and double daggers denote changeable assignment); ^{13}C NMR δ 133.56, 132.09, 128.95, 127.38, 123.60, 122.27, 56.95, 47.43, 31.14, 27.80; IR ν_{max} 3072, 3032, 1479, 1429, 1219 cm^{-1}; MS (FAB^+) *m/z* 225 {$M^+(^{35}Cl)$ + 1}; HRMS calcd for $C_{12}H_{13}{}^{35}ClS + H^+$: 225.0505, found 225.0485. Anal. Calcd for $C_{12}H_{13}ClS$: C, 64.13; H, 5.83. Found: C, 63.92; H, 5.93%. This adduct (10.26 g, 46 mmol) was dissolved in dry CH_2Cl_2 (500 mL) and cooled to 0 °C. Commercially available *m*CPBA (purity: *ca*. 70%; 24.1 g, 92 mmol) was slowly added and the mixture was stirred at room temperature overnight. The resulting suspension was filtered through a Celite pad. The filtrate was washed with a saturated aqueous solution of $NaHCO_3$, water, and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed on silica gel to give 7.55 g (64%) of (4*R**,5*R**)-4-chloro-5-phenylsulfonylcyclohexene as colorless oil: ^{1}H NMR δ 7.93 (m, 2H), 7.69 (m, 1H), 7.59 (m, 2H), 5.68 (m, 1H, H^{2}*), 5.67 (m, 1H, H^{1}*), 4.64 (q, *J* 4.7 Hz, 1H, H^5), 3.58 (dt, *J* 6.9, 4.7 Hz, 1H, H^4), 2.94 (dm, *J* 18.7 Hz, 1H, $H^{3eq\dagger}$), 2.65 (m, 1H, $H^{6eq\dagger}$), 2.56 (dm, *J* 17.6 Hz, $H^{6ax\ddagger}$), 2.38 (br d, *J* 18.6 Hz, 1H, $H^{3ax\ddagger}$) (asterisks, daggers, and double daggers denote changeable assignment); ^{13}C NMR δ 138.22, 133.90, 129.19, 128.57, 122.81, 122.23, 63.69, 51.48, 32.44, 22.08; IR ν_{max} (KBr) 3037, 1431, 1308, 1144, 1084 cm^{-1}; MS (FAB^+) *m/z* 257 {$M^+(^{35}Cl)$ + 1}; HRMS calcd for $C_{12}H_{13}{}^{35}ClSO_2 + H^+$: 257.0403, found 257.0408. To a stirred solution of the sulfone (3.87 g, 15.1 mmol) in dry CH_2Cl_2 (56 mL) was added DBU (2.24 mL, 15.1 mmol) at 0 °C and the mixture was allowed to warm up to room temperature. After 3 h, the mixture was sequentially washed with a 1-M solution of HCl, a saturated aqueous solution of $NaHCO_3$, water, and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was

chromatographed on silica gel to give 2.06 g (62%) of a diene mixture, which consisted of 1-phenylsulfonyl-1,4-cyclohexadiene {**5b**, ^{1}H NMR δ 7.87 (m, 2H), 7.62 (m, 1H), 7.54 (m, 2H), 7.05 (m, 1H, H2), 5.68 (m, 1H, H^4*), 5.65 (m, 1H, H^5*), 2.96 (m, 2H, H^3*), 2.81 (m, 2H, H^6*), asterisks denote changeable assignment.} and 5-phenylsulfonyl-1,3-cyclohexadiene {**6**, ^{1}H NMR *δ* 7.86 (m, 2H), 7.62 (m, 1H), 7.49 (m, 2H), 6.09 (dd, *J* 10.2, 4.8 Hz, 1H, H^2), 5.80 (dd, *J* 9.6 Hz, 1H, H^3), 5.60-5.48 (m, 2H, H^1 and H^4), 3.88 (dtd, *J* 10.7, 5.4, 1.0 Hz, H^5), 2.99 (dt, *J* 19.4, 4.9 Hz, 1H, H^{6eq}), 2.67 (ddt, *J* 19.4, 10.9, 2.4 Hz, 1H, H^{6ax})} in a ratio of 2:1. This mixture was used in the next step without further purification. The diene sulfone mixture (1.08 g, 4.9 mmol) was dissolved in dry THF (40 mL) and ethyl isocyanoacetate (0.65 mL, 6 mmol) was added. To the cooled mixture at 0 °C was added a 1-M solution of KO^{t}Bu in THF (12 mL, 12 mmol) and the mixture was allowed to warm up to room temperature. After being stirred for 12 h, the reaction mixture was quenched with a 1-M solution of HCl. The mixture was extracted with EtOAc. The organic extract was washed with a saturated aqueous solution of $NaHCO_3$, water, and brine, dried over Na_2SO_4, and concentrated. The residue was chromatographed on silica gel to give 500 mg (53%) of the title compound as colorless crystals: mp 94 °C; ^{1}H NMR δ 8.88 (br, 1H, NH), 6.71 (m, 1H), 5.88 (m, 2H), 4.30 (q, 2H, *J* 7.0 Hz), 3.44 (m, 2H), 3.22 (m, 2H), 1.35 (t, 3H, *J* 7.0 Hz); ^{13}C NMR δ 161.55, 124.79, 124.31, 123.72, 118.83, 118.44, 117.42, 59.88, 24.14, 22.44, 14.63; IR ν_{max} (KBr) 3288, 1685, 1675, 1323, 1250, 1154 cm^{-1}; MS (FAB$^+$) *m/z* 192 (M$^+$ + 1). HRMS calcd for $C_{11}H_{13}NO_2$ + H$^+$: 192.1025, found 192.1014. Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 68.92; H, 7.03; N, 7.42%.

Ethyl (5*S,6*S**)-5-chloro-6-phenylsulfanyl-4,5,6,7-tetrahydroisoindole-1-carboxylate** (**8a**) and **ethyl (5*S**,6*S**)-6-chloro-5-phenylsulfanyl-4,5,6,7-tetrahydroisoindole-1-carboxylate** (**8b**): Phenylsulfenyl chloride (1.99 mL, 17 mmol) was added to a stirred solution of dihydroisoindole **7** (3.35 g, 17.5 mmol) in dry CH_2Cl_2 (150 mL) at −78 °C and the mixture was allowed to warm to room temperature. After 1 h, the mixture was sequentially washed with a saturated aqueous solution of $NaHCO_3$, water, and brine, dried over Na_2SO_4, and concentrated. The residue was purified by silica-gel chromatography to give 4.95 g (84%) of a 1:1 diastereomer mixture of the title compounds as a pale yellow powdery solid: mp 110-112 °C; ^{1}H NMR *δ* 8.94 (br, 1H, both NH), 7.47 (m, 2H, both), 7.36-7.27 (m, 3H, both), 6.74 (m, 1H, both H^3), 4.45 (m, 1H, one of C*H*S), 4.40 (m, 1H, another C*H*S), 4.30 (m, 2H, both OCH_2), 3.84 (m, 2H, both C*H*Cl), 3.63 (dd, *J* 18.9, 5.3 Hz, 1H, one), 3.52 (d, *J* 17.7 Hz, 1H, another), 3.52 (dt, *J* 17.7, 5.3 Hz, 1H, one), 3.40 (dd, *J* 18.9, 5.3 Hz, 1H, another), 3.34 (dd, *J* 18.9, 5.3 Hz, 1H,one), 3.23 (dd, *J* 18.9, 5.3 Hz, 1H, another), 2.93 (dd, *J* 16.9, 5.3 Hz, 1H, one), 2.84 (dd, *J* 16.9, 5.3 Hz, 1H, another), 1.36 (t, *J* 7.1 Hz, 3H, one), 1.34 (t, *J* 7.1 Hz, 3H, another); ^{13}C NMR (typical signals) *δ* 161.39, 161.33, 133.66, 133.63, 132.27, 132.14, 129.19, 129.18, 127.64, 127.60, 122.66, 121.91, 119.42, 119.25, 118.57, 118.34, 116.85, 116.17, 60.02, 60.00, 57.51, 57.43, 47.94, 47.80, 28.81, 27.31, 25.07, 23.54, 14.49, 14.45; IR ν_{max} (KBr)

3278, 1684, 1429, 1331, 1147 cm^{-1}; MS (FAB^+) *m/z* 336 {$M^+(^{35}Cl)$ + 1}; HRMS calcd for $C_{17}H_{18}{}^{35}ClNO_2S$: 336.0825, found 336.0824. Anal. Calcd for $C_{17}H_{18}ClNO_2S$: C, 60.80; H, 5.40; N, 4.17. Found: C, 61.10; H, 5.67; N, 3.84%.

Ethyl (5*S,6*S**)-5-chloro-6-phenylsulfonyl-4,5,6,7-tetrahydroisoindole-1-carboxylate** (**9a**) and **ethyl (5*S**,6*S**)-6-chloro-5-phenylsulfonyl-4,5,6,7-tetrahydroisoindole-1-carboxylate** (**9b**): To a stirred solution of the mixture of **8a** and **8b** (4.95 g, 14.7 mmol) in dry CH_2Cl_2 (150 mL) was added *m*CPBA (purity *ca*. 70%; 7.05 g, 29.4 mmol) at 0 °C. The mixture was allowed to warm up to room temperature and stirred for 16 h. The resulting suspension was filtered through a Celite pad. The filtrate was washed with a saturated aqueous solution of $NaHCO_3$, water, and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica-gel chromatography to give 5.40 g (99%) of a mixture of the title compounds as a pale yellow solid: mp 80-82 °C; ^1H NMR δ 8.95 (br, 1H, both NH), 7.92 (m, 2H, both), 7.68 (m, 1H, both), 7.58 (m, 2H, both), 6.73 (m, 1H, both H^3), 5.05 (m, 1H, one), 4.94 (m, 1H, another), 4.30 (m, 2H, both), 3.79-3.70 (m, 1H, both), 3.61 (dd, *J* 18.7, 4.5 Hz, 1H, one), 3.50 (dd, *J* 17.1, 4.1 Hz, 1H, one), 3.44 (m, 2H, another), 3.31 (dd, *J* 18.7, 7.2 Hz, 1H, one), 3.21 (dd, *J* 17.9, 6.6 Hz, 1H, another), 3.16 (dd, *J* 17.9, 2.4 Hz, 1H, another), 3.04 (dd, *J* 17.1, 1.5 Hz, 1H, one), 1.35 (t, *J* 7.1 Hz, one), 1.31 (t, *J* 7.1 Hz, another); ^{13}C NMR (typical signals) δ 161.1, 161.0, 138.1, 137.9, 134.4, 134.0, 132.2, 130.0, 129.6, 129.3, 129.2, 128.7, 128.6, 125.6, 121.7, 121.1, 119.5, 118.8, 118.5, 118.0, 116.2, 115.2, 64.1, 64.0, 60.2, 60.1, 52.6, 52.4, 30.9, 30.2, 28.8, 19.5, 18.2, 14.5; IR ν_{max} (KBr) 3313, 1697, 1419, 1319, 1144, 727 cm^{-1}; MS (FAB^+) *m/z* 368 {$M^+(^{35}Cl)$ + 1}; HRMS calcd for $C_{17}H_{18}ClNO_4S$: 368.0723, found 368.0688.

Diethyl 4,8-dihydropyrrol[3,4-*f*]isoindole-1,5-dicarboxylate (*anti*-**4**) and **Diethyl 4,8-dihydropyrrol[3,4-*f*]isoindole-1,7-dicarboxylate** (*syn*-**4**): To a stirred solution of a mixture of **9a** and **9b** (1.12 g, 3.05 mmol) in dry THF (30 mL) was added a 1-M solution of KO^tBu (3.04 mL, 3.04 mmol) at 0 °C. The mixture was allowed to warm up to room temperature and stirred for 4 h. The reaction mixture was quenched with a 1-M solution of HCl and the mixture was extracted with EtOAc. The organic extract was washed with a saturated aqueous solution of $NaHCO_3$, water, and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was dissolved in $CHCl_3$ and passed through a short silica-gel column. The filtrate was concentrated to give 770 mg (76%) of a 5:4 mixture of ethyl 6-phenylsulfonyl-4,7-dihydroisoindole-1-carboxylate {^1H NMR δ 8.94 (br, 1H, NH), 7.91 (m, 2H), 7.59 (m, 1H), 7.54 (m, 3H), 6.72 (d, *J* 2.7 Hz, 1H, H^5), 4.28 (q, *J* 7.1 Hz, 2H, OCH_2), 3.73 (m, 1H), 3.59 (m, 1H), 3.52 (m, 1H), 3.38 (m, 1H), 1.36 (t, *J* 7.1 Hz, 3H)} and ethyl 5-phenylsulfonyl-4,7-dihydroisoindole-1-carboxylate {^1H NMR δ 8.93 (br, 1H, NH), 7.93 (m, 2H), 7.59 (m, 1H), 7.54 (m, 3H), 6.70 (d, *J* 2.6 Hz, 1H, H^6), 4.31 (q, *J* 7.1 Hz, 2H, OCH_2), 3.73 (m, 1H), 3.59 (m, 1H), 3.52 (m, 1H), 3.38 (m, 1H), 1.33 (t, *J* 7.1 Hz, 3H)}; MS (FAB^+) *m/z* 332 (M^+ + 1). This material was used in the next step without further

purification. The isomeric mixture of vinyl sulfones (680 mg, 2.05 mmol) and ethyl isocyanoacetate (0.27 mL, 2.5 mmol) were dissolved in dry THF (20 mL). After the solution was cooled to 0 °C, a 1-M solution of KO^{t}Bu in THF (5.1 mL, 5.1 mmol) was added. The mixture was allowed to warm up to room temperature and stirred for 12 h. The mixture was quenched with a 1-M solution of HCl and extracted with EtOAc. The organic extract was washed with a saturated aqueous solution of $NaHCO_3$, water, and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The solid residue was treated with a small amount of ether and then the triturated powdery solid was subject to the chromatographic purification on silica gel ($CHCl_3$). The analytically pure title compounds were obtained in 24% (150 mg) yield in a ratio of 10:3. Recrystallization of the mixture from acetone/hexane gave 70 mg (11%) of pure *anti*-**4** as a pale brown powdery solid: mp 173 °C (decomp); ^{1}H NMR δ 8.95 (br, 2H, NH), 6.86 (d, *J* 2.7 Hz, 2H, H^3 and H^7), 4.35 (d, *J* 7.2 Hz, 4H, OCH_2), 3.99 (s, 4H, H^4 and H^8), 1.39 (t, *J* 7.2 Hz, 6H, CH_3); IR ν_{max} (KBr) 3294, 1666, 1311, 1151, 1028, 775, 600 cm^{-1}; MS (FAB$^+$) *m/z* 303 (M$^+$ + 1); HRMS calcd for $C_{16}H_{18}N_2O_4$: 303.1345, found 303.1348. *syn*-**4**: ^{1}H NMR δ 8.95 (br, 2H, NH), 6.83 (d, *J* 2.7 Hz, 2H, H^3 and H^7), 4.35 (d, *J* 7.6 Hz, 4H, OCH_2), 4.21 (s, 2H, H^8), 3.75 (s, 2H, H^4), 1.40 (t, *J* 7.6 Hz, 6H, CH_3).

Diethyl 3,7-bis(5'-ethoxycarbonyl-3',4'-diethylpyrrol-2'-yl)-4,8-dihydropyrrol[3,4-*f*]isoindole-1,7-dicarboxylate (**10**): Pyrrolisoindole *anti*-**4** (68 mg, 0.27 mmol) and ethyl 5-acetoxymethyl-3,4-diethylpyrrole-2-carboxylate (143 mg, 0.53 mmol) was dissolved in acetic acid (7 mL) and then *p*-toluenesulfonic acid monohydrate (23 mg, 0.12 mmol) was added. After the mixture was stirred at room temperature for 3 h, the reaction was quenched with water. The mixture was extracted with $CHCl_3$. The organic extract was washed with a saturated aqueous solution of $NaHCO_3$, water, and brine, dried over Na_2SO_4, and concentrated. The residual solid was triturated with a mixture of acetone/hexane (1/10) to give 98 mg (50%) of the title compound as a pale purple solid: ^{1}H NMR δ 8.83 (m, 2H, NH), 8.70 (m, 2H, NH), 4.25-4.33 (m, 12H), 3.96 (m, 4H), 3.83 (m, 4H), 2.75 (q, *J* 6.8 Hz, 4H), 2.45(q, *J* 6.8 Hz, 4H), 1.27-1.40 (m, 12H), 1.85 (m, *J* 6.8 Hz, 6H), 1.09 (m, *J* 7.6 Hz, 6H); IR ν_{max} (KBr) 3294, 1670, 1419, 1311, 1153 cm^{-1}; MS (FAB) *m/z* 717 (M$^+$ + 1).

1,2,8,9-Tetraethyl-4,4,11,11-tetrafluoro-3,5,10,12-tetramethyl-4,11-dibora-3a,4a,10a,11a-tetraaza-6,11-dihydrobenzo[1,2-*a*:4,5-*a'*]di-*s*-indacene (**12**): Bisdipyrromethane tetraester **10** (74 mg, 0.1 mmol) was dissolved in dry THF (10 mL) and cooled at 0 °C under an inert atmosphere. Lithium aluminum hydride (76 mg, 2 mmol) was slowly added and then the mixture was heated under reflux conditions for 3 h. After being cooled to room temperature, the reaction mixture was quenched with an aqueous solution of NaOH. The resulting suspension was filtered through a Celite pad and the filtrate was extracted with EtOAc. The organic extract was washed with water and brine, dried over Na_2SO_4, and concentrated. The residue was passed through a short silica-gel column. The filtrate was concentrated *in vacuo* to leave 33 mg (68%) of a mixture of 3,7-bis(3',4'-diethyl-5'-methylpyrrol-2'-yl)-1,7-dimethyl-4,8-dihydro-

pyrrol[3,4-*f*]isoindole and its mono-dehydrogenated product {**11**: MS (MALDI-TOF) *m/z* 484 (M^+), 482 (M^+-2)}, which was used in the next step without purification. This material was dissolved in dry CH_2Cl_2 (5 mL) and chloranil (35 mg, 0.14 mml) was added with stirring at room temperature. After 1 h, diisopropylethylamine (0.17 mL, 0.97 mmol) and $BF_3 \cdot Et_2O$ (0.13 mL, 1.1 mmol) were added. After 2 h, the mixture was quenched with water. The resulting suspension was filtered through a Celite pad. The filtrate was washed with a saturated aqueous solution of $NaHCO_3$, water, and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed on silica gel (CH_2Cl_2) to give 33 mg (56%, 2 steps) of the title compound as a purple solid: ^{1}H NMR δ 6.99 (m, 2H), 3.66 (m, 4H), 2.60 (m, 4H), 2.57 (s, 6H), 2.53 (s, 6H), 2.41 (m, 4H), 1.19-1.26 (m, 12H); IR ν_{max} (KBr) 2972, 1602, 1408, 1180 cm^{-1}; UV-vis ($CHCl_3$) λ 551 nm; MS (FAB$^+$) *m/z* 576 (M^+); HRMS calcd for $C_{32}H_{38}B_2F_4N_4$: 576.3219, found: 576.3207.

1,2,8,9-Tetraethyl-4,4,11,11-tetrafluoro-3,5,10,12-tetramethyl-4,11-dibora-3a,4a,10a,11a-tetraaza-benzo[1,2-*a*:4,5-*a′*]di-*s*-indacene (**3a**):[6] Dihydro-bisBODIPY **11** (1 mg, 0.002 mmol) was dissolved in dry CH_2Cl_2 (5 mL) and chloranil (0.5 mg, 0.002 mmol) was added and the mixture was stirred for 4 h. The mixture was quenched with a saturated aqueous solution of $NaHCO_3$, washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to leave 1 mg of the title compound as a purple solid: ^{1}H NMR δ 8.15 (s, 2H), 7.27 (s, 2H), 3.03 (s, 6H), 2.65 (q, 4H, *J* 7.6 Hz), 2.52 (s, 6H), 2.43 (q, 4H, *J* 7.6 Hz), 1.25 (t, 6H, *J* 7.6 Hz), 1.12 (t, 6H, *J* 7.6 Hz); UV-vis ($CHCl_3$) λ 758 ($\varepsilon = 1.90 \times 10^5$ $M^{-1} \cdot cm^{-1}$) nm.

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REFERENCES

1. L. Luan, L. Ding, W. Zhang, J. Shi, X. Yu, and W. Liu, *Bioorg. Med. Chem. Lett.*, 2013, **23**, 3775.
2. T. Funayama, M. Sakane, T. Abe, and N. Ochiai, *Photomed. Laser Surg.*, 2012, **30**, 47; Y. Yang, Q. Guo, H. Chen, Z. Zhou, Z. Guo, and Z. Shen, *Chem. Commun.*, 2013, **49**, 3940; J. Tian, L. Ding, H.-J. Xu, Z. Shen, H. Ju, L. Jia, L. Bao, and J.-S. Yu, *J. Am. Chem. Soc.*, 2013, **135**, 18850.
3. P. Sarder, S. Yazdanfar, W. J. Akers, R. Tang, G. P. Sudlow, C. Egbulefu, and S. Achilefu, *J. Biomed. Opt.,* 2013, **18**, 106012.
4. L. Yao, S. Zhang, R. Wang, W. Li, F. Shen, B. Yang, and Y. Ma, *Angew. Chem. Int. Ed.*, 2014, **53**, 2119.
5. H. Uno, ‘Methods and Applications of Cycloaddition Reactions in Organic Syntheses,’ ed. by N.

Nishiwaki, "Cycloreversion Approach For Preparation of Large π-Conjugated Compounds" John Wiley & Sons Inc., Chap 15, 429–470, 2014.

6. M. Nakamura, M. Kitatsuka, K. Takahashi, T. Nagata, S. Mori, D. Kuzuhara, T. Okujima, H. Yamada, T. Nakae, and H. Uno, *Org. Biomol. Chem.*, 2014, **12**, 1309; M. Nakamura, H. Tahara, K. Takahashi, T. Nagata, H. Uoyama, D. Kuzuhara, S. Mori, T. Okujima, H. Yamada, and H. Uno, *Org. Biomol. Chem.*, 2012, **10**, 6840.
7. H. Uno, S. Ito, M. Wada, H. Watanabe, M. Nagai, A. Hayashi, T. Murashima, and N. Ono, *J. Chem. Soc., Perkin Trans. 1*, 2000, 4347.
8. P. S. Clezy, C. J. R. Fookes, and A. H. Mirza, *Aust. J. Chem.*, 1977, **30**, 1337.
9. M. A. Filatov, A. V. Cheprakov, and I. P. Beletskaya, *Eur. J. Org. Chem.*, 2007, 3468.
10. T. Okujima, G. Jin, Y. Hashimoto, H. Yamada, H. Uno, and N. Ono, *Heterocycles*, 2006, **70**, 619.
11. H. Uno, M. Nakamura, and K. Takahashi, *Jpn. Kokai Tokkyo Koho*, JP 2013177551, A 20130909 (2013); V. V. Roznyatovskiy, R. Carmieli, S. M. Dyar, K. E. Brown, and M. R. Wasielewski, *Angew. Chem. Int. Ed.*, 2014, **53**, 3457.