SYNTHESIS OF 2,4-DIHYDROPYRROLO[3,4-*b*]PYRROLES AND 4,6-DIHYDRO-2*H*-DIPYRROLO [3,4-*b*:3',4'-*d*]PYRROLES

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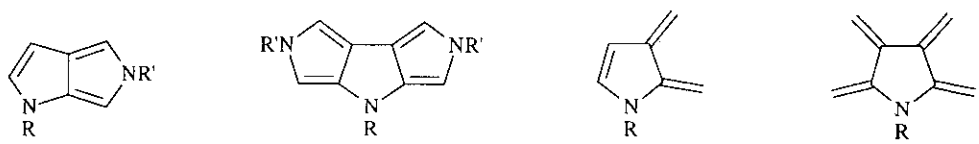
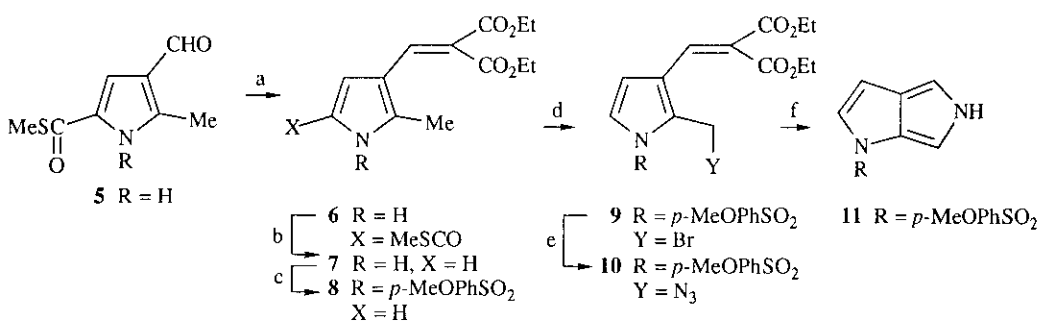
Abstract - The labile heterocyclic ring systems, 2,4-dihydropyrrolo[3,4-*b*]pyrrole **1** and 4,6-dihydro-2*H*-dipyrrolo[3,4-*b*:3',4'-*d*]pyrrole **2**, were prepared readily by the phosphineimine-alkylidenemalonate cyclization reaction or the retro-malonate addition reaction. An *X*-ray structure analysis confirmed that three pyrrole rings of **2** are coplanar.

2,4-Dihydropyrrolo[3,4-*b*]pyrrole and 4,6-dihydro-2*H*-dipyrrolo[3,4-*b*:3',4'-*d*]pyrrole[1] ring systems are cyclic analogues of the interesting radialenes **3** and **4** respectively.[2] According to theoretical calculations, **1** and **2** are highly unstable heteroaromatic ring systems.[3] To date ring system **1** is still unknown. Herein we report the facile syntheses of **1** and **2** based on our new methods, the phosphineimine-alkylidenemalonate cyclization,[4] or the retro-malonate addition reaction.[5]



1 **2** **3** **4**

Starting from the known aldehyde **5**,[6] we synthesized 2,4-dihydropyrrolo[3,4-*b*]pyrroles **11-14** with the 4-position protected with a *p*-methoxyphenylsulfonyl group. Knoevenagel condensation of **5** with diethyl malonate gave **6**. Reductive cleavage of the thioester group of **6** with Raney nickel afforded **7**. Treatment of **7** with potassium hydride followed by *p*-methoxybenzenesulfonyl chloride gave the *N*-protected pyrrole **8**. Bromination of **8** with *N*-bromosuccinimide and dibenzoyl peroxide gave bromide **9**. Reaction of bromide **9** with sodium azide in aqueous THF gave the azido compound **10**. Treatment of **10** with triphenylphosphine followed by hydrolysis afforded the pyrrolo[3,4-*b*]pyrrole **11**, Scheme 1. Attempted removal of the *p*-methoxyphenylsulfonyl protecting group led to the decomposition of the product. Apparently the parent system of 2,4-dihydropyrrolo[3,4-*b*]pyrrole is too labile to isolate.



5 R = H

b: **6** R = H, X = MeSCO
c: **7** R = H, X = H; **8** R = *p*-MeOPhSO$_2$, X = H

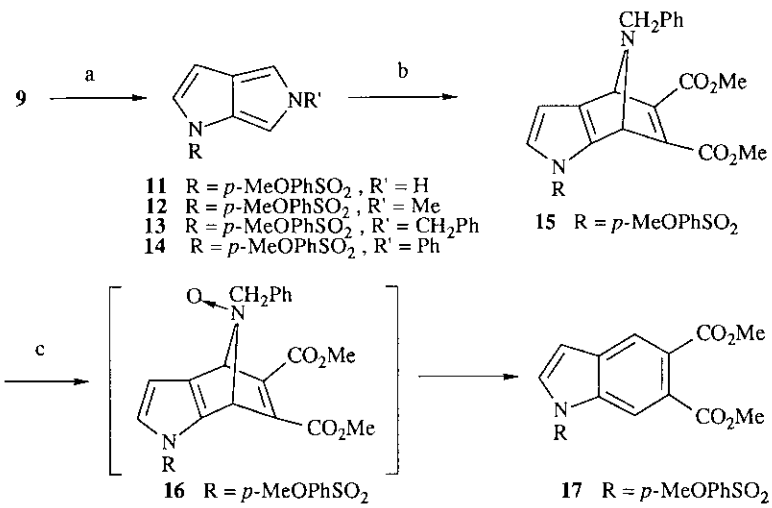
e: **9** R = *p*-MeOPhSO$_2$, Y = Br; **10** R = *p*-MeOPhSO$_2$, Y = N$_3$

11 R = *p*-MeOPhSO$_2$

a. $CH_2(CO_2Et)_2$, piperidine, benzene, reflux, 32 h, 90%. b. Raney nickel, acetone, reflux, 30 min, 77%. c. i) KH / THF, -78°C, 30 min; ii) *p*-MeOPhSO$_2$Cl, -78°C→0°C, 87%. d. NBS, dibenzoyl peroxide, CCl_4, reflux, 30 min, 72%. e. NaN_3, THF / H_2O (1 : 1), 25°C, 12 h, 98%. f. i) Ph_3P, THF, 25°C, 12 h; ii) H_2O, 25°C, 12 h, 48%.

Scheme 1

On the other hand, reactions of bromide **9** directly with ammonia, methylamine, benzylamine, or aniline produced the pyrrolo[3,4-*b*]pyrroles **11-14** in good yields. Furthermore, compound **13** was selected to react with dimethyl acetylenedicarboxylate in a Diels-Alder reaction to give the cycloadduct **15**. *m*-Chloroperbenzoic acid oxidation[7] of **15** followed by thermolysis afforded indole **17**[8] via the *N*-oxide **16**, Scheme 2.



11 R = *p*-MeOPhSO$_2$, R' = H
12 R = *p*-MeOPhSO$_2$, R' = Me
13 R = *p*-MeOPhSO$_2$, R' = CH_2Ph
14 R = *p*-MeOPhSO$_2$, R' = Ph

15 R = *p*-MeOPhSO$_2$

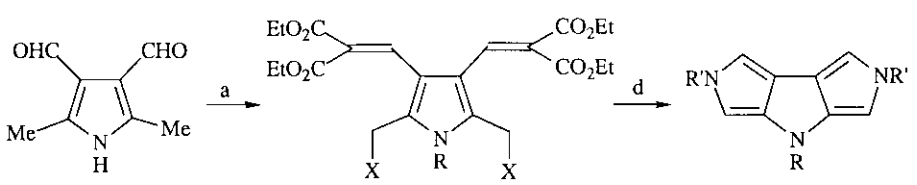
16 R = *p*-MeOPhSO$_2$

17 R = *p*-MeOPhSO$_2$

a. 25% NH_3, absolute ethanol, 25°C, 20 h, **11** (33%); 40% CH_3NH_2, absolute ethanol, 25°C, 30 h, **12** (47%); benzylamine, 95% ethanol, 25°C, 24 h, **13** (50%); aniline, 95% ethanol, 25°C, 48 h,**14** (61%).
b. dimethyl acetylenedicarboxylate, benzene, 25°C, 4 h, 84%. c. MCPBA, CH_2Cl_2, 25°C, 1 h, 63%.

Scheme 2

Similarly dipyrrolo[3,4-*b*:3',4'-*d*]pyrroles **22** and **23** were synthesized starting from the known dialdehyde **18.**[9] Double Knoevenagel condensations of **18** with diethyl malonate gave **19**. Treatment of **19** with potassium hydride followed by benzenesulfonyl chloride gave **20.** Bromination of **20** with *N*-bromosuccinimde and dibenzoyl peroxide gave dibromide **21.** Treatment of **21** with ammonia in ethanol produced 4,6-dihydro-2*H*-dipyrrolo[3,4-*b*:3',4'-*d*]pyrrole **22.** Reaction of **21** with benzylamine afforded 4,6-dihydro-2*H*-dipyrrolo[3,4-*b*:3',4'-*d*]pyrrole **23**, Scheme 3.



18

b **19** R = H , X = H
20 R = $PhSO_2$, X = H
c **21** R = $PhSO_2$, X = Br

22 R = $PhSO_2$, R' = H
23 R = $PhSO_2$, R' = CH_2Ph

a. $CH_2(CO_2Et)_2$, piperidine, benzene, reflux, 48 h, 70%. b. i) KH / THF, -78°C, 30 min; ii) $PhSO_2Cl$, -78°C→O°C, 86%. c. NBS, dibenzoyl peroxide, CCl_4, reflux, 2 h, 85%. d. 25% NH_3, absolute ethanol, 25°C, 20 h, **22** (35%); benzylamine, 95% ethanol, 35°C, 18 h, **23** (34%).

Scheme 3

Compound **23** is a white crystalline solid, mp 212 - 213°C dec. A single-crystal *X*-ray analysis was performed to analyze the structure in detail. Three fused pyrrole rings of 4,6-dihydro-2*H*-dipyrrolo[3,4-*b*:3',4'-*d*]pyrrole **23** were found in a plane. A

molecular drawing of **23** is shown in Figure 1. Atomic coordinates and equivalent isotropic displacement parameters are given in Table 1.

In summary, 2,4-dihydropyrrolo[3,4-*b*]pyrroles **11-14** and 4,6-dihydro-2*H*-dipyrrolo[3,4-*b*:3',4'-*d*]pyrroles **22-23** were synthesized readily by our phosphineimine-alkylidenemalonate cyclization reaction or the retro-malonate addition reaction. From a single-crystal *X*-ray analysis of compound **23**, three fused pyrrole rings were found to be coplanar. In addition a new synthesis of indole **17** was achieved by the Diels-Alder reaction of **13** with dimethyl acetylenedicarboxylate followed by oxidative extrusion of the imine nitrogen.

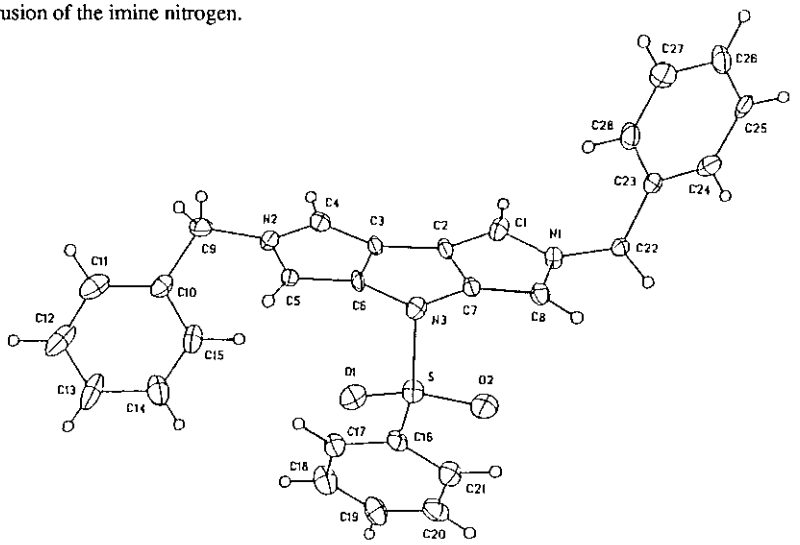


Figure 1: Molecular drawing of **23** generated by SHELXTL PLUS.

Table 1. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameter (Å x 10^3)

Atom	X	Y	Z	U (eq)	Atom	X	Y	Z	U (eq)
S	2318 (4)	4586	5627 (1)	41 (1)	C23	-3667 (14)	1648 (7)	6978 (4)	40 (3)
O1	4348 (10)	4856 (5)	5533 (3)	53 (2)	C28	-1811 (17)	1449 (8)	7224 (4)	58 (4)
O2	1133 (11)	4887 (5)	6139 (3)	55 (2)	C27	-1605 (17)	946 (8)	7729 (5)	68 (4)
N1	-2118 (11)	2429 (6)	6098 (3)	44 (2)	C26	-3268 (20)	623 (7)	8020 (5)	65 (4)
N2	5315 (12)	2392 (6)	4611 (3)	46 (2)	C25	-5160 (21)	817 (7)	7792 (5)	66 (4)
N3	2427 (12)	3569 (5)	5723 (3)	42 (2)	C24	-5328 (17)	1317 (8)	7276 (5)	60 (4)
C16	950 (13)	4742 (5)	4929 (4)	41 (3)	C6	3478 (14)	3082 (6)	5259 (3)	37 (3)
C21	-1038 (16)	4972 (7)	4963 (5)	53 (4)	C3	2436 (14)	2347 (6)	5126 (3)	37 (2)
C20	-2080 (17)	5098 (7)	4403 (6)	65 (4)	C4	3629 (14)	1931 (6)	4719 (4)	45 (3)
C19	-1100 (21)	4979 (8)	3850 (6)	69 (4)	C5	5278 (13)	3110 (6)	4942 (4)	37 (3)
C18	897 (20)	4753 (7)	3812 (5)	68 (4)	C9	6888 (15)	2180 (6)	4169 (5)	53 (3)
C17	1948 (14)	4650 (7)	4360 (4)	50 (3)	C10	6981 (16)	2708 (7)	3595 (4)	51 (3)
C2	615 (13)	2357 (6)	5512 (4)	41 (3)	C11	8741 (20)	2781 (8)	3276 (6)	74 (4)
C7	590 (13)	3103 (6)	5846 (3)	36 (3)	C12	8790 (27)	3241 (10)	2738 (6)	96 (6)
C1	-1107 (16)	1924 (7)	5691 (4)	51 (3)	C13	7102 (27)	3636 (10)	2515 (5)	99 (6)
C8	-1089 (14)	3162 (6)	6209 (3)	41 (3)	C14	5351 (24)	3566 (8)	2840 (5)	82 (5)
C22	4001 (13)	2194 (6)	6423 (4)	47 (3)	C15	5244 (20)	3104 (7)	3377 (4)	66 (4)

* Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor

EXPERIMENTAL

General : Melting points were determined with a Yanaco micro melting point apparatus. ^{1}H Nmr spectra were recorded on a Varian EM-390, JEOL HX-100 or Bruker AM-400 spectrometer. ^{13}C Nmr spectra were recorded on a JEOL HX-100 or Bruker AM-400 spectromether. Mass spectra refer to the electron impact mass spectra and were recorded on a JEOL TMS-D-100 mass spectrometer. High resolution mass spectra were taken on a JEOL HX-110 mass spectrometer. Ir spectra were recorded on a Perkin-Elmer 781 spectrophotometer, and uv spectra were recorded on a Perkin-Elmer Lambda 5 UV-VIS spectrophotometer. Solvents were distilled before use and were dried, as necessary, according to literature procedures. All reactions were conducted under a nitrogen atmosphere.

X-Ray analysis **23**, $C_{28}H_{23}N_3O_2S$: M = 465.6, orthorhombic, space group $Pc2_1b$, a = 6.589(2), b = 16.218 (4), c = 21.480 (6) Å, V = 2295 (1)Å^3, Z = 4, D_c = 1.347 g/cm^3. 2151 Independent reflections were measured of which 1104 were considered observed [(I)>2.5 σ(I)]. The structure was solved by direct methods to an R value of 0.0413. All calculations were performed on a Micro Vax II based Nicolet SHELXTL PLUS system.

Diethyl [(2-Carbothiomethoxy-5-methyl-4-pyrrolyl)methylene]propanedioate **6**

To a solution of methyl 2-methyl-3-formylpyrrole-5-thiocarboxylate **5**[6] (0.1 g, 0.55 mmol) in dry benzene (30 ml) were added diethyl malonate (0.13 g, 0.81 mmol) and piperidine (0.1 ml). The mixture was heated to reflux for 32 h with separation of water by a Dean-Stark apparatus. The solvent was then removed on a rotary evaporator . The residue was chromatographed on silica gel (hexane-ethyl acetate; 6:1) to give the title product **6** (159.8 mg, 90%). Recrystallization (ethyl acetate-hexane) gave **6** as pale yellow crystals: mp 157-158°C; ir (KBr) 3290, 1730, 1700, 1620 cm^{-1}; ^{1}H nmr (90 MHz, $CDCl_3$) δ 1.20-1.53 (q, J = 7 Hz, 6 H), 2.43 (broad s, 6 H), 2.43 (broad s, 6H), 4.13-4.60 (m, 4 H), 7.03 (broad d, 1 H), 7.63 (s, 1 H), 9.83 (broad s, 1H); ms *m/z* (relative intensity) 325 (M$^+$, 16), 279 (26), 278 (26), 183 (68), 136 (100); hrms *m/z* 325.0989 (calcd for $C_{15}H_{19}NO_5S$: 325.0984). Anal. Calcd for $C_{15}H_{19}NO_5S$: C, 55.37; H, 5.89; N, 4.30. Found: C, 55.33; H, 5.89; N, 4.29.

Diethyl [(2-Methyl-3-pyrroloyl)methylene]propanedioate **7**

W-2 Raney nickel (4 g) was added to acetone (30 ml) and stirred at room temperature for 15 min. A solution of the thioester **6** (495 mg, 1.52 mmol) in acetone (20 ml) was added, and the mixture was refluxed for 30 min. The reaction mixture was then cooled and filtered through a short pad of Celite. The filtrate was concentrated and the residue was purified by silica gel chromatography (hexane-ethyl acetate; 1:1) to give the product **7** (293 mg, 77%). Recrystallization (ethyl acetate-hexane) gave **1** as white crystals: mp 130-132°C; ir (KBr) 3300, 1725, 1660, 1605 cm^{-1}; ^{1}H nmr (90 MHz, $CDCl_3$) δ 1.17-1.47 (m, 6 H), 2.33 (s, 3 H), 4.10-4.53 (m, 4 H), 6.23 (deformed triplet, 1 H), 6.58 (deformed triplet, 1 H), 7.68 (s, 1 H), 8.57 (broad s, 1 H); ms *m/z* (relative intensity) 251 (M$^+$, 57), 205 (100); hrms *m/z* 251.1164 (calcd for $C_{13}H_{17}NO_4$: 251.1158). Anal. Calcd for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82; N, 5.57. Found: C, 62.05; H, 6.81; N, 5.54.

Diethyl {[1-(*p*-Methoxyphenylsulfonyl)-2-methyl-3-pyrrolyl]methylene}propanedioate **8**

To a suspension of potassium hydride (10.25 mg, 0.26 mmol) in dry THF (3 ml) was added dropwise a solution of compound **7** (40 mg, 0.095 mmol) in dry THF (3 ml) at -78°C. The reaction mixture was stirred at -78°C for 30 min. A solution of *p*-methoxybenzenesulfonyl chloride (43.9 mg, 0.21 mmol) in dry THF (3 ml) was then added dropwise. The reaction mixture was warmed up to room temperature and water (10 ml) was immediately added for quenching with external cooling. The aqueous solution was extracted with dichloromethane (20 ml × 3). The organic layer was dried over $MgSO_4$ and concentrated. Silica gel chromatography (hexane-ethyl acetate, 6:1) gave compound **8** as a colorless oil (58 mg, 87%); ir (neat) 1725, 1630, 1595 cm^{-1}; ^{1}H nmr (90 MHz, CCl_4) δ 1.13-1.43 (m, 6 H), 2.40 (s, 3 H), 3.80 (s, 3 H), 4.03-4.50 (m, 4 H), 6.27 (d, J = 3 Hz, 1 H), 6.83, 6.93 (d, J = 9 Hz, 2 H), 7.17 (d, J = 3 Hz, 1 H), 7.37 (s, 1 H), 7.67 (d, J = 9 Hz, 2 H); ms *m/z* (relative intensity) 421 (M$^+$, 56), 375 (84), 204 (59), 171 (100); hrms *m/z* 421.1224 (calcd for $C_{20}H_{23}NO_7S$: 421.1195).

Diethyl {[1-(*p*-Methoxyphenylsulfonyl)-2-bromomethyl-3-pyrrolyl]methylene}propanedioate **9**

To a mixture of compound **8** (68.7 mg, 0.16 mmol) and *N*-bromosuccinimide (35 mg, 0.20 mmol) in carbon tetrachloride (40 ml) was added dibenzoyl peroxide (10 mg). The reaction mixture was heated to reflux for 30 min, then was diluted with dichloromethane (20 ml), and washed with water (2 × 15 ml) and brine (20 ml). The aqueous layer was extracted with dichloromethane (2 × 20 ml). The combined organic layers were dried over $MgSO_4$ and concentrated. Silica gel chromatography (hexane-ethyl acetate, 12:1) gave compound **9** (58.7 mg, 72%). Recrystallization (ethyl acetate-hexane) gave **9** as white needles: mp 143-145°C; ir (KBr) 1730, 1717, 1630, 1595 cm^{-1}; ^1H nmr (100 MHz, $CDCl_3$) δ 1.23-1.56 (m, 6 H), 3.87 (s, 3 H), 4.16-4.53 (m, 4H) , 4.90 (s, 2 H), 6.37 (d, J = 3.7 Hz, 1 H), 6.99 (d, J = 9 Hz, 2 H), 7.33 (d, J = 3.7 Hz, 1 H), 7.57 (s, 1 H), 7.88 (d, J = 9 Hz, 2 H); ^{13}C nmr (400 MHz, $CDCl_3$) 13.98 (q), 14.09 (q), 19.19 (t), 55.82 (q), 61.62 (t), 61.76 (t), 110.29 (d), 114.79 (d), 122.50 (s), 124.74 (d), 125.28 (d), 129.13 (s), 130.17 (d), 131.06 (s), 132.26 (s), 164.07 (s), 164.50 (s), 166.64 (s); ms *m/z* (relative intensity) 499 (M^+, 10), 501 (M+2, 10), 420 (100); hrms *m/z* 499.0302. (calcd for $C_{20}H_{22}NO_7SBr$: 499.0301). Anal. Calcd for $C_{20}H_{22}NO_7SBr$: C, 48.01; H, 4.43; N, 2.80. Found: C, 47.96; H, 4.45; N, 2.80.

Diethyl {[1-(*p*-Methoxyphenylsulfonyl)-2-azidomethyl-3-pyrrolyl]methylene}propanedioate **10**

To a solution of compound **9** (95.7 mg, 0.19 mmol) in THF (15 ml) was added a solution of sodium azide (62 mg, 0.95 mmol) in H_2O (15 ml). The reaction mixture was stirred in dark at room temperature for 12 h, then was extracted with ether (2 × 30 ml). The combined ether layers were dried over $MgSO_4$ and concentrated. Silica gel chromatography (hexane-ethyl acetate 6:1) gave oil compound **10** (87 mg, 98%); ir ($CHCl_3$) 2120, 1730, 1630, 1600 cm^{-1}; ^1H nmr (100 MHz, $CDCl_3$) δ 1.25-1.40 (m, 6 H), 3.87 (s, 3 H), 4.23-4.53 (m, 4 H), 4.70 (s, 2 H), 6.39 (d, J = 3 Hz, 1 H), 6.99 (d, J = 9 Hz, 2 H), 7.35 (d, J = 3 Hz, 1 H), 7.53 (s, 1 H), 7.84 (d, J = 9 Hz, 2 H); ms *m/z* (relative intensity) 434 (M^+ - 28, 19), 361 (28), 276 (66), 186 (72), 167 (100).

1-(*p*-Methoxyphenylsulfonyl)-1,5-dihydropyrrolo[3,4-*b*]pyrrole **11**

Method A: To a solution of compound **10** (87 mg, 0.32 mmol) in THF (10 ml) was added triphenylphosphine (100 mg, 0.38 mmol) in dry THF (15 ml). The reaction mixture was stirred at room temperature for 12 h. Thin layer chromatography (hexane-ethyl acetate, 2:1) indicated that no starting material left. Excess water (3 ml) was then added to the reaction mixture. The mixture was stirred for additional 12 h at room temperature, then extracted with ether (3 × 20 ml). The combined ether layers were dried over $MgSO_4$ and concentrated. Silica gel chromatography (hexane-ethyl acetate, 4:1) gave a solid compound **11** (25 mg, 48%). Method B: To a solution of compound **10** (36 mg, 0.072 mmol) in absolute ethanol (10 ml) was added 25% ammonia solution (2ml, 26 mmol). The reaction mixture was stirred at room temperature in dark for 20 h, then was concentrated by a rotary evaporator. Silica gel chromatography (hexane-ethyl acetate, 4:1) gave a solid compound **11** (7.02 mg, 32.6%); ir ($CHCl_3$) 3470, 1600, 1580, 1500 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ 3.77 (s, 3 H), 6.30 (d, J = 3.6 Hz, 1 H), 6.56 (deformed triplet, 1 H), 6.84 (d, J = 8.8 Hz, 2 H), 6.87 (broad s, 1 H), 7.03 (d, J = 3.6 Hz, 1 H), 7.76 (d, J = 8.8 Hz, 2 H), 8.42 (broad s, 1 H); ms *m/z* (relative intensity) 276 (M^+, 100), 171 (9), 105 (45); hrms *m/z* 276.0562 (calcd for $C_{13}H_{12}N_2O_3S$: 276.0569).

1-(*p*-Methoxyphenylsulfonyl)-5-methyl-1,5-dihydropyrrolo[3,4-*b*]pyrrole **12**

To a solution of compound **9** (41 mg, 0.082 mmol) in absolute ethanol (10 ml) was added 40% methylamine (2ml, 23 mmol). The reaction mixture was stirred at room temperature in dark for 30 h, then was concentrated by a rotary evaporator. Silica gel chromatography (hexane-ethyl acetate, 4:1) gave a solid compound **12** (11 mg, 47%); ir ($CHCl_3$) 1595, 1575, 1495 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ 3.76 (s, 3 H), 3.80 (s, 3 H), 6.25, 6.26 (d, J = 3.6 Hz, 1 H), 6.39 (d, J = 1.6 Hz, 1 H), 6.72 (d, J = 1.6 Hz, 1 H), 6.86 (d, J = 8.8 Hz, 2 H), 6.98 (d, J = 3.6 Hz, 1 H), 7.77 (d, J = 8.8 Hz, 2 H); ms *m/z* (relative intensity) 290 (M^+, 100), 278 (46), 171 (19), 119 (27); hrms *m/z* 290.0721 (calcd for $C_{14}H_{14}N_2O_3S$: 290.0725).

1-(*p*-Methoxyphenylsulfonyl)-5-benzyl-1,5-dihydropyrrolo[3,4-*b*]pyrrole **13**

To a solution of compound **9** (40.4 mg, 0.11 mmol) in 95% ethanol (8 ml) was added benzylamine (98 mg, 0.92 mmol). The reaction mixture was stirred at room temperature in dark for 24 h, then was concentrated by a rotary evaporator. Silica gel chromatography (hexane-ethyl acetate, 4:1) gave compound **13** (14.9 mg, 50%). Recrystallization (ethyl acetate-hexane) gave **13** as white crystals: mp 128-129°C; ir ($CHCl_3$) 1590, 1585 cm^{-1}; ^1H nmr (100 MHz, $CDCl_3$) δ 3.79 (s, 3 H), 5.12 (s, 2 H), 6.24 (d, J = 3 Hz, 1 H), 6.46 (d, J = 2 Hz, 1 H), 6.78-7.33 (m, 9 H), 7.73 (d, J = 9 Hz, 2 H); ms *m/z* (relative

intensity) 366 (M^+, 100), 195 (13); hrms *m/z* 366.1039 (calcd for $C_{20}H_{18}N_2O_3S$: 366.1038).

1-(*p*-Methoxyphenylsulfonyl)-5-phenyl-1,5-dihydropyrrolo[3,4-*b*]pyrrole **14**

To a solution of compound **9** (38 mg, 0.076 mmol) in 95% ethanol (10 ml) was added aniline (21 mg, 0.23 mmol). The reaction mixture was stirred at room temperature in dark for 48 h, then was concentrated by a rotary evaporator. Silica gel chromatography (hexane-ethyl acetate, 4:1) gave compound **14** (15.6 mg, 61%). Recrystallization (ethyl acetate-hexane) gave **14** as pale yellow crystals: mp 127-128°C; ir ($CHCl_3$) 1595, 1585, 1500 cm^{-1}; ^1H nmr (90 MHz, $CDCl_3$) δ 3.73 (s, 3 H), 6.24 (d, J = 3 Hz, 1 H), 6.75-6.90 (m, 3 H), 6.98 (d, J = 3 Hz, 1 H), 7.10-7.50 (m, 6 H), 7.75 (d, J = 9 Hz, 2 H); ms *m/z* (relative intensity) 352 (M^+, 100), 181 (27); hrms *m/z* 352.0898 (calcd for $C_{19}H_{16}N_2O_3S$: 352.0882). Anal. Calcd for $C_{19}H_{16}N_2O_3S$: C, 64.76; H, 4.58; N, 7.95. Found: C, 64.33; H, 4.61; N, 7.78.

Dimethyl 1-(*p*-Methoxyphenylsulfonyl)-4,7-dihydro-8-benzylindole-4,7-imine-5,6-dicarboxylate **15**

Compound **13** (8.9 mg, 0.024 mmol), dimethyl acetylenedicarboxylate (4.1 mg, 0.028 mmol) and benzene (2 ml) were stirred at room temperature for 4 h. The solvent was evaporated and the residue was separated by silica gel chromatography (hexane-ethyl acetate, 4:1) to give compound **15** as a colorless oil (10.9 mg, 84%); ir ($CHCl_3$) 1720, 1660, 1590 cm^{-1}; ^1H nmr (100 MHz, $CDCl_3$) δ 3.58 (s, 2 H), 3.67 (s, 3 H), 3.70 (s, 3 H), 3.79 (s, 3 H), 4.68 (d, J = 1.5 Hz, 1 H), 4.99 (broad s, 1 H), 6.21 (d, J = 2.9 Hz, 1 H), 6.75 (d, J = 2.9 Hz, 1 H), 6.87 (d, J = 9.1 Hz, 2 H), 7.03-7.30 (m, 5 H), 7.73 (d, J = 9.1 Hz, 2 H); ms *m/z* (relative intensity) 508 (M^+, 2), 366 (100), 195 (28), 111 (94); hrms *m/z* 508.1306 (calcd for $C_{26}H_{24}N_2O_7S$: 508.1304).

Dimethyl 1-(*p*-Methoxyphenylsulfonyl)indole-5,6-dicarboxylate **17**

To a solution of compound **15** (10.9 mg, 0.025 mmol) in dichloromethane (2 ml) was added a solution of MCPBA (5 mg, 0.029 mmol) in dichloromethane (2 ml). The reaction mixture was stirred at room temperature for 1 h, then was washed with 5% aqueous Na_2CO_3 (2 ml × 2). The organic layer was dried over $MgSO_4$ and concentrated. Silica gel chromatography (hexane-ethyl acetate, 4:1) gave compound **17** as a colorless oil (5.3 mg, 63%); ir ($CHCl_3$) 1725, 1590, 1585, 1500 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ 3.78 (s, 3 H), 3.88 (s, 3 H), 3.93 (s, 3 H), 6.70 (d, J = 3.6 Hz, 1 H), 6.88 (d, J = 8.8 Hz, 2 H), 7.69 (d, J = 3.6 Hz, 1 H), 7.81 (d, J = 8.8 Hz, 2 H), 7.88 (s, 1 H), 8.35 (s, 1 H); ms *m/z* (relative intensity) 403 (M^+, 100), 201 (26), 171 (22); hrms *m/z* 403.0719 (calcd for $C_{19}H_{17}NO_7S$: 403.0726).

Tetraethyl [(2,5-Dimethyl-3,4-pyrrolediyl)dimethylene]bis(propanedioate) **19**

To a solutuon of 3,4-diformyl-2,5-dimethylpyrrole **18**[9] (0.82 g, 5.4 mmol) in dry benzene (80 ml) were added diethyl malonate (1.9 g, 11.9 mmol) and piperidine (0.5 ml). The mixture was heated to reflux for 48 h with separation of water by a Dean-Stark apparatus. Benzene was then removed by a rotary evaporator. The residue was chromatographed on silica gel (hexane-ethyl acetate; 6:1) to give compound **19** (1.65 g, 70%). Recrystallization (ethyl acetate-hexane) gave **19** as yellow crystals: mp 95-97°C; ir ($CHCl_3$) 3440, 1710, 1610 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ 1.22 (t, J = 7.2 Hz, 6 H), 1.29 (t, J = 7.2 Hz, 6 H), 2.09 (s, 6 H), 4.16 (q, J = 7.2 Hz, 4 H), 4.23 (q, J = 7.2 Hz, 4 H), 7.60 (s, 2 H), 8.43 (s, 1 H); ms *m/z* (relative intensity) 435 (M^+, 100), 389 (46), 343 (62); hrms *m/z* 435.1894 (calcd for $C_{22}H_{29}NO_8$: 435.1893).

Tetraethyl [(1-Phenylsulfonyl-2,5-dimethyl-3,4-pyrrolediyl)dimethylene]bis(propanedioate) **20**

To a suspension of potassium hydride (0.127 g, 3.18 mmol) in dry THF (20 ml) was added dropwise a solution of compound **19** (0.59 g, 1.59 mmol) in dry THF (10 ml) at -78°C. The reaction mixture was stirred at -78°C for 30 min. A solution of benzenesulfonyl chloride (0.34 g, 1.91 mmol) in dry THF (5 ml) was then added dropwise. The reaction mixture was warmed up to room temperature and immediately, added water (10 ml) for quenching with external cooling. The aqueous solution was extracted with dichloromethane (30 ml × 3). The organic layer was dried over $MgSO_4$ and concentrated. Silica gel chromatography (hexane-ethyl acetate; 6:1) gave compound **20** as a colorless oil (0.786 g, 86%); ir ($CHCl_3$) 1720, 1630 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ 1.13 (t, J = 7.2 Hz, 6 H), 1.28 (t, J = 7.2 Hz, 6 H), 2.29 (s, 6 H), 4.09 (q, J = 7.2 Hz, 4 H), 4.23 (q, J = 7.2 Hz, 4 H), 7.44 (s, 2 H), 7.49-7.53 (m, 2 H), 7.58-7.64 (m, 3 H); ms *m/z* (relative intensity) 575 (M^+, 95), 529 (38), 483 (19), 434 (57), 388 (100), 342 (67); hrms *m/z* 575.1833 (calcd for $C_{28}H_{33}NO_{10}S$: 575.1826).

Tetraethyl [(1-Phenylsulfonyl-2,5-dibromomethyl-3,4-pyrrolediyl)dimethylene]bis(propanedioate) **21**

To a mixture of compound **20** (0.53 g, 0.92 mmol) and *N*-bromosuccinimide (0.36 g, 2.02 mmol) in carbon tetrachloride (40 ml) was added dibenzoyl peroxide (50 mg). The reaction mixture was heated to reflux for 2 h, then was diluted with

dichloromethane (20 ml), and washed water (2 × 20 ml) and brine (30 ml). The aqueous layers were extracted with dichloromethane (3 × 30 ml). The combined organic layers were dried over $MgSO_4$ and concentrated. Silica gel chromatography (hexane-ethyl acetate, 4:1) gave a soild compound **21** (0.57 g, 85%); ir ($CHCl_3$), 1730 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ 1.14 (t, J = 6.8 Hz, 6 H), 1.30 (t, J = 6.8 Hz, 6 H), 4.12 (q, J = 6.8 Hz, 4 H), 4.28 (q, J = 6.8 Hz, 4 H), 4.74 (s, 4 H), 7.44 (s, 2 H), 7.53-7.57 (m, 2 H), 7.64-7.68 (m, 1 H), 7.91-7.93 (m, 2 H); ms *m/z* (relative intensity) 731 (M^+, 0.8), 733 (M+2, 0.8), 652 (11), 654 (11), 572 (89), 432 (100).

4-Phenylsulfonyl-4,6-dihydro-2*H*-dipyrrolo[3,4-*b*;3',4'-*d*]pyrrole **22**

To a solution of compound **21** (93.2 mg, 0.127 mmol) in absolute ethanol (10 ml) was added 25% ammonia solution (2ml, 26 mmol). The reaction mixture was stirred at room temperature in dark for 20 h, then was concentrated by a rotary evaporator. Silica gel chromatography (hexane-ethyl acetate; 4:1) gave a soild compound **22** (12.7 mg, 35%); ir ($CHCl_3$) 3470, 1580, 1500 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ 6.60 (t, J = 2.1 Hz, 2 H), 6.92 (t, J = 2.3 Hz, 2 H), 7.22-7.31 (m, 2 H), 7.43 (t, J = 7.2 Hz, 1 H), 7.76 (d, J = 7.6 Hz, 2 H), 8.00 (broad s, 2 H); ms *m/z* (relative intensity) 285 (M^+, 11), 157 (100); hrms *m/z* 285.0583 (calcd for $C_{14}H_{11}N_3O_2S$: 285.0572).

4-Phenylsulfonyl-2,6-dibenzyl-4,6-dihydro-2*H*-dipyrrolo[3,4-*b*; 3',4'-*d*]pyrrole **23**

To a solution of compound **21** (124.8 mg, 0.17 mmol) in 95% ethanol (10 ml) was added benzylamine (55 mg, 5.12 mmol). The reaction mixture was stirred at 35°C in dark for 18 h, then was concentrated by a rotary evaporator. Silica gel chromatography (hexane-ethyl acetate; 4:1) gave compound **23** (26 mg, 34%). Recrystallization (ethyl acetate-hexane) gave **23** as white crystals: mp 212-213°C dec.; ir ($CHCl_3$) 1600, 1580, 1540, 1530 cm^{-1} ; ^1H nmr (400 MHz, $CDCl_3$) δ 5.06 (s, 4 H), 6.43 (d, J = 1 Hz, 2 H), 6.82 (d, J = 1.2 Hz, 2 H), 7.03 (d, J = 7.6 Hz, 4 H), 7.21-7.31 (m, 9 H), 7.64 (d, J = 8 Hz, 2 H); ms *m/z* (relative intensity) 465 (M^+, 100), 324 (69); hrms *m/z* 465.1499 (calcd for $C_{28}H_{23}N_3O_2S$: 465.1511).

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