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Synthesis and Diels-Alder Reaction of Thieno[2,3-*c*:4,5-*c*']dipyrroles

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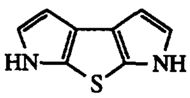
Abstract: An efficient method for the synthesis of the thieno[2,3-*c*:4,5-*c*']dipyrrole ring system is described. Reaction of **13** with sodium azide followed by the treatment with triphenylphosphine and water gave parent compound **4**. Reaction of **13** with benzylamine or aniline afforded *N,N'*-disubstituted derivatives **15** and **16** respectively. Diels-Alder reaction of **15** with DMAD gave cycloadducts **17** and **18**. Oxidative removal of the imine bridge from **17** and **18** gave dibenzothiophene **19**.

Thienodipyrroles **1-6** are theoretically interesting 14 π-electron heteroaromatic compounds. While the parent compounds **1-3** were synthesized by Farnier and co-workers in 1976,[1] compounds **4-6** are still unknown. Among them ring system **4** is of special interest because it can be considered as a cyclic analogue of the highly labile radialene **7**.[2] In addition, thienodipyrroles **1-6** could also be used as novel monomers for the preparation of new conducting polymers.[3] In this paper, we report the first synthesis of the parent compound thieno[2,3-*c*:4,5-*c*']dipyrrole **4** and *N,N'*-disubstituted derivatives **15** and **16**, as well as the Diels-Alder reaction of **15** with dimethyl acetylenedicarboxylate (DMAD).



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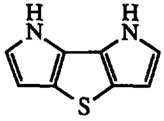

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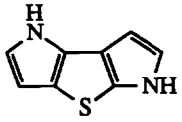

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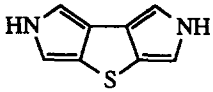

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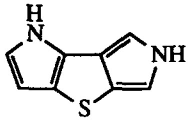

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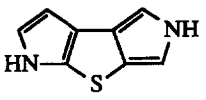

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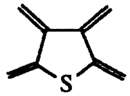

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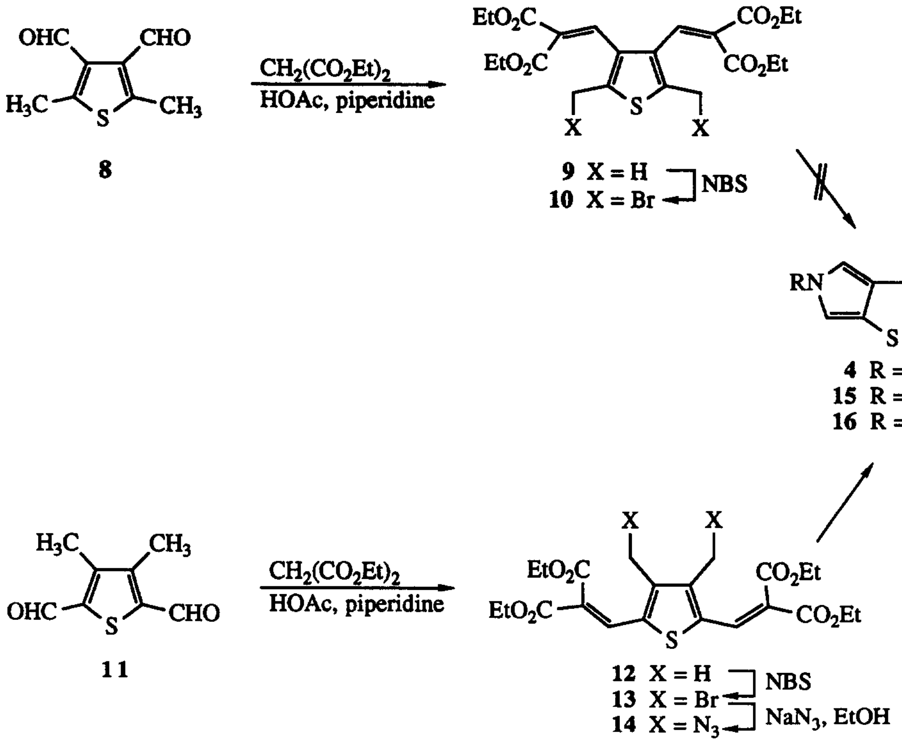
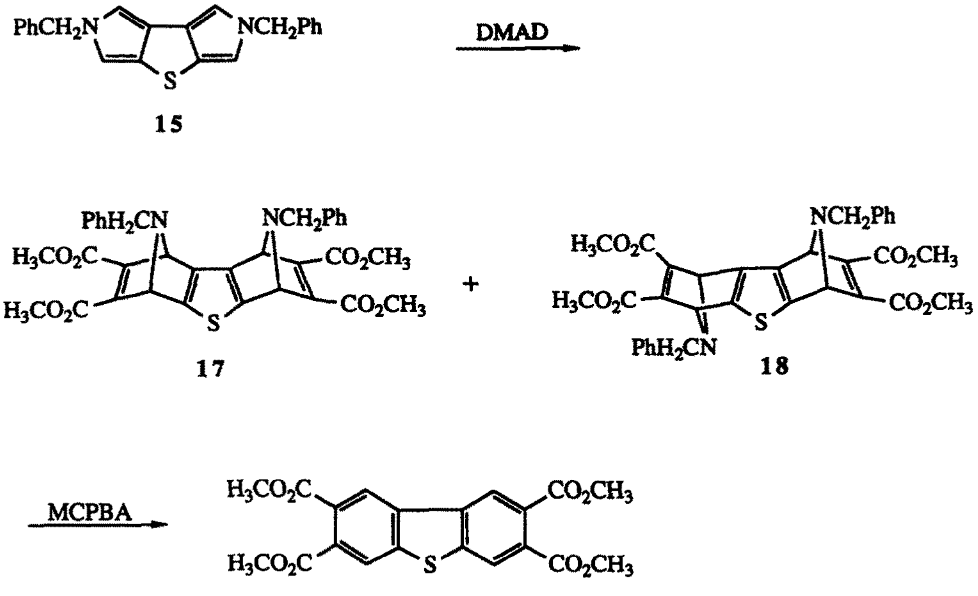
Double Knoevenagel condensation of dialdehyde **8** with diethyl malonate gave dialkylidenemalonate **9**. Double bromination of **9** with *N*-bromosuccinimide afforded dibromide **10**. However, attempted reaction of **10** with sodium azide or with benzylamine both produced complex mixtures of products. To circumvent this problem, dialdehyde **11** was prepared and used as the starting material.[4] Double Knoevenagel condensation of **11** with diethyl malonate yielded dialkylidenemalonate **12**. Bromination of **12** with NBS gave dibromide **13**. Reaction of dibromide **13** with sodium azide in ethanol gave diazide **14** smoothly. Treatment of **14** with triphenylphosphine and then water[5] produced the labile parent compound **4** which easily polymerized at room temperature into dark material. Reaction of **13** with benzylamine or aniline afforded *N,N'*-disubstituted thieno[2,3-*c*:4,5-*c'*]dipyrroles **15** or **16** respectively,[6] Scheme 1.

Scheme 1



Diels-Alder reaction of **15** with DMAD at room temperature gave cycloadducts **17** and **18**. Oxidative extrusion of the imine bridge from the mixture of **17** and **18** by *m*-chloroperbenzoic acid[7] gave dibenzothiophene **19**, Scheme 2.

Scheme 2



In summary, we report an efficient synthesis and the Diels-Alder reaction of the thieno[2,3-*c*:4,5-*c*']dipyrrole ring system. The potential of this heterocyclic system to be used in the conducting polymer synthesis is currently under investigation in our laboratory.

Experimental Section

General. Melting points were determined with a Büchi 530 melting point apparatus. ^1H NMR spectra were recorded on a JEOL HX-100, Varian GEMINI-300, or Bruker AM-400 spectrometer. ^{13}C NMR spectra were recorded in a Bruker AM-400 spectrometer. 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 Bomem MB-100 FT spectrometer, and UV spectra were recorded on a Perkin-Elmer Lambda 5 UV-VIS spectrometer. Solvents were distilled before use, and were dried as necessary according to literature procedures. All reactions were conducted under a nitrogen atmosphere. Elemental analyses were performed by the Microanalytical Laboratory of the NSC Regional Instrumentation Center operated by Department of Chemistry, National Cheng Kung University, Tainan, Taiwan.

Tetraethyl [(2,5-Dimethyl-3,4-thienyl)dimethylene]bispropandioate (9). Method A: To a solution of dialdehyde **8** (360 mg, 2.14 mmol) in benzene (20 mL) was added diethyl malonate (831 mg, 5.14

mmol), piperidine (70 mg), and acetic acid (50 mg). The reaction mixture was refluxed for 23 h with a Dean-Stark water separator attached. Concentration and silica gel flash column chromatography (hexane-ethyl acetate, 4:1) gave **9** (640 mg, 68%). **Method B**: A solution of titanium tetrachloride (0.8 mL, 5.6 mmol) in dry carbon tetrachloride (2 mL) was added dropwise to tetrahydrofuran (6 mL) under a calcium chloride drying tube with efficient stirring at 0°C for 1 h. To the resulting yellow suspension was added a solution of diethyl malonate (480 mg, 3.0 mmol) and dialdehyde **8** (237 mg, 1.41 mmol) in tetrahydrofuran (6 mL) dropwise, and stirred for 1 h. A solution of dry pyridine (0.9 mL, 12.0 mmol) in tetrahydrofuran (3 mL) was then added slowly in a period of 1 h. The resulting mixture was stirred at 0°C for an additional 12 h and then at room temperature for 12 h. The reaction mixture was quenched with H_2O (10 mL) and ether (10 mL), and the layers were separated. The aqueous layer was extracted with ether (10 mL x 3) and the combined organic layers were washed with 0.5 N hydrochloric acid, brine, and then dried ($MgSO_4$). Concentration and silica gel flash column chromatography (hexane: ethyl acetate, 4:1) gave **9** (523 mg, 82%) as a yellow oil: IR (KBr) 2850, 1719, 1667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.52 (s, 2 H), 4.29 (q, 4 H, *J* = 7.3 Hz), 4.17 (q, 4 H, *J* = 7.3 Hz), 2.28 (s, 6 H), 1.33 (t, 6 H, *J* = 7.3 Hz), 1.16 (t, 6 H, *J* = 7.3 Hz); MS *m/z* (relative intensity) 452 (M^+, 37), 406 (47), 360 (100); HRMS calcd for $C_{22}H_{28}O_8S$ 452.1505, found 452.1514.

Tetraethyl [(3,4-Dimethyl-2,5-thienyl)dimethylene]bispropanedioate (12). By the same procedure as method B for **9**, dialdehyde **11** (118 mg 0.71 mmol) was reacted with diethyl malonate (231 mg, 1.44 mmol) to give **12** (295 mg, 92 %) as yellow crystals: mp 118-119°C; IR (KBr) 2850, 1735, 1610 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 2 H), 4.38 (q, 4 H, *J* = 7.3 Hz), 4.27 (q, 4 H, *J* = 7.3 Hz), 2.24 (s, 6 H), 1.35 (t, 6 H, *J* = 7.3 Hz), 1.29 (t, 6 H, *J* = 7.3 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 165.90 (s), 163.81 (s), 143.58 (s), 133.48 (s), 131.19 (d), 123.74 (s), 61.99 (t), 61.43 (t), 13.67 (q), 13.62 (q), 12.97 (q); MS *m/z* (relative intensity) 452 (M^+, 100) 406 (38), 360 (20); HRMS calcd for $C_{22}H_{28}O_8S$ 452.1505, found 452.1495. Anal. calcd for $C_{22}H_{28}O_8S$: C, 58.37; H, 6.24. Found C, 58.35; H, 6.24.

Tetraethyl [(2,5-Dibromomethyl-3,4-thienyl)dimethylene]bispropanedioate (10). To a solution of **9** (145 mg 0.32 mmol) in carbon tetrachloride (20 mL) was added *N*-bromosuccinimide (136 mg, 0.76 mmol) and dibenzoyl peroxide (2 mg). The reaction mixture was stirred and heated at reflux for 2.5 h. After the mixture was cooled in an ice bath, the solid was removed by filtration and washed with carbon tetrachloride. Concentration and silica gel flash column chromatography (hexane-ethyl acetate, 4:1) gave **10** (161 mg, 82 %) as a white solid: mp 94.5-97.0°C; IR (KBr) 3042, 2980, 1737, 1699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 2 H), 4.53 (s, 4 H), 4.32 (q, 4 H, *J* = 7.2 Hz), 4.16 (q, 4 H, *J* = 7.2 Hz), 1.35 (t, 6 H, *J* = 7.2 Hz), 1.14 (t, 6 H, *J* = 7.2 Hz); MS *m/z* (relative intensity) 612 (M^++4, 21) 610 (M^++2, 33), 608 (M^+, 18), 531 (100), 529 (92), 485 (63), 483 (56), 393 (6).

Tetraethyl [(3,4-Dibromomethyl-2,5-thienyl)dimethylene]bispropanedioate (13). By the same procedure as that for **10**, compound **12** (270 mg 0.60 mmol) was treated with *N*-bromosuccinimide (246 mg, 1.38 mmol) to give **13** (336 mg, 92 %) as a yellow solid: mp 123-124°C; IR (KBr) 2980, 1722, 1613 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 2 H), 4.59 (s, 4 H), 4.38 (q, 2 H, *J* = 7.2 Hz), 4.29(q, 2H, *J* = 7.2Hz), 1.35 (t, 6 H, *J* = 7.2 Hz), 1.31 (t, 6 H, *J* = 7.1 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 165.51 (s), 163.46 (s), 140.65 (s), 136.92 (s), 129.20 (d), 126.72 (s), 62.53 (t), 62.12 (t), 20.72 (t), 14.02 (q), 13.83

(q); MS *m/z* (relative intensity) 612 (M^++4, 59), 610(100), 608(57), 531(50), 529(50); HRMS calcd for $C_{22}H_{26}Br_2O_8S$ 607.9716, found 607.9717; Anal. calcd for $C_{22}H_{26}Br_2O_8S$: C, 43.3; H, 4.30. Found C, 43.30; H, 4.35.

Tetraethyl [(3,4-Diazidomethyl-2,5-thienyl)dimethylene]bispropanedioate (14). To a solution of **13** (122 mg 0.2 mmol) in 95 % ethanol (10 mL) and dichloromethane (2.5 mL) was added sodium azide (65 mg, 1.0 mmol). The reaction mixture was stirred at room temperature for 2.5 h. Concentration and silica gel flash column chromatography (hexane-ethyl acetate, 4:1) gave **14** (79 mg, 74 %) as a yellow solid: mp 57-59 °C; IR (KBr) 2982, 2103 (N_3), 1717, 1614 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 7.87 (s, 2 H), 4.49 (s, 4 H), 4.41 (q, 4 H, *J* = 7.1 Hz), 4.32 (q, 4 H, *J* = 7.1 Hz), 1.37 (t, 6 H, *J* = 7.1 Hz), 1.33 (t, 6 H, *J* = 7.1 Hz); MS *m/z* (relative intensity) 478 (M^+-56, 31), 405 (19), 320 (56), 247 (47), 162 (69), 133 (94), 115 (100); HRMS calcd for $C_{22}H_{26}N_2O_8S$ (M^+-56) 478.1410, found 478.1385.

3*H*,6*H*-Thieno[2,3-*c*:4,5-*c*']dipyrrole (4). To a solution of **14** (26.6 mg, 0.05 mmol) in tetrahydrofuran (2 mL) was added triphenylphosphine (34.0 mg, 0.13 mmol). The reaction mixture was stirred at room temperature for 2.5 h. Water (0.2 mL) was then added, and the mixture was stirred for 12 h. Concentration and silica gel flash column chromatography (hexane-ethyl acetate, 1:1) gave **4** (4.8 mg, 59 %) as a pale yellow solid: mp 172-175 °C (dec.); IR (KBr) 3375, 3120 cm^{-1}; UV (CH_2Cl_2) λ_{max} 326 (ε 9.2 x 10^2), 233 (ε 1.9 x 10^4); ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 (br s, 2 H), 6.96-6.95 (m, 2 H), 6.74-6.72 (m, 2 H); MS *m/z* (relative intensity) 162 (M^+, 100); HRMS calcd for $C_8H_6N_2S$ 162.0252, found 162.0245.

3,6-Dibenzylthieno[2,3-*c*:4,5-*c*']dipyrrole (15). To a solution of **13** (292 mg, 0.48 mmol) in dichloromethane (5 mL) was added benzylamine (123 mg, 1.15 mmol) and triethylamine (182 mL, 1.80 mmol). The reaction mixture was stirred at room temperature for 3 h. Ethanol (2 mL) was added. The reaction mixture was refluxed for 7 h. Concentration and silica gel flash column chromatography (hexane-ethyl acetate, 7:1) gave **15** (71 mg, 43 %) as a pale yellow oil: IR ($CHCl_3$) 3120 cm^{-1}; UV (CH_2Cl_2) λ_{max} 236 (ε 4.00 x 10^4); ^1H NMR (400 MHz, $CDCl_3$) δ 7.12-7.05 (m, 6 H), 6.93 (d, 4 H, *J* = 6.8 Hz), 6.62 (d, 2 H, *J* = 1.5 Hz), 6.65 (d, 2 H, *J* = 1.9 Hz), 4.92 (s, 4 H); MS *m/z* (relative intensity) 342 (M^+, 100); HRMS calcd for $C_{22}H_{18}N_2S$ 342.1191, found 342.1190.

3,6-Diphenylthieno[2,3-*c*:4,5-*c*']dipyrrole (16). A solution of **13** (65.0 mg, 0.11 mmol), aniline (23.1 mg, 0.26 mmol) and triethylamine (45.0 mg, 0.45 mmol) in 5:1 ethanol-dichloromethane (1.8 mL) was stirred at room temperature for 2 h. Ethanol (4 mL) was then added. The reaction mixture was refluxed for 84 h. Concentration and silica gel flash column chromatography (hexane-ethyl acetate, 6:1) gave **16** (12 mg, 36 %) as a white solid: mp 178-179°C; IR (KBr) 3120, 1597, 1503 cm^{-1}; UV (CH_2Cl_2) λ_{max} 293 (ε 3.13 x 10^4), 242 (ε 1.72 x 10^4); ^1H NMR (400 MHz, $CDCl_3$) δ 7.43-7.42 (m, 8 H), 7.28 (d, 2H, *J* = 1.8Hz), 7.26-7.24 (m, 2H), 7.05 (d, 2 H, *J* = 1.8 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) 141.12 (s), 129.63 (d), 125.63 (d), 123.12 (s), 120.50 (d), 109.76 (d), 108.82 (d); MS *m/z* (relative intensity) 314 (M^+, 100); HRMS calcd for $C_{20}H_{14}N_2S$ 314.0878, found 314.0874. Anal. calcd for $C_{20}H_{14}N_2S$: C, 76.40; H, 4.49; N, 8.91. Found C, 75.98; H, 4.40; N, 8.85.

Cycloadducts 17 and 18 of 3,6-Dibenzylthieno[2,3-*c*:4,5-*c*']dipyrrole (15) and Dimethyl Acetylenedicarboxylate. A solution of **15** (42.0 mg, 0.12 mmol) and dimethyl acetylenedicarboxylate

(63.2 mg, 0.45 mmol) in benzene (2.5 mL) were stirred at room temperature for 12 h. Concentration afforded a mixture of **17** and **18**. Silica gel flash column chromatography (hexane-ethyl acetate, 1:1) gave a major product (47.3 mg, 63 %) and a minor product (11.0 mg, 15 %). The major product is a yellow oil: IR (KBr) 3011, 2951, 2831, 1723 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$, 21°C) δ 7.33-7.28 (m, 10 H), 4.94 (br s, 2 H), 4.85 (br s, 2 H), 3.80, 3.77 and 3.80-3.50 (two singlets and a broad peak, 16 H); MS *m/z* (relative intensity) 626 (M$^+$, 1), 484 (23), 342 (11), 273 (20), 142 (26), 112, (100); HRMS calcd for $C_{34}H_{30}N_2O_8S$ 626.1723, found 626.1721. The minor product is a yellow oil: IR (CHCl$_3$) 1725 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$, 21°C) δ 7.36 (s, 6 H), 7.38-7.24 (m, 4 H), 4.89 (br s, 4 H), 3.79, 3.75 and 3.88-3.60 (two singlets and a broad peak, 16 H); MS *m/z* (relative intensity) 626 (M$^+$, 2), 484 (4), 342 (100).

Tetramethyl Dibenzothiophene-2,3,7,8-tetracarboxylate (19). To a solution of the mixture of **17** and **18** (48.0 mg, 0.08 mmol) in dichloromethane(2 mL) was added dropwise a solution of *m*-chloroperbenzoic acid (35.0 mg, 0.16 mmol) in dichloromethane (1 mL).The reaction mixture was stirred at room temperature for 1.5 h, and then diluted with dichloromethane (7 mL). The reaction mixture was then washed with saturated sodium thiosulfate solution, sodium carbonate solution, water, and brine. Concentration and silica gel flash column chromatography (hexane-ethyl acetate, 2:1) gave **19** (22.0 mg, 69 %) as a yellow solid: mp 167-168°C; IR (KBr) 2940, 1729 cm^{-1}; UV (CH$_2$Cl$_2$) λ_{max} 341 (ε 3.55 x 10^3), 263 (ε 6.67 x 10^4), 219 (ε 2.4 x 10^4); ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.64 (s, 2 H), 8.25 (s, 2 H), 4.00 (s, 6 H), 3.98 (s, 6 H); ^{13}C NMR (100.6 MHz, CDCl$_3$) 167.65 (s), 167.37(s), 143.24(s), 135.90 (s), 131.56 (s), 128.53 (s), 123.74 (d), 123.36 (d), 52.95 (q), 52.87 (q); MS *m/z* (relative intensity) 416 (M$^+$, 100), 385 (19); HRMS calcd for $C_{20}H_{16}O_8S$ 416.0566, found 416.0552.

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