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Synthesis and Diels–Alder reactions of the benzo[4,5]thieno [2,3-*c*]pyrrole ring system

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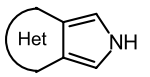
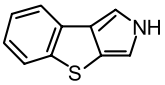
Abstract—The first synthesis of the parent compound of the benzo[4,5]thieno[2,3-*c*]pyrrole ring system and its derivatives, as well as their Diels–Alder reactions with DMAD and *N*-phenylmaleimide are reported. A new synthesis of the benzo[4,5]thieno[2,3-*d*]pyridazine ring system is also described. © 2003 Elsevier Science Ltd. All rights reserved.

iso-Condensed heteroaromatic pyrroles **1** are versatile heterocycles.[1] They can be used as diene components in Diels–Alder reactions[2] and as monomers for preparation of conducting polymers.[3] In our previous papers, we reported three methods for the synthesis of these useful heterocyclic structures, namely: (1) 1,3-dipolar cycloaddition and cycloreversion,[4] (2) retro-malonate addition,[5] and (3) phosphoimine–alkylidenemalonate cyclization.[6] Herein, we report the first synthesis of the parent compound **2** of benzo[4,5]thieno[2,3-*c*]pyrrole ring system and its derivatives[3a] using methods (1) and (2), as well as their Diels–Alder reactions with dimethyl acetylenedicarboxylate (DMAD) and *N*-phenylmaleimide. Using similar approach, a new synthesis of the benzo[4,5]thieno[2,3-*d*]pyridazine ring system is also described.

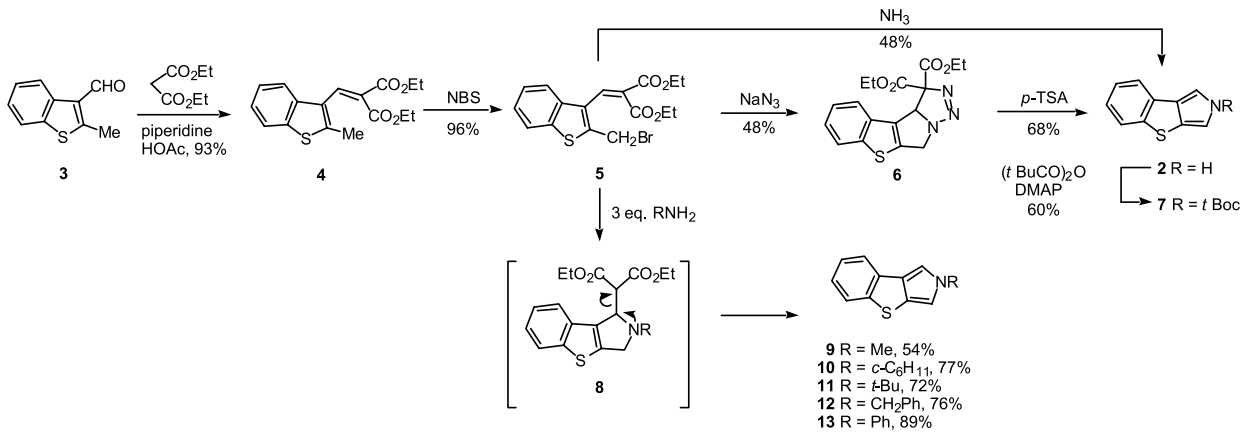


1



2

Knoevenagel condensation of 2-methylbenzo[*b*]thiophene-3-carbaldehyde (**3**)[7] with diethyl malonate gave compound **4** (Scheme 1). NBS bromination of **4** afforded bromo compound **5**. Treatment of bromo compound **5** with sodium azide in ethanol led to the stable triazoline **6**. 1,3-Dipolar cycloreversion of **6** was induced by a catalytic amount of *p*-TSA to give the parent 2*H*-benzo[4,5]thieno[2,3-*c*]pyrrole (**2**) in 68% yield. Alternatively, direct treatment of bromo compound **5** with excess ammonia furnished **2** in 48% yield



Scheme 1.

Keywords: benzo[4,5]thieno[2,3-*d*]pyridazine; retro-malonate addition; 1,3-dipolar cycloaddition–cycloreversion; Knoevenagel condensation; dibenzothiophene.

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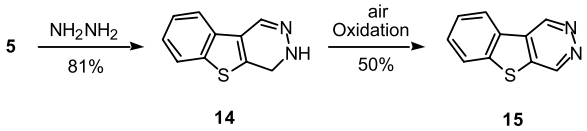
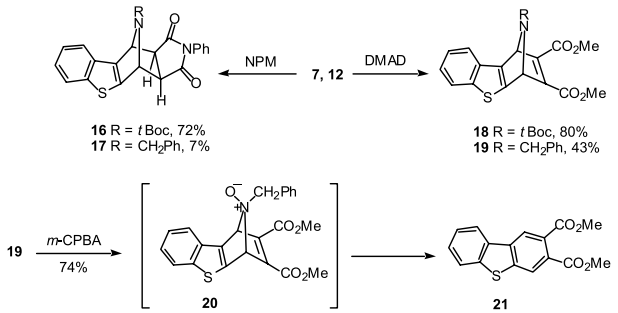
in one step. Compound **2** was treated with di-*tert*-butyl dicarbonate and 4-(dimethylamino)pyridine to give *N*-*tert*-butoxycarbonyl derivative **7**. We then reacted bromo compound **5** with methylamine, cyclohexylamine, *tert*-butylamine, benzylamine, and aniline, respectively, to give the *N*-substituted benzo[4,5]thieno[2,3-*c*]pyrroles **9**–**13** via a retro-malonate addition which occurred in intermediate **8**.

Similarly, the benzo[4,5]thieno[2,3-*d*]pyridazine ring system **15** can also be synthesized from compound **5** (Scheme 2). Treatment of **5** with hydrazine in ethanol gave 3,4-dihydrobenzo[4,5]thieno[2,3-*d*]pyridazine (**14**) in 81% yield. Air oxidation of **14** afforded benzo[4,5]thieno[2,3-*d*]pyridazine (**15**)[8] in 50% yield.



Scheme 2.

Furthermore, Diels–Alder reactions of the benzo[4,5]-thieno[2,3-*c*]pyrrole ring system were studied. *N*-*tert*-Butoxycarbonyl derivative **7** was reacted with *N*-phenylmaleimide to give the *exo* cycloadduct **16** in 72% yield, Scheme 3. The stereochemistry of cycloadduct **16** was determined from the coupling pattern of the bridgehead protons in the ^{1}H NMR spectrum.[6] Cycloaddition of **7** with DMAD gave cycloadduct **18** in 80% yield. However, the Diels–Alder reaction of 2-benzyl-2*H*-benzo[4,5]thieno[2,3-*c*]pyrrole (**12**) with *N*-phenylmaleimide and DMAD under identical conditions gave only 7 and 43% yields of corresponding cycloadducts **17** and **19**. Oxidation of cycloadduct **19** with *m*-CPBA in dichloromethane led to spontaneous extrusion of 1-(nitrosomethyl)benzene[6] to give dibenzothiophene derivative **21**.[9]



Scheme 3.

In conclusion, we have demonstrated that 1,3-dipolar cycloaddition-cycloreversion and retro-malonate addition methods can be used to synthesize parent compound **2** as well as several *N*-substituted derivatives **9**–**13** of the benzo[4,5]thieno[2,3-*c*]pyrrole ring system in good yield. Using this method, the benzo[4,5]thieno[2,3-*d*]pyridazine ring system **15** was also prepared. Diels–Alder reactions of *N*-substituted benzo[4,5]thieno[2,3-*c*]pyrroles **7** and **12** with *N*-phenylmaleimide and DMAD gave the corresponding cycloadducts **16**–**19**. Oxidative extrusion of the nitrogen bridge in cycloadduct **19** via intermediate **20** afforded dibenzothiophene derivative **21**.

1. Experimental

1.1. General

Melting points were determined with a Yanaco-MP-S melting-point apparatus. IR spectra were recorded on a Perkin–Elmer 781 spectrometer. UV spectra were measured on a Perkin–Elmer Lambda 5 UV–VIS spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-400 or a Varian UNITYInova-500 spectrometer. Mass spectra were recorded on a JEOL TMS-D-100 mass spectrometer. High-resolution mass spectra were recorded on a JEOL HX-110 mass spectrometer.

1.1.1. Diethyl 2-[(2-methylbenzo[*b*]thiophen-3-yl)-methylene] malonate (4). To a solution of aldehyde **3** (1.46 g, 8.31 mmol) in dry benzene (50 mL), diethyl malonate (1.60 g, 9.98 mmol), piperidine (350 mg, 4.16 mmol) and glacial acetic acid (100 mg, 1.66 mmol) were added. The reaction mixture was heated to reflux for 12 h. Water was separated with a Dean–Stark trap. Concentration and silica gel column chromatography (EtOAc/hexane, 1:4) gave compound **4** (2.64 g, 93%) as a yellow liquid; IR ($CHCl_3$): 2980, 1725, 1640, 1250, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.89 (t, 3H, J=7.2 Hz), 1.35 (t, 3H, J=7.2 Hz), 2.49 (s, 3H), 3.79 (q, 2H, J=7.2 Hz), 4.33 (q, 2H, J=7.2 Hz), 7.25–7.33 (m, 2H), 7.53 (d, 1H, J=8.0 Hz), 7.70 (d, 1H, J=7.2 Hz), 7.93 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 13.3, 13.9, 14.7, 61.0, 61.5, 121.6, 121.7, 124.0, 124.2, 126.4, 129.8, 137.7, 138.1, 138.3, 140.8, 163.9, 165.1; MS (EI): m/z 318 (M^+, 100), 272 (19), 176 (36); HRMS (FAB): calcd for (M+H) $C_{17}H_{19}O_4S$ 319.1004, found 319.0998.

1.1.2. Diethyl 2-{[2-(bromomethyl)benzo[*b*]thiophen-3-yl] methylene} malonate (5). To a solution of substrate **4** (1.91 g, 6.0 mmol) in dry CCl_4 (30 mL), *N*-bromosuccinimide (1.07 g, 6.0 mmol) and dibenzoyl peroxide (20 mg) were added. The reaction mixture was heated at reflux for 4 h and cooled to room temperature. The solvent was removed under reduced pressure. The crude product was purified by silica gel column chromatography (EtOAc/hexane, 1:4) to give bromo compound **5** (2.31 g, 96%) as white crystals; mp 66.9–67.6°C; IR ($CHCl_3$): 2980, 1725, 1630, 1260, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.79 (t, 3H, J=7.2 Hz), 1.33 (t, 3H, J=7.2 Hz), 3.91 (q, 2H, J=7.2 Hz), 4.31 (q, 2H, J=7.2 Hz), 4.67 (s, 2H), 7.30–7.32 (m, 2H), 7.53 (m, 1H), 7.70 (m, 1H), 7.84 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 13.4, 14.1, 61.5, 62.0, 122.4, 123.0, 124.9, 125.6, 129.1, 132.4, 126.8, 137.7, 138.9, 139.1, 163.4, 164.7; MS (EI): m/z 398 (M^++2, 41), 396 (M^+, 40), 317 (M^+−80, 49), 271 (100), 243 (17), 217 (10), 199 (5); HRMS (EI): calcd for $C_{17}H_{17}BrO_4S$ 396.0031, found 396.0033.

1.1.3. Diethyl 5,10c-dihydro-1*H*-benzo[4′,5′]-thieno[3′,2′:3,4] pyrrolo[1,2-*c*][1,2,3]triazole-1,1-dicarboxylate (6). To a solution of bromo compound **5** (209 mg, 0.53 mmol) in 95% ethanol (5 mL), NaN_3

(171 mg, 2.64 mmol) was added. The reaction mixture was stirred at room temperature for 4 h. Removal of solvent followed by silica gel column chromatography (EtOAc/hexane, 1:5) gave triazoline **6** (91 mg, 48%) as a colorless liquid; IR ($CHCl_3$): 3000, 1740, 1500, 1470, 1430, 1370, 1250, 1060 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.73 (t, 3H, J=7.2 Hz), 1.37 (t, 3H, J=7.2 Hz), 3.78–3.84 (m, 2H), 4.31–4.37 (m, 1H), 4.44–4.50 (m, 1H), 4.73 (dd, 1H, J=15.2, 2.4 Hz), 5.34 (dd, 1H, J=15.2, 1.7 Hz), 5.86 (s, 1H), 7.24–7.32 (m, 2H), 7.53–7.55 (m, 1H), 7.72–7.74 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 13.1, 14.0, 53.7, 63.0, 63.4, 67.0, 92.8, 121.9, 123.6, 124.5, 124.7, 132.6, 134.4, 139.1, 145.3, 165.3, 165.4; MS (EI): *m*/*z* 359 (M^+, 5), 331 (36), 173 (100); HRMS (EI): calcd for $C_{17}H_{17}N_3O_4S$ 359.0940, found 359.0945.

1.1.4. 2*H*-Benzo[4,5]thieno[2,3-*c*]pyrrole (2). *By 1,3-dipolar cycloreversion of triazoline* **6**. To a solution of triazoline **6** (91 mg, 0.25 mmol) in dry ether (5 mL), catalytic amount of *p*-toluenesulfonic acid was added. The reaction mixture was stirred at room temperature for 3 min. The solvent was then removed, and the crude product was purified by silica gel column chromatography (EtOAc/hexane, 1:8) to give compound **2** (30 mg, 68%) as a yellow liquid; UV (CH_2Cl_2) λ_{max} (nm) (log ε): 316.6 (3.50), 255.3 (4.36), 234.3 (4.36); IR ($CHCl_3$): 3460, 3300, 3060, 3000, 1600, 1570, 1445, 1250, 1150, 1110, 1040, 900 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 6.85–6.86 (m, 1H), 7.22–7.30 (m, 3H), 7.64 (d, 1H, J=7.2 Hz), 7.76–7.78 (m, 1H), 8.66 (br s, 1H); MS (EI): *m*/*z* 173 (M^+, 100); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 107.3, 108.1, 121.2, 121.8, 123.3, 124.0, 124.5, 128.4, 131.3, 143.9; HRMS (EI): calcd for $C_{10}H_7NS$ 173.0300, found 173.0312.

By retro-malonate addition to compound **5**. To a solution of bromo compound **5** (450 mg, 1.13 mmol) in 95% ethanol (6 mL) was added saturated ammonia water (0.3 mL). The reaction mixture was stirred at room temperature for 45 min. Concentration and silica gel chromatography (EtOAc/hexane, 1:6) gave compound **2** (95 mg, 48%) as a yellow liquid.

1.1.5. *tert*-Butyl 2*H*-benzo[4,5]thieno[2,3-*c*]pyrrole-2-carboxylate (7). To a solution of substrate **2** (95 mg, 0.55 mmol) in dry CH_2Cl_2 (2 mL), 4-(dimethylamino)pyridine (134 mg, 1.10 mmol) was added. The reaction mixture was stirred at room temperature for 5 min. To this reaction mixture, di-*tert*-butyl dicarbonate (239 mg, 1.10 mmol) was added. After 30 min, solvent was removed and the crude product was chromatographed on silica gel (EtOAc/hexane, 1:4) to give compound **7** (89 mg, 60%) as a yellow liquid; UV (CH_2Cl_2) λ_{max} (nm) (log ε): 274.2 (4.61), 249.0 (4.55), 228.9 (4.53); IR ($CHCl_3$): 2980, 1740, 1600, 1570, 1450, 1390, 1270, 1150, 970 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.64 (s, 9H), 7.26–7.31 (m, 3H), 7.57–7.58 (m, 1H), 7.68 (d, 1H, J=1.2 Hz), 7.74–7.76 (m, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 27.8, 84.1, 109.0, 109.7, 122.1, 123.3, 124.4, 125.2, 126.1, 130.2, 131.1, 144.8, 148.9; MS (EI): *m*/*z* 273 (M^+, 70), 217 (100), 173 (27); HRMS (EI): calcd for $C_{15}H_{15}NO_2S$ 273.0823, found 273.0824.

1.1.6. 2-Methyl-2*H*-benzo[4,5]thieno[2,3-*c*]pyrrole (9). To a solution of bromo compound **5** (32 mg, 0.81 mmol) in 95% ethanol (2 mL), methylamine (76 mg, 2.4 mmol) in 95% ethanol (1 mL) was added. The reaction mixture was stirred at room temperature for 2 h. Concentration and silica gel column chromatography (EtOAc/hexane, 1:10) gave compound **9** (83 mg, 54%) as a yellow liquid; UV (CH_2Cl_2) λ_{max} (nm) (log ε): 262.1 (4.38), 241.8 (4.35), 229.7 (4.34); IR ($CHCl_3$): 3060, 2940, 1680 (broad), 1600, 1550, 1440, 1390, 1250, 1180, 1120, 1060, 1020 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 3.81 (s, 3H), 6.69 (d, 1H, J=1.6 Hz), 7.09 (d, 1H, J=1.6 Hz), 7.21–7.30 (m, 2H), 7.65 (d, 1H, J=7.6 Hz), 7.73 (d, 1H, J=8.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 37.3, 111.1, 112.1, 120.9, 121.5, 123.3, 123.9, 124.1, 128.1, 131.5, 143.3; MS (EI): *m*/*z* 187 (M^+, 100), 176 (35), 162 (12); HRMS (EI): calcd for $C_{11}H_9NS$ 187.0456, found 187.0439.

1.1.7. 2-Cyclohexyl-2*H*-benzo[4,5]thieno[2,3-*c*]pyrrole (10). The procedure was similar to that of compound **9**. The reaction mixture, containing bromo compound **5** (214 mg, 0.84 mmol), cyclohexylamine (251 mg, 2.54 mmol) and 95% ethanol (3 mL), was stirred at room temperature for 1 h. Concentration and silica gel column chromatography (EtOAc/hexane, 1:8) gave compound **10** (166 mg, 77%) as a yellow liquid; UV (CH_2Cl_2) λ_{max} (nm) (log ε): 261.9 (5.0), 241.8 (5.0), 229.4 (5.0); IR ($CHCl_3$): 3060, 3000, 2940, 2860, 1600, 1550, 1450, 1380, 1350, 1170, 1120, 1060, 1020 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.23–1.30 (m, 1H), 1.38–1.48 (m, 2H), 1.66–1.77 (m, 3H), 1.89–1.93 (m, 2H), 2.15–2.19 (m, 2H), 3.91–3.97 (m, 1H), 6.81 (d, 1H, J=1.6 Hz), 7.16–7.26 (m, 3H), 7.61 (d, 1H, J=8.0 Hz), 7.70 (d, 1H, J=8.4 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 25.4, 25.7, 35.0, 60.2, 108.2, 109.0, 120.8, 123.3, 123.9, 124.0, 127.4, 131.7, 143.3; MS (EI): *m*/*z* 255 (M^+, 100), 173 (46); HRMS (EI): calcd for $C_{16}H_{17}NS$ 255.1082, found 255.1076.

1.1.8. 2-(*tert*-Butyl)-2*H*-benzo[4,5]thieno[2,3-*c*]pyrrole (11). The procedure was similar to that of compound **9**. The reaction mixture, containing bromo compound **5** (135 mg, 0.34 mmol), *t*-butylamine (75 mg, 1.0 mmol) and 95% ethanol (3 mL), was stirred at room temperature for 6 h. Concentration and silica gel column chromatography (EtOAc/hexane, 1:5) gave compound **11** (66 mg, 72%) as a yellow liquid; UV (CH_2Cl_2) λ_{max} (nm) (log ε): 262.0 (4.5), 229.9 (4.5); IR ($CHCl_3$): 3060, 2980, 1680, 1600, 1560, 1440, 1370, 1350, 1250, 1120, 1090, 1060, 1020 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.63 (s, 9H), 6.95 (d, 1H, J=1.6 Hz), 7.20–7.33 (m, 2H), 7.35 (d, 1H, J=1.7 Hz), 7.65 (d, 1H, J=7.6 Hz), 7.75 (d, 1H, J=7.6 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 31.0, 56.2, 107.3, 108.1, 120.8, 121.0, 123.3, 123.9, 124.0, 127.4, 131.7, 143.4; MS (EI): *m*/*z* 229 (M^+, 47), 173 (100); HRMS (EI): calcd for $C_{14}H_{15}NS$ 229.0925, found 229.0930.

1.1.9. 2-Benzyl-2*H*-benzo[4,5]thieno[2,3-*c*]pyrrole (12). The procedure was similar to that of compound **9**. The reaction mixture, containing bromo compound **5** (215 mg, 0.54 mmol), benzylamine (174 mg, 1.62 mmol) and 95% ethanol (6 mL), was stirred at room temperature for 1 h. Concentration and silica gel column chromatography (EtOAc/hexane, 1:5) gave compound **12** (111 mg, 76%) as a yellow liquid; UV (CH_2Cl_2) λ_{max} (nm) (log ε): 257.7 (4.5), 229.3 (4.4); IR ($CHCl_3$): 3060, 3000, 1690, 1600,

1500, 1440, 1390, 1350, 1250, 1170, 1120, 1060, 1020 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.22 (s, 2H), 6.78 (d, 1H, J=2.0 Hz), 7.15–7.32 (m, 8H), 7.62 (d, 1H, J=8.0 Hz), 7.69–7.71 (m, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 54.4, 110.7, 111.6, 121.0, 121.8, 123.3, 124.0, 124.2, 127.0, 127.8, 128.3, 128.7, 131.4, 137.5, 143.4; MS (EI): m/z 263 (M^+, 100); HRMS (EI): calcd for $C_{17}H_{13}NS$ 263.0769, found 263.0769.

1.1.10. 2-Phenyl-2*H*-benzo[4,5]thieno[2,3-*c*]pyrrole (13). The procedure was similar to that of compound **9**. The reaction mixture, containing bromo compound **5** (369 mg, 0.93 mmol), aniline (259 mg, 2.8 mmol) and 95% ethanol (6 mL), was stirred at room temperature for 8 h. Concentration and silica gel column chromatography (EtOAc/hexane, 1:5) gave compound **13** (207 mg, 89%) as white crystals; mp 118.9–119.5°C; UV (CH_2Cl_2) λ_{max} (nm) (log ε): 284.1 (4.6), 257.7 (4.5), 224.8 (4.4); IR ($CHCl_3$): 1600, 1560, 1500, 1440, 1390, 1340, 1270, 1040 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.19 (d, 1H, J=2.1 Hz), 7.27–7.34 (m, 3H), 7.47–7.50 (m, 4H), 7.57 (d, 1H, J=1.6 Hz), 7.68–7.70 (m, 1H), 7.81–7.83 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 109.1, 109.7, 121.2, 121.4, 123.4, 124.0, 124.3, 125.0, 126.3, 129.7, 131.1, 141.0, 143.7; MS (EI): m/z 249 (M^+, 100); HRMS (EI): calcd for $C_{16}H_{11}NS$ 249.0612, found 249.0592.

1.1.11. 3,4-Dihydrobenzo[4,5]thieno[2,3-*d*]pyridazine (14). To a solution of bromo compound **5** (416 mg, 1.05 mmol) in 95% ethanol (5 mL), hydrazine (101 mg, 3.15 mmol) was added and stirred at room temperature for 30 min. Removal of solvent followed by silica gel column chromatography (EtOAc/hexane, 2:1) gave compound **14** (159 mg, 81%) as white crystals; IR ($CHCl_3$): 3400, 3000, 2800, 1550, 1470, 1430, 1315, 1070 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 4.47 (s, 2H), 5.90 (br s, 1H), 7.24–7.34 (m, 2H), 7.63 (s, 1H), 7.69–7.75 (m, 2H); MS (EI): m/z 188 (M^+, 67), 187 (100).

1.1.12. Benzo[4,5]thieno[2,3-*d*]pyridazine (15). Substrate **14** (159 mg, 0.85 mmol) was kept under open atmosphere for 4 days. Crude product was purified by silica gel column chromatography (EtOAc/hexane, 2:1) to give compound **15** (80 mg, 50%) as a brown solid; mp 125.8–126.5°C (lit.;[8] mp 126°C); UV (CH_2Cl_2) λ_{max} (nm) (log ε): 325.3 (3.85), 251.7 (4.5), 233.0 (4.8); IR ($CHCl_3$): 1600, 1550, 1520, 1430, 1320, 1230, 1100, 1030 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.50–7.60 (m, 2H), 7.89–7.92 (m, 1H), 8.22–8.25 (m, 1H), 9.61 (d, 1H, J=1.2 Hz), 9.72 (d, 1H, J=2.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 123.0, 123.4, 126.1, 130.0, 131.9, 132.6, 139.8, 140.5, 144.3, 146.8; MS (EI): m/z 186 (M^+, 100), 158 (29), 114 (32); HRMS (EI): calcd for $C_{10}H_6N_2S$ 186.0252, found 186.0234.

1.1.13. Diels–Alder reaction of compound 7 with *N*-phenylmaleimide. To a solution of compound **7** (16 mg, 0.06 mmol) in dry benzene (5 mL), *N*-phenylmaleimide (31 mg, 0.18 mmol) was added. The reaction mixture was then heated at reflux for 3 h. The solution was then filtered and concentrated to give *exo* cycloadduct **16** (19 mg, 72%) as a white solid; mp 222.2–223.5°C; IR (KBr): 2980, 1780, 1710, 1685, 1490, 1415, 1280, 1200, 1100 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.32 (s, 9H), 2.98 (ABq, 2H, J=23.5, 6.8 Hz), 5.69 (br s, 1H), 5.79 (br s, 1H), 7.29–7.50 (m, 7H), 7.80–7.84 (m, 2H); MS (EI): m/z 446 (M^+, 12), 273 (74), 217 (100), 173 (74); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 28.0, 29.7, 50.4, 63.0, 64.5, 82.1, 122.2, 123.8, 125.0, 125.3, 126.5, 128.9, 129.3, 131.3, 131.6, 145.5, 155.0, 174.1, 174.4; HRMS (EI): calcd for $C_{25}H_{22}N_2O_4S$ 446.1300, found 446.1301.

1.1.14. Diels–Alder reaction of compound 12 with *N*-phenylmaleimide. The reaction was carried out at room temperature for 24 h using compound **12** (62 mg, 0.24 mmol) and *N*-phenylmaleimide (122 mg, 0.71 mmol) in dry benzene. Concentration and silica gel column chromatography (EtOAc/hexane, 1:8) gave *exo* cycloadduct **17** (6.8 mg, 7%) as a white solid; mp 143.9–144.5°C; IR ($CHCl_3$): 1770, 1700, 1590, 1515, 1390, 1290, 1190, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.97 (ABq, 2H, J=18.5, 6.8 Hz), 3.64 (s, 2H), 4.81 (s, 1H), 4.90 (s, 1H), 7.15–7.54 (m, 12H), 7.75 (d, 1H, J=8.0 Hz), 7.84 (d, 1H, J=8.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 50.0, 50.5, 51.3, 65.9, 67.8, 122.0, 124.0, 124.5, 125.1, 126.6, 127.4, 128.2, 128.6, 128.8, 129.3, 132.1, 132.7, 138.1, 144.6, 146.3, 146.8, 175.4, 175.7; MS (EI): m/z 263 (M^+-173, 100), 173 (M^+-263, 60); HRMS (FAB): calcd for (M+H) $C_{27}H_{21}N_2O_2S$ 437.1324, found 437.1319.

1.1.15. Diels–Alder reaction of compound 7 with dimethyl acetylenedicarboxylate. To a solution of compound **7** (11 mg, 0.04 mmol) in dry ether (5 mL), dimethyl acetylenedicarboxylate (6.4 mg, 0.045 mmol) was added. The reaction mixture was heated at reflux for 12 h. Concentration and silica gel column chromatography (EtOAc/hexane, 1:1) gave compound **18** (14 mg, 80%) as a yellow liquid; IR ($CHCl_3$): 2985, 1725, 1630, 1440, 1370, 1330, 1260, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.34 (s, 9H), 3.72 (s, 3H), 3.74 (s, 3H), 5.91 (br s, 1H), 6.03 (br s, 1H), 7.20–7.24 (m, 1H), 7.30–7.34 (m, 1H), 7.69–7.73 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 28.0, 52.5, 52.5, 67.9, 68.3, 69.2, 69.5, 82.0, 121.3, 121.6, 123.6, 124.3, 125.0, 132.9, 144.3, 152.5, 153.1, 154.0, 162.8; MS (EI): m/z 415 (M^+, 55), 217 (100); HRMS (EI): calcd for $C_{21}H_{21}NO_6S$ 415.1090, found 415.1096.

1.1.16. Diels–Alder reaction of compound 12 with dimethyl acetylenedicarboxylate. The reaction was carried out at room temperature for 12 h using compound **12** (80 mg, 0.30 mmol) and dimethyl acetylenedicarboxylate (56 mg, 0.39 mmol) in dry benzene. Concentration and silica gel column chromatography (EtOAc/hexane, 3:1) gave compound **19** (66 mg, 43%) as a yellow liquid; IR ($CHCl_3$): 3000, 2950, 2840, 1725, 1630, 1440, 1295, 1200, 1100 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 3.62–3.68 (m, 8H), 5.01 (br s, 1H), 5.13 (br s, 1H), 7.15–7.28 (m, 7H), 7.60 (d, 1H, J=8.0 Hz), 7.68 (d, 1H, J=8.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 52.3, 53.4, 54.0, 71.1, 72.5, 121.3, 123.8, 124.9, 127.5, 128.6, 129.3, 137.1, 153.3; MS (EI): m/z 405 (M^+, 46), 263 (M^+-142, 100); HRMS (EI): calcd for $C_{23}H_{19}NO_4S$ 405.1035, found 405.1032.

1.1.17. Dimethyl dibenzo[*b*,*d*]thiophene-2,3-dicarboxylate (21). To a solution of substrate **19** (10 mg, 0.026 mmol) in dry CH_2Cl_2 (1 mL), a solution of *m*-CPBA (4.5 mg, 0.026 mmol) in dry CH_2Cl_2 (1 mL) was slowly added. The

reaction mixture was stirred at room temperature for 30 min and then diluted with CH_2Cl_2 (10 mL). Organic layer was washed with saturated solution of $NaHCO_3$ (10 mL) and water (10 mL), and then dried ($MgSO_4$). Concentration and silica gel column chromatography (EtOAc/hexane, 1:3) gave compound **21** (5.5 mg, 74%) as a yellow solid; mp 106.8–107.4°C (lit.;[9] mp 102–104°C); UV (CH_2Cl_2) λ_{max} (nm) (log ε): 266.2 (4.5), 246.1 (4.6), 224.2 (4.4); IR ($CHCl_3$): 3000, 2950, 1720, 1440, 1360, 1320, 1280, 1100 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 4.00 (s, 3H), 4.01 (s, 3H), 7.53–7.58 (m, 2H), 7.91–7.93 (m, 1H), 8.24–8.26 (m, 2H), 8.56 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 52.8, 52.9, 122.4, 122.5, 123.0, 123.7, 125.1, 128.0, 128.1, 130.0, 134.4, 137.2, 140.7, 142.1, 168.0, 168.1; MS (EI): *m/z* 300 (M^+, 100); HRMS (EI): calcd for $C_{16}H_{12}O_4S$ 300.0456, found 300.0461.

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