

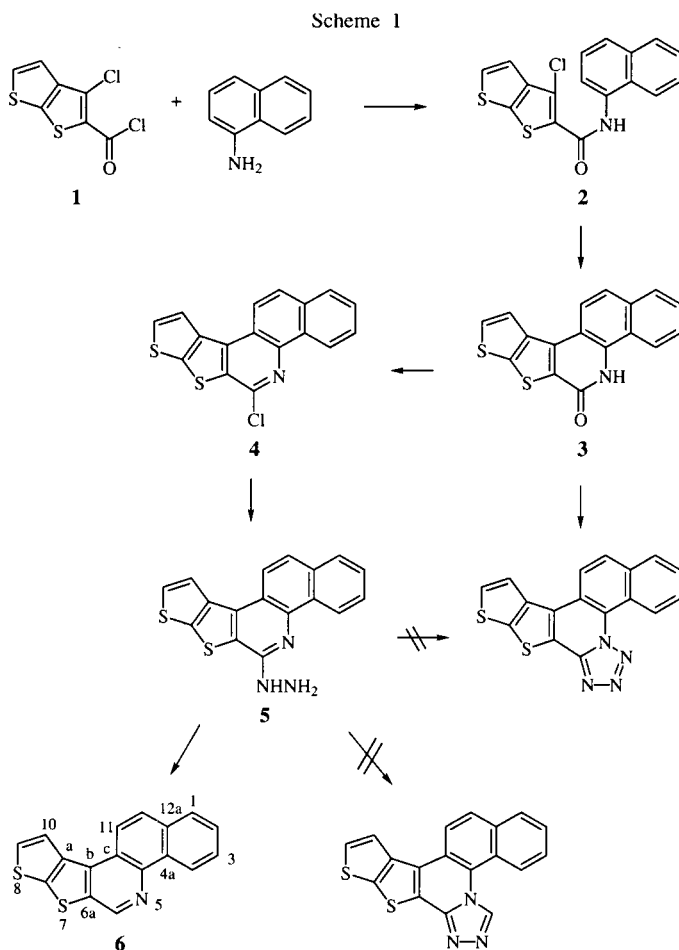
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Four previously unknown polycyclic heterocyclic ring systems, namely, benzo[*h*]thieno[3',2':4,5]-thieno[2,3-*c*]quinoline (**6**), benzo[*h*]thieno[3',2':4,5]thieno[2,3-*c*]quinoline (**11**), benzo[*f*]thieno[3',2':4,5]thieno[2,3-*c*]tetrazolo[1,5-*a*]quinoline (**12**) and benzo[*f*]thieno[3',2':4,5]thieno[2,3-*c*][1,2,4]-triazolo[4,3-*a*]quinoline (**13**), were synthesized via oxidative photocyclization. Unequivocal total assignments of the proton and carbon nmr spectra of **6** and **11** were made through the concerted usage of COSY, HMQC and HMBC two-dimensional nmr spectroscopic methods.

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Recently we have employed the oxidative photocyclization of the appropriate amides to synthesize novel polycyclic heterocyclic ring systems [1]. As a continuing study we report in this paper the synthesis of four previously unknown heterocyclic ring systems, namely, benzo[*h*]thieno[3',2':4,5]thieno[2,3-*c*]quinoline (**6**), benzo[*f*]thieno[3',2':4,5]thieno[2,3-*c*]quinoline (**11**), benz[*f*]thieno[3',2':4,5]thieno[2,3-*c*]tetrazolo[1,5-*a*]quinoline (**12**) and benzo[*f*]thieno[3',2':4,5]thieno[2,3-*c*][1,2,4]triazolo[4,3-*a*]quinoline (**13**) via photocyclization.

Condensation of 3-chlorothiophene[2,3-*b*]thiophene-2-carbonyl chloride (**1**) [1a,3,4] with 1-naphthylamine in benzene solution afforded 3-chloro-*N*-(1-naphthyl)thiophene[2,3-*b*]thiophene-2-carboxamide (**2**) in 62% yield (Scheme 1). Irradiation of the amide **2** in benzene solution containing triethylamine with a 450 watt medium pressure mercury vapor lamp for four hours gave benzo[*h*]thieno[3',2':4,5]thieno[2,3-*c*]quinolin-6(*5H*)-one (**3**) in 81% yield. Chlorination of lactam **3** was performed by refluxing **3** with phosphorus oxychloride to obtain 6-chlorobenzo[*h*]thieno[3',2':4,5]thieno[2,3-*c*]quinoline (**4**) in 77% yield. Attempts to synthesize the unsubstituted ring system **6** by catalytic dechlorination of **4** with 10% Pd-C failed as reported previously [1a,o]. Therefore, a two-step procedure was required to obtain the unsubstituted ring system **6**. Thus, upon hydrazination of chloride **4** with anhydrous hydrazine in a refluxing mixture of benzene and ethanol, 6-hydrazinobenzo[*h*]thieno[3',2':4,5]thieno[2,3-*c*]quinoline (**5**) was obtained in 92% yield. When **5** was allowed to react with a mixture of a 10% copper sulfate solution and aqueous acetic acid, the unsubstituted ring system **6**, benzo[*h*]thieno[3',2':4,5]thieno[2,3-*c*]quinoline, was obtained in 66%. Attempts to synthesize triazole and tetrazole derivatives of **6** by reacting **5** with trimethyl orthoformate or nitrous acid, were unsuccessful possibly due to the poor solubility of the hydrazine **5** in the reaction media.



Likewise, 3-chloro-*N*-(2-naphthyl)thiophene[2,3-*b*]thiophene-2-carboxamide (**7**) was obtained in 76% yield by refluxing the carbonyl chloride **1** with 2-naphthylamine in benzene solution. Oxidative photocyclization of amide **7** in benzene solution provided benzo[*f*]thieno[3',2':4,5]thieno[2,3-*c*]-

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. The ir spectra were recorded on a Beckmann FT1100 spectrometer as potassium bromide pellets and frequencies are expressed in cm^{-1} . The ^1H nmr spectra of the intermediates were obtained on a JEOL FX-90Q or on a Bruker AMX360 MHz NMR spectrometer in the solvent indicated with tetramethylsilane as the internal standard; chemical shifts are reported in ppm (δ) and J values in Hz. Analysis (tlc) were performed on Sigma precoated silica gel plates containing a fluorescent indicator. Elemental analyses were performed by M-H-W Laboratories, Phoenix, Arizona.

The ^1H and ^{13}C spectra of **6** and **11** were acquired on a Bruker AMX360 MHz NMR spectrometer operating at an observation frequency of 360.13 MHz for ^1H and 90.56 for ^{13}C . All experiments were performed using an inverse-geometry 5 mm broad band probe. Pulse widths (90°) for ^1H and ^{13}C were 7.2 and 14.4 μsec , respectively. The COSY spectra were recorded using the Bruker pulse program (COSY90) [5]. The HMQC experiments were performed using the Bruker pulse program (invbdgpt) with the BIRD sequence optimized for direct couplings (165 Hz $^1\text{J}_{\text{CH}}$) [6]. The HMBC spectra were obtained using the Bruker pulse program (inv4lplrnd) [7] optimized for 10 Hz $^3\text{J}_{\text{CH}}$ couplings.

3-Chloro-N-(1-naphthyl)thieno[2,3-*b*]thiophene-2-carboxamide (2).

A mixture of 3.0 g (12.65 mmoles) of 3-chlorothieno[2,3-*b*]thiophene-2-carbonyl chloride (**1**) [1a,3,4] and 1.81 g (12.65 mmoles) of 1-naphthylamine in 100 ml of benzene was heated under reflux for 4 hours. After cooling to room temperature, the solid was collected by filtration and then recrystallized from benzene to afford 2.69 g (7.82 mmoles, 62%) of amide **2** as colorless crystals, mp 183-184° dec; tlc (benzene) R_f 0.49; ir (potassium bromide): 3415 (NH stretching), 3099, 3083 (aromatic CH stretching), 1665 (C=O stretching); ^1H nmr (deuteriochloroform): δ 7.27 (d, $J_{4,5} = 5.2$ Hz, 1H, H4), 7.47 (d, $J_{4,5} = 5.2$ Hz, 1H, H5), 7.54-8.26 (m, 7H, ArH), 9.18 (br, 1H, NH).

Anal. Calcd. for $\text{C}_{17}\text{H}_{10}\text{ClNOS}_2$: C, 59.38; H, 2.93; N, 4.07; Cl, 10.31; S, 18.65. Found: C, 59.70; H, 3.17; N, 3.92, Cl, 10.12; S, 18.35.

Benzo[*h*]thieno[3',2':4,5]thieno[2,3-*c*]quinolin-6(5*H*)-one (3).

A mixture of 0.5 g (1.45 mmoles) of amide **2**, 0.15 g of triethylamine, and 450 ml of benzene was irradiated with a 450 watt Hanovia medium pressure mercury vapor lamp for 4 hours. A slow stream of air was passed through the solution during the course of the reaction. After cooling to room temperature the solid was collected by filtration and washed with water to give 0.36 g (1.17 mmoles, 81%) of lactam **3**, mp >300°; ir (potassium bromide): 3155 (NH stretching), 3050 (aromatic CH stretching), 1635 (C=O stretching); ^1H nmr (dimethyl- d_6 sulfoxide): δ 7.36-8.13 (m, 5H, ArH), 8.31 (d, $J_{9,10} = 5.4$ Hz, 1H, H10), 8.56 (d, $J_{11,12} = 8.5$ Hz, 1H, H11), 8.98 (dd, $J_{3,4} = 6.2$ Hz, $J_{2,4} = 3.3$ Hz, 1H, H4). This compound was used in the next reaction without further purification due to its low solubility.

6-Chlorobenzo[*h*]thieno[3',2':4,5]thieno[2,3-*c*]quinoline (4).

A mixture of 1.82 g (5.92 mmoles) of lactam **3** and 80 ml of phosphorus oxychloride was heated at 110-115° for 4 hours. After cooling to room temperature the solution was slowly poured into 500 ml of ice-water with caution. The solid was collected by filtration

and rinsed with water. The solid was recrystallized from benzene to afford 1.49 g (4.57 mmoles, 77%) of chloride **4** as off-white crystals, mp 208-210°; tlc (benzene) R_f 0.88; ir (potassium bromide): 3052 (aromatic CH stretching); ^1H nmr (deuteriochloroform): δ 7.54-7.83 (m, 5H, ArH), 7.89 (d, $J_{9,10} = 5.4$ Hz, 1H, H10), 8.29 (d, $J_{11,12} = 9.0$ Hz, 1H, H11), 9.18-9.29 (m, 1H, H4).

Anal. Calcd. for $\text{C}_{17}\text{H}_8\text{ClNS}_2$: C, 62.66; H, 2.48; N, 4.30; S, 19.68. Found: C, 62.89; H, 2.70; N, 4.11; S, 19.41.

6-Hydrazinobenzo[*h*]thieno[3',2':4,5]thieno[2,3-*c*]quinoline (5).

To a boiling mixture of 0.44 g (1.35 mmoles) of chloride **4** in 75 ml of absolute ethanol and 20 ml of benzene was added dropwise 10 ml of anhydrous hydrazine over a period of 30 minutes. The mixture was heated at 100-110° for 24 hours. After cooling to room temperature the solid was collected by filtration, washed with ethanol and recrystallized from a benzene-ethanol mixture to give 0.40 g (1.24 mmoles, 92%) of hydrazine derivative **5** as colorless crystals, mp 228-230° dec; tlc (benzene) R_f 0.09; ir (potassium bromide): 3304, 3263 (NH_2 stretching), 3042 (aromatic CH stretching), 1617 (NH bending); ^1H nmr (dimethyl- d_6 sulfoxide): δ 3.40 (br s, 3H, NH and NH_2), 7.55-8.00 (m, 5H, ArH), 8.07 (d, $J_{9,10} = 5.4$ Hz, 1H, H10), 8.44 (d, $J_{11,12} = 9.0$ Hz, 1H, H11), 9.16-9.27 (m, 1H, H4).

Anal. Calcd. for $\text{C}_{17}\text{H}_{11}\text{N}_3\text{S}_2$: C, 63.53; H, 3.45; N, 13.07. Found: C, 63.30; H, 3.32; N, 12.85.

Benzo[*h*]thieno[3',2':4,5]thieno[2,3-*c*]quinoline (6).

A mixture of 0.25 g (0.78 mmole) of hydrazine **5** in 10 ml of water and 5 ml of glacial acetic acid was heated to boiling. To the boiling mixture 10 ml of a 10% copper sulfate solution was added dropwise. The resulting mixture was heated under reflux for 5 hours. After cooling to room temperature the mixture was basified with 2*N* sodium hydroxide solution. The mixture was extracted with dichloromethane (100 ml x 3) and dried over anhydrous magnesium sulfate. After filtration and removal of solvent, the solid was recrystallized from benzene to afford 0.15 g (0.52 mmole, 67%) of **6** as brownish prisms, mp 215-216°; tlc (benzene) R_f 0.52; ir (potassium bromide): 3049, 3076, 3089 (aromatic CH stretching).

Anal. Calcd. for $\text{C}_{17}\text{H}_8\text{NS}_2$: C, 70.32; H, 2.78; N, 4.82. Found: C, 70.08; H, 2.82; N, 4.75.

3-Chloro-N-(2-naphthyl)thieno[2,3-*b*]thiophene-2-carboxamide (7).

A mixture of 2.0 g (8.43 mmoles) of 3-chlorothieno[2,3-*b*]thiophene-2-carbonyl chloride (**1**) [1a, 3,4] and 1.21 g (8.43 mmoles) of 2-naphthylamine in 50 ml of benzene was heated under reflux for 4 hours. After cooling to room temperature the mixture was evaporated to dryness *in vacuo*. The solid was recrystallized from benzene to afford 2.50 g (7.27 mmoles, 86%) of amide **7** as colorless needles, mp 196-197°; tlc (benzene) R_f 0.47; ir (potassium bromide): 3317 (NH stretching), 1635 (C=O stretching); ^1H nmr (deuteriochloroform): δ 7.20-7.63 (m, 5H, ArH), 7.74-7.87 (m, 3H, ArH), 8.32 (d, $J_{1',3'} = 2.0$ Hz, 1H, H1'), 8.87 (br s, 1H, NH).

Anal. Calcd. for $\text{C}_{17}\text{H}_{10}\text{ClNOS}_2$: C, 59.38; H, 2.93; N, 4.07; S, 18.65. Found: C, 59.41; H, 3.02; N, 3.86; S, 18.84.

Benzo[*f*]thieno[3',2':4,5]thieno[2,3-*c*]quinolin-8(7*H*)-one (8).

A mixture of 0.5 g (1.45 mmoles) of amide **7** and 0.15 g of triethylamine in 500 ml of benzene was irradiated with a 450 watt Hanovia medium pressure mercury vapor lamp for 4 hours. A slow stream of air was passed through the solution during the

course of the reaction. The solid was collected by filtration and washed with water to give 0.4 g (1.30 mmoles, 89%) of lactam **8**, mp >300°; ir (potassium bromide): 3140 (NH stretching), 1635 (C=O stretching), 1617 (NH bending); ¹H nmr (dimethyl-d₆ sulfide): 130°, δ 7.33-8.06 (m, 7H, ArH), 8.67 (dd, J_{1,2} = 7.6 Hz, J_{1,3} = 1.5 Hz, 1H, H1). This compound was used for the next reaction without further purification because of its low solubility.

8-Chlorobenzo[f]thieno[3',2':4,5]thieno[2,3-c]quinoline (**9**).

A mixture of 2.27 g (7.39 mmoles) of lactam **8** and 80 ml of phosphorus oxychloride was heated under reflux for 4 hours. The mixture was slowly poured into 600 ml of ice-water with caution. The precipitate was collected by filtration and washed with water. The dried solid was recrystallized from benzene to afford 1.70 g (5.22 mmoles, 71%) of chloride **9** as off-white crystals, mp 197-200°; tlc (benzene) R_f 0.62; ir (potassium bromide): 3050 (aromatic CH stretching); ¹H nmr (deuteriochloroform): 50°, δ 7.53 (d, J_{11,12} = 5.4 Hz, 1H, H11), 7.64-7.79 (m, 2H, ArH), 7.98-8.10 (m, 4H, ArH), 8.94 (m, 1H, H1).

Anal. Calcd. for C₁₇H₈ClNS₂: C, 62.66; H, 2.48; N, 4.30; S, 19.68. Found: C, 62.67; H, 2.37; N, 4.19; S, 19.55.

8-Hydrazinobenzo[f]thieno[3',2':4,5]thieno[2,3-c]quinoline (**10**).

To a boiling mixture of 1.56 g (4.79 mmoles) of chloride **9** in 100 ml of ethanol and 50 ml of benzene 15 ml of anhydrous hydrazine was added dropwise over a period of 30 minutes. The mixture was heated under reflux for 10 hours. After cooling to room temperature the solid was collected by filtration and washed with ethanol. The solid was recrystallized from ethanol to give 1.33 g (4.14 mmoles, 86%) of hydrazine derivative **10** as fine pinkish needles, mp 230-233° dec; tlc (benzene) R_f 0.049; ir (potassium bromide): 3346, 3178 (NH₂ stretching); ¹H nmr (dimethyl-d₆ sulfide): δ 3.70 (br s, 2H, NH₂), 7.51-8.04 (m, 7H, ArH), 8.50 (br s, 1H, NH), 8.66 (dd, J_{1,2} = 7.1 Hz, J_{1,3} = 1.5 Hz, 1H, H1).

Anal. Calcd. for C₁₇H₁₁N₃S₂: C, 63.53; H, 3.45; N, 13.07. Found: C, 63.50; H, 3.46; N, 13.17.

Benzo[f]thieno[3',2':4,5]thieno[2,3-c]quinoline (**11**).

A mixture of 0.90 g (2.80 mmoles) of hydrazine **10** in 20 ml of water and 10 ml of glacial acetic acid was heated to boiling and then treated with 15 ml of a 10% copper sulfate solution. The mixture was heated under reflux for 4 hours. After cooling to room temperature the mixture was basified with 2 N sodium hydroxide solution. The mixture was extracted with dichloromethane (100 ml x 3), dried over anhydrous magnesium sulfate. After filtration and removal of the solvent the solid was recrystallized from benzene to yield 0.40 g (1.38 mmoles, 49%) of **11** as off-white crystals, mp 174-176°; tlc (dichloromethane) R_f 0.13; ir (potassium bromide): 3039 (aromatic CH stretching).

Anal. Calcd. for C₁₇H₈NS₂: C, 70.32; H, 2.78; N, 4.82. Found: C, 70.37; H, 3.00; N, 4.66.

Benzo[f]thieno[3',2':4,5]thieno[2,3-c]tetrazolo[1,5-a]quinoline (**12**).

To a mixture of 0.19 g (0.59 mmole) of hydrazine **10** in 10 ml of 50% acetic acid in an ice bath was added dropwise a solution of 0.10 g (1.45 mmoles) of sodium nitrite in 5 ml of water with vigorous stirring. The reaction mixture was stirred at room temperature for 4 hours. The precipitate was collected by filtration, washed with water, and dried. The solid was recrystallized from benzene to afford 0.10 g (0.3 mmole, 51%) of tetrazole **12** as light brown prisms, mp 236-238° dec; tlc (dichloromethane) R_f 0.71; ir

(potassium bromide): 3067 (aromatic CH stretching); ¹H nmr (deuteriochloroform): δ 7.53 (d, J_{11,12} = 5.5 Hz, 1H, H12), 7.66-7.77 (m, 2H, H2 and H3), 7.84 (d, J_{11,12} = 5.5 Hz, 1H, H11), 8.02-8.09 (m, 1H, H7), 8.17 (d, J_{5,6} = 8.8 Hz, 1H, H6), 8.72 (d, J_{5,6} = 8.8 Hz, 1H, H5), 8.86 (dd, J_{1,2} = 6.2 Hz, J_{1,3} = 3.5 Hz, 1H, H10).

Anal. Calcd. for C₁₇H₈N₄S₂: C, 61.41; H, 2.43; N, 16.85. Found: C, 61.36; H, 2.39; N, 16.87.

Benzo[f]thieno[3',2':4,5]thieno[2,3-c][1,2,4]triazolo[4,3-a]quinoline (**13**).

A mixture of 0.20 g (0.62 mmole) of hydrazine **10**, 10 ml of triethyl orthoformate and 15 ml of ethanol was heated at 95-100° for 12 hours. After cooling to room temperature the mixture was evaporated to dryness *in vacuo* and the solid was recrystallized from benzene to afford 0.18 g (0.54 mmole, 88%) of triazole **13** as off-white prisms, mp 150-152° dec; tlc (dichloromethane/ethyl acetate 1:1) R_f 0.26; ir (potassium bromide): 3110, 3095 (aromatic CH stretching), 1617 (C=N stretching); ¹H nmr (deuteriochloroform): δ 7.41 (d, J_{11,12} = 5.6 Hz, 1H, H12), 7.56-7.70 (m, 3H, ArH), 7.83-8.05 (m, 3H, ArH), 8.67 (dd, J_{9,10} = 6.1 Hz, J_{8,10} = 3.4 Hz, 1H, H10), 9.21 (s, 1H, H3).

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