The Synthesis of Novel Polycyclic Heterocyclic Ring Systems *via* Photocyclization. 7 [1]. [1]Benzothieno[2,3-*c*]naphtho[2,1-*h*]quinoline and [1]Benzothieno[2,3-*c*]naphtho[2,1-*h*][1,2,4]triazolo[4,3-*a*]quinoline

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Received April 15, 1992

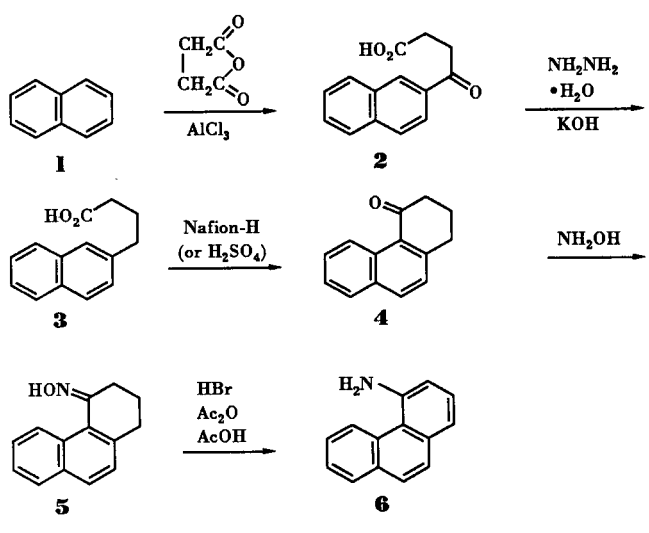
The synthesis of two novel polycyclic heterocyclic ring systems *via* photocyclization is described. These are [1]benzothieno[2,3-*c*]naphtho[2,1-*h*]quinoline and [1]benzothieno[2,3-*c*]naphtho[2,1-*h*][1,2,4]triazolo[4,3-*a*]-quinoline. In the ^{1}H nmr spectrum the proton at position 6 is strongly deshielded in the first ring system while the proton at position 6 in the second ring system is shifted considerably upfield while the proton at position 8 in the second ring system is the most deshielded proton in that ring system. The bay regions in both ring systems are severely congested.

J. Heterocyclic Chem., **29**, 963 (1992).

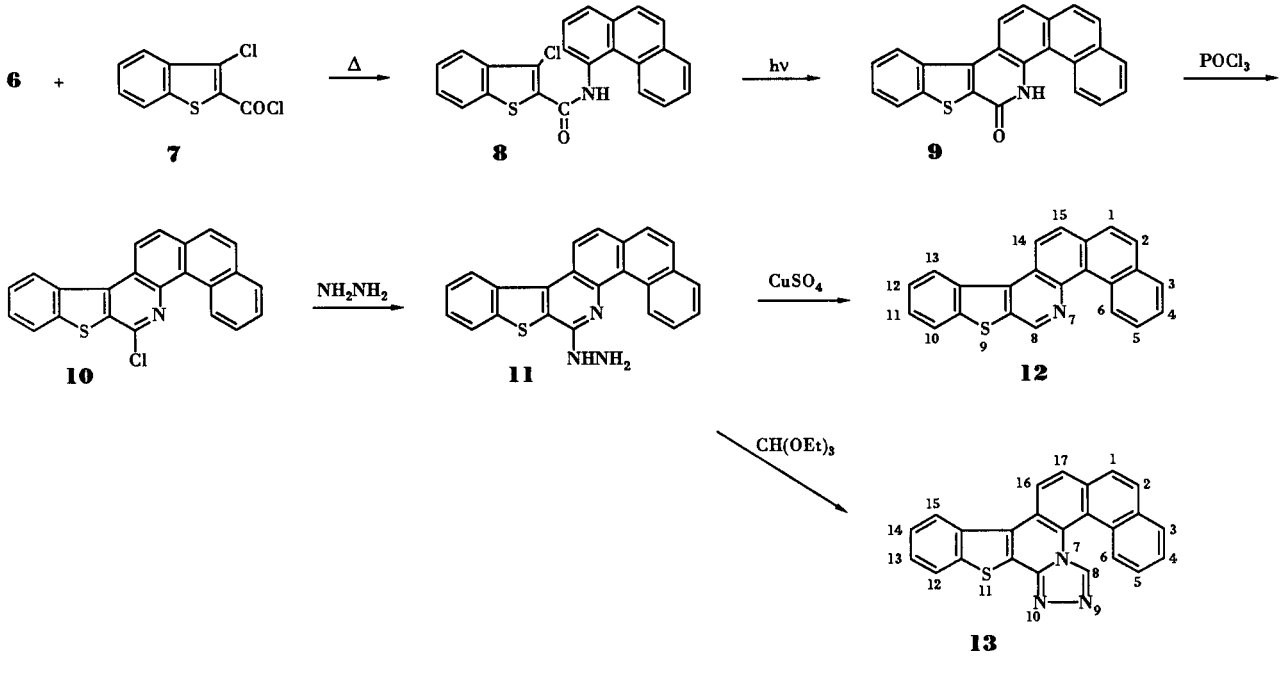
In continuation of our program designed to synthesize novel polycyclic heterocyclic ring systems *via* photocyclization [1a-f] we now report the synthesis of two novel unsubstituted polycyclic heterocyclic ring systems. These are [1]benzothieno[2,3-*c*]naphtho[2,1-*h*]quinoline (**12**) and [1]benzothieno[2,3-*c*]naphtho[2,1-*h*][1,2,4]triazolo[4,3-*a*]-quinoline (**13**). Both ring systems display a rather congested bay region involving H-6 in both **12** and **13**.

As shown in Scheme 1, the requisite key intermediate, 4-aminophenanthrene (**6**) was prepared by essentially the same route reported by Haworth [3] and Beringer *et al.* [4]. Clemmensen reduction had been carried out in the process from 3-(2′-naphthoyl)propionic acid (**2**) to 4-(2′-naphthyl)butyric acid (**3**) [3], but purification of the reduction product was troublesome in our hands. Therefore we performed a Huang-Minlon reaction [5] for this reduction because of its high yield (93%) and ease of purification. Re-

Scheme 1



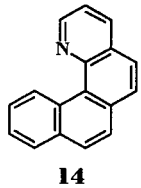
Scheme 2



cently, it was reported that 4-phenylbutyric acid cyclized in refluxing *p*-xylene in 88% yield in the presence of Nafion-H (Aldrich) [6]. Thus, a similar cyclization of compound **3** using Nafion-H was performed (Method A). This reaction proceeded in 75% yield, however purification of the desired product was complicated because of the presence of a less polar impurity. Therefore, cyclization of compound **3** was also performed using sulfuric acid to promote the reaction (Method B). This reaction gave the desired product in lower yield (68%) than Method A, but purification was easier and the desired product was obtained as almost a single spot on tlc at the end of an extraction. After conversion of ketone **4** to oxime **5** in quantitative yield with hot ethanolic hydroxylamine and pyridine, compound **6** was obtained from **5** by the method of Beringer *et al.* [4].

As shown in Scheme 2 compound **6** was allowed to react with 3-chlorobenzo[*b*]thiophene-2-carbonyl chloride (**7**) [1b] in benzene solution, and 3-chloro-*N*-(4′-phenanthryl)-benzo[*b*]thiophene-2-carboxamide (**8**) was obtained in 65% yield. Irradiation of amide **8** in cyclohexane-benzene solution containing triethylamine with a 450 watt medium pressure mercury vapor lamp gave the cyclized product **9** in 86% yield. Chlorination of compound **9** was accomplished by refluxing in phosphorus oxychloride to yield 6-chloro[1]benzothieno[2,3-*c*]naphtho[2,1-*h*]quinoline (**10**) in 87% yield. Compound **10** reacted with anhydrous hydrazine in ethanol to afford 6-hydrazino[1]benzothieno[2,3-*c*]-naphtho[2,1-*h*]quinoline (**11**) in 82% yield. This hydrazino derivative **11** in a refluxing mixture of acetic acid and water with a 10% solution of copper sulfate produced the unsubstituted compound **12** in 92% yield whereas refluxing a suspension of **11** in ethanol with triethyl orthoformate resulted in a 67% yield of compound **13**.

We have observed the most deshielded proton at 11.09 ppm in the ^{1}H nmr spectrum of **12** and have assigned it to H-6 in the congested bay region. This same proton (H-6) in compound **13** is shifted upfield to 8.21 ppm because of the proximity of H-8 appearing at 9.22 ppm, the furthest downfield proton in this ring system **13**. These observations are consistent with the remarkable deshielding of H-12 (11.25 ppm) reported by Martin *et al.* [7] in the bay region of naphtho[2,1-*h*]quinoline (**14**).



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EXPERIMENTAL

Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. The ir spectra were recorded on a Beckman FT 1100 spectrometer as potassium bromide pellets and frequencies are expressed in cm^{-1}. The ^{1}H nmr spectra were obtained on a JEOL FX-90Q spectrometer in the solvent indicated with TMS as the internal standard and chemical shifts are reported in ppm (δ) and J values in Hz. Elemental analyses were performed by M-H-W Laboratories, Phoenix, Arizona.

3-(2′-Naphthoyl)propionic Acid (**2**).

The title compound was prepared by the method of Haworth [3] in 36% yield as colorless plates, mp 171-174° (from methanol, lit [3] mp 171-173°, lit [8] mp 174°).

4-(2′-Naphthyl)butyric Acid (**3**).

A mixture of 22.8 g (0.10 mole) of 3-(2′-naphthoyl)propionic acid (**2**), 19.0 g (0.34 mole) of potassium hydroxide, 14 ml of 85% hydrazine hydrate, and 140 ml of diethylene glycol was refluxed for 1 hour 40 minutes. The water formed in the reaction mixture was evaporated and the temperature allowed to raise to 200°. Refluxing of the reaction mixture was continued for an additional 5 hours. After cooling, the reaction mixture was diluted with 300 ml of water and the mixture was poured slowly into 200 ml of 6*N* hydrochloric acid. The precipitated pale brown solid was collected by filtration and dissolved in 500 ml of ether. The ether solution was washed with water, dried over anhydrous sodium sulfate, and evaporated to dryness. Recrystallization of the residue from cyclohexane gave 19.9 g (93%) of **3** as pale brown scales, mp 97-98° (lit [3] mp 94-95°, lit [8] mp 95°).

4-Oxo-1,2,3,4-tetrahydrophenanthrene (**4**).

Method A.

A mixture of 6.5 g (30.4 mmoles) of compound **3**, 2.0 g (30 wt%) of Nafion-H, and 100 ml of *p*-xylene was refluxed for 40 hours. After cooling, the reaction mixture was filtered and the filtrate was evaporated to give a viscous red-brown oil. Crystallization and recrystallization of the hot-cyclohexane soluble fraction of this oily residue were repeated from cyclohexane to afford 4.4 g (75%) of the compound as pale reddish-brown prisms, mp 65-68° (lit [3] mp 69°, lit [8] mp 69°). The compound was identified with the product obtained by Method B by comparison of the spectral data and by mixed melting point determination.

Method B.

Compound **4** was prepared by the method of Haworth [3] in 68% yield as pale brown prisms, mp 66.5-68° (from cyclohexane).

4-Oxo-1,2,3,4-tetrahydrophenanthrene Oxime (**5**).

This compound was prepared by the method of Beringer *et al.* [4] in 95% yield as colorless prisms, mp 173-175° (from benzene, lit [8] mp 172-173°).

4-Aminophenanthrene (**6**).

This compound was prepared by the method of Beringer *et al.* [4] in 36% yield as pale brown prisms, mp 61-63° (lit [4] mp 64-65°, lit [9] mp 55°, lit [10] mp 62.5-63.5°).

3-Chloro-*N*-(4′-phenanthryl)benzo[*b*]thiophene-2-carboxamide (**8**).

A solution of 1.50 g (7.77 mmoles) of compound **6** and 1.80 g (7.79 mmoles) of compound **7** in 50 ml of benzene was refluxed for 4 hours. After cooling, the reaction mixture was concentrated to about 10 ml and the precipitated pale gray solid was collected by filtration. The solid, which behaved as almost a single spot on tlc, was recrystallized from benzene to give 1.97 g (65%) of **8** as

pale brown needles, mp 219-221°; ir (potassium bromide): 3224 (N-H stretching), 3050 (aromatic C-H stretching), 1625 (C=O stretching); ^{1}H nmr (DMSO-d_6): δ 7.56-7.72 (m, 6H, Ar-H), 7.89-8.25 (m, 6H, Ar-H), 9.35-9.46 (m, 1H, Ar-H), 10.97 (s, 1H, NH).

Anal. Calcd. for $C_{23}H_{14}ClNOS$: C, 71.21; H, 3.63; N, 3.61; S, 8.26. Found: C, 71.28; H, 3.66; N, 3.58; S, 8.43.

[1]Benzothieno[2,3-*c*]naphtho[2,1-*h*]quinolin-6(5*H*)-one (**9**).

To a solution of 500 mg (1.29 mmoles) of compound **8** in 500 ml of a mixture of cyclohexane and benzene (2:1, v/v), 0.2 ml of triethylamine was added and the solution was irradiated with a 450 watt Hanovia medium pressure mercury lamp for 12.5 hours. The pale yellow solid which precipitated during the reaction was collected by filtration and the filtrate was evaporated to dryness. The brown residue was triturated with 2 ml of benzene and the undissolved solid was collected by filtration and combined with the solid which was obtained from the former filtration. The combined solid was washed thoroughly with water, dried at 100° for 3 hours to give 389 mg (86%) of **9**, mp 272-274°; ir (potassium bromide): 3134 (N-H stretching), 3057 (aromatic C-H stretching), 1635 (C=O stretching); ^{1}H nmr (DMSO-d_6): δ 7.67-8.36 (m, 9H, Ar-H), 8.95-9.09 (2 doublets partially overlapped, 2H, H-13, H-14), 9.60 (m, 1H, H-6). This compound was used in the next step without further purification because of its low solubility.

6-Chloro[1]benzothieno[2,3-*c*]naphtho[2,1-*h*]quinoline (**10**).

A mixture of 1.38 g (3.93 mmoles) of compound **9** and 40 ml of phosphorus oxychloride was refluxed for 17 hours. After cooling, the reaction mixture was evaporated to dryness and 30 ml of ice-water was poured carefully onto the residue. The mixture was basified with sodium hydrogen carbonate and the mixture was extracted with benzene. The undissolved solid in both layers during the extraction was filtered. The organic layer was washed with water, dried over anhydrous sodium sulfate and evaporated to give 800 mg of a crystalline yellow solid which was combined with the hot-benzene soluble fraction of the above filtered solid. The mixture was recrystallized from benzene to afford 1.26 g (87%) of compound **10** as pale yellow needles, mp 202-204°; ir (potassium bromide): 3055, 3124 (aromatic C-H stretching); ^{1}H nmr (deuteriochloroform): δ 7.52-8.03 (m, 9H, Ar-H), 8.73 (dd, 1H, $J_{13,12}$ = 5.7 Hz, $J_{13,11}$ = 4.0 Hz, H-13), 8.79 (d, 1H, J = 8.8 Hz, H-14), 10.85 (dd, 1H, $J_{6,5}$ = 7.9 Hz, $J_{6,4}$ = 1.5 Hz, H-6).

Anal. Calcd. for $C_{23}H_{12}ClNS$: C, 74.68; H, 3.27; N, 3.78; S, 8.66. Found: C, 74.64; H, 3.28; N, 3.56; S, 8.61.

6-Hydrazino[1]benzothieno[2,3-*c*]naphtho[2,1-*h*]quinoline (**11**).

To a stirred suspension of 1.10 g (2.98 mmoles) of compound **10** in 50 ml of ethanol was added 8.0 ml (255 mmoles) of anhydrous hydrazine over a period of 30 minutes. The mixture was refluxed for 24 hours. After cooling the precipitate in the reaction mixture was collected by filtration and crystallized from ethyl acetate. The crystals were recrystallized from benzene to afford 886 mg (82%) of compound **11** as pale brown needles, mp 228-230° dec; ir (potassium bromide): 3327, 3250, 3129 (N-H stretching), 3047 (aromatic C-H stretching); ^{1}H nmr (DMSO-d_6): δ 4.98 (s, 2H, NH_2), 7.64-8.33 (m, 9H, Ar-H), 8.88 (s, 1H, NH), 9.06 (d, 1H, J = 5.3 Hz, H-13), 9.08 (d, 1H, J = 8.8 Hz, H-14), 11.37 (dd, 1H, $J_{6,5}$ = 7.9 Hz, $J_{6,4}$ = 1.8 Hz, H-6).

Anal. Calcd. for $C_{23}H_{15}N_3S$: C, 75.59; H, 4.13; N, 11.49. Found: C, 75.76; H, 4.25; N, 11.28.

[1]Benzothieno[2,3-*c*]naphtho[2,1-*h*]quinoline (**12**).

A suspension of 200 mg (0.55 mmole) of compound **11** in 4 ml of water and 4 ml of acetic acid was heated to boiling and treated dropwise with 3 ml of a 10% solution of copper sulfate. The mixture was refluxed for 3 hours. After cooling, the reaction mixture was poured into 40 ml of ice-water, and the mixture was basified with 2*N* sodium hydroxide. The mixture was extracted with dichloromethane and the organic layer was washed with water, dried over anhydrous sodium sulfate and evaporated to dryness. The crystalline residue was recrystallized from benzene to give 169 mg (92%) of compound **13** as pale yellow needles, mp 240-242°; ir (potassium bromide): 3050, 3116 (aromatic C-H stretching); ^{1}H nmr (deuteriochloroform): δ 7.60-7.76 (m, 3H, Ar-H), 7.82-8.19 (m, 6H, Ar-H), 8.93 (dd, 1H, $J_{13,12}$ = 5.2 Hz, $J_{13,11}$ = 2.2 Hz, H-13), 9.04 (d, 1H, J = 8.6 Hz, H-14), 9.62 (s, 1H, H-8), 11.09 (dd, 1H, $J_{6,5}$ = 8.3 Hz, $J_{6,4}$ = 1.5 Hz, H-6).

Anal. Calcd. for $C_{23}H_{13}NS$: C, 82.35; H, 3.90; N, 4.17. Found: C, 82.17; H, 4.12; N, 4.12.

[1]Benzothieno[2,3-*c*]naphtho[2,1-*h*][1,2,4]triazolo[4,3-*a*]quinoline (**13**).

A suspension of 200 mg (0.55 mmole) of compound **11** in 8 ml of triethyl orthoformate and 16 ml of ethanol was refluxed for 24 hours. After cooling, the crystalline precipitate was collected by filtration and recrystallized from benzene to give 137 mg (67%) of compound **13** as pale yellow prisms, mp >300°; ir (potassium bromide): 3052, 3122 (aromatic C-H stretching); ^{1}H nmr (deuteriochloroform): δ 7.49-8.01 (m, 9H, Ar-H), 8.19 (br d, 1H, J = 9.2 Hz, H-6), 8.71 (br d, 1H, J = 7.6 Hz, H-15), 8.86 (d, 1H, J = 8.6 Hz, H-16), 9.19 (s, 1H, H-8).

Anal. Calcd. for $C_{24}H_{13}N_3S$: C, 76.77; H, 3.48; N, 11.19. Found: C, 76.89; H, 3.60; N, 11.00.

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