The Synthesis of Novel Polycyclic Heterocyclic Ring Systems *via* Photocyclization. 3 [1]. 12-Methylbenzo[*h*][1]benzothieno[2,3-*c*][1,6]naphthyridine

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The synthesis of the 12-methyl derivative of a novel heterocyclic ring system, namely benzo[*h*][1]benzothieno[2,3-*c*][1,6]naphthyridine (**8**) was prepared by photocyclization of 3-chloro-*N*-(2′-methyl-4′-quinolyl)benzo[*b*]thiophene-2-carboxamide (**5**) to 12-methylbenzo[*h*][1]benzothieno[2,3-*c*][1,6]naphthyridin-6(5*H*)-one (**6**). Chlorination of **6** afforded 6-chloro-12-methylbenzo[*h*][1]benzothieno[2,3-*c*][1,6]naphthyridine (**7**) which upon dechlorination provided the novel title compound **8**.

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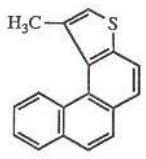
We have become interested in the synthesis and the spectral evaluation of polycyclic aromatic thiophenes [3] and related heterocycles [4]. We reported in a previous study [5] the determination of the tertiary structure in solution and in the crystalline state of 1-methylphenanthro[3,4-*b*]thiophene (**1**). The related phenanthro[3,4-*b*]-thiophene and benzo[*b*]phenanthro[4,3-*c*]thiophene (**2**) [6] also have pronounced tertiary helical structures in solution. Therefore, we wish to report the synthesis of a new heterocyclic ring system that possesses a methyl group in the bay region similar to **1**.

When 3-chlorobenzo[*b*]thiophene-2-carbonyl chloride (**3**) was treated with 4-amino-2-methylquinoline (**4**), a 70% yield of 3-chloro-*N*-(2′-methyl-4′-quinolyl)benzo[*b*]thiophene-2-carboxamide (**5**) resulted. Dehydrochlorinative photocyclization of the carboxamide **5** was carried out under oxidative conditions to furnish 12-methylbenzo[*h*][1]benzothieno[2,3-*c*][1,6]naphthyridin-6(5*H*)-one (**6**) (85%). The photocyclization was carried out in benzene in the presence of equal molar amounts of triethylamine. The lactam **6** was chlorinated in refluxing phosphorus oxychloride to give 6-chloro-12-methylbenzo[*h*][1]benzothieno[2,3-*c*][1,6]-naphthyridine (**7**) (47%). 6-Chloro-12-methylbenzo[*h*][1]-benzothieno[2,3-*c*][1,6]naphthyridine (**7**) was dechlorinated with 10% Pd/C in a solution of sodium hydroxide, methanol, and benzene under a hydrogen atmosphere to yield 12-methylbenzo[*h*][1]benzothieno[2,3-*c*][1,6]naphthyridine (**8**) (59%). The structure of **8** was established by a COSY spectrum which confirmed the presence of two four spin systems. The details of a 2D-nmr study will be published later in a full paper establishing the tertiary structure of **8**.



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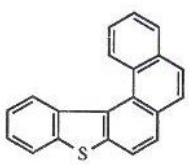

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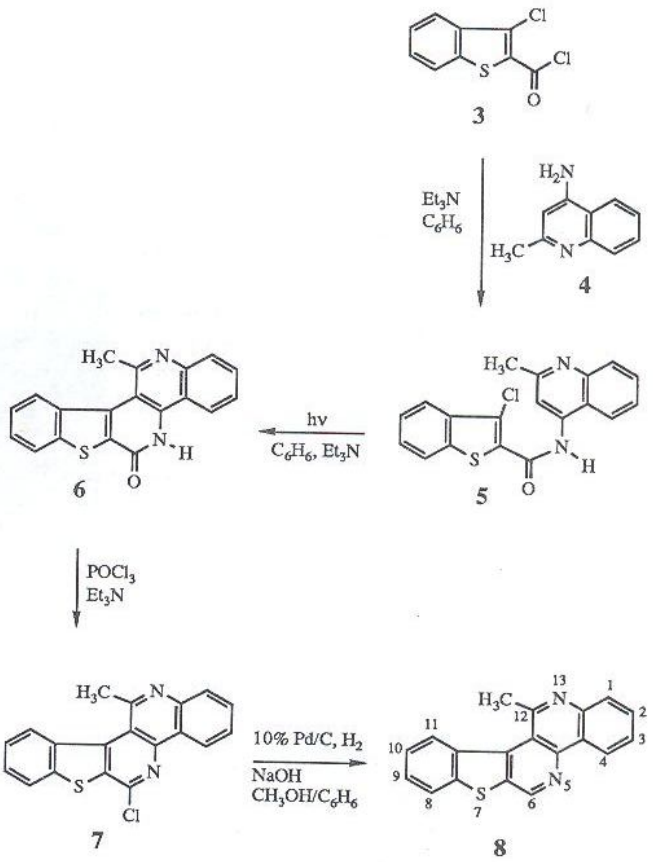

EXPERIMENTAL

Melting points were determined on a Thomas Hoover melting point apparatus and are uncorrected. The ir spectra were recorded on a Beckmann FT 1100 spectrometer as potassium bromide pellets and frequencies are expressed in cm^{-1}. The ^1H and ^{13}C nmr spectra were obtained on a Bruker AMX 360 in the solvent indicated with TMS as the internal standard and chemical shifts reported in ppm (δ) and J values in Hz. Elemental analyses were performed by M-H-W Laboratories, Phoenix, Arizona.

3-Chloro-*N*-(2′-methyl-4′-quinolyl)benzo[*b*]thiophene-2-carboxamide (**5**).

A solution of 4-amino-2-methylquinoline (**4**) (0.68 g, 4.3 mmoles) and triethylamine (0.6 ml, 4.3 mmoles) in benzene (50 ml) was added dropwise to a stirred solution of 3-chlorobenzo[*b*]-thiophene-2-carbonyl chloride (**3**) (1 g, 4.3 mmoles) in benzene (50 ml) at room temperature. After the addition was complete, the mixture was stirred for 12 hours at *ca* 50°. Excess solvent was removed under reduced pressure to give a light-brown solid. This solid was suspended in water (15 ml) to remove quaternary salts, stirred for 15 minutes and then filtered. The resulting solid was dissolved in hot benzene (200 ml), the solution was treated with charcoal, then allowed to cool and stand at room temperature overnight. The precipitate was collected by filtration and dried to afford 1.12 g (70%) of **5** as faint-brown needles, mp 276-280° dec; ir (potassium bromide): 1687, 1650, 1609, 1583, 1509, 1342, 1092, 930, 851, 755 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 8.55 (bs, amide NH, 1H), 8.4 (d, 1H, J = 8 Hz), 7.94 (m, 4H), 7.50 (m, 3H), 6.64 (s, 3'H, 1H), 2.64 (s, 3H, methyl).

Anal. Calcd. for $C_{19}H_{13}ClN_2OS\cdot 2.5H_2O$: C, 57.35; H, 4.56; N, 7.04; S, 8.06. Found: C, 57.60; H, 3.94; N, 6.84; S, 7.72 [7].

12-Methylbenzo[*h*][1]benzothieno[2,3-*d*][1,6]naphthyridin-6(5*H*)-one (**6**).

A stirred solution of 3-chloro-*N*-(2'-methyl-4'-quinolyl)benzo-[*b*]thiophene-2-carboxamide (**5**) (1 g, 2.8 mmoles) and triethylamine (0.4 ml, 2.9 mmoles) in benzene (500 ml) was irradiated for 8 hours with a 450 watt Hanovia medium pressure mercury lamp under a slow stream of air. The material was collected, the solvent removed under reduced pressure, and washed with water (2 x 10 ml) then dried to give 0.81 g (85%) of **6** as very light yellowish crystals, mp 258-260°; Beilstein test negative; ir (potassium bromide): 1684, 1558, 1504, 1419, 1272, 1227, 766, 741 cm^{-1}. This material was used without further purification because of the lack of solubility in crystallization solvents.

6-Chloro-12-methylbenzo[*h*][1]benzothieno[2,3-*c*][1,6]naphthyridine (**7**).

A stirred mixture of 12-methylbenzo[*h*][1]benzothieno[2,3-*c*]-[1,6]naphthyridin-6(5*H*)-one (**6**) (0.75 g, 2.4 mmoles) in phosphorus oxychloride (30 ml) and triethylamine (0.4 ml, 2.8 mmoles) was refluxed for 12 hours then excess solvent removed under reduced pressure. The resulting viscous material was cooled to ice bath temperature where residual phosphorus oxychloride was decomposed by the portionwise addition of crushed ice (*ca* 75 g). The precipitate was collected by filtration and dried. This solid was dissolved in hot benzene (200 ml), treated with charcoal, allowed to cool and stand at room temperature overnight. The precipitate was collected by filtration and recrystallized from benzene (2x) to give 0.37 g (47%) of **7** as thin white needles. The compound started to decompose at 180° and turned black at 220°; ir (potassium bromide): 1553, 1501, 1437, 1203, 912, 761 s, 746 s cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 9.08 (d, 1H, J = 8 Hz), 8.48 (d, 1H, J = 7.7 Hz), 8.12 (m, 2H), 7.84 (m, 1H), 7.67 (m, 3H), 3.18 (s, 3H, methyl).

Anal. Calcd. for $C_{19}H_{11}ClN_2S\cdot 0.25H_2O$: C, 67.05; H, 3.70; N, 8.23; S, 9.42. Found: C, 67.18; H, 3.98; N, 8.29; S, 9.66.

12-Methylbenzo[*h*][1]benzothieno[2,3-*c*][1,6]naphthyridine (**8**).

A 10% Pd/C catalyst (0.2 g) was added to a stirred solution of 6-chloro-12-methylbenzo[*h*][1]benzothieno[2,3-*c*][1,6]naphthyridine (**7**) (0.15 g, 0.45 mmole) in a solution of sodium hydroxide (0.018 g, 0.45 mmole), methanol (100 ml) and benzene (100 ml). The mixture was stirred under a hydrogen atmosphere for 3 days at room temperature. The catalyst was removed by filtration through a Celite pad and the filtrate concentrated to dryness under reduced pressure. The solid residue was dissolved in hot benzene (100 ml) and treated with charcoal. To the hot filtrate an equal volume of cyclohexane was added, the solution was allowed to cool and then stand at room temperature overnight. The solid was collected and recrystallized from cyclohexane:benzene (3:2) to afford 80 mg (59%) of off-white crystals, mp 192-194°; Beilstein test negative; ir (potassium bromide): 1578, 1556, 1509, 1450, 764 s, 738 s cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 9.55 (s, H6, 1H), 9.14 (dd, 1H, J = 8.1, 1.2 Hz, H11), 8.50 (dd, 1H, J = 7, 1.6 Hz, H1), 8.15 (m, 1H), 8.09 (m, 1H), 7.83 (m, 1H), 7.73 (m, 1H), 7.64 (m, 2H), 3.18 (s, 3H, methyl). The COSY spectrum confirmed the presence of two four spin systems; ^{13}C-nmr (dimethyl sulfoxide-d_6): protonated carbons at δ 27.64, 123.65, 123.94, 124.82, 126.54, 127.60, 128.76, 129.09, 129.84, 148.40, and quaternary carbons at δ 115.48, 123.35, 133.44, 135.35, 136.36, 141.43, 144.42, 145.15, 155.78.

Anal. Calcd. for $C_{19}H_{12}N_2S$: C, 75.97; H, 4.03; N, 9.33. Found: C, 75.80; H, 4.00; N, 9.48.

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[7] A more satisfactory value for hydrogen was not obtainable.