Synthesis of [1]Benzothienonaphthyridines

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3-Chlorobenzo[*b*]thiophene-2-carbonyl chloride reacted readily with 2-amino-, 3-amino-, or 4-aminopyridine to give the corresponding amides. Photocyclization of the amides afforded the following lactams: [1]benzothieno[2,3-*c*][1,5]naphthyridin-6(5*H*)-one (**14**), [1]benzothieno[2,3-*c*][1,6]naphthyridin-6(5*H*)-one (**7**), [1]benzothieno[2,3-*c*][1,7]naphthyridin-6(5*H*)-one (**11**), and [1]benzothieno[2,3-*c*][1,8]naphthyridin-6(5*H*)-one (**3**). These lactams have been converted to other derivatives including in two instances the unsubstituted ring system.

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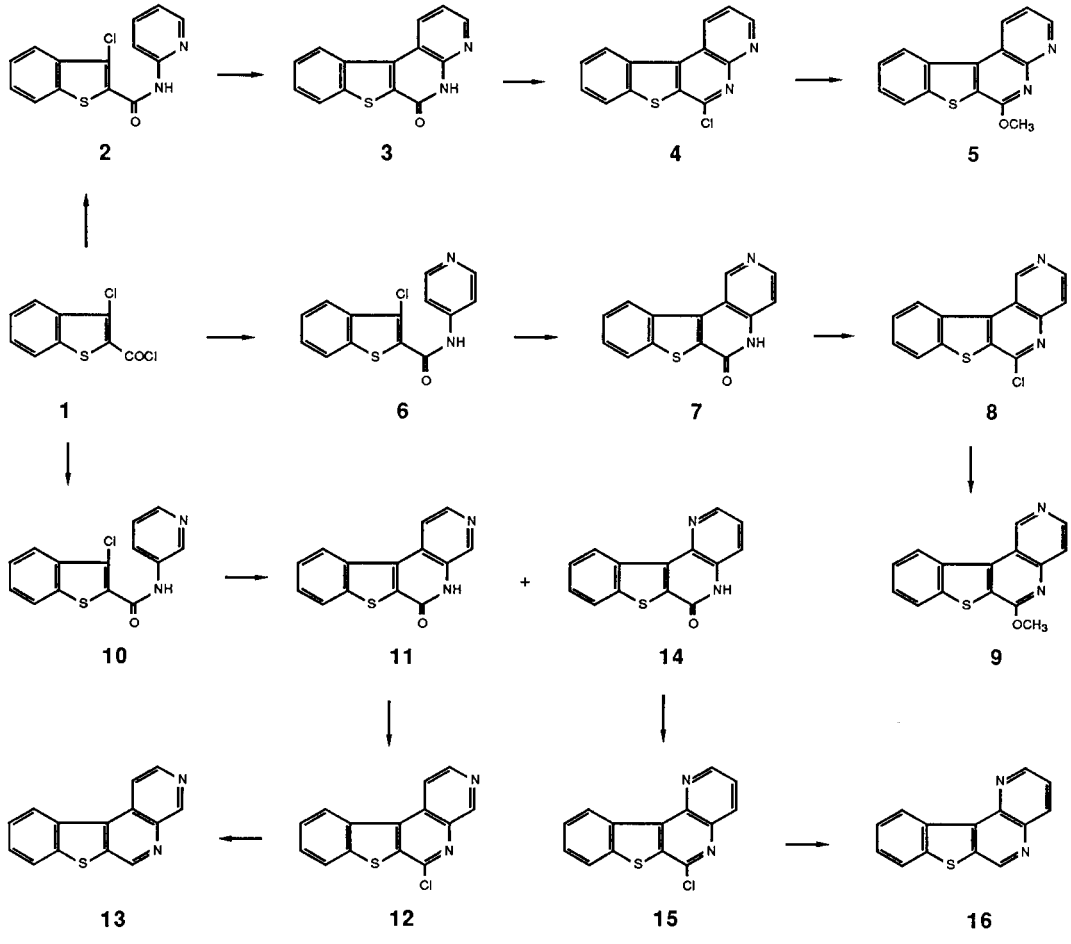
In order to continue our efforts to synthesize polycyclic heterocycles which are suspected of occurring in coal liquids, shale oils and related coal-derived products, we have undertaken the synthesis of the following ring systems: [1]benzothieno[2,3-*c*][1,5]naphthyridine, [1]benzothieno[2,3-*c*][1,6]naphthyridine, [1]benzothieno[2,3-*c*][1,7]naphthyridine, and [1]benzothieno[2,3-*c*][1,8]naphthyridine so that representative compounds in these ring sys-

Scheme 1



tems could be sought in coal-derived products.

These four [1]benzothienonaphthyridines have been reported in the form of the lactams only in a preliminary communication without adequate published characterization [4].

When 3-chlorobenzo[*b*]thiophene-2-carbonyl chloride (**1**) [5] was allowed to react with 2-aminopyridine, 3-chloro-*N*-(2-pyridyl)benzo[*b*]thiophene-2-carboxamide (**2**) was obtained in 86% yield. Photocyclization of **2** afforded [1]benzothieno[2,3-*c*][1,8]naphthyridin-6(5*H*)-one (**3**) [4] in 54% yield. Phosphorus oxychloride chlorination of **3** provided 6-chloro[1]benzothieno[2,3-*c*][1,8]naphthyridine (**4**) in 18% yield. The catalytic dehalogenation (5% Pd-C) of **4** in methanolic potassium hydroxide did not provide the unsubstituted ring system, rather 6-methoxy[1]benzothieno-[2,3-*c*][1,8]naphthyridine (**5**) was obtained in 57% yield.

The reaction of **1** with 4-aminopyridine gave 3-chloro-*N*-(4-pyridyl)benzo[*β*]thiophene-2-carboxamide (**6**) in 81% yield. Photocyclization of the amide **6** afforded [1]benzothieno[2,3-*c*][1,6]naphthyridine-6(5*H*)-one (**7**) [4] in 90% yield. Chlorination of the lactam **7** with phosphorus oxychloride gave 6-chloro[1]benzothieno[2,3-*c*][1,6]naphthyridine (**8**) in 18% yield. The attempts to catalytically dechlorinate **8** (5% Pd-C, methanolic potassium hydroxide) again afforded only 6-methoxy[1]benzothieno[2,3-*c*][1,6]-naphthyridine (**9**) in 57% yield.

3-Chloro-*N*-(3-pyridyl)benzo[*b*]thiophene-2-carboxamide (**10**) was obtained in 90% yield when **1** was allowed to react with 3-aminopyridine. Photocyclization of **10** afforded a separable mixture of two lactams. [1]Benzothieno-[2,3-*c*][1,7]naphthyridine-6(5*H*)-one (**11**) was obtained in 88% yield while the more soluble [1]benzothieno[2,3-*c*]-[1,5]naphthyridin-6(5*H*)-one (**14**) [4] was obtained in 7% yield in contrast to the yields previously reported [4]. In our hands 95% of the amide **10** photocyclized. When **11** was allowed to react with phosphorus oxychloride, 6-chloro[1]benzothieno[2,3-*c*][1,7]naphthyridine (**12**) was obtained in 44% yield. Catalytic dechlorination of **12** (5% Pd-C, methanol, potassium hydroxide and benzene) provided [1]benzothieno[2,3-*c*][1,7]naphthyridine (**13**) in 67% yield. In this instance no methoxy derivative was detected. Phosphorus oxychloride chlorination of **14** afforded 6-chloro[1]-benzothieno[2,3-*c*][1,5]naphthyridine (**15**) in 64% yield. Catalytic dechlorination of **15** under the same conditions as for the preparation of **13** also provided [1]benzothieno-[2,3-*c*][1,5]naphthyridine (**16**) in 58% yield. Likewise in this instance a methoxy derivative was not obtained.

All compounds have been characterized by spectral methods and all compounds except the lactams have been further characterized by elemental analyses for CHNS.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. The ^{1}H nmr spectra were obtained on a Varian EM 360 spectrometer or on a JEOL FX 90Q Fourier Transform spectrometer in the solvent indicated. Mass spectra were obtained on a Hewlett Packard model 5980A mass spectrometer. Elemental analyses were performed by MHW Laboratories, Phoenix, Arizona.

3-Chloro-*N*-(2-pyridyl)benzo[*b*]thiophene-2-carboxamide (**2**).

A mixture of **1** (3.5 g, 0.015 mole), 2-aminopyridine (1.4 g, 0.015 mole), pyridine (1.2 g, 0.015 mole), and benzene (50 ml) was heated on a steam bath for 1 hour. After removal of benzene, the residue was washed with water and 3.7 g (86%) of product was obtained. The analytical sample was recrystallized from absolute ethanol, white prisms, mp 167-168°; ^{1}H nmr (deuteriochloroform): δ 7.35-8.12 (m, 6H), 8.21-8.54 (m, 2H), 9.56 (br s, 1H); ms: m/e (relative intensity) 288 (M^+, 5), 286 (M^+, 12), 196 (40), 194 (100).

Anal. Calcd. for $C_{14}H_9ClN_2OS$: C, 58.23; H, 3.14; N, 9.70; S, 11.10. Found: C, 58.19; H, 3.21; N, 9.62; S, 11.07.

[1]Benzothieno[2,3-*c*][1,8]naphthyridin-6(5*H*)-one (**3**).

A solution of **2** (0.5 g, 0.0017 mole) and triethylamine (0.0017 mole) in dry benzene (500 ml) was irradiated for 2 hours with a 450 watt Hanovia medium pressure mercury lamp. During the course of the reaction, a slow stream of air was passed through the solution. The solvent was evaporated *in vacuo* and the residue was washed with water and used in the next reaction. There was obtained 0.2 g (54%) of colorless prisms, mp >270°; ^{1}H nmr (deuteriochloroform + deuteriotrifluoroacetic acid): δ 7.17-8.26 (m, 4H), 8.47-8.93 (m, 2H), 9.55-9.83 (m, 1H); ms: m/e (relative intensity) 252 (M^+, 18), 251 (M^+-1, 100). This compound was used in the next reaction without further purification.

6-Chloro[1]benzothieno[2,3-*c*][1,8]naphthyridine (**4**).

A mixture of **3** (1.9 g, 0.08 mole) and phosphorus oxychloride (40 ml) was gently refluxed for 3.5 hours. After removal of the excess phosphorus oxychloride, the residue was poured into ice water (100 ml). The precipitate (0.4 g, 18%) was collected by filtration. The analytical sample was recrystallized from benzene, pale yellow prisms, mp 220-221°; ^{1}H nmr (deuteriochloroform + deuteriotrifluoroacetic acid): δ 7.75-8.27 (m, 4H), 8.31-8.71 (m, 1H), 9.14-9.44 (m, 1H), 9.99-10.32 (m, 1H); ms: m/e (relative intensity) 272 (M^+, 31) 270 (M^+, 100).

Anal. Calcd. for $C_{14}H_7ClN_2S$: C, 62.11; H, 2.61; N, 10.35; S, 11.84. Found: C, 62.28; H, 2.77; N, 10.36; S, 11.73.

6-Methoxy[1]benzothieno[2,3-*c*][1,8]naphthyridine (**5**).

A solution of **4** (0.2 g, 0.0007 mole) and potassium hydroxide (0.04 g, 0.0007 mole) in methanol (40 ml) and benzene (40 ml) was hydrogenated catalytically using 5% Pd-C catalyst (0.5 g) at atmospheric pressure and room temperature. After the uptake of an equimolar amount of hydrogen, the catalyst was filtered and the solvent was removed under reduced pressure. The product was treated with water, extracted with benzene, dried over anhydrous sodium sulfate, and evaporated to afford 0.1 g (57% of product). The analytical sample was recrystallized from benzene, pale yellow prisms, mp 190-191°; ^{1}H nmr (deuteriochloroform): δ 4.29 (s, 3H), 7.33-7.56 (m, 3H), 7.82-7.92 (m, 1H), 8.37-8.48 (m, 1H), 8.77-8.90 (m, 2H).

Anal. Calcd. for $C_{15}H_{10}N_2OS$: C, 67.65; H, 3.78; N, 10.51; S, 12.04. Found: C, 67.72; H, 4.14; N, 10.35; S, 11.80.

3-Chloro-*N*-(4-pyridyl)benzo[*β*]thiophene-2-carboxamide (**6**).

This compound was synthesized from **1** (3.5 g, 0.015 mole), 4-aminopyridine (1.4 g, 0.015 mole), pyridine (1.2 g, 0.015 mole), and benzene (50 ml) in a manner similar to that described for **2**, and there was obtained 3.5 g (81%) of product. The analytical sample was recrystallized from absolute ethanol to give pale yellow prisms, mp 219-220°; ^{1}H nmr (deuteriochloroform + deuteriotrifluoroacetic acid): δ 7.08-8.68 (m); ms: m/e (relative intensity) 289 (M^+-1, 7), 287 (M^+-1, 19), 196 (38), 194 (100).

Anal. Calcd. for $C_{14}H_9ClN_2OS$: C, 58.23; H, 3.14; N, 9.70; S, 11.10. Found: C, 58.21; H, 3.33; N, 9.43; S, 11.26.

[1]Benzothieno[2,3-*c*][1,6]naphthyridine-6(5*H*)-one (**7**).

This compound was synthesized from **6** (0.5 g, 0.0017 mole), triethylamine (0.17 g, 0.0017 mole), benzene (450 ml), and methanol (50 ml) in a manner similar to **3**, and there was obtained 0.4 g (90%) of white prisms, mp >270°, and used in the next reaction without additional purification; ^{1}H nmr (deuteriochloroform + deuteriotrifluoroacetic acid): δ 7.66-8.35 (m, 5H), 8.51-8.92 (m, 2H), 10.2 (br s, 1H); ms: m/e (relative intenstiy) 252 (M^+, 12), 251 (M^+-H, 100).

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

This compound was synthesized from **7** (1.9 g, 0.008 mole), phosphorus oxychloride (40 ml) and triethylamine (0.8 g, 0.008 mole) in a manner similar to the preparation of **4**. Compound **8** was obtained in 71% yield (1.3 g). The analytical sample was recrystallized from benzene to give pale yellow prisms, mp 259-260°; ^{1}H nmr (deuteriochloroform + deuteriotrifluoroacetic acid): δ 7.41-8.46 (m, 5H), 8.68-9.08 (m, 2H); ms: m/e (relative intensity) 272 (M^+, 29), 270 (M^+, 100).

Anal. Calcd. for $C_{14}H_7ClN_2S$: C, 62.11; H, 2.61; N, 10.35; S, 11.84. Found: C, 62.30; H, 2.79; N, 10.39; S, 11.91.

6-Methoxy[1]benzothieno[2,3-*c*][1,6]naphthyridine (**9**).

This compound was synthesized from **8** (0.2 g, 0.0007 mole), potassium hydroxide (0.04 g, 0.0007 mole), 5% Pd-C (0.5 g), methanol (40 ml), and benzene (40 ml) in a manner similar to that described for the preparation of **5**, and there was obtained 0.1 g (57%) of product. The analytical sample was recrystallized from benzene to give yellow needles, mp 211-212; ^{1}H nmr (deuteriochloroform): δ 4.27 (s, 3H), 7.55-8.05 (m, 4H), 8.67-8.77 (m, 2H), 10.07 (s, 1H); ms: m/e (relative intensity) 266 (M^+, 100), 265 (M^+-1, 81).

Anal. Calcd. for $C_{15}H_{10}N_2OS$: C, 67.65; H, 3.78; N, 10.51; S, 12.04. Found: C, 67.93; H, 4.12; N, 10.39; S, 12.07.

3-Chloro-*N*-(3-pyridyl)benzo[*β*]thiophene-2-carboxamide (**10**).

This compound was synthesized from **1** (13.9 g, 0.06 mole), 3-aminopyridine (5.6 g, 0.06 mole), pyridine (4.7 g, 0.06 mole), and benzene (150 ml) in a manner similar to that described for the preparation of **2**, and there was obtained 15.3 g (90%) of product. The analytical sample was recrystallized from methanol, white prisms, mp 240-241°; ^{1}H nmr (deuteriochloroform + deuteriotrifluoroacetic acid): δ 7.50-8.26 (m, 5H), 8.62-9.07 (m, 2H), 9.71 (s, 1H); ms: m/e (relative intensity) 289 (M^+-1, 7), 287 (M^+-1, 20), 196 (38), 194 (100).

Anal. Calcd. for $C_{14}H_9ClN_2OS$; C, 58.23; H, 3.41; N, 9.70; S, 11.10. Found: C, 58.07; H, 3.29; N, 9.56; S, 10.96.

[1]Benzothieno[2,3-*c*][1,7]naphthyridin-6(5*H*)-one (**11**), and [1]Benzothieno[2,3-*c*][1,5]naphthyridin-6(5*H*)-one (**14**).

These compounds were synthesized from **10** (0.5 g, 0.0017 mole), triethylamine (0.17 g, 0.0017 mole), benzene (450 ml), and methanol (50 ml) in a manner similar to that described for the preparation of **3**. Compound **11** (0.4 g, 88%) was obtained as a precipitate from the reaction mixture. When the filtrate was evaporated to dryness *in vacuo*, compound **14** (30 mg, 7%) was obtained.

Compound **11** had ^{1}H nmr (deuteriochloroform + deuteriotrifluoroacetic acid): δ 7.73-8.02 (m, 2H), 8.06-8.36 (m, 1H), 8.63-8.98 (m, 2H), 9.07-9.45 (m, 2H).

Compound **14** had ^{1}H nmr (deuteriochloroform + deuteriotrifluoroacetic acid): δ 7.56-8.30 (m, 4H), 8.48-9.27 (m, 3H). Compounds **11** and **14** were used for the next reactions without further purification.

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

This compound was synthesized from **11** (1.5 g, 0.006 mole), phosphorus oxychloride (40 ml) and triethylamine (0.6 g, 0.006 mole) in a manner similar to that described for the preparation of **4**, and there was obtained 0.7 g (44%) of product. The analytical sample was recrystallized from benzene, pale yellow prisms, mp 237-238°; ^{1}H nmr (deuteriochloroform + deuteriotrifluoroacetic acid): δ 7.79-8.07 (m, 2H), 8.17-8.50 (m, 1H), 8.77-9.14 (m, 2H), 9.30-9.61 (m, 2H), 9.91 (s, 1H); ms: m/e (relative intensity) 272 (M^+, 40), 270 (M^+, 100).

Anal. Calcd. for $C_{14}H_7ClN_2S$: C, 62.11; H, 2.61; N, 10.35; S, 11.84. Found: C, 62.14; H, 2.70; N, 10.45; S, 11.91.

[1]Benzothieno[2,3-*c*][1,7]naphthyridine (**13**).

This compound was synthesized from **12** (0.7 g, 0.0026 mole), 5% Pd-C (0.5 g), potassium hydroxide (150 mg), methanol (40 ml), and benzene (40 ml) in a manner similar to that described for the preparation of **5**, and there was obtained 0.4 g (66%) of product. The analytical sample was recrystallized from benzene to give yellow prisms, mp 170-171°; ^{1}H nmr (deuteriochloroform): δ 7.51-7.66 (m, 2H), 7.95-8.02 (m, 1H), 8.37-8.77 (m, 3H), 9.31 (s, 1H), 9.58 (s, 1H); ms: m/e (relative intensity) 236 (M^+, 100), 235 (M^+-1, 49).

Anal. Calcd. for $C_{14}H_8N_2S$: C, 71.16; H, 3.41; N, 11.86; S, 13.57. Found: C, 71.18; H, 3.57; N, 11.90; S, 13.39.

6-Chloro[1]benzothieno[2,3-*c*][1,5]naphthyridine (**15**).

This compound was synthesized from **14** (250 mg, 0.00092 mole), phosphorus oxychloride (50 ml), and triethylamine (0.4 g, 0.004 mole) in a manner similar to that described for the preparation of **4**, and there was obtained 150 mg (64%) of product. The analytical sample was recrystallized from hexane, pale yellow prisms, mp 200-201°; ^{1}H nmr (deuteriochloroform): δ 7.47-7.68 (m, 3H), 7.78-7.96 (m, 1H), 8.23-8.42 (m, 1H), 8.87-9.03 (m, 1H), 9.39-9.64 (m, 1H); ms: m/e (relative intensity) 272 (M^+, 38), 270 (M^+, 100).

Anal. Calcd. for $C_{14}H_7ClN_2S$: C, 62.11; H, 2.61; N, 10.35; S, 11.84. Found: C, 62.05; H, 2.67; N, 10.22; S, 11.67.

[1]Benzothieno[2,3-*c*][1,5]naphthyridine (**16**).

This compound was synthesized from **15** (100 mg, 0.0003 mole), 5% Pd-C (0.5 g), potassium hydroxide (100 mg), ethanol (50 ml), and benzene (50 ml) in a manner similar to that described for the preparation of **5** and there was obtained 50 mg (58%) of product. The analytical sample was recrystallized from hexane-benzene (3:1) to give a colorless powder, mp 181-183°; ^{1}H nmr (deuteriochloroform): δ 7.57-7.72 (m, 3H), 7.94-8.04 (m, 1H), 8.45-8.57 (m, 1H), 9.04-9.10 (m, 1H), 9.35 (s, 1H), 9.63-9.73 (m, 1H); ms: m/e (relative intensity) 236 (M^+, 100), 235 (M^+-1, 32).

Anal. Calcd. for $C_{14}H_8N_2S$: C, 71.16; H, 3.41; N, 11.86; S, 13.57. Found: C, 71.23; H, 3.45; N, 11.74; S, 13.49.

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