The Synthesis of Novel Polycyclic Heterocyclic Ring System *via* Photocyclization. **18** [1,2]. Benzo[*h*]naphtho-[1',2':4,5]thieno[2,3-*c*]quinoline and Benzo[*h*]naphtho-[1',2':4,5]thieno[2,3-*c*] [1,2,4]triazolo[4,3-*a*]quinoline

Jiann-Kuan Luo, Ronald F. Federspiel and Raymond N. Castle* [3]

Department of Chemistry, University of South Florida
Tampa, FL 33620-5250
Received February 23, 1996

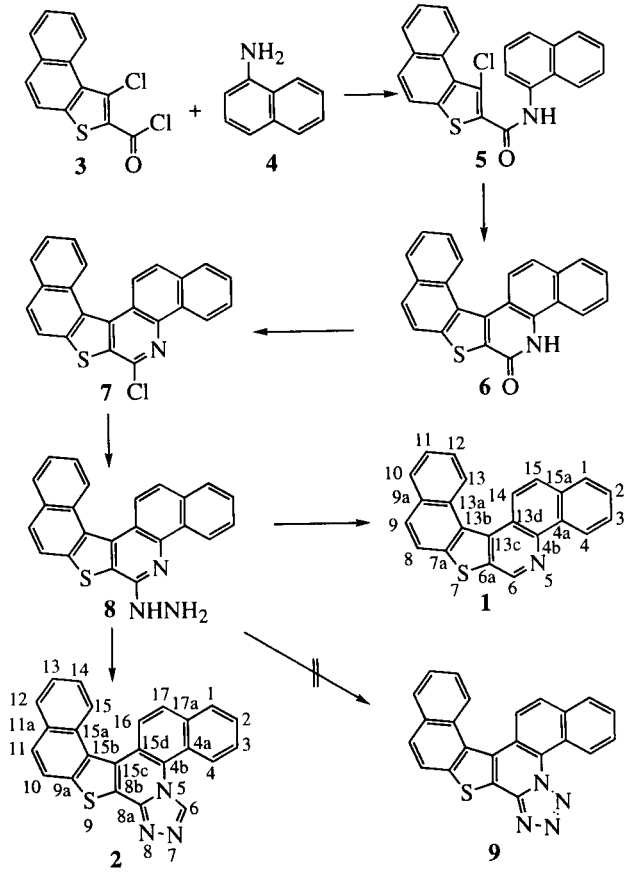
Dedicated to the memory of Professor Nicholas Alexandrou

The synthesis of two previously unknown polycyclic ring systems, benzo[*h*]naphtho[1'2':4,5]-thieno[2,3-*c*]quinoline (**1**) and benzo[*h*]naphtho[1',2':4,5]thieno[2,3-*c*][1,2,4]triazolo[4,3-a]quinoline (**2**), was achieved *via* oxidative photocyclization of 1-chloro-*N*-(1-naphthyl)naphtho[2,1-*b*]thiophene-2-carboxamide (**5**). The total assignment of their ^1H and ^{13}C nmr spectra was determined by the concerted use of two-dimensional nmr methods.

J. Heterocyclic Chem., **33**, 923 (1996).

In our recent reports [2], we have demonstrated that oxidative photocyclization of appropriate anilides is extremely useful for the synthesis of polycyclic heterocycles. As a continuing study of novel polycyclic heterocyclic ring systems, we now describe in this paper the synthesis of two previously unknown heterocyclic ring systems, benzo[*h*]naphtho[1',2':4,5]thieno[2,3-*c*]quinoline (**1**) and benzo[*h*]naphtho[1',2':4,5]thieno[2,3-*c*][1,2,4]-triazolo[4,3-*a*]quinoline (**2**).

Scheme 1



The synthetic pathway to compounds **1** and **2** is illustrated in Scheme 1. The reaction of 1-chloronaphtho[2,1-*b*]-thiophene-2-carbonyl chloride (**3**) [4,5] with 1-naphthylamine (**4**) in benzene gave 1-chloro-*N*-(1-naphthyl)-naphtho[2,1-*b*]thiophene-2-carboxamide (**5**) in 87% yield. Irradiation of the carboxamide **5** in benzene solution containing triethylamine with a 450 watt medium pressure mercury vapor lamp provided benzo[*h*]naphtho[1',2':4,5]thieno-[2,3-*c*]quinolin-6(5*H*)-one (**6**) in 88% yield. Chlorination of **6** was carried out by refluxing in phosphorus oxychloride to afford 6-chlorobenzo[*h*]naphtho[1',2':4,5]thieno[2,3-*c*]-quinoline (**7**) in 82% yield. When **7** was allowed to react with anhydrous hydrazine in a refluxing mixture of benzene and ethanol, 6-hydrazinobenzo[*h*]naphtho[1',2':4,5]-thieno[2,3-*c*]quinoline (**8**) was obtained in 98% yield. Treatment of **8** with a 10% copper sulfate solution in refluxing aqueous acetic acid resulted in a 23% yield of the unsubstituted novel ring system, benzo[*h*]naphtho[1',2':4,5]-thieno[2,3-*c*]quinoline (**1**) after column chromatography. The hydrazine derivative **8** in refluxing triethyl orthoformate and ethanol furnished benzo[*h*]naphtho[1',2':4,5]-thieno[2,3-*c*][1,2,4]triazolo[4,3-*a*]quinoline (**2**) in 40% yield. Attempts to obtain benzo[*h*]naphtho[1',2':4,5]-thieno[2,3-*c*]tetrazolo[1,5-*a*]quinoline (**9**) by diazotization of **8** with sodium nitrite in acetic acid were met with failure.

NMR Spectroscopy.

The COSY [6] spectrum of **1** revealed two two-spin and four four-spin systems and an isolated spin, H6 resonating at 9.50 ppm, as expected. The spectrum also exhibited the connectivities between one of the protons in each four-spin and two-spin systems through five-bond epi zig-zag couplings, *i.e.* H4/H15 and H9/H13. However, the long-range coupling across the "bay" between H13 and H14 engendered the differentiation among those spin systems and established their orientations, too. The

observation of the nuclear Overhauser effect between H13 and H14 shown in the NOESY [7] spectrum of **1** further supported our assignment. With all protons accounted for, the protonated carbons could be determined by its HMQC [8] spectrum except C1 and C8, since H1 and H8 have identical chemical shifts at 7.98 ppm. The assignment of the remaining quaternary carbons and the differentiation of C1 and C8 were achieved by the HMBC [9] spectrum of **1** (Table 1).

Table 1

^{1}H and ^{13}C-NMR Chemical Shift Assignments and Observed Proton-Carbon Multiple-Bond Correlations for Compound **1** in Deuteriochloroform at 298°K at Observation Frequencies of 360.13 and 90.6 MHz, Respectively

Position	δH	δC	Two-Bond Correlation	Three-Bond Correlation
1	7.98	127.6		H3, H15
2	7.72	127.6		H4
3	7.79	127.2		H1
4	9.44	125.1		H2
4a		132.2 [a]		H1, H3, H15
4b		143.3		H4, H6, H14
6	9.50	143.5		
6a		134.0	H6	
7a		141.5		H9
8	7.98	121.0		
9	8.04	130.0		H10
9a		132.1 [a]	H9, H10	H8, H11, H13
10	8.05	128.8		H9, H12
11	7.63	125.8		H13
12	7.63	125.9		H10
13	8.85	126.1		H11
13a		130.3		H9, H10, H12
13b		130.0		H8, H13
13c		138.1		H6, H14
13d		122.2		H15
14	8.70	123.7		
15	7.90	125.9		H1
15a		132.8	H1, H15	H2, H4, H14

[a] Assignments for the resonances noted may be interchanged. Unequivocal assignment could not be made with the digital resolution available.

For instance, the singlet resonating at 9.50 ppm assigned as H6 showed long-range couplings to three quaternary carbons resonating at 134.0, 138.1, and 143.3 ppm. The quaternary carbon resonating at the furthest downfield of this group displays long-range couplings to H4 and H14 and is logically assigned as C4b. The carbon resonating at 138.1 ppm exhibits a long-range coupling to H14 and is reasonable to be attributed to C13c. The remaining quaternary carbon at 134.0 ppm showing no further long-range correlation is expected for C6a. The quaternary C4a resonating at 132.1 ppm is derived from its long-range responses to H1, H3, and H15. Similarly, C13d can be assigned through its long-range correlation to H15, whereas C15a through the correlations to H2, H4, H14 and H15. Likewise, the assignment of quaternary carbons C7a, C9a, C13a and C13b was established in a manner as described above.

The aforementioned C1 (*vide supra*) can be differentiated from C8 by the use of HMBC spectrum, for C1 exhibiting long-range couplings to H3 and H15, whereas C8 showing none. Thus, a complete assignment of ^{1}H and ^{13}C nmr spectra of **1** was accomplished by the concerted use of two-dimensional nmr methods.

The spectral assignment of **2** was analyzed and determined in a manner similar to that described in the assignment of the spectra of **1**. The ^{1}H and ^{13}C assignments are summarized in Table 2. The vicinal proton-proton connectivities were obtained by using the COSY experiment. However, unambiguous assignment from the COSY spectrum is unlikely without the assistance of NOESY spectrum. In the NOESY spectrum of **2** the observation of nOe responses between the proton pairs H4/H6 and H15/H16 among others furnishes the recognition of the connectivity and orientation of two two-spin and two four-spin systems. The assigned protons led to the identification of the protonated carbons except C10 and C11 by the usage of the HMQC spectrum. The differentiation of C10 and C11 was induced through the HMBC experiment. The remaining quaternary carbons were also assigned through the HMBC spectrum. An HMQC-TOCSY [10] experiment of **2** further confirmed the assignment of protons and their corresponding carbons.

Table 2

^{1}H and ^{13} C-NMR Chemical Shift Assignments and Observed Proton-Carbon Multiple-Bond Correlations for Compound **2** in Deuteriochloroform at 298°K at Observation Frequencies of 360.13 and 90.6 MHz, Respectively

Position	δH	δC	Two-Bond Correlation	Three-Bond Correlation
1	8.14	129.2		H3, H17
2	7.78	127.4		H4
3	7.91	128.1		H1
4	8.85	122.8		H2
4a		124.0		H1, H3, H17
4b		126.4		H4, H16
6	10.13	137.6		
8a		145.9		H6
8b		125.4		
9a		140.5		H11
10	8.04	120.9		
11	8.04	128.9		H12
11a		132.4		H10, H13, H15
12	8.08	129.0		H11, H14
13	7.64	126.0		H15
14	7.57	125.8		H12
15	8.60	125.9		H13
15a		129.5		H11, H12, H14
15b		130.6		H10, H15
15c		132.3		H16
15d		119.9	H16	H17
16	8.69	125.0		
17	7.94	125.2		H1
17a		133.4		H2, H4, H16

In summary, synthesis of two previously unknown polycyclic heterocyclic ring systems has been achieved *via* oxidative photocyclization. Two-dimensional nmr techniques were employed to accomplish the total assignments of ^{1}H and ^{13}C nmr spectra of **1** and **2**.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover melting apparatus and are uncorrected. The ir spectra were recorded on a Beckman 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 TMS as the internal standard and chemical shifts are reported in ppm (δ) and J values in Hz. Analyses (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 nmr spectra of **1** and **2** were acquired on a Bruker AMX360 MHz NMR spectrometer operating at an observation frequency of 360.13 MHz for ^1H and 90.56 MHz 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. The COSY spectra were recorded using the Bruker pulse program (*COSY90*) [6]. The NOESY experiments were performed using the Bruker pulse program (*noesytp*) [7]. The HMQC experiments were performed using the Bruker pulse program (*invbdgtp*) with the BIRD sequence optimized for direct couplings (165 Hz $^1J_{CH}$) [8]. The HMBC spectra were obtained using the Bruker pulse program (*inv4lplrnd*) [9] optimized for 10 Hz $^3J_{CH}$ couplings. The HMQC-TOCSY experiment was acquired using the standard Bruker pulse program (*invbmltp*) [10].

1-Chloro-*N*-(1-naphthyl)naphtho[2,1-*b*]thiophene-2-carboxamide (**5**).

A mixture of 2.57 g (9.15 mmoles) of carbonyl chloride **3** [4,5] and 1.31 g (9.15 mmoles) of 1-aminonaphthalene (**4**) in 80 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 3.10 g (7.99 mmoles, 87%) of amide **5** as colorless fine needles, mp 210-212°; ir (potassium bromide): 3242 (NH stretching), 3047 (aromatic CH stretching), 1635 (C=O stretching); ^1H nmr (deuteriochloroform): 50°, δ 7.42-8.31 (m, 12H, ArH), 9.36 (br s, 1H, NH), 9.42 (dd, $J_{4,5}$ = 6.6 Hz, $J_{4,6}$ = 2.5 Hz, 1H, H-4).

Anal. Calcd. for $C_{23}H_{14}ClNOS$: C, 71.22; H, 3.64; N, 3.61; S, 8.27. Found: C, 71.23; H, 3.70; N, 3.56; S, 8.12.

Benzo[*h*]naphtho[1',2':4,5]thieno[2,3-*c*]quinolin-6(5*H*)-one (**6**).

A mixture of 0.50 g (1.29 mmoles) of amide **5** and 0.13 g (1.29 mmoles) of triethylamine in 480 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 precipitate was collected by filtration and washed with water to afford 0.40 g (1.14 mmoles, 88%) of lactam **6**, mp >300°; ir (potassium bromide): 3165 (NH stretching), 3052 (aromatic CH stretching), 1653 (C=O stretching); ^1H nmr (DMSO-d_6): 150°, δ 7.60-7.78 (m, 5H, ArH), 7.96-8.20 (m, 4H, ArH), 8.47 (d, $J_{14,15}$ = 8.8 Hz, 1H, H14), 8.71 (dd, $J_{12,13}$ = 6.2 Hz, $J_{11,13}$ = 3.3 Hz, 1H, H13), 8.95 (dd, $J_{3,4}$ = 6.4 Hz, $J_{2,4}$ = 3.4 Hz, 1H, H4). This compound was used in the next step without further purification because of its low solubility.

6-Chlorobenzo[*h*]naphtho[1',2':4,5]thieno[2,3-*c*]quinoline (**7**).

A mixture of 2.33 g (6.63 mmoles) of lactam **6** and 80 ml of phosphorus oxychloride was heated at 100-110° for 4 hours. After cooling to room temperature, the mixture was poured into 600 ml of ice water with vigorous stirring. The precipitate was collected by filtration, washed with water, and then dried. The solid was recrystallized from benzene to obtain 2.00 g (5.41 mmoles, 82%) of chloride **7** as yellow fine needles, mp 242-244°; ir (potassium bromide): 3044 (aromatic CH stretching); ^1H nmr (deuteriochloroform): δ 7.58-8.11 (m, 9H, ArH), 8.70 (d, $J_{14,15}$ = 9.3 Hz, 1H, H14), 8.81 (dd, $J_{12,13}$ = 7.6 Hz, $J_{11,13}$ = 3.7 Hz, 1H, H13), 9.37 (dd, $J_{3,4}$ = 8.0 Hz, $J_{2,4}$ = 2.9 Hz, 1H, H4).

Anal. Calcd. for $C_{23}H_{12}ClNS$: C, 74.69; H, 3.27; N, 3.79; S, 8.67. Found: C, 74.57; H, 3.40; N, 3.47; S, 8.56.

6-Hydrazinobenzo[*h*]naphtho[1',2':4,5]thieno[2,3-*c*]quinoline (**8**).

To a mixture of 1.80 g (4.87 mmoles) of chloride **7** in 120 ml of boiling ethanol and 50 ml of benzene was added dropwise 20 ml of anhydrous hydrazine over a period of one hour. The resulting mixture was heated under reflux for 48 hours. After cooling to room temperature, the solid was collected by filtration, washed with benzene and ethanol, and recrystallized from ethanol to give 1.75 g (4.79 mmoles, 98%) of hydrazine derivative **8** as yellow needles, mp 259-262°dec; ir (potassium bromide): 3266 (NH stretching), 3037 (aromatic CH stretching), 1615 (NH bending); ^1H nmr (DMSO-d_6): δ 4.97 (br s, 2H, NH_2), 7.64-7.98 (m, 5H, ArH), 8.15-8.25 (m, 4H, ArH), 8.47 (d, $J_{14,15}$ = 9.0 Hz, 1H, H14), 8.72 (s, 1H, NH), 8.75 (dd, $J_{12,13}$ = 7.2 Hz, $J_{11,13}$ = 2.2 Hz, 1H, H13), 9.24 (dd, $J_{3,4}$ = 6.1 Hz, $J_{2,4}$ = 2.9 Hz, 1H, H4).

Anal. Calcd. for $C_{23}H_{15}N_3S$: C, 75.59; H, 4.14; N, 11.50. Found: C, 75.49; H, 4.18; N, 11.33.

Benzo[*h*]naphtho[1',2':4,5]thieno[2,3-*c*]quinoline (**1**).

A mixture of 0.80 g (2.19 mmoles) of hydrazine derivative **8** in 15 ml of water and 20 ml of glacial acetic acid was heated under reflux. To the boiling mixture a 15 ml of 10% aqueous copper sulfate solution was added dropwise. The mixture was heated under reflux for 24 hours. After cooling to room temperature, the mixture was basified with a 2*N* sodium hydroxide solution. The mixture was extracted with ethyl acetate (3 x 150 ml), dried over anhydrous magnesium sulfate. After filtration, the filtrate was evaporated to dryness *in vacuo*. The solid was dissolved in 15 ml of chloroform and was chromatographed over silica gel eluting with a chloroform-cyclohexane (1:5) mixture to give 0.17 g (0.51 mmole, 23%) of **1** as brown prisms after recrystallization from cyclohexane-benzene mixture, mp 193-196°; tlc (chloroform) R_f 0.68; ir (potassium bromide): 3044 (aromatic CH stretching).

Anal. Calcd. for $C_{23}H_{13}NS$: C, 82.36; H, 3.91; N, 4.18. Found: C, 82.52; H, 4.16; N, 4.21.

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

A mixture of 0.37 g (1.01 mmoles) of hydrazine derivative **8** and 12 ml of triethyl orthoformate in 45 ml of ethanol was heated at 100-110° for 24 hours. After cooling to room temperature, the mixture was evaporated to dryness *in vacuo* and the solid was recrystallized from benzene to afford 0.15 g (0.40 mmole, 40%) of triazole **2** as yellowish prisms, mp 296-298°dec; tlc (di-

chloromethane:ethyl acetate, 1:4) R_f 0.26; ir (potassium bromide): 3055 (aromatic CH stretching).

Anal. Calcd. for $C_{24}H_{13}N_3S$: C, 76.78; H, 3.49; N, 11.19. Found C, 76.83; H, 3.52; N, 10.97.

Acknowledgment.

The authors wish to thank the National Science Foundation (CHE-8813620) for providing funds for the acquisition and operation of the Bruker AMX360 NMR spectrometer used in this work.

REFERENCES AND NOTES

[1] Presented at the XVIth European Colloquium on Heterocyclic Chemistry, Bled, Slovenia, September 25-28, 1994.

[2a] Part **1**: S. L. Castle, J.-K. Luo, H. Kudo and R. N. Castle, *J. Heterocyclic Chem.*, **25**, 1363 (1988); [b] Part **2**: J.-K. Luo and R. N. Castle, *J. Heterocyclic Chem.*, **27**, 1031 (1990); [c] Part **3**: M. J. Musmar and R. N. Castle, *J. Heterocyclic Chem.*, **28**, 203 (1991); [d] Part **4**: J.-K. Luo, A. S. Zektzer and R. N. Castle, *J. Heterocyclic Chem.*, **28**, 737 (1991); [e] Part **5**: J.-K. Luo and R. N. Castle, *J. Heterocyclic Chem.*, **28**, 1825 (1991); [f] Part **6**: R. N. Castle, S. Pakray and G. E. Martin, *J. Heterocyclic Chem.*, **28**, 1997 (1991); [g] Part **7**: K. Sasaki and R. N. Castle, *J. Heterocyclic Chem.*, **29**, 963 (1992); [h] Part **8**: K. Sasaki and R. N. Castle, *J. Heterocyclic Chem.*, **29**, 1613 (1992); [i] Part **9**: Ch. Camoutsis and R. N. Castle, *J. Heterocyclic Chem.*, **30**, 153 (1993); [j] Part **10**: M. J. Musmar, A. S. Zektzer, R. N. Castle and N. K. Dalley, *J. Heterocyclic Chem.*, **30**, 487 (1993); [k] Part **11**: J.-K. Luo, A. S. Zektzer, R. N. Castle, R. C. Crouch, J. P. Shockcor and G. E. Martin, *J. Heterocyclic Chem.*, **30**, 453 (1993); [l] Part **12**: J.-K. Luo, S. L. Castle and R. N. Castle, *J. Heterocyclic Chem.*, **30**, 653 (1993); [m] Part **13**: J.-K. Luo and R. N. Castle, *J. Heterocyclic Chem.*, **30**, 1167 (1993); [n] Part **14**: M. J. Musmar and R. N. Castle, *J. Heterocyclic Chem.*, **31**, 553 (1994); [o] Part **15**: J.-K. Luo, R. F. Federspiel and R. N. Castle, *J. Heterocyclic Chem.*, **32**, 317 (1995); [p] Part **16**: J.-K. Luo, R. F. Federspiel and R. N. Castle, *J. Heterocyclic Chem.*, **32**, 659 (1995); [q] K. Sasaki, O. Tokuda, T. Hirota, J.-K. Luo and R. N. Castle, *J. Heterocyclic Chem.*, **32**, 1735 (1995); [r] Part **17**: J.-K. Luo, R. F. Federspiel and R. N. Castle, *J. Heterocyclic Chem.*, **33**, 185 (1996).

[3] To whom correspondence should be addressed at the Department of Chemistry, University of South Florida, Tampa, FL 33620-5250 USA

[4] T. N. Sidorenko, G. A. Terent'eva, O. S. Andrienko, Yu. V. Savinykh and V. S. Askenov, *J. Heterocyclic Compd.*, (USSR), **19**, 156 (1983).

[5] W. B. Wright, Jr. and H. J. Brabander, *J. Heterocyclic Chem.*, **8**, 711 (1972).

[6] A. Bax and R. J. Freeman, *J. Magn. Reson.*, **44**, 542 (1981).

[7] J. Jeener, B. H. Meier, P. Bachmann and R. R. Ernst, *J. Chem. Phys.*, **71**, 4546 (1979).

[8] A. Bax and S. Subramanian, *J. Magn. Reson.*, **67**, 565 (1986).

[9] A. Bax and F. Summers, *J. Am. Chem. Soc.*, **108**, 2093 (1986).

[10] L. Lerner and A. Bax, *J. Magn. Reson.*, **69**, 375 (1986).