The Synthesis of Novel Polycyclic Heterocyclic Ring Systems *via* Photocyclization. **14**. 14-Methylbenzo[*h*]naphtho-[1'2':4,5]thieno[2,3-*c*][1,6]naphthyridine

M. J. Musmar and Raymond N. Castle* [1]

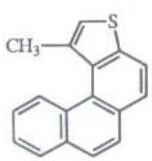
Department of Chemistry, University of South Florida, Tampa, Florida 33620-5250 USA

Received November 24, 1993

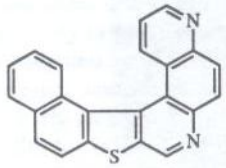
Benzo[*h*]naphtho[1'2':4,5]thieno[2,3-*c*][1,6]naphthyridine, a novel polycyclic heterocyclic ring system, has been synthesized as the 14-methyl derivative **8** in four steps from known intermediates. The structure of **8** is supported by assignment of the proton and the protonated carbon atoms by 2D-nmr techniques (COSY and a carbon-hydrogen one-bond coupling experiment).

J. Heterocyclic Chem., **31**, 553 (1994).

We report the synthesis of an additional novel polycyclic ring system *via* photocyclization, benzo[*h*]naphtho-[1'2':4,5]thieno[2,3-*c*][1,6]naphthyridine as the 14-methyl analogue which we add to those ring systems already reported in this series [2a-m]. The 14-methyl analogue is important because it provides yet another example of a methyl group in the bay region [2c,3] which will permit us to study further the twisting out of plane in detail as was accomplished for 1-methylphenanthro[3,4-*b*]thiophene (**1**) [3] and for naphtho[1'2':4,5]thieno[3,2-*a*]-4,7-phenanthroline (**2**) [2j].



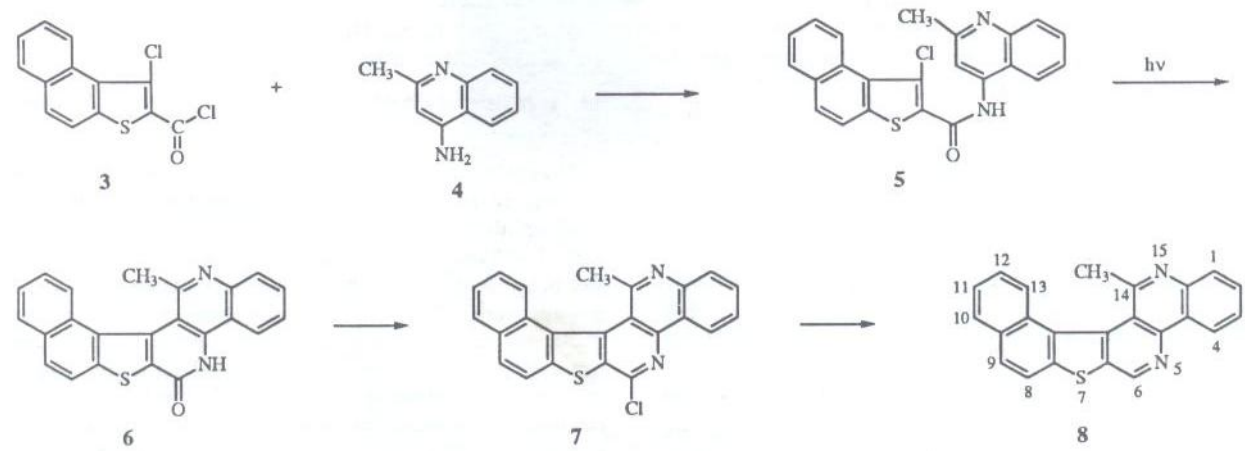
1



2

1-Chloronaphtho[2,1-*b*]thiophene-2-carbonyl chloride (**3**) [4] served as the starting material for the synthesis of 12-methylbenzo[*h*]naphtho[1'2':4,5]thieno[2,3-*c*][1,6]-naphthyridine (**8**). When **3** was allowed to react with 4-amino-2-methylquinoline (**4**) (Aldrich), 1-chloro-*N*-4'-(2'-methylquinolyl)naphtho[2,1-*b*]thiophene-2-carboxamide (**5**) was obtained in 82% yield. Photocyclization of **5** afforded 14-methylbenzo[*h*]naphtho[1'2':4,5]thieno[2,3-*c*][1,6]naphthyridin-6(5*H*)-one (**6**) in 45% yield. Phosphoryl chloride chlorination of **6** gave 6-chloro-14-methylbenzo[*h*]naphtho[1',2':4,5]thieno[2,3-*c*][1,6]naphthyridine (**7**) in 53% yield. Catalytic dechlorination of **7** provided 14-methylbenzo[*h*]naphtho[1'2':4,5]thieno[2,3-*c*][1,6]naphthyridine (**8**) in 68% yield. The structure of **8** is supported by COSY and CH one bond HETCOR experiments.

Scheme



3 **4** **5** **6** **7** **8**

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 ^1H and ^{13}C nmr spectra were obtained on a Bruker AMX360 in deuteriochloroform 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.

Proton and carbon nmr spectra were acquired at ambient temperature. A carbon frequency of 90.56 MHz was used with broad band decoupling using a pulse flip angle of 35°. The one-dimensional carbon spectrum was obtained with a spectral width of 1500.5 Hz and 2.5 seconds between transients. Routine proton spectra were obtained at a proton frequency of 360.13 MHz, with a pulse flip angle of 48.6° and a 5 μs pulse. An acquisition time of 5 seconds was used between transients to ensure accurate integrals. The two-dimensional experiments were acquired using standard automation microprograms provided with the Bruker Aspect 3000 data system and a Bruker inverse geometry probe. A typical proton-proton phase-sensitive double quantum filtered COSY experiment was acquired using the spectral width 992.06 Hz in the F_2 domain. The spectra were acquired with 1K data points in F_2 (one order of zero filling in the F_1 domain) with four transients (two dummy scans) and 512 t_1 increments of 504 μs used to encode the second dimension. The delay between scans was 1.4 seconds. A 90° phase shifted sine-bell multiplication was applied to avoid truncation artifacts. The matrix was symmetrized about the diagonal. Proton-carbon correlation experiments were acquired using an inverse-detected technique. Evolution times of 3.0 ms and 47.0 ms were used for direct and long-range methods, respectively. For the phase-sensitive direct correlation technique, 256 t_1 increments of 156 μs were used to encode a spectral width of 3205.1 Hz.

1-Chloro-*N*-(2'-methyl-4'-quinolyl)naphtho[2,1-*b*]thiophene-2-carboxamide (**5**).

A solution of 4-amino-2-methylquinoline (**4**) (2.813 g, 17.8 mmoles) and triethylamine (2.5 ml, 18 mmoles) in benzene (50 ml) was added dropwise to a stirred solution of 1-chloronaphtho[2,1-*b*]thiophene-2-carbonyl chloride (5 g, 17.8 mmoles) in benzene (50 ml) at room temperature. After the addition was complete, the mixture was stirred for 12 hours at *ca* 70°. Excess solvent was removed under reduced pressure to give a light-brown solid. This solid was suspended in water (25 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 at room temperature. Compound **5** was obtained (5.875 g 82%) as faint brown needles, mp 238-240° dec; ir (potassium bromide): 3397, 1653, 1648, 1527, 805, 738 cm^{-1}.

Anal. Calcd. for $C_{23}H_{15}ClN_2OS$: C, 68.57; H, 3.75; N, 6.95. Found: C, 68.46; H, 3.82; N, 6.88.

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

A stirred solution of 1-chloro-*N*-(2'-methyl-4'-quinolyl)-naphtho[2,1-*b*]thiophene-2-carboxamide (**5**) (0.75 g, 1.86 mmoles) and triethylamine (0.3 ml, 2.2 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 **6** as a beige colored powder. A total of 4.5 g (11.17 mmoles) of **5** afforded after irradiation 1.842 g (5.0 mmoles, 45%) of **6**, mp >300°; Beilstein test negative; ir (potassium bromide): 3291, 1646, 1327, 805, 761, 676 cm^{-1}. This material was used without further purification because of poor solubility in crystallization solvents. The analytical sample was obtained by crystallization from 95% ethanol.

Anal. Calcd. for $C_{23}H_{14}N_2OS \cdot 0.33H_2O$: C, 74.17; H, 3.97; N, 7.52. Found: C, 74.30; H, 3.99; N, 7.30.

6-Chloro-14-methylbenzo[*h*]naphtho[1'2':4,5]thieno[2,3-*c*][1,6]-naphthyridine (**7**).

A stirred mixture of 14-methylbenzo[*h*]naphtho[1'2':4,5]-thieno[2,3-*c*][1,6]naphthyridin-6-(5*H*)-one (**6**) (1.5 g, 4.1 mmoles) in phosphorus oxychloride (40 ml) and triethylamine (0.6 ml, 4.1 mmoles) was refluxed for 12 hours then excess phosphorus oxychloride was removed under reduced pressure. The resulting thick viscous material was cooled to ice bath temperature where residual phosphorus oxychloride was decomposed by the portionwise addition of crushed ice (~ 100 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 (2 x) to give 0.835 g (53%) of **7** as thin pale colored needles. This compound started to decompose at *ca* 200° then turned black and melted at 246-248°; ^1H-nmr (deuteriochloroform): δ 9.09 (dd, 1H, J = 1, 8 Hz) not fully resolved, 8.27 (dd, 1H, J = 1, 9 Hz) not fully resolved, 8.17 (d, 1H, J = 9 Hz), 8.14 (d, 1H, J = 9.3 Hz), 8.06 (d and m, 2H, J = 8.8 Hz), 7.89 (dt, 1H, not fully resolved), 7.75 (dt, 1H, not fully resolved), 7.61 (m, 2H), 2.60 (s, 3H, methyl); ^{13}C-nmr (deuteriochloroform): protonated carbons at δ 131.3, 130.3, 128.7, 127.7, 126.9, 126.7, 126.4, 124.7, 124.3, 120.6, 27.6, and quaternary carbons at δ 156.4, 147.7, 146.4, 145.3, 142.1, 139.2, 134.2, 131.4, 131.0, 130.7, 122.8, 116.2.

Anal. Calcd. for $C_{23}H_{13}ClN_2S$: C, 71.78; H, 3.40; N, 7.28. Found: C, 72.00; H, 3.54; N, 7.21.

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

The catalyst (10% Pd/C, 0.3 g) was added to a stirred solution of 6-chloro-14-methylbenzo[*h*]naphtho[1'2':4,5]thieno[2,3-*c*]-[1,6]naphthyridine (**7**) (0.6 g, 1.56 mmoles) in a solution of potassium hydroxide (0.062 g, 1.56 mmoles), methanol (100 ml) and benzene (100 ml). The mixture was stirred under a hydrogen atmosphere for 72 hours 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 (200 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 (1:1) to yield 0.371 g (68%) of off-white crystals, mp 222-224°; Beilstein test negative; ^1H-nmr (deuteriochloroform): δ 9.58 (s, 1H, H-6), 9.10 (d, 1H, J = 8.7 Hz, H-4), 8.38 (m, 1H, H-13), 8.19 (d, 1H, J = 9 Hz, H-10), 8.16-8.20 (m, 3H, H-9, H-1, H-8), 7.86 (dt, 1H, not fully resolved, H-2), 7.74 (dt, 1H, not fully resolved, H-12), 7.61 (m, 2H, H-3 and H-11), 2.62 (s, 3H, methyl). The COSY spectra for

7 and **8** confirmed the presence of a two spin system and a pair of four spin systems in each compound; ^{13}C-nmr (deuteriochloroform): protonated carbons at δ 147.1, 130.9, 129.8, 128.7, 127.7, 126.8, 126.6, 126.3, 124.8, 124.1, 120.9, and 27.7; quaternary carbons at δ 156.8, 146.0, 145.1, 142.0, 136.7, 134.8, 131.3, 129.5, 126.8, 123.7, and 116.9.

Anal. Calcd. for $C_{23}H_{14}N_2S \cdot 0.75H_2O$: C, 76.22; H, 4.31; N, 7.72. Found: C, 76.24; H, 4.61; N, 7.45.

REFERENCES AND NOTES

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

[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).

[3] M. J. Musmar, G. E. Martin, R. T. Gampe, Jr., V. M. Lynch, S. H. Simonsen, M. L. Lee, M. J. Tedjamulia, and R. N. Castle, *J. Heterocyclic Chem.*, **22**, 545 (1985).

[4] S. Pakray and R. N. Castle, *J. Heterocyclic Chem.*, **24**, 231 (1987).