Chemistry of Condensed Thiophenes. IV. Acetylation of Phenanthro[4,5-*bcd*]thiophene

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Treatment of phenanthro[4,5-*bcd*]thiophene (**2**) with acetyl chloride and aluminum chloride in nitrobenzene gives acetylation of positions *ortho* and *para* to the heteroatomic sulfur atom. In separate experiments, mixtures of 1- and 3-acetyl (50% yield, ratio 1.9:1) or of 1,5-, 1,7-, and 3,5-diacetyl (79% yield, ratio 3:1:1) derivatives were obtained. Isolated as isomerically pure products were the 1-acetyl and the 1,5-diacetyl compounds, as well as the oximes of the 1- and 3-acetyl derivatives. Comparison of these results is made with those reported for nitration of **2**, which also occurs *ortho* and *para* to the sulfur atom, and with nitration and acetylation of pyrene (the benzolog of **2**) which substitutes in the corresponding positions.

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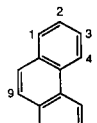
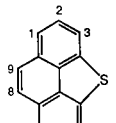
In a previous paper we reported that phenanthro[4,5-*bcd*]thiophene (**2**) undergoes nitration with nitric acid in acetic anhydride to give mixtures of 1- and 3-nitro derivatives, *i.e.* products which result from electrophilic substitution *ortho* and *para* to the heteroatomic sulfur atom [3]. The present paper concerns Friedel-Crafts acetylation of compound **2** by means of acetyl chloride and aluminum chloride in nitrobenzene as the solvent at 6-25°.

Mixtures of **2** and phenanthrene (**1**) were available from sulfur bridging of the latter [3]. Initially we fractionated this mixture in order to remove all but 5 mole % of **1** before proceeding with acetylation. Since, however, the presence of phenanthrene in **2** did not cause problems in processing the acetylation reaction mixture [4], subsequent experiments were conducted on crude product mixtures (67 mole % **2**, 33 mole % **1**, freed from elemental sulfur) from sulfur bridging. Reaction of equimolar amounts of purified **2** and acetyl chloride gave monoacetyl **2** (50%), obtained as a non-separated mixture of the 1 (**2a**) and 3 (**2b**) isomers in a ratio of 1.9:1, as based on the ^{1}H nmr spectrum. This mixture was obtained analytically pure. Chromatography and recrystallization of the mixed product from a subsequent monoacetylation yielded isomerically pure **2a**, identified primarily by the presence of a downfield doublet (δ 9.16, J = 9.3 Hz) for one proton (H-9) in its ^{1}H nmr spectrum. Although **2b** was not obtained isomerically pure, its structural assignment was apparent from the difference in the nmr spectrum of the isomeric mixture and that of pure **2a**. This difference spectrum included a downfield doublet (δ 8.24, J = 7.2 Hz) for H-2 and a triplet for H-6. These features are inconsistent with location of the acetyl group at an alternative position of C-2 or C-8.



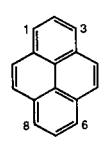
1

a, x-C(=NOH)-CH$_3$



2

a, 1-Ac
b, 3-Ac
c, 1,5-diAc
d, 1,7-diAc
e, 3,5-diAc
f, 1-C(=NOH)-CH$_3$
g, 3-C(=NOH)-CH$_3$



3

Corroborating structural assignments for the acetyl isomers resulted from oximation of the preceding mixture in a solvent of pyridine-absolute ethanol-conditions expected to form the *E*-stereoisomers **2f** and **2g** only [5]. In fact, the crude, crystalline oxime mixture (28%) which was isolated was readily separated into the 1-isomer **2f** (R_f 0.08, mp 204°) and the 3-isomer **2g** (R_f 0.23, mp 193°) in a ratio of 30:1 by chromatography with silica gel/chloroform. Unexpectedly, the oximation mixture contained a large amount of gray, clay-like solid plus a dark green material, both soluble in chloroform, but not investigated further. Structural assignment of the 1-isomer was again made primarily on the basis of a downfield doublet (δ 8.57, J = 9 Hz) for H-9 in the ^{1}H nmr spectrum. This chemical shift is ascribed to proximity of the non-bonding electron-pair on the oxime nitrogen atom to H-9 in the molecule. In contrast, the doublet which falls furthest downfield in the 3-isomer occurs at δ 8.21 (J = 8 Hz) for H-2. In fact, molecular mechanics calculations indicate an N to H-9 internuclear distance of 2.47 Å in **2f** and an N to H-2 internuclear distance of 2.65 Å in **2g** [6].

Treatment of a mixture of phenanthro[4,5-*bcd*]thiophene (**2**) and phenanthrene (molar ratio 1.5:1) with a 2.55-molar quantity of acetyl chloride in the presence of anhydrous aluminum chloride and nitrobenzene produced a mixture of diacetyl-**2** isomers (79%), ascribed to the presence of 1,5 (**2c**), 1,7 (**2d**), and 3,5 (**2e**) compounds in the ratio of about 3:1:1, respectively, on the basis of its ^{1}H nmr spectrum. Thick layer chromatography of this mixture gave isomerically pure **2c** as bright yellow needles, mp 235°. Location of one of the acetyl groups at C-1 is based on the presence of a downfield doublet (δ 9.27, J = 9.3 Hz) for H-9, while that of the other acetyl group is placed at C-5, consistent with the presence of 2 overlapping doublets (J = 7.8 Hz) at 8.46 and 8.45 ppm for H-2 and

H-6. These latter doublets are inconsistent with the presence of the second acetyl group at C-2, C-3, C-6, C-7 or C-8 (C-9 already eliminated as a possibility). Although neither **2d** nor **2e** was isolated in an isomerically pure state structural assignments were facilitated by the isolation of a 4:1 mixture of these two components (free from **2c**) on further processing. The ^{1}H nmr spectrum of this mixture indicated the presence of two symmetrically substituted diacetyl derivatives. The more abundant isomer (*i.e.* 1,7-diacetyl, **2d**) showed a singlet at δ 9.18 for protons at H-8 and H-9, while the other isomer (3,5-diacetyl, **2e**) also exhibited a singlet for H-8 and H-9 but further upfield at δ 8.39.

The foregoing results show that **2** undergoes Friedel-Crafts acetylation at positions *ortho* and *para* to the heterocyclic sulfur atom, just as occurs in the process of nitration. Previously it was noted that **2** and its benzolog pyrene (**3**) undergo nitration in analogous positions, *i.e.* to yield 1-nitro- or even 1,3,6,8-tetranitropyrenes [7]. This correlation between substitution patterns for **2** and **3** can now be extended to the acetylation reaction where 1-acetylpyrene is produced [8]. A discussion of similar correlations for other thienolog-benzolog *peri*-condensed systems has been presented [9] and may indicate that general topology of the molecule could be significant in the orientation of entering substituents into these parent systems.

Limited effort was made to obtain an identifiable, pure dioxime from the mixture of residues (284 mg) which remained after isolation of isomer **2c**. Oximation of these residues gave a mixture of numerous components (as based on tlc) which was subjected to chromatography (column and thick layer), recrystallization, and finally fractional vacuum sublimation at 130°. This effort was unsuccessful at producing a pure dioxime, but it did result in the isolation of 5 mg of a white solid, mp 126-127°, tentatively assigned the structure of an acetylphenanthrene oxime (**1a**) on the basis of elemental analysis (fits molecular formula $C_{16}H_{13}NO$), ^{1}H nmr (singlet for oxime OH at δ 10.6), and mass spectrum. The mass spectrum exhibited abundant ions at m/e 235 (molecular ion), 218 (loss of OH), 203 (loss of methanol), and 177 (loss of the acetoxime unit), a pattern expected for structure **1a**. Including both positional and geometric (*E* and *Z*) isomers there are ten possible structural formulas to consider for **1a**. Four of these ten have been reported in the literature and have melting points in the range of 144-197°, considerably higher than that of **1a** [10]. Our sample was too small to permit us to establish its structure definitively.

EXPERIMENTAL [11]

Monoacetylation of Phenanthro[4,5-*bcd*]thiophene (**2**).

To a stirred solution (at about 5°) of 2.9 g (14 mmoles) of **2** (95% pure, 5% **1**) in 10 ml of dry nitrobenzene was added dropwise a solution of 5.57 g (42 mmoles) of anhydrous aluminum chloride and 1.48 ml (20.8 mmoles) of acetyl chloride in 25 ml of nitrobenzene. The mixture immediately changed from yellow to dark red. After 24 hours, during which time the mixture was allowed to warm to room temperature, tlc (silica gel/carbon tetrachloride) showed that all **2** (R_f 0.62) had reacted to give acetylated product (R_f 0.2). Excess 18% hydrochloric acid was added and the two-phased mixture was steam distilled to remove the nitrobenzene. The acidic residue was extracted with chloroform. Chloroform extracts were washed with water until neutral, dried (sodium sulfate), and evaporated to give crude, dark brown product. Recrystallization from absolute ethanol gave 1.66 g (50%) of yellow prisms of monoacetylphenanthro[4,5-*bcd*]thiophenes, mp 138-141°, ascribed to a mixture of 1-acetyl (**2a**) and 3-acetyl (**2b**) isomers in a ratio of 1.9:1, respectively [12]. Recrystallization from the same solvent produced colorless prisms, mp 144-145°; ir: 1660 (carbonyl), 1558, 1489, 1398, 1252, 828 cm^{-1}; uv (ethanol): λ max 248 nm (log ϵ 4.41), 283 (4.22), 344 (4.12), 370 (3.92); ms: m/e 250 (M^+, 65), 235 (M^+-Me, 100), 207 (M^+-Ac, 89), 163 (207^+ - CS, 44), 103.5 (207^{++}, 33). The ^{1}H nmr spectrum (deuteriochloroform) exhibited all of the signals found for purified **2a** (*vide infra*) plus these separately discernible signals ascribed to **2b**: δ 8.24 (d, $J_{1,2}$ = 7.2 Hz, 1 H, H-2), 7.94 (t, J = 7.2 Hz, 1 H, H-6), 2.92 (s, 3 H, Ac).

Anal. Calcd. for $C_{16}H_{10}OS$: C, 76.77; H, 4.03. Found: C, 76.88; H, 3.87.

1-Acetylphenanthro[4,5-*bcd*]thiophene (**2a**).

A sample of mixed monoacetyl derivatives [13] (mp 134-140°) was chromatographed on a thick layer plate of silica gel with methylene chloride. Solid collected from the middle zone (of three formed) was recrystallized successively from ethanol-acetone and methanol and deposited on a thin layer Si-C_{18} reversed-phase plate. Extraction of the whole plate with acetone gave a solution of isomerically pure (as based on ^{1}H nmr) **2a**, mp 148-150°, raised to 150-151° by sublimation at 140° (0.1 mm), obtained as nearly colorless prisms; ir: 1661 (carbonyl), 1250, 828 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 9.16 (d, $J_{8,9}$ = 9.3 Hz, 1 H, H-9), 8.41 (d, $J_{2,3}$ = 8.1 Hz, 1 H, H-2), 8.18 (d, 1 H, H-8), 8.13 (d, J = 7.8 Hz, 1 H, H-5 or H-7), 8.11 (d, 1 H, H-3), 8.05 (d, J = 7.2 Hz, 1 H, H-7 or H-5), 7.93 (t, J $\approx$ 7.8 Hz, 1 H, H-6), 2.89 (s, 3 H, Ac); ms: m/e 250 (M^+, 73), 235 (M^+-Me, 100), 207 (M^+-Ac, 73), 163 (207^+-CS, 31), 103.5 (30).

Anal. Calcd. for $C_{16}H_{10}OS$: C, 76.77; H, 4.03; S, 12.81. Found: C, 76.85; H, 4.16; S, 12.98.

Diacetylation of Phenanthro[4,5-*bcd*]thiophene (**2**).

A 2.16-g mixture of **2** (6.6 mmoles) and phenanthrene (4.4 mmoles), obtained from sulfur bridging, was dissolved in 10 ml of nitrobenzene and treated, with stirring at about 6°, with a solution of acetyl chloride (2 ml, 28.1 mmoles) and anhydrous aluminum chloride (5.55 g, 41.6 mmoles) over a period of 50 minutes. Stirring was continued while the mixture was allowed to warm to room temperature and for nearly 3 days longer. The very dark red mixture was processed, in the same manner as used in monoacetylation of **2**, to give a crude, brown product, partially purified by molecular distillation at 190° (0.04 mm) to a semi-solid, yellow mixture of diacetylphenanthro[4,5-*bcd*]thiophenes, yield 1.52 g (79%); ^{1}H nmr (deuteriochloroform): δ 9.2 (superim-

posed s and d, rel. area 1), 8.4 (m, rel. area 2), 8.0-8.3 (4 d, rel. area 3), 2.9 (overlapping singlets, Ac groups, rel. area 6) [14]; three main spots (plus some minor ones) by tlc; ascribed to the presence of 1,5-, 1,7-, and 3,5-diacetyl isomers in the ratio of 3:1:1, respectively. Repetitive thick layer chromatography (silica gel/chloroform or methylene chloride) furnished an intermediate zone (R_f 0.33 on silica gel/methylene chloride) of isomerically pure 1,5-diacetylphenanthro[4,5-*bcd*]thiophene (**2c**).

An analytically pure sample of **2c** was obtained by recrystallization of the preceding product from acetonitrile plus sublimation at 208° (0.1 mm) to give bright yellow needles, mp 233-235°; ir: 1667 and 1661 (2 carbonyls), 1552, 1368, 1268, 954 cm^{-1}; ^1H nmr (deuteriochloroform): δ 9.27 (d, $J_{8,9}$ = 9.3 Hz, 1 H, H-9), 8.46 and 8.45 (2 overlapping doublets, J = 7.8 Hz, 2 H total, H-2 and H-6), 8.26 (d, 1 H, H-3), 8.20 (d, 1 H, H-8), 8.10 (d, 1 H, H-7), 2.93 and 2.91 (2s, 3 H each, 2 Ac groups); ms: m/e 293 (15), 292 (M^+, 66), 278 (23), 277 (M^+-CH_3, 100), 234 (M^+-Ac-CH_3, 38), 206 (M^+ - 2 Ac, 36).

Anal. Calcd. for $C_{18}H_{12}O_2S$: C, 73.95; H, 4.14; S, 10.97. Found: C, 73.96; H, 4.16; S, 11.21.

Through a series of other purification steps there was obtained an isomerically enriched sample of 1,7-diacetylphenanthro[4,5-*bcd*]thiophene (**2d**) (*ca.* 80% **2d**, 20% **2e**); ^1H nmr for **2d** (deuteriochloroform): δ 9.18 (s, 2 H, H-8 and H-9), 8.23 (AB system, J_{AB} = 8.1 Hz, $\Delta\delta$ = 93.5 Hz, 4 H, H-2, H-3, H-5, H-6), 2.89 (s, 6H, 2 Ac groups). Pertinent features of the ^1H nmr spectrum of the third isomer 3,5-diacetylphenanthro[4,5-*bcd*]thiophene (**2e**) were obtained by difference: δ 8.39 (s, H-8 and H-9) superimposed on a doublet (H-2 and H-6), 8.10 (d, J = 7.8 Hz, H-1 and H-7), 2.9 (s, Ac groups).

Oximation of Monoacetylphenanthro[4,5-*bcd*]thiophene Mixture.

A mixture of 1.0 g (4 mmoles) of preceding monoacetyl derivatives (mp 138-141°; isomeric ratio **2a**:**2b** = 1.9:1), 0.83 g (12 mmoles) of hydroxylammonium chloride, 1.3 ml of anhydrous pyridine, and 4.6 ml of absolute ethanol was refluxed for 3.5 hours, whereupon the color of the solution had changed from yellow to dark green and tlc (silica gel/chloroform) showed that acetyl components (R*f* 0.39) were absent. A chloroform solution of the colored clay-like residue from evaporation of the reaction mixture was washed with water several times, treated with charcoal once, dried (sodium sulfate), and evaporated to dryness. Recrystallization of the residue from chloroform gave 300 mg (28%, based on total acetyl derivative used) of nearly white oxime, mp 184.5-190.5°, and a dark green mother liquor (*vide infra*). Column chromatography (silica gel/chloroform) of the solid yielded 8.8 mg of crude 3-(1-hydroxyiminoethyl)phenanthro-[4,5-*bcd*]thiophene (**2g**), mp 184.5-185.5°, R_f 0.23, and 265 mg (38%, based on **2a** used) of 1-(1-hydroxyiminoethyl)phenanthro-[4,5-*bcd*]thiophene (**2f**), mp 195.5-197.5°, R_f 0.08.

Isomer **2f** was purified further by recrystallization from 95% ethanol and sublimed at 150° (0.5 mm) to produce white needles, mp 203.5-204°; ir: 3191 (OH), 1363, 1022, 941, 816, 750 cm^{-1}; ^1H nmr (hexadeuterioacetone): δ 10.57 (s, 0.25 H, NOH), 8.57 (d, $J_{8,9}$ = 9 Hz, 1 H, H-9), 8.23 (d, $J_{2,3}$ = 7.8 Hz, 1 H, H-2) which overlaps 8.22 (d, $J_{5,6}$ = 7.5 Hz, 1 H, H-5), 8.10 (d, 1 H, H-8), 8.06 (d, $J_{6,7}$ = 7.8 Hz, 1 H, H-7), 7.99 (d, 1 H, H-3), 7.93 (t, 1 H, H-6), 2.50 (s, 3 H, methyl group); ms: m/e 265 (M^+, 100), 248 (M^+-OH, 40), 233 (35), 208 (37), 207 (M^+-CH_3C=NOH, 80).

Anal. Calcd. for $C_{16}H_{11}NOS$: C, 72.43; H, 4.18; N, 5.28. Found: C, 72.34; H, 4.14; N, 5.31.

The preceding sample of crude **2g** plus additional product obtained from processing of the green mother liquor was chromatographed on a 20 x 20-cm thick layer of silica gel with chloroform. The components of a dark band (5 cm wide) were collected and sublimed at 150° (0.5 mm) to give first a yellow resinous condensate (discarded) and then analytically pure, nearly white prisms of **2g**, yield 9.3 mg (3%), mp 192-193°, R_f 0.41 (silica gel/dichloromethane) [15]; ir: 3395 (OH), 1556, 1388, 1291, 1009, 944, 831, 759 cm^{-1}; ^1H nmr (hexadeuterioacetone): δ 10.84 (s, 0.42 H, NOH), 8.21 (d, $J_{1,2}$ = $J_{5,6}$ = 8 Hz, 2 H, H-2 and H-5), 8.12 (d, 1 H, H-1), 8.08 (s, 2 H, H-8 and H-9), 8.06 (d, $J_{6,7}$ = 8 Hz, 1 H, H-7), 7.92 (t, 1 H, H-6), 2.60 (s, 3 H, methyl group); ms: m/e 266 (20), 265 (M^+, 100), 248 (M^+-OH, 17), 233 (M^+-CH_3OH, 26), 208 (29), 207 (M^+-CH_3C=NOH, 65).

Anal. Found: C, 72.31; H, 4.11; N, 5.06.

Isolation of Acetylphenanthrene Oxime **1a**.

A solution of 284 mg of residues from the isolation of diacetyl derivative **2c** plus 405 mg of hydroxylammonium chloride in 3 ml of absolute ethanol and 0.63 ml of anhydrous pyridine was refluxed for 4 hours. The green reaction mixture was evaporated to dryness. A hot ethanol extract of the residue was evaporated and this resultant residue was extracted into hot chloroform. Successive fractionations of the soluble portion by column chromatography (silica gel/methylene chloride-ethyl acetate, 4:1)–collection of early fractions; thick layer chromatography (silica gel/methylene chloride)–collection of fraction of $R_f \geq 0.28$, blue fluorescent zone; and sublimation at 130° (0.1 mm)–collection of white needles only, gave 5 mg of **1a**, mp 126-127°; ^1H nmr (hexadeuterioacetone): δ 10.6 (s, NOH), 7-9 (m, aromatic protons), 2.48 (s, methyl group); ms: m/e 235 (M^+, 100), 218 (M^+-OH, 22), 204 (22), 203 (M^+-CH_3OH, 24), 178 (43), 177 (M^+-CH_3C=NOH, 55), 176 (59).

Anal. Calcd. for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.58; H, 5.35; N, 5.94.

No attempt was made to purify other fractions from the oximation product mixture.

REFERENCES AND NOTES

[1] Undergraduate Research Assistant, summer 1987.

[2] Undergraduate Research Assistant, 1988-1990.

[3] L. H. Klemm, R. Tsuchiya, E. K. L. Wong, M. P. Stevens, J. J. Lu, and C. E. Klopfenstein, *J. Heterocyclic Chem.*, **24**, 357 (1987).

[4] Apparently **1** is considerably less reactive than **2**. In any event **1** or its acetylation product(s) was not encountered during processing of reaction mixtures. However, see footnote [14].

[5] The use of pyridine and absolute ethanol as a solvent mixture for oximation of acetylarenes was first described by W. E. Bachmann and C. H. Boatner, *J. Am. Chem. Soc.*, **58**, 2097 (1936), who noted predominant formation of the *E*-isomer as based on Beckmann rearrangement preferentially to an acetylaminoarene product by means of phosphorus pentachloride [P. A. S. Smith, The Chemistry of Open-Chain Organic Nitrogen Compounds, Vol **2**, W. A. Benjamin, Inc., New York, NY, 1966, p 49]. The oximation procedure is presented by R. L. Shriner, R. C. Fuson, and D. Y. Curtin, The Systematic Identification of Organic Compounds, 5th Ed, John Wiley and Sons, Inc., New York, NY 1967, p 289. Oximation and Beckmann rearrangement steps for the conversion of 2-acetylthieno[2,3-*b*]pyridine into 2-acetylaminothieno[2,3-*b*]pyridine were also reported from our laboratory [L. H. Klemm, R. Zell, I. T. Barnish, R. A. Klemm, C. E. Klopfenstein, and D. R. McCoy, *J. Heterocyclic Chem.*, **7**, 373 (1970)]. It seems likely that the oxime *E*-isomer is the thermodynamically controlled product, especially since it forms by a slow reaction.

[6] Molecular mechanics calculations were made on a Silicon Graphics model 40-70G computer with SYBYL software (version 5.3, Tripos Associates, St. Louis). The total steric energy for the molecule was first minimized for a conformation in which the nonbonding electron-pair on the nitrogen atom is directed toward the closest aromatic proton and then the internuclear distance was computed.

[7] E. Clar, Polycyclic Hydrocarbons, Vol **2**, Academic Press, New York, NY, 1964, p 120.

[8] H. Vollmann, H. Becker, M. Corell, and H. Streeck, *Liebigs Ann. Chem.*, **531**, 1 (1937).

[9] L. H. Klemm, *Heterocycles*, **30**, 1219 (1990).

[10] Melting points have been reported for one oxime each from 1-, 2-, 3-, and 9-acetylphenanthrenes. See Bachmann and Boatner in footnote [5]; E. Mosettig and J. van de Kamp, *J. Am. Chem. Soc.*, **52**, 3704 (1930); **55**, 3442 (1933).

[11] Infrared spectra were determined on potassium bromide wafers by means of a Nicolet 5-DXB FTIR instrument, ^{1}H nmr spectra by means of a General Electric QE-300 instrument, and ultraviolet absorption spectra by means of a Perkin-Elmer Lambda 6 spectrophotometer. We thank Eliot Hall for assistance with some of these spectra. Electron-impact mass spectra were obtained at 70 eV by Dr. Richard Wielesek of this laboratory on a VG 12-250 instrument. Elemental analyses were conducted by Desert Analytics, Tucson, Arizona.

[12] The isomeric ratio is based on integrations of the methyl signals in the ^{1}H nmr spectrum.

[13] Obtained from acetylation of a 2:1 molar mixture of **2** to **1**.

[14] Although tlc indicates that trace amounts of unreacted **1** and/or **2**, as well as monoacetylphenanthrene, could be present in this mixture the ^{1}H nmr failed to show the presence of such impurities. Also, the ratio of integrations for aromatic protons/acetyl protons of 1:1 implies the absence of monoacetyl derivatives. It seems likely that most of these components were removed during the lengthy steam and molecular distillations used in processing. As noted later, however, a trace amount (<5 mg) of acetylphenanthrene was actually isolated as its oxime (**1a**) from this mixture.

[15] Apparently oxime **2g** is considerably less stable than **2f** in the oximation reaction.