distillation alone at pressures near 1 atm and below since the vapor is richer in *ether* than is the solution.[7] However, the composition of the homogeneous ether–water azeotrope is so close to that of water-saturated ether[8] that even saturated brine alone can remove enough water for the composition of the ether solution to move to the ether-rich side of azeotrope. Distillation of a brine-treated ether solution is not very efficient for drying since the azeotrope boils only slightly lower than pure ether,[8] but at worst the water concentration in the distalland will not increase.

Registry No. NaCl, 7647-14-5.

(7) Othmer, D. F.; Wentworth, T. O. *Ind. Eng. Chem.* **1940**, *32*, 1590. This is easily confirmed by distilling a two-phase ether–water mixture and noting that the distillate is homogeneous (ref 4b, p 1366, verified by author). The author has also observed that even ether just saturated with water at 20 °C upon distillation at normal pressure (bp 34 °C) gives separation of an aqueous phase in the *pot*.

(8) Horsley, L. H. In "Azeotropic Data-III"; American Chemical Society: Washington, DC, 1973; *Adv. Chem. Ser.* No. 116, p 23. The data in note 7 also shows that the azeotrope must be homogeneous, contrary to the statement in Lurie, A. P., ref 3b, 1965; Vol. 8, p 478.

Bromination of Some *c*-Fused Thiophenes. Thioanhydrides from Thiophenes

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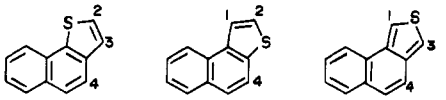
Fusion of a thiophene ring to the 1,2-positions of naphthalene can give three isomeric naphthothiophenes **1**–**3**, each of which is a phenanthrene analogue. Electro-



philic substitution has been studied with **1**[1,2] and **2**[3] but not with the *c*-fused thiophene **3**.[4] We report here the first studies on electrophilic substitution in **3** and the novel conversion of the thiophene ring in **3** to a thioanhydride.

Molecular orbital calculations[1,5] on the preferred sites of electrophilic substitution in **1** and **2** are not in agreement with experiment. For example, the preferred positions of attack in **1** are predicted[4] to be 3 > 2 > 5, whereas bromination, formylation, and acetylation occurred predominantly in the 2-position, and nitration gave a mixture of 2- and 5-nitro products. Only if the 2-position was blocked with a methyl substituent did substitution occur in the supposedly preferred 3-position.[2] With **2**, the predicted[5] preferences were for positions 1 > 2 > 5; experimentally,[3] nitration, bromination, formylation, and acetylation occurred in the 2-position, and *not* in the 1-position. There are no MO predictions for substitution in **3**, nor is there any experimental information.

(1) Clarke, K.; Gregory, D. N.; Scrowston, R. M. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2956.

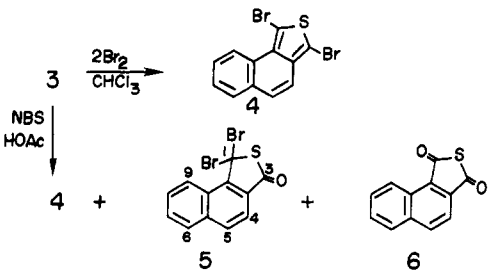
(2) Clarke, K.; Gregory, D. N.; Scrowston, R. M. *J. Chem. Soc., Perkin Trans. 1* **1977**, 63.

(3) Clarke, K.; Rawson, G.; Scrowston, R. M. *J. Chem. Soc. C* **1969**, 537. For studies on the closely related benzodithiophenes, see: Gronowitz, S.; Dahlgren, T. *Chem. Scr.* **1977**, *12*, 97.

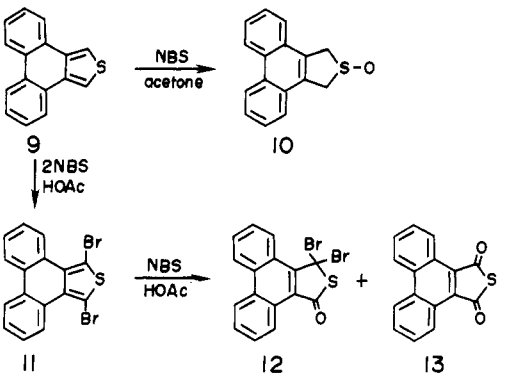
(4) Cava, M. P.; Pollack, N. M.; Mamer, O. A.; Mitchell, M. J. *J. Org. Chem.* **1971**, *36*, 3932.

(5) Zahradnik, R.; Párkányi, C. *Collect. Czech. Chem. Commun.* **1965**, *30*, 195.

Scheme I



Scheme II

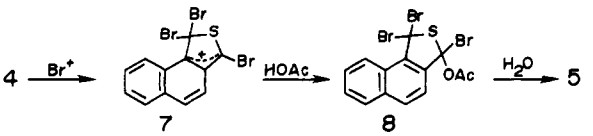


Bromination of **3**[4,6] in chloroform with 1 equiv of bromine gave a mixture of mono- and dibromo products which could not be readily resolved into its components. With 2 equiv of bromine, the 1,3-dibromo derivative **4** was obtained (Scheme I). The ^{1}H NMR spectrum of **4** showed that the two vinyl protons at C4 and C5 were still present (δ 7.27, 7.28, J = 10 Hz). As with **1** and **2**, substitution occurred in the thiophene ring and not at the "vinyl" positions, as in phenanthrene.

Bromination of **3** with *N*-bromosuccinimide (NBS) in acetic acid gave, in addition to **4**, the thiolactone **5** and the thioanhydride **6**. Similar bromination of **4** also gave **5** and **6**, and long exposure of **5** to laboratory air gave **6**. The structure of **6** was proved not only by its spectral properties but also by hydrolysis to the known[7] naphthalene-1,2-dicarboxylic acid.

The relative positions of the bromines and carbonyl group in **5** are based on an analysis of the NMR spectrum in the presence of shift reagent. Lactone **5** showed peaks at δ 8.97 and 7.81 assigned to the C9 and C4 protons, respectively. It was the latter peak (a doublet, coupled with the C5 proton at δ 8.09, J = 8 Hz) which was most shifted downfield with europium shift reagent.

We conclude that while there is not a large difference in the bromination rates of **3** at C1 or at C3, the former position probably has a slight advantage. The formation of **5** can be rationalized via the intermediates **7** and **8**. One



possible driving force for electrophilic attack at C1 is to convert that carbon from sp^2 to sp^3 hybridization, thus reducing the "peri" interaction with the C9 proton.

To examine the possible generality of the conversion of a thiophene to a thioanhydride via bromination/hydrolysis,

(6) Horner, C. J.; Saris, L. E.; Lakshmikantham, M. V.; Cava, M. P. *Tetrahedron Lett.* **1976**, 2581.

(7) Fieser, L. F. *J. Am. Chem. Soc.* **1929**, *51*, 951.

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we examined the reaction with phenanthro[9,10-c]-thiophene (9).[8] Treatment of 9 with NBS in acetone is reported to cause oxidation to sulfoxide 10 (Scheme II). We found that NBS in acetic acid, however, gave the dibromo compound 11 which, on further bromination gave 12 and 13.

We note that in the conversion of 4 to 5 and 11 to 12, one destroys the aromaticity of a thiophene ring but gains a benzenoid ring, and this may be a factor which facilitates the observed further electrophilic bromination.

Experimental Section

Bromination of Naphtho[1,2-c]thiophene (3). (a) With Bromine. Bromine (320 mg, 2 mmol) in 5 mL of chloroform was added to a solution of 3 (180 mg, 1 mmol) in 10 mL of chloroform. The mixture was stirred at room temperature for 2 min and then was washed with aqueous sodium bisulfite, sodium bicarbonate, and water. The organic layer was dried over magnesium sulfate, and the solvent was removed under vacuum. The residue was chromatographed on silica gel with 30% of benzene in hexane as the eluent to give 140 mg (41%) of 1,3-dibromonaphtho[1,2-c]thiophene (4), which could be recrystallized from hexane: mp 89–91 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.25 (m, 1 H), 7.65 (m, 1 H), 7.52 (m, 2 H), 7.28 (d, J = 10 Hz, 1 H), 7.27 (d, J = 10 Hz, 1 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 132.00, 131.53, 128.64, 128.06, 127.88, 127.59, 127.11, 127.06, 123.65, 119.41, 104.94, 103.24; IR (KBr) 3060 (m), 1460 (s), 1380 (s), 1220 (m), 890 (s), 870 (w) cm^{-1}; mass spectrum, m/e (relative intensity) 344 (50), 342 (100), 340 (53), 263 (22), 261 (22); high-resolution mass spectrum calcd for $C_{12}H_6Br_2S$ m/e 341.853 83, found m/e 341.854 12.

(b) With 2 Equiv of N-Bromosuccinimide. NBS (360 mg, 2 mmol) was added to a solution of 3 (180 mg, 1 mmol) in 20 mL of acetic acid. The mixture was stirred at room temperature for 20 min, and then 100 mL of water was added. The solution was extracted with 30 mL of ether three times. The combined organic layers were washed with aqueous sodium bicarbonate and dried over magnesium sulfate. The solvent was removed under vacuum to give a solid which was chromatographed on silica gel with 20% of benzene in hexane as the eluent to give 74 mg (22%) of 4, mp 89–91 °C.

In addition to 4, compounds 5 and 6 were isolated in 13% and 21% yields respectively. For 5: mp 113–114 °C; ^{1}H NMR (250 HMz, $CDCl_3$) δ 8.97 (m, 1 H), 8.10 (m, 1 H), 8.09 (d, J = 8.0 Hz, 1 H), 7.85 (m, 2 H), 7.81 (d, J = 8.0 Hz, 1 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 189.18, 148.42, 137.49, 133.10, 129.58, 129.52, 129.25, 127.66, 127.37, 126.70, 118.27, 44.43; IR (KBr) 3080 (w), 1700 (s), 1500 (m), 1350 (m) cm^{-1}; mass spectrum, m/e (relative intensity) 360 (0.78), 358 (1.6), 356 (0.73), 279 (73.6), 277 (77.4), 198 (17), 170 (100); high-resolution mass spectrum calcd for $C_{12}H_6Br_2OS$ m/e 357.848 75, found m/e 357.846 07.

For 6: mp 115–117 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.17 (m, 1 H), 8.23 (d, J = 8.5 Hz, 1 H), 7.95 (m, 1 H), 7.94 (d, J = 8.5 Hz, 1 H), 7.77 (m, 2 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 190.50, 190.04, 139.46, 136.84, 136.17, 133.55, 130.67, 129.58, 128.53, 128.14, 126.20, 118.53; IR (KBr) 3060 (m), 1690 (s), 1400 (m), 1250 (m) cm^{-1}; mass spectrum, m/e (relative intensity) 214 (79.6), 186 (31), 158 (20), 126 (100); high-resolution mass spectrum calcd for $C_{12}H_6O_2S$ m/e 214.008 85, found m/e 214.009 07.

Hydrolysis of 6. Compound 6 (30 mg, 0.14 mmol) was suspended in 30 mL of hydrochloric acid (20%), and the mixture was refluxed for 6 h. After the solution was cooled to room temperature, it was extracted with 25 mL of ether. The organic layer was washed with water and dried over magnesium sulfate. The solvent was evaporated to give a yellow solid which was recrystallized from ethanol to give 15 mg (50%) of naphthalene-1,2-dicarboxylic acid: mp 175–176 °C (lit.[7] mp 175 °C); mass spectrum, m/e (relative intensity) 216 (29), 198 (81), 172 (10), 154 (65.6), 126 (100).

Bromination of Phenanthro[9,10-c]thiophene (9). Bromination of 9[8] (85 mg, 0.36 mmol) with NBS (150 mg, 0.72 mmol) in 30 mL of acetic acid was carried out as described for the preparation of 4. The workup gave a solid which was recrystallized from hexane to yield 100 mg (65%) of 11: mp 170–172 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.33 (m, 2 H), 8.40 (m, 2 H), 7.55 (m, 4 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 131.79, 130.55, 127.97, 127.67, 127.09, 124.32, 123.44, 105.04; IR (KBr) 3010 (w), 1450 (s), 1040 (w), 750 (s), 720 (s) cm^{-1}; mass spectrum, m/e (relative intensity) 394 (53), 392 (100), 390 (50), 313 (21), 311 (22); high-resolution mass spectrum calcd for $C_{16}H_8Br_2S$ m/e 391.869 49, found m/e 391.870 42.

Treatment of 11 with NBS. Compound 11 (80 mg, 0.2 mmol) was treated with NBS (36 mg, 0.2 mmol) in 20 mL of acetic acid with stirring at room temperature for 20 min. Then water (20 mL) was added, and the solution was extracted with ether (20 mL) three times. The combined organic layers were washed with aqueous sodium bicarbonate and water. The organic solution was dried over magnesium sulfate and evaporated to give a residue. The residue was chromatographed on silica gel with 20% of benzene in hexane as the eluent to yield 12 (62%) and 13 (15%).

For 12: mp 150–152 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.90 (m, 2 H), 7.83 (m, 2 H), 7.76 (m, 2 H), 7.73 (m, 2 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 190.07, 150.84, 134.32, 131.85, 131.84, 129.44, 129.08, 128.44, 126.61, 125.97, 125.50, 125.14, 122.79, 43.69; IR (KBr) 3030 (w), 1695 (s), 1495 (m), 1380 (m), 1080 (m) cm^{-1}; mass spectrum, m/e (relative intensity) 410 (2), 408 (3.5), 406 (1.8), 329 (83), 327 (70), 220 (100); high-resolution mass spectrum calcd for $C_{16}H_8Br_2OS$ m/e 407.864 40, found m/e 407.868 41.

For 13: mp 160–162 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.35 (m, 2 H), 8.71 (m, 2 H), 7.82 (m, 4 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 191.38, 135.46, 133.87, 130.04, 129.22, 127.93, 125.81, 122.99; IR (KBr) 3020 (w), 1690 (s), 1500 (w), 1360 (w) cm^{-1}; mass spectrum, m/e (relative intensity) 264 (76), 236 (45), 208 (30), 176 (100); high-resolution mass spectrum calcd for $C_{16}H_8O_2S$ m/e 264.024 50, found m/e 264.024 50.

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Registry No. 3, 232-81-5; 4, 82338-26-9; 5, 82338-27-0; 6, 82338-28-1; 9, 235-95-0; 11, 82338-29-2; 12, 82338-30-5; 13, 82338-31-6; naphthalene-1,2-dicarboxylic acid, 2088-87-1.

(8) Shields, J. E.; Remy, D. E.; Bornstein, J. J. Org. Chem. 1975, 40, 477.

C(13) and C(14) Configurations of 8,13- and 8,13β-Epoxylabdane-14,15-diols: A Method Based on Boric Acid Induced ^{13}C NMR Shifts[1]

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Among natural substances of the diterpene type there exist an increasing number containing a vicinal glycol unit in the form of a 13-dihydroxyethyl group.[3] Whereas the stereochemistry of their rigid nuclear framework and of the substituents attached to it could be easily determined by spectral methods, the configuration of their secondary hydroxy group of the dihydroxyethyl moiety has remained

(1) Dedicated to Professor Dr. Ignacio Ribas, University of Santiago de Compostela, Spain, on the occasion of his 80th birthday.

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(3) (a) Wenkert, E.; Ceccherelli, P.; Raju, M. S.; Polonsky, J.; Tingoli, M. J. Org. Chem. 1979, 44, 146, and references therein. (b) Rodríguez, B.; Valverde, S. Tetrahedron 1973, 29, 2837. (c) Valverde, S.; Rodríguez, B. Phytochemistry 1977, 16, 1841. (d) de Quesada, T. G.; Rodríguez, B.; Valverde, S. Phytochemistry 1975, 14, 517. (e) von Carstenn-Lichterfelde, C.; Rodríguez, B.; Valverde, S. Experientia 1975, 31, 757.

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