Synthesis of 4,5-Dihydro-1*H*,3*H*-thieno[3,4-*c*]thiophene and 4,5-Dihydro-1*H*,3*H*-thieno[3,4-*c*]furan

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4,5-Dihydro-1*H*,3*H*-thieno[3,4-*c*]thiophene and 4,5-dihydro-1*H*,3*H*-thieno[3,4-*c*]furan were synthesized by retro Diels-Alder reactions under flash vacuum thermolysis conditions.

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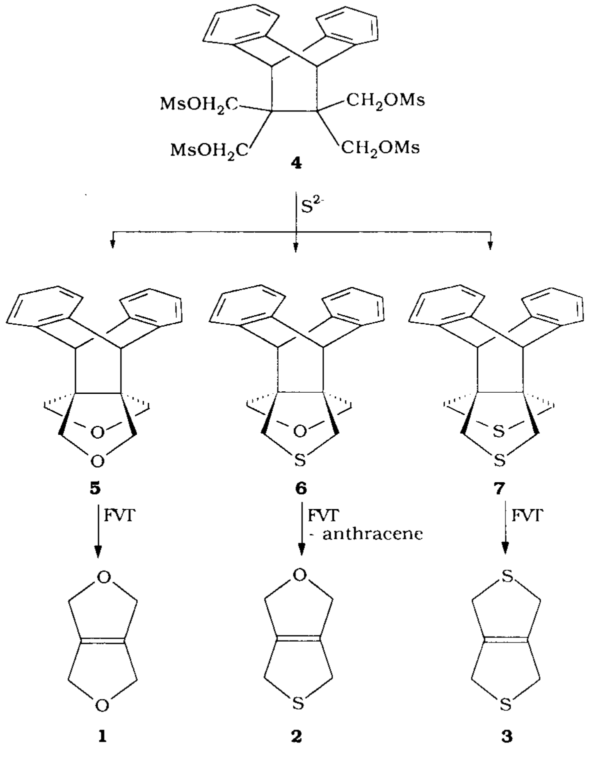
The simple symmetric heterocycle **1**, 4,5-dihydro-1*H*,3*H*-furano[3,4-*c*]furan, was obtained in our laboratory in 1974 [1,2] and its photoelectron spectrum has been studied [3]. In contrast, its corresponding monothia-, 4,5-dihydro-1*H*,3*H*-thieno[3,4-*c*]furan **2**, and dithia-analogue, 4,5-dihydro-1*H*,3*H*-thieno[3,4-*c*]thiophene **3**, remained unknown until now. Even substituted heterocycles of these families have been scarcely studied. Tetramethyl and dibromotetramethyl derivatives of 4,5-dihydro-1*H*,3*H*-thieno[3,4-*c*]thiophene have been obtained from 1,1,4,4-tetramethyl-1*H*,4*H*-thieno[3,4-*c*]thiophene [4]. The monosulfone of compound **3** has been synthesized by reaction of the unstable 3,4-dimethylenethiolane with sulfur dioxide [5,6]. The only well-known derivative in the dihydrothieno[3,4-*c*]furan series is a dioxo compound, the anhydride of 2,5-dihydrothiophene-3,4-dicarboxylic acid [7-9].

The retro Diels-Alder reaction [10,11] has proved to be a useful tool for the formation of C = C double bonds and was used in the synthesis of compound **1** [1,2]. The required precursor was obtained by dehydration of the corresponding tetraalcohol but also by reaction of the tetrakismethanesulfonate **4** with sodium sulfide in DMSO at 100°. The reaction of anhydrous sodium sulfide with *cis*-tetralin-1,2-bis-methanesulfonate giving the corresponding cyclic sulfide [12,13], we have re-investigated this cyclisation when minimizing the amount of water in the reaction mixture.

The replacement of the sodium sulfide nonahydrate used in reference [2] by commercially available trihydrate, or by a "dried" sulfide obtained by azeotropic distillation of the water from the nonahydrate with toluene, led us to a mixture of the three ethanoanthracenic compounds **5**, **6** and **7**, easily separated by liquid chromatography. The molar ratio **5**:**6**:**7** was not reproducible and varied from 17:82:1 to nearly 50:50:0. Further drying of sodium sulfide at 300° during 20 hours under a stream of nitrogen led to the major formation of the bis-sulfide **7**. However, in this case **7** was accompanied by by-products (probably di- or polysulfides) and could not be isolated in pure form.



Finally, **7** was synthesized in 35% yield by using dry lithium sulfide obtained by bubbling hydrogen sulfide through a solution of butyl lithium. In this experiment, the diether **5** was not formed. The ether-sulfide **6** was isolated in 30% yield.

Upon flash vacuum thermolysis (FVT) [14] at 700° (oven l = 18 cm, d = 1.5 cm) compounds **6** and **7** were cleaved, *via* a retro Diels-Alder reaction, to anthracene and the expected heterocycles. Anthracene crystallized at the oven exit. The heterocycle **2** was trapped on a cold finger in nearly pure form. Compound **3** was collected with anthracene at the oven exit and purified by liquid chromatography. Yields of **2** and **3** were nearly quantitative. The ^{1}H nmr spectrum of the thienofuran **2** showed two singlets of equal intensities at 3.60 and 4.52 ppm (**1**, δ = 4.51 ppm [1,2]). Compound **3** was characterized by a singlet at 3.50 ppm. The ^{13}C nmr spectra (**2**, 32.47, 71.88, 142.14; **3**, 34.38, 142.35) were also in good agreement with the proposed structures.

EXPERIMENTAL

Melting points were determined on a Gallenkamp apparatus and are uncorrected. The ^{1}H nmr spectra were recorded on a Varian EM 360 spectrometer (60 MHz). Chemical shifts are reported in ppm from TMS as an internal standard and given in δ units. The ^{13}C nmr spectra were recorded on a Bruker WP 80 SY spectrometer. The ir spectra were obtained on a Perkin-Elmer 1420 apparatus. The mass spectra were recorded on a Nermag 10-10H spectrometer (70 eV, electron impact).

Reaction of the Tetrakis-methanesulfonate **4** with Sodium Sulfide Trihydrate.

The tetrakis-methanesulfonate **4** (4.0 g, 6.27 mmoles) and sodium sulfide trihydrate (4.0 g, 30 mmoles) were added to dry DMSO (50 ml). The mixture was stirred and heated at 100° for 48 hours and afterwards poured into cold water and extracted with dichloromethane. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate. After removal of the solvent under reduced pressure, a white solid (2.06 g) was obtained and chromatographed on silica gel. Compound **7** (95 mg, 0.5% yield) was eluted with petroleum ether:dichloromethane (2:1, v/v). Compound **6** (1.38 g, 72%) was eluted with dichloromethane. The diether **5** (280 mg, 15%) was eluted with dichloromethane:ethanol (1:1, v/v).

(9,10-Dihydro-9,10-anthracenylene)-3a,6a-(4,5-dihydro-1*H*,3*H*-thieno[3,4-*c*]furan) (**6**).

This compound was isolated as a white solid, mp 244°; ^{1}H nmr (carbon tetrachloride): δ 2.32 and 2.41 (2 d, J = 11 Hz, 4H, 2 SCH_2), 2.52 and 3.87 (2 d, J = 8.5 Hz, 4H, 2 OCH_2), 3.93 (s, 2H, bridgehead protons), 6.91-7.31 (m, 8H, aromatic protons); ^{13}C nmr (deuteriochloroform): δ 40.25, 53.02, 68.78, 78.93, 124.56, 125.77, 126.21, 126.35, 141.75, 142.11; ir (potassium bromide): ν 1462, 1454, 1096, 941, 762, 743, 571 cm^{-1}; ms: m/z 306 (molecular ion, 34%), 178 (anthracene ion, 100%).

Anal. Calcd. for $C_{20}H_{18}OS$ (306.42): C, 78.39; H, 5.92; O, 5.21; S, 10.46. Found: C, 77.99; H, 5.95; O, 5.21; S, 10.81.

Reaction of the Tetrakis-methanesulfonate **4** with Dry Lithium Sulfide.

Hydrogen sulfide was bubbled through a solution of *n*-butyllithium in hexane at −20° under a nitrogen atmosphere in order to obtain 15 mmoles of dry lithium sulfide. To this mixture was added dry DMSO (50 ml) and the hexane was distilled off under reduced pressure. Compound **4** (1.95 g, 3 mmoles) was poured into the solution and the obtained mixture was stirred for 48 hours at 100°. The workup was identical to the one described above. The bis-sulfide **7** (338 mg, 35%) and the ether-sulfide **6** (275 mg, 30%) were easily separated by liquid chromatography.

(9,10-Dihydro-9,10-anthracenylene)-3a,6a-(4,5-dihydro-1*H*,3*H*-thieno[3,4-*c*]thiophene) (**7**).

This compound was isolated as a white solid, mp 189-194°; ^{1}H nmr (carbon tetrachloride): δ 2.72 (broad s, 8H, 4 SCH_2), 4.02 (s, 2H, bridgehead protons), 6.40-7.32 (m, 8H, aromatic protons); ^{13}C nmr (deuteriochloroform): δ 45.52, 54.89, 70.56, 125.14, 126.31, 142.18; ir (potassium bromide): ν 1460, 1451, 1434, 1422, 1169, 755, 660, 570 cm^{-1}; ms: m/z 322 (molecular ion, 6%), 178 (anthracene ion, 100%).

Anal. Calcd. for $C_{20}H_{18}S_2$ (322.49): C, 74.48; H, 5.62; S, 19.89. Found: C, 74.35; H, 5.68; S, 19.93.

Flash Vacuum Thermolysis of Compound **6**.

Compound **6** (200 mg, 0.65 mmole) was vaporized through a quartz oven (length = 18 cm, internal diameter = 1.5 cm) heated at 700° under 10^{-3} mbar. The heterocycle **2** was collected in a cold trap (liquid nitrogen, −196°). The crude product was purified by liquid chromatography on a silica gel column using pentane:dichloromethane (1:1, v/v) as eluant to yield 75 mg (90%) of **2**.

4,5-Dihydro-1*H*,3*H*-thieno[3,4-*c*]furan (**2**).

This compound was obtained as a colorless oil; ^{1}H nmr (carbon tetrachloride): δ 3.60 (s, 4H, 2 SCH_2), 4.52 (s, 4H, 2 OCH_2); ^{13}C nmr (deuteriochloroform): δ 32.47, 71.88, 142.14; ir (carbon tetrachloride): ν 2960, 2920, 2890, 2858, 1445, 1261, 1164, 1101, 1055, 1025, 894 cm^{-1}; ms: m/z 128 (molecular ion, 35%), 100 (24%), 99 (46%), 97 (100%), 85 (44%), 81 (40%).

Anal. Calcd. for C_6H_8SO (128.19): C, 56.22; H, 6.29. Found: C, 56.01; H, 6.04.

Flash Vacuum Thermolysis of Compound **7**.

The thermolysis was conducted in the same conditions as above from 230 mg of **7** (0.71 mmole). The heterocycle **3** and anthracene crystallized at the oven exit and were separated by liquid chromatography (eluant: petroleum ether; **3**, 85 mg, 83%; anthracene, 114 mg, 90%).

4,5-Dihydro-1*H*,3*H*-thieno[3,4-*c*]thiophene (**3**).

This compound was obtained as a white solid, mp 125°; ^{1}H nmr (carbon tetrachloride): δ 3.50 (s); ^{13}C nmr (deuteriochloroform): δ 34.38, 142.35; ir (potassium bromide): ν 2900, 2830, 1445, 1420, 1195, 760, 742 cm^{-1}; ms: m/z 144 (molecular ion, 100%), 111 (32%), 99 (30%), 98 (37%), 97 (97%), 77 (17%).

Anal. Calcd. for $C_6H_8S_2$ (144.26): C, 49.95; H, 5.59. Found: C, 50.31; H, 5.70.

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