Rearrangements in the 11-Thia-9,10-dihydro-9,10-ethanoanthracene Series. Synthesis of a Bridged Thienooxepin†

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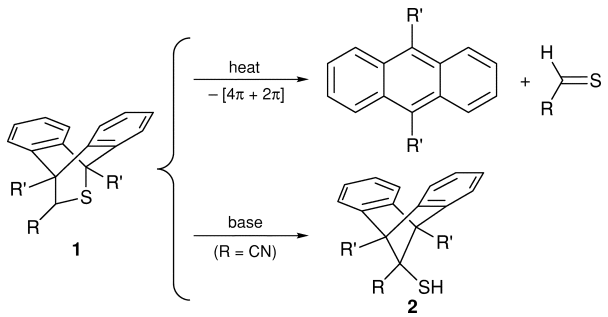
A rearrangement from 11-thia-9,10-dihydro-9,10-ethanoanthracene derivatives into a thienooxepin is reported; the structure of the bridged oxepin is confirmed by X-ray analysis.

11-Thiaethanoanthracenic derivatives **1** (Scheme 1) are excellent precursors for thiocarbonyl compounds.[1] When heated they undergo a retro-Diels–Alder cleavage, giving anthracene or a substituted analog and a compound containing a C=S double bond. However, these bridged heterocycles, as other Diels–Alder adducts of thioaldehydes, can readily undergo rearrangements. We have recently reported a ring contraction under basic conditions allowing the transformation of thiaethanoanthracenic derivatives bearing an electron-withdrawing group in position 12 (*e.g.* **1**, R = CN) into 9,10-methanoanthracene derivatives **2**.[2]

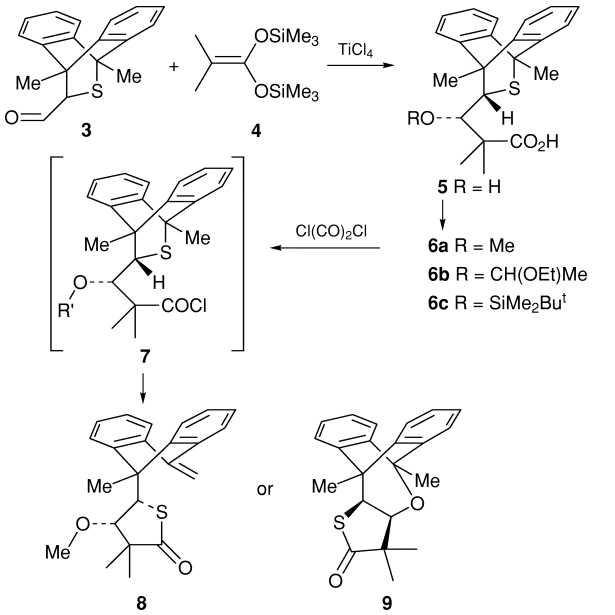


Scheme 1

Pursuing our work on the synthesis of unstable thiocarbonyl compounds,[3] we needed to prepare the hydroxy-acid **5** (Scheme 2) and to transform it, or one of its protected derivatives **6a**–**c**, into an acyl chloride. By making use of these chlorides, we would have been able to introduce various functional groups. Here we report that the expected acyl chlorides are not stable and that they undergo rearrangements into thiolactones.

The first step of the synthesis was planned to be an aldol reaction of the known aldehyde **3**.[4] In order to avoid any problem related to the use of basic conditions (see the rearrangement described in Scheme 1), we decided to perform the aldol reaction under acidic conditions. Compound **3** was treated with 1.4 equiv. of the bis[trimethylsilyl]ketene acetal **4**,[5] in the presence of $TiCl_4$. After a usual workup, the corresponding β-hydroxy acid was obtained in good yield (80%). The ^{1}H NMR spectrum revealed an excellent diastereoselectivity during this reaction. Apparently only one diastereoisomer was formed. However, at this stage, we were unable to determine its configuration.

Various protective groups were used to mask the hydroxyl function. The methyl ether **6a** was obtained by treatment of compound **5** with sodium hydride and methyl iodide (10 equiv.) at 0 °C during 18 h (yield = 57%). The ethoxyethyl group was introduced under acidic conditions to give quantitatively the adduct **6b**. Finally, the *tert*-butyldimethylsilyl derivative **6c** was obtained with a low yield (17%). This may be due to the steric hindrance around the hydroxyl group.



Scheme 2

These acids (**5**, **6a**–**c**) were then treated with oxalyl chloride in order to give the corresponding acyl chlorides. However, we were unable to isolate the expected compound **7**. When **6a** was used the resulting product was the thiolactone **8**. This compound showed a characteristic $\nu_{C=O}$ band in its IR spectrum (1690 cm^{-1}). Its ^{1}H NMR spectrum showed two ethylenic protons (δ 5.70 and 5.73), and only four methyl groups (δ 0.79, 1.02, 2.10 and 3.23 ppm) in place of the five methyl groups expected for compound **7a**. The presence of a methylidene group (δ 109.7) and of four methyl groups (17.3, 19.2, 23.7 and 58.9 ppm) was confirmed by ^{13}C NMR spectroscopy.

On the other hand, when **5, 6b** and **6c** were treated with oxalyl chloride, a new compound was isolated which was identical regardless of the starting material (quantitative yields). Even though its IR spectrum displayed a carbonyl vibration at 1702 cm^{-1} possibly attributed to a thiolactone, this compound did not show any ethylenic proton signal in its ^{1}H NMR spectrum, so that it cannot be attributed a structure analogous to **8**. Finally, a single crystal was

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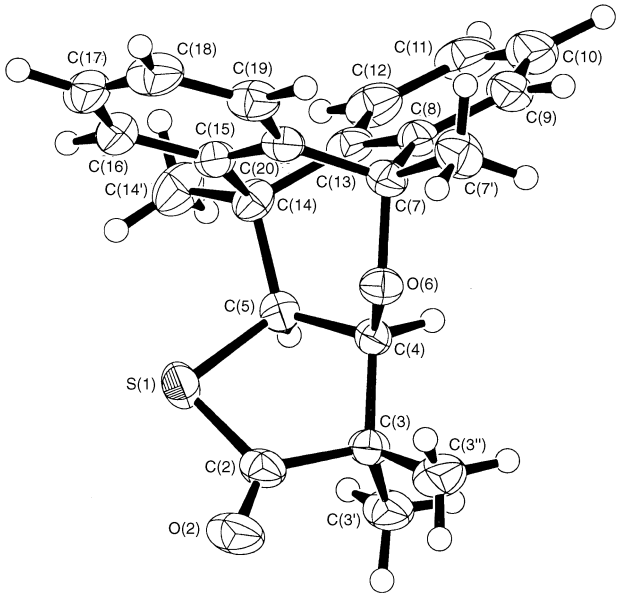
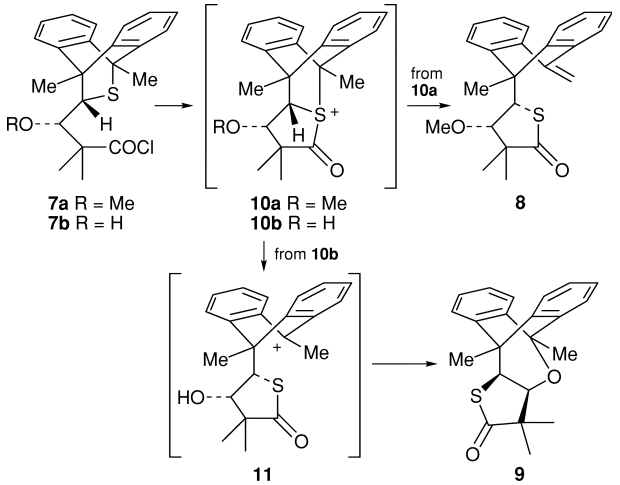


Fig. 1 X-Ray structure of bridged oxepin **9**

obtained and its X-ray analysis (Fig. 1) demonstrated that the obtained compound was the bridged oxepin **9**.

We propose that the formation of both **8** and **9** can be explained by the formation of an intermediate acyl sulfonium (Scheme 3). Similar intramolecular sulfur acylation has been already described by Truce and Abraham.[6] The sulfonium **10a**, formed from **6a**, undergoes proton abstraction (maybe *via* a transient carbocation) from the bridgehead methyl group to give the alkene **8**. Starting from **5**, the sulfonium **10b** is formed and is rearranged into the oxepin **9** *via* a nucleophilic substitution. As obviously no Walden inversion is possible here, we suppose that the carbocation **11** is an intermediate in this ('SN_1') intramolecular substitution. As **9** is also obtained from **6b**,**c**, we suppose that the protecting groups in these starting materials are rapidly cleaved by the HCl formed during the reaction of oxalyl chloride with the carboxylic acid prior to rearrangement.



Scheme 3

The observed relative configuration of **9** (*S**,*S**) can be related to the stereochemistry of the acid **5**, demonstrating that this acid also has a (*S**,*S**) relative configuration.

Experimental

Preparation of Compound **5**.—A solution of **4** (1.5 equiv) in methylene chloride was added dropwise, at −78 °C under an argon atmosphere, into a mixture of aldehyde **3**[7] (1 equiv.) and of $TiCl_4$ 91.3 equiv.) in methylene chloride. The reaction mixture was stirred for 3 h at room temperature. After a usual aqueous work-up, compound **5** was obtained in 80% yield; MS: 368 ($M^{\bullet+}$); δ_H (250 MHz, $CDCl_3$) 7.4–7.1 (m, 8 H, ArH), 4.31 (s, 1H, CHO*H*), 3.39 (s, 1 H, CHS), 2.31 (s, 3 H, Me), 2.30 (br s, 1 H, OH), 2.24 (s, 3 H, Me), 1.04 (s, 3 H, me), 0.98 (s, 3 H, Me) (Found: C, 71.85; H, 6.34. $C_{22}H_{22}O_2S$ requires C, 71.71; H, 6.56%).

Protection of the Hydroxy Group of Compound **5**.—All reactions were performed under classical conditions. For typical procedures see ref. 8. **6a**: δ_H (200 MHz, $CDCl_3$) 7.3–7.0 (m, 8 H, ArH), 3.91 (s, 1 H, CHOMe), 3.14 (s, 1 H, CHS), 2.55 (s, 3 H, OCH_3), 2.20 (s, 3 H, Me), 2.10 (s, 3 H, me), 1.03 (s, 3 H, Me), 1.00 (s, 3 H, Me). **6b**: MS: 440 ($M^{\bullet+}$); δ_H (250 MHz, $CDCl_3$) 7.5–7.1 (m, 8 H, ArH), 5.9–5.8 (m, 1 H, OCHO), 4.36 (s, 1 H, CHOEE), 3.6–3.35 (m, 2 H, CH_2), 3.34 (s, 1 H, CHS), 2.26 (s, 3 H, me), 1.38 (t, 3 H, C$H_3$$CH_2$), 1.3–0.9 (m, 9 H, 3Me). **6c**: δ_H (250 MHz, $CDCl_3$) 7.6–7.1 (m, 8 H, ArH), 4.26 (s, 1 H, C*HO*t*B*DMS), 3.32 (s, 1 H, CHS), 2.24 (s, 3 H, me), 2.17 (s, 3 H, Me), 1.16 (s, 3 H, Me), 0.98 (s, 3 H, Me), 0.85 [s, 9 H, $Si(CH_3)_3$], 0.03 (s, 6 H, H_3CSiCH_3).

Reactions of Compounds **5**, **6a**–**c** *with Oxalyl Chloride*.—Compound **5** (or **6**) was dissolved in methylene chloride. 2.5 equiv. of oxalyl chloride were added at 0 C. The reaction mixture was then stirred at room temperature for 2.5 h. Removal of solvent and of excess oxalyl chloride under reduced pressure gave product **9** (or **8**) which was purified by liquid chromatography on silica gel (eluant:methylene chloride). **8** (yield: 73%): MS: 364 ($M^{\bullet+}$); δ_H (200 MHz, $CDCl_3$) 7.6–7.2 (m, 8 H, ArH), 5.66 and 5.63 (2 s, 2 H, $=CH_2$), 4.19 (s, 1 H, C*H*OMe), 3.22 (s, 3 H, OCH_3), 2.64 (s, 1 H, CHS), 2.10 (s, 3 H, Me), 1.17 (s, 3 H, Me), 0.79 (s, 3 H, Me) (Found: C, 75.51; H, 6.62; S, 8.65. $C_{23}H_{24}O_2S$ requires C, 75.79; H, 6.46; S, 8.80%).

9 (nearly quantitative yields): MS: 350 ($M^{\bullet+}$); δ_H (200 MHz, $CDCl_3$) 7.6–7.1 (m, 8 H, ArH), 3.75 (s, 1 H, $J = 3.1$ Hz, C*H*OR), 3.44 (s, $J = 3.1$ Hz, 1 H, CHS), 2.05 (s, 3 H, Me), 1.96 (s, 3 H, me), 1.21 (s, 3 H, Me), 1.00 (s, 3 H, Me) (Found: C, 75.04; H, 6.34; S, 8.95. $C_{22}H_{22}O_2S$ required C, 75.40; H, 6.33; S, 9.13%).

X-Ray Crystallography.—Crystals of compound **9** were grown from a methylene chloride solution. The space group is $P2_1/c$ (no. 14). The cell parameters were determined on an Enraf Nonius CAD4 four circle diffractometer ($\lambda = 0.7107$ Å) as $a = 9.555(4)$, $b = 17.952(5)$, $c = 10.971(4)$ Å, $\beta = 106.64(3)°$, with $Z = 4$. The volume of the unit cell is 1803(1) Å^3, $F(000) = 744$, $\mu = 0.191$ mm^{-1} and $D_c = 1.291$. The structure was solved by direct methods[8] using 3152 reflections [with $I > 2\sigma(I)$]. The final R value is 0.041 ($R_w = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w F_o^2)]^{1/2}$) with $w = [\sigma^2(F_o) + 0.00027\ |F_o|^2]^{-1}$ and $S = 1.88$.

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