AN OXIDATIVE 1,3-DITHIOLANE — DIHYDRO-1,4-DITHIIN REARRANGEMENT

Luis Angel Maldonado* and Norberto Manjarrez
División de Estudios de Posgrado, Facultad de Química, UNAM,
04510 México D.F., México

Abstract - In hot DMSO, compound 1 is converted into 2 in excellent yield. This conversion involves a 1,3-dithiolane — dihydro-1,4-dithiin rearrangement to 3, followed by oxidation of the allylic CH₂. Appropriate experiments established the mechanism of this rearrangement-oxidation sequence.

The rearrangement of 1,3-dithiolanes to dihydro-1,4-dithiins is a well known reaction. It can be initiated by an external oxidative reagent (peracids, halonium ions)¹ or by an appropriately located leaving group². We wish to report a new example of this rearrangement under conditions in which oxidation of an allylic position of the resulting dihydro-1,4-dithiin occurs concomitantly.

The ethylene thioketal of 3-bromo[1]chroman-4-one 1 was prepared from [1]chroman-4-one by standard methods involving bromination and thioketalization:

When a DMSO solution of 1 was heated in a water bath for 2 h, a 83 % yield of a pale yellow crystalline solid, mp 189-190°C, was obtained. The ir spectrum of this substance showed a 1700 cm⁻¹ absorption band and from its ¹H-nmr spectrum only aromatic (δ 7.10-7.80) and protons vicinal to sulfur (δ 3.40) can be observed in a 1 : 1 ratio. From the above data, its molecular weight (236 by ms) and its elemental analysis (C₁₁H₈O₂S₂), structure 2 was assigned to this compound³:
The reaction should involve a 1,3-dithiolane → dihydro-1,4-dithiin rearrangement (1 → 3, bromide ion as the leaving group), followed by oxidation of the allylic CH₂ of the intermediate 3:

\[ \text{1} \xrightarrow{\Delta} (\text{DMSO}) \xrightarrow{\text{[O]}} \text{2} \]  

Evidence for this sequence of events was obtained in the following way. Although the \(^1\)H-nmr spectrum of 1 in CDCl₃ at rt showed the expected signals (\(\delta 7.75\) (dd, \(J_o = 7.5\) Hz, \(J_m = 2\) Hz, H-5), 6.70-7.15 (complex signals, three aromatic protons), 4.30-4.80 (ABC system, BrCH-CH₂O) and 3.55 (s, SCH₂CH₂S)), in DMSO-d₆ at 73°C a completely different spectrum was recorded. Thus the four aromatic protons are observed between \(\delta 6.80-7.30\) and a high field shift to \(\delta 3.35\) for the SCH₂CH₂S group is also evident. It is most important that the complex signal due to the ABC system for the BrCH-CH₂O group is no longer present, being replaced by a singlet at \(\delta 4.55\). All these changes can be explained by the structure 3, the unoxidized dihydro-1,4-dithiin proposed as intermediate.

The above experiment strongly suggested that intermediate 3 could be isolated under appropriate reaction conditions and this proved to be the case by performing the rearrangement of 1 in the presence of powdered NaHCO₃. Vigorous gas evolution (CO₂) was observed and a 93% yield of 3 was obtained as an unstable oil. Although an analytical sample of 3 could not be prepared, its spectroscopic properties were in accord with the proposed structure (\(^1\)H-nmr (CDCl₃) \(\delta 6.70-7.33\) (complex signals, four aromatic protons), 4.50 (s, allylic CH₂O) and 3.26 (s, SCH₂CH₂S)):
Since the isolated intermediate 3 could not be oxidized to 2 with DMSO alone (water bath, with or without added NaHCO₃), we turned our attention to HBr, the expected by-product of the rearrangement 1 → 3 (see reaction 2). When a DMSO solution of 3 was heated in a water bath, while passing into a slow stream of gaseous HBr, a 75% yield of oxidized product 2 was obtained:

\[
3 \xrightarrow{\text{HBr (DMSO), } \Delta} 2 \tag{4}
\]

Therefore, we propose that HBr is first oxidized by DMSO to give bromine⁴ and this attacks the allylic position of 3 to afford the intermediate α-bromo ether 4. This is finally oxidized by DMSO in the usual fashion⁵ to give 2:

\[
2 \text{HBr} + \text{DMSO} \rightarrow \text{H}_2\text{O} + \text{DMS} + \text{Br}_2 \tag{5}
\]

Accordingly with the above explanation, the oxidation 3 → 2 could also be accomplished in DMSO with bromine or NBS.

**EXPERIMENTAL**

Melting points are uncorrected. IR and ¹H-nmr spectra were recorded on Perkin-Elmer 337 and Varian EM-390 or HA-100 instruments, respectively. Mass spectra were taken at an ionizing voltage of 70 eV on a Hewlett-Packard 5985 GC/ms instrument. Elemental analyses were performed at Galbraith Laboratories Inc.

**Ethylene thiketal of 3-bromo[1]chroman-4-one, 1**

To a solution of 3-bromo[1]chroman-4-one⁶, mp 67-69°C (2 g, 8.8 mmol), in 1 ml of glacial AcOH containing 2 ml (2.24 g, 23.8 mmol) of 1,2-ethanediethiol, was added dropwise 1 ml of BF₃-Et₂O. The crystalline derivative thus formed was diluted with 1 ml of glacial AcOH, 0.2 ml of BF₃-Et₂O was added and the suspension allowed to stand at rt for 15 min. The pink crystalline product was filtered off and washed with cold MeOH to give 2.2 g of 1, mp 112-115°C (dec.) (83% yield). The analytical sample was obtained as white prisms with a pinkish tint, by crystallization from AcOEt, mp 120-121°C (dec.). Anal. calcd. for C₁₁H₁₁BrOS₂: C, 43.56; H, 3.63; Br, 26.40; S, 21.12; found: C,
43.71; H, 3.72; Br, 26.40; S, 21.25. Ir (KBr) : ν 1610, 1580, 1490, 1460, 1220, 1080 and 750 cm⁻¹. ¹H-nmr (CDCl₃) : δ 7.70 (dd, J₀ = 7.5 Hz, Jₘ = 2 Hz, H-5), 6.70 -7.15 (complex signals, three aromatic protons), 4.30-4.80 (ABC system, BrCH-CH₂O) and 3.55 (s, SCH₂CH₂S).

In another route to 1, [1] chroman-4-one was first thiketalized as above in 94 % yield, but bromination of the resulting thiketel with phenyl trimethyl ammonium tribromide in THF proceeded in low yield (28 %). Compound 1 is unstable turning dark even in the refrigerator.

2,3-Dihydro-5H-[1] chromano[2,3-c]-1,4-dithiin-5-one, 2 : A solution of 1 (0.75 g, 2.47 mmol) in 20 ml of DMSO was heated in a water bath for 6 h and allowed to stand at rt overnight. The reaction mixture was diluted with H₂O and the crystalline material filtered off to give 480 mg of 2, mp 178°C (83 % yield). The analytical sample was prepared by crystallizations from CHCl₃-MeOH, mp 189-190°C (pale yellow needles). Anal. calcd. for C₁₁H₈O₂S₂ : C, 55.94; H, 3.41; S, 27.10; found : C, 55.78; H, 3.41; S, 26.95. Ir (KBr) : ν 1700, 1610, 1590, 1530 and 750 cm⁻¹. ¹H-nmr (CDCl₃) : δ 7.10-7.80 (complex signals, four aromatic protons) and 3.40 (s, SCH₂-CH₂S). Ms (m/z, rel intensity) : 236 (M⁺, 100 %), 237 (M⁺ + 1, 16.6 %), 180 (42.7 %) and 120 (74.5 %).

2,3-Dihydro-5H-[1] chromano[2,3-c]-1,4-dithiin, 3 : To a mixture of bromo thiketel 1 (0.5 g, 1.65 mmol) and powdered NaHCO₃ (0.5 g, 5.95 mmol), 6 ml of DMSO were added and the yellow suspension was heated in a water bath. After a few min the suspension turned pink and vigorous gas evolution was observed which in about 2 min subsided. The reaction mixture was heated 15 min further, cooled to rt, diluted with H₂O (15 ml) and extracted with Et₂O. The combined organic extracts were washed with cold H₂O (5 x 5 ml), and after the usual workup, a red oil (339 mg, 93 % yield) was obtained. Analytical tlc (hex-AcOEt, 5 : 1, 2 elutions) showed that a main component was present. This compound decomposed on the attempted distillation at reduced pressure and its impurities could not be removed completely by preparative tlc. Therefore, an analytical sample of 3 was not obtained.

In order to record the spectroscopic data of 3, partial purification could be achieved by rapid filtration of the crude product through Florisil, eluting with hex-C₆H₆ (2 : 1). The almost colorless oil thus obtained was immediately analyzed by ir and ¹H-nmr spectroscopies which showed the expected data. Ir (film) : ν 1595,
1570, 1500, 1240, 1220, 1040, 1015 and 755 cm\(^{-1}\). \(^1\)H-nmr (CDCl\(_3\)) : \(\delta\) 6.70-7.30 (complex signals, four aromatic protons), 4.50 (s, CH\(_2\)O) and 3.25 (s, SCH\(_2\)CH\(_2\)S).

Oxidation of 3 to 2: All the experiments were run under somewhat standard conditions using 0.76-0.95 mmol of 3 in 5-7 ml of DMSO at \(\approx 90^\circ\)C for 2 h.

a) With gaseous HBr: A slow stream of gaseous HBr was passed into a hot solution of 0.76 mmol of 3 in 5 ml of DMSO for 1 h. After heating for another 1 h, it was allowed to stand at rt overnight, diluted with H\(_2\)O (exothermic reaction) and extracted with AcOEt. The organic extracts were washed with H\(_2\)O, 10 % aqueous solution of Na\(_2\)SO\(_3\) and H\(_2\)O. Usual workup gave 205 mg of crude yellow crystals 2, which was purified by crystallizing from CHCl\(_3\)-MeOH, mp 185-187°C (136 mg, 75 % yield).

b) With Br\(_2\): Bromine (8 drops) was cautiously added (exothermic reaction) to a hot solution of 0.95 mmol of 3 in 7 ml of DMSO. After 2 h in a water bath, the mixture was allowed to stand at rt overnight and worked up as in the above case. The crude product (218 mg) was crystallized as before to give almost pure 2, mp 187-189°C.

c) With NBS: 160 mg (0.89 mmol) of solid NBS were added in two portions to a hot solution of 3 (0.86 mmol) in DMSO (6 ml). Heating and workup were the same as in the previous cases to afford an orange solid (163 mg) identified as 1 by mp and tlc comparison with an authentic sample.

REFERENCES AND NOTES


3. Compound 2 dissolves with difficulty in hot ethanolic NaOH, being recovered unchanged after acidification.


Received, 9th May, 1985