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

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Abstract - In hot DMSO, compound 1 is converted into 2 in excel-
lent yield. This conversion involves a 1,3-dithiolane —► dihydro-
1,4-dithiin rearrangement to 3, followed by oxidation of the al-
lylic CH$_2$. 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 re-
action. It can be initiated by an external oxidative reagent (peracids, halonium
ions)[1] or by an appropriately located leaving group[2]. We wish to report a new ex-
ample of this rearrangement under conditions in which oxidation of an allylic po-
sition 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 :
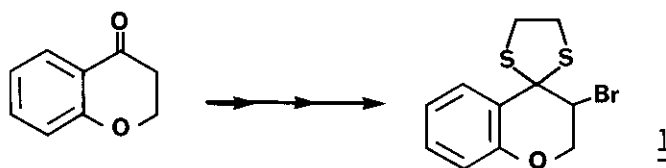
When a DMSO solution of 1 was heated in a water bath for 2 h, a 83 % yield of a
pale yellow crystalline solid, mp 189-190°C, was obtained. The ir spectrum of this
substance showed a 1700 cm^{-1} absorption band and from its [1]H-nmr spectrum only aro-
matic (δ 7.10-7.80) and protons vicinal to sulfur (δ 3.40) can be observed in a
1 : 1 ratio. From the above data, its molecular weight (236 by ms) and its elemen-
tal analysis (C$_{11}$H$_8$O$_2$S$_2$), structure 2 was assigned to this compound[3] :

$$\underline{1} \quad \xrightarrow[\text{(DMSO)}]{\Delta} \quad \underline{2} \qquad (1)$$
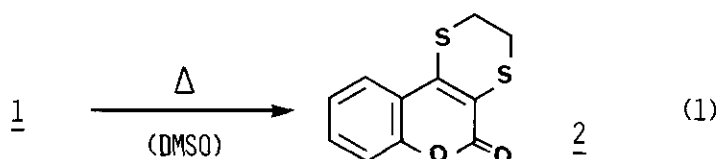
The reaction should involve a 1,3-dithiolane $\longrightarrow$ dihydro-1,4-dithiin rearrangement ($\underline{1} \longrightarrow \underline{3}$, bromide ion as the leaving group), followed by oxidation of the allylic CH_2 of the intermediate $\underline{3}$:

$$\underline{1} \quad \xrightarrow{-HBr} \quad \left[\quad \underline{3} \quad \right] \quad \xrightarrow{[O]} \quad \underline{2} \qquad (2)$$
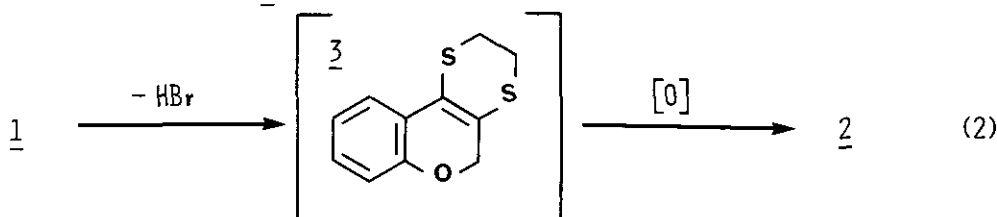
Evidence for this sequence of events was obtained in the following way. Although the [1]H-nmr spectrum of $\underline{1}$ in $CDCl_3$ at rt showed the expected signals (δ 7.75 (dd, J_o = 7.5 Hz, J_m = 2 Hz, H-5), 6.70-7.15 (complex signals, three aromatic protons), 4.30-4.80 (ABC system, BrCH-CH_2O) and 3.55 (s, SCH_2CH_2S)), in DMSO-d_6 at 73°C a completely different spectrum was recorded. Thus the four aromatic protons are observed between δ 6.80-7.30 and a high field shift to δ 3.35 for the SCH_2CH_2S group is also evident. It is most important that the complex signal due to the ABC system for the BrCH-CH_2O group is no longer present, being replaced by a singlet at δ 4.55. All these changes can be explained by the structure $\underline{3}$, the unoxidized di-hydro-1,4-dithiin proposed as intermediate.
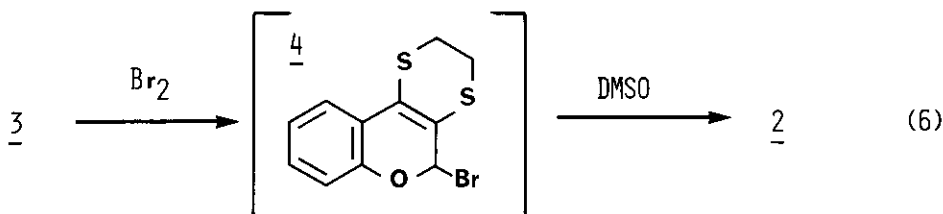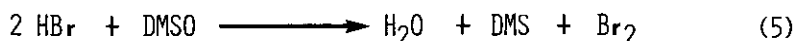
The above experiment strongly suggested that intermediate $\underline{3}$ could be isolated under appropriate reaction conditions and this proved to be the case by performing the rearrangement of $\underline{1}$ in the presence of powdered $NaHCO_3$. Vigorous gas evolution (CO_2) was observed and a 93 % yield of $\underline{3}$ was obtained as an unstable oil. Although an analytical sample of $\underline{3}$ could not be prepared, its spectroscopic properties were in accord with the proposed structure ([1]H-nmr ($CDCl_3$) δ 6.70-7.33 (complex signals, four aromatic protons), 4.50 (s, allylic CH_2O) and 3.26 (s, SCH_2CH_2S)) :

$$\underline{1} \quad \xrightarrow[\text{(DMSO)}, \Delta]{NaHCO_3} \quad \underline{3} \qquad (3)$$
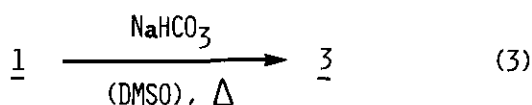
Since the isolated intermediate $\underline{3}$ could not be oxidized to $\underline{2}$ with DMSO alone (water bath, with or without added $NaHCO_3$), we turned our attention to HBr, the expected by-product of the rearrangement $\underline{1} \rightarrow \underline{3}$ (see reaction 2). When a DMSO solution of $\underline{3}$ was heated in a water bath, while passing into a slow stream of gaseous HBr, a 75 % yield of oxidized product $\underline{2}$ was obtained :

$$\underline{3} \xrightarrow[\text{(DMSO)}, \Delta]{\text{HBr}} \underline{2} \qquad (4)$$
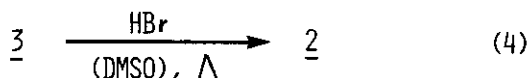
Therefore, we propose that HBr is first oxidized by DMSO to give bromine[4] and this attacks the allylic position of $\underline{3}$ to afford the intermediate α-bromo ether $\underline{4}$. This is finally oxidized by DMSO in the usual fashion[5] to give $\underline{2}$:

$$2\ HBr\ +\ DMSO\ \longrightarrow\ H_2O\ +\ DMS\ +\ Br_2 \qquad (5)$$

$$\underline{3} \xrightarrow{Br_2} \left[\ \underline{4}\ \right] \xrightarrow{DMSO} \underline{2} \qquad (6)$$

Accordingly with the above explanation, the oxidation $\underline{3} \rightarrow \underline{2}$ could also be accomplished in DMSO with bromine or NBS.

EXPERIMENTAL

Melting points are uncorrected. Ir and ^{1}H-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 thioketal of 3-bromo[1]chroman-4-one, $\underline{1}$: To a solution of 3-bromo[1]chroman-4-one[6], 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-ethanedithiol, was added dropwise 1 ml of BF_3-Et_2O. The crystalline derivative thus formed was diluted with 1 ml of glacial AcOH, 0.2 ml of BF_3-Et_2O 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 $\underline{1}$, mp 112-115°C (dec.) (83 % yield). The analytical sample was obtained as white prisms with a pinkish tint, by crystallizations from AcOEt, mp 120-121°C (dec.). Anal. calcd. for $C_{11}H_{11}BrOS_2$: 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}. ^{1}H-nmr (CDCl$_3$) : δ 7.70 (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-CH$_2$O) and 3.55 (s, SCH$_2$CH$_2$S).

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

2,3-Dihydro-5H- [1] chromano[2,3-c]-1,4-dithiin-5-one, $\underline{2}$: A solution of $\underline{1}$ (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 H$_2$O and the crystalline ma-terial filtered off to give 480 mg of $\underline{2}$, mp $\simeq$ 178°C (83 % yield). The analytical sample was prepared by crystallizations from CHCl$_3$-MeOH, mp 189-190°C (pale yellow needles). Anal. calcd. for C$_{11}$H$_8$O$_2$S$_2$: 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}. ^{1}H-nmr (CDCl$_3$) : δ 7.10-7.80 (complex signals, four aromatic protons) and 3.40 (s, SCH$_2$-CH$_2$S). 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, $\underline{3}$: To a mixture of bromo thioketal $\underline{1}$ (0.5 g, 1.65 mmol) and powdered NaHCO$_3$ (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 H$_2$O (15 ml) and extracted with Et$_2$O. The combined organic extracts were washed with cold H$_2$O (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 ana-lytical sample of $\underline{3}$ was not obtained.

In order to record the spectroscopic data of $\underline{3}$, partial purification could be a-chieved by rapid filtration of the crude product through Florisil, eluting with hex-C$_6$H$_6$ (2 : 1). The almost colorless oil thus obtained was immediately analyzed by ir and ^{1}H-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$_3$) : δ 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 $\simeq$ 90°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 2 by mp and tlc comparison with an authentic sample.

REFERENCES AND NOTES

1.- C.H. Chen, Tetrahedron Lett., 1976, 25; C.H. Chen and B.A. Donatelli, J. Org. Chem., 1976, 41, 3053; H. Yoshino, Y. Kawazoe and T. Taguchi, Synthesis, 1974, 713.

2.- H. Rubinstein and M. Wuerthele, J. Org. Chem., 1969, 34, 2762; J.L. Massingill Jr., M.G. Reinecke and J.E. Hodgkins, ibid., 1970, 35, 823 and references cited therein.

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

4.- W.W. Epstein and F.W. Sweat, Chem. Rev., 1967, 67, 247 and appropriate references cited therein.

5.- N. Kornblum, W.J. Jones and G.J. Anderson, J. Am. Chem. Soc., 1959, 81, 4113.

6.- J. Cologne and C. Guyot, Bull. Soc. Chim. France, 1957, 1228.