

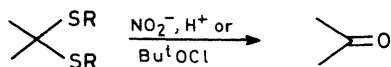
The *S,S*-Acetal to Carbonyl Transformation using the Soft NO^+ or Cl^+ Species

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A series of *S,S*-acetals (spiro-1,3-dithiolanes, 1,3-dithiolanes, and *S,S*-dibenzyl acetals) have been converted into the corresponding carbonyl compounds by sodium nitrite in aqueous solution (NO^+ , H_2ONO^+ , ClNO) or with *t*-butyl hypochlorite (Cl^+) in anhydrous CCl_4 . Mechanisms for these transformations are suggested, based on the Hard and Soft Acids and Bases (HSAB) principle.

The transformation of *S,S*-acetals into the corresponding carbonyl compounds is an important reaction.¹ For it to be successful it is important that a soft (borderline) acid² (soft acids: low energy of the frontier unoccupied orbitals²) attacks the soft base (the sulphur of the *S,S*-acetal; soft bases: high energy of the occupied frontier orbitals²). A variety of procedures for the title transformation are known, as for example use of transition-metal ions (Ti^{4+} , Cu^{2+} , Cd^{2+} , Ag^+ , and Hg^{2+}), oxidation of sulphur to a higher oxidation state, or *S*-alkylation.¹ As a continuation of our work on reactions of soft (borderline) electrophiles with thiocarbonyl compounds³ we have studied the transformation of *S,S*-acetals into the corresponding carbonyl compounds (Scheme 1) by two different methods: sodium nitrite in aqueous acid solution (NO^+) (Method A) and *t*-butyl hypochlorite (Cl^+) in anhydrous CCl_4 (Method B).



Scheme 1.

Results and Discussion

A series of spiro-1,3-dithiolanes (1), (3), and (5), 1,3-dithiolanes (6), (8), and (10), and *S,S*-dibenzyl acetals (2), (4), (7), (9), and (11) have been prepared by standard methods⁴ and treated with sodium nitrite in 4*M*-HCl solution (Method A) or *t*-butyl hypochlorite in anhydrous CCl_4 (Method B) at room temperature.

When 3 mol equiv. of NaNO_2 (excess) are allowed to react with *S,S*-acetals in 4*M*-HCl or 2 mol equiv. of Bu^tOCl (excess) with *S,S*-acetals in CCl_4 at room temperature the corresponding carbonyl compounds are formed after a relatively short time (see Table) and isolated in most cases in reasonable yield.

Inspection of these results (see Table) reveals that aromatic *S,S*-acetals are transformed into the corresponding carbonyl compounds in reasonable yields by both Method A and Method B. For the alicyclic *S,S*-acetals the yields of the transformation are somewhat lower. Further, it should be noted that *S,S*-acetals of heptanal produce low yields of heptanal, besides a number of by-products when treated according to both methods.

The advantages of using sodium nitrite in 4*M*-HCl or *t*-butyl hypochlorite in anhydrous CCl_4 for the deprotection of the *S,S*-acetals are the mild reaction conditions and the simplicity of work-up together with the ready availability and cheapness of the compounds.

Comparing the transformation of *O,O*-acetals and *S,S*-acetals into their corresponding carbonyl compounds, it should be noted, that the choice of reagents is crucial. Hydrolysis of *O,O*-acetals and orthoesters is carried out by

Table. Reaction of *S,S*-acetals with NaNO_2 in 4*M*-HCl (Method A) or Bu^tOCl in anhydrous CCl_4 (Method B)

Compd.	Method A		Method B	
	Reaction time (h)	%	Reaction time (h)	%
(1)	1	7	1	88
(2)	1	94	1	100
(3)	4	43	20	24
(4)	20	42	20	55
(5)	0.25	88	1.50	65
(6)	1	67	2	94
(7)	5	100	0.25	90
(8)	1	100	1	80
(9)	1	100	1	83
(10)	1	70*	†	
(11)	6	48	24	51

* Together with some unidentified products. † Complicated mixture of by-products (seems to contain carbonyl compound).

mineral acids (H^+), whereas *S,S*-acetals are transformed into the corresponding carbonyl compounds by transition-metal ions (Ti^{4+} , Cu^{2+} , Ag^+ , Cd^{2+} , Hg^{2+}), oxidation of sulphur, or *S*-alkylation. These differences can be accounted for by MO theory and the theory of Hard and Soft Acids and Bases (HSAB).

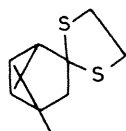
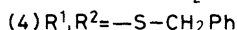
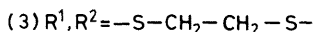
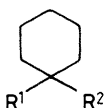
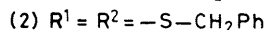
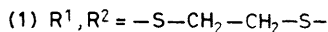
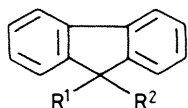
Hard acids (electrophiles) are generally positively charged and have a relatively high LUMO energy (*e.g.* cations of the more positive elements of the Periodical Table: H^+ , Li^+ , Na^+ , K^+) whereas soft acids (electrophiles) have low energy and do not necessarily have a positive charge. Hard nucleophiles (bases) are generally negatively charged and have a relatively low HOMO energy [anions centred on the electronegative elements (*e.g.* OH^-)] and soft nucleophiles have a relatively high HOMO energy and do not necessarily have a negative charge (*e.g.* thiocyanates).

O,O-Acetals are hard, and are hydrolysed by the hard H^+ ,⁵ due to the favourable hard-hard interaction, which gives a significant contribution to the Coulomb term in the Klopman equation⁶ [equation (1)]

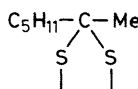
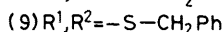
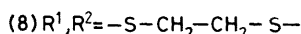
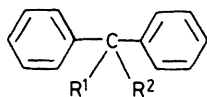
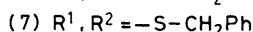
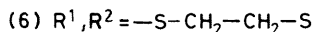
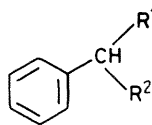
$$\Delta E = \frac{q_{\text{nuc1}} \cdot q_{\text{elec}}}{\epsilon} \Gamma + \frac{2(c_{\text{nuc1}} \cdot c_{\text{elec}} \beta)^2}{E_{\text{HOMO}} - E_{\text{LUMO}}} \quad (1)$$

S,S-Acetals are soft, and are transformed into the corresponding carbonyl synthons by soft acids, and the orbital term in equation (1) is most important. Orbital-controlled reactions are soft-soft interactions and are exothermic; some of the reactions studied in this investigation are, in fact, exothermic.

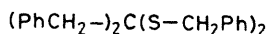
The electrophiles used here for the *S,S*-acetal \rightarrow carbonyl



(5)

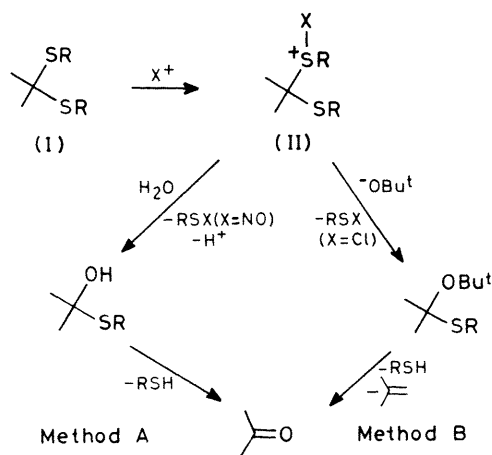


(10)



(11)

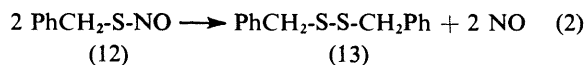
transformation are NO^+ (H_2ONO^+ and $CINO^+$ of which the last one is assumed to be present when HCl is used as acid) or Cl^+ . Both NO^+ (borderline) and Cl^+ are soft.² The first step in the reaction is the attack of X^+ ($X = NO$ or Cl) at the soft sulphur of the *S,S*-acetal (I) giving (II):



Scheme 2.

By Method A RSNO is substituted by water, and subsequent decomposition produces the carbonyl compound and the thiol. Similarly, *t*-butoxide and (II) give the sulphenyl chloride and an *O,S*-acetal, of which the last one decomposes to give

isobutylene, the thiol, and the corresponding carbonyl compound. *S*-Benzyl thionitrite⁷ (12) has been isolated in low yield and was characterized on the basis of i.r.⁷ and mass spectral evidence [see equation (2)]. Compound (12) is also



known to form dibenzyl disulphide (13) and nitrogen oxide,⁷ which accounted for the isolation of (13) from all the reactions with *S,S*-dibenzyl acetals. It is also envisaged, that the soft sulphenyl chloride (RSCl), formed by Method B can also attack the soft sulphur of (I) or (II) to give (13).

It is well known from nitrosation reactions that anions such as Cl^- and SCN^- increase the reaction rate and yields.⁸ Preliminary investigations seem to indicate that when Method A is used for the transformation of (1) and (3) into the corresponding carbonyl compounds by the presence of SCN^- in the reaction mixture, the yields of the carbonyl compounds increase by 14 and 63%, respectively (the same reaction time). Further work is in progress to elucidate the effect.

Experimental

¹H N.m.r. spectra were recorded at 60 MHz on a Varian EM 360 spectrometer, SiMe₄ being used as an internal standard. I.r. spectra were recorded on a Beckman IR 18 spectrometer. Mass spectra were recorded on a Micromass 7070F spectrometer operating at 70 eV using a direct inlet. Microanalyses were carried out by Løvens Kemiske Fabrik, DK-2750 Ballerup (Microanalytical Lab.). The starting compounds were prepared according to known methods.⁴

General Procedure.—Sodium nitrite in aqueous acid solution.

Method A. The *S,S*-acetal (5 mmol) was mixed with 4M-HCl (15–20 ml) (CH_2Cl_2 was also used if the *S,S*-acetal was insoluble in the acidic medium) and NaNO₂ (15 mmol) in water (5–10 ml) was added dropwise with vigorous stirring at room temperature; the reaction times are given in Table 1. The reaction mixture was extracted with CH_2Cl_2 and the combined organic layers were washed with water and dried (MgSO₄). The organic phase was evaporated and then subjected to column chromatography on silica gel with CH_2Cl_2 as eluant. The products were identical (¹H n.m.r., i.r. and mass spectra and m.p.) with authentic samples of the carbonyl compounds.

t-Butyl hypochlorite in anhydrous CCl₄. *Method B.* The *S,S*-acetal (5 mmol) was mixed with anhydrous CCl₄ (15–20 ml) and Bu^oOCl (10 mmol) in anhydrous CCl₄ (5 ml) was added dropwise with vigorous stirring at room temperature; the reaction mixture was worked up as above.

Acknowledgements

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