

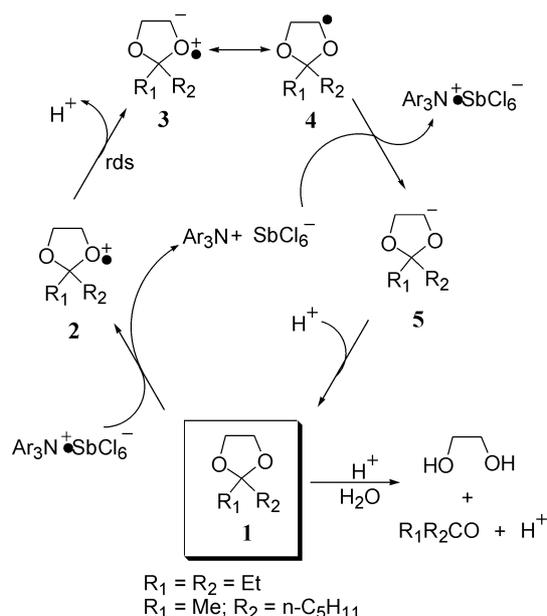
A Mechanistic Reinvestigation of *tris*-(*p*-Bromophenyl)aminium Hexachloroantimonate Induced Deketalization

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Received July 8, 2003

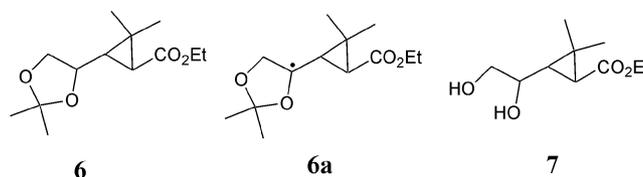
Key Words : Deketalization, *tris*-(*p*-Bromophenyl)aminium hexachloroantimonate, Mechanism

In 1986 Kim *et al.* reported¹ an interesting property of the title compound in its ability to deprotect in sub-stoichiometric amounts, functionalities such as acetals, ketals, silylethers, tritylether and tetrahydropyranyl ether in moist acetonitrile (% H₂O not reported). They proposed that the hydrolysis of 1,3-dioxalanes such as **1** involved a SET mechanism² (Scheme 1). Thus, treatment of **1** with *tris*-(*p*-bromophenyl)aminium hexachloroantimonate (Ar₃N⁺SbCl₆⁻) was assumed to generate **2** which on H⁺ loss originated the radical **3** ↔ **4**. At this stage two concurrent reactions are envisaged to occur. In the first, a part of H⁺ formed is utilised catalytically, in conjunction with the water contained in the solvent, to regenerate the ketone, and in the second, the other part of H⁺ protonates the carbanion **5** formed by the reduction of **4** by the tertiary amine (Ar₃N → Ar₃N⁺SbCl₆⁻) thus rendering the overall reaction catalytic for both the aminium salt and acid. Presumably, the purported failure of Et₄N⁺SbCl₆⁻ to bring about the ketal hydrolysis under similar conditions, led the authors to suppose that the first step was oxidative in nature.



Scheme 1. Mechanism proposed by Kim *et al.*

In connection with other studies currently in progress in our laboratory it became necessary to confirm the validity of this assumption. Therefore the cyclopropyl ketal **6**,³ with a built-in bias to undergo ring-opening in the event of the formation of a radical **6a**, akin to **4**, was selected for our study.



Exposure of **6** to Ar₃N⁺SbCl₆⁻, under standard conditions,⁴ furnished the diol-ester **7** in good yield, with the cyclopropane group remaining intact (Table; entry 1a). The regeneration of **9** from ketal-acrylate **8**³ (entry 2a) also proceeded in an analogous manner in near quantitative yield. While largely confirming the other results of Kim we, however, found that Et₄N⁺SbCl₆⁻ did indeed regenerate the diols **7** and **9** from **6** and **8** respectively, in excellent yields (entries 1b and 2b). These results therefore prompted us to consider the possibility that the process could be simply due to the dissociation of the SbCl₆⁻ anion in water, by which the acid required for the hydrolysis is formed. In fact Neumann⁵ had provided evidence for the existence of the following equilibrium:

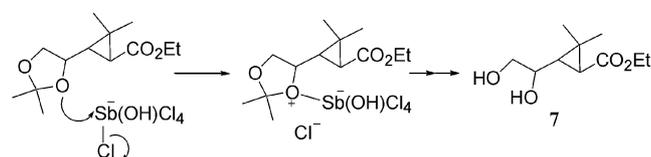


Germane in this context is the observation that the ¹H-NMR signal due to the H₂O present in commercial CD₃CN (0.3% water),⁶ at δ 2.15, underwent a small but significant shift on addition of Et₄N⁺SbCl₆⁻ and (*p*-BrC₆H₄)₃N⁺SbCl₆⁻ (at 6 × 10⁻³ M each) to δ 2.23 and 2.76 respectively. We attribute⁷ this shift to the existence of species, such as D₂HO⁺, DH₂O⁺ and/or H₃O⁺. Similar δ values of 2.24 and 2.72 were observed for solutions of HCl in moist acetonitrile at concentrations of 6.8 × 10⁻⁴ M and 4.8 × 10⁻³ M respectively. Our results gathered in the Table show that deketalisation reactions, can also be brought about solely by mineral acids, but at *vastly different rates*, at H⁺ concentrations that elicited comparable δ values shifts. Interestingly a reversal of similar significant rate difference was noted for the desilylation of

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Table 1. Deketalisation and desilylation reactions with aminium and ammonium salts and mineral acids

Entry	Compound	Product	Reagent	Time (h)	Yield (%)
1a			$\text{Ar}_3\text{N}^+\text{SbCl}_6^-$	72	70
1b			$\text{Et}_4\text{N}^+\text{SbCl}_6^-$	96	87
1c			HCl	3	93
2a			$\text{Ar}_3\text{N}^+\text{SbCl}_6^-$	92	98
2b			$\text{Et}_4\text{N}^+\text{SbCl}_6^-$	96	79
2c			HCl	2	92
3a			$\text{Ar}_3\text{N}^+\text{SbCl}_6^-$	6	79
3b			$\text{Et}_4\text{N}^+\text{SbCl}_6^-$	7 days	NR ^d
3c			HCl	87	86

^dNR—no reaction.**Scheme 2.** Proposed mechanism for a Lewis acid induced deketalisation.silyl ether **10** with HCl to **11** (entry 3c versus 1c and 2c).

On these grounds we consider that the weight of evidence is in favour of an essentially Lewis acid catalysed mechanism that is probably assisted by the HCl present in the reaction mixture. The hydrolysis of other substances studied by Kim probably occurs via an analogous process (Scheme 2).

Acknowledgements. We thank Fundação para a Ciência e a Tecnologia (FC&T, Lisbon, Portugal) for partial financial support (Project POCTI/QUI/36456). One of us (P. M. C. G) is grateful for the award of a doctoral fellowship from FC&T.

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- Typical procedure for deketalisation of **6** and **8**: To a stirred solution of the ketal **6** (58 mg; 1 eq.; 0.06 M) in 4 mL of acetonitrile (0.1% water) was added the radical cation $\text{Ar}_3\text{N}^+\text{SbCl}_6^-$ (19.6 mg; 0.1 eq), under an atmosphere of nitrogen and at room temperature. On completion of the reaction (72 h; TLC control; AcOEt/Hex 4 : 1) the product was isolated by evaporation of the solvent, treating the resulting residue with aq. NaHCO_3 (1%) and extraction with CH_2Cl_2 . The diol **7** (33.9 mg; 70%) isolated by PTLC (AcOEt/Hex 4 : 1), was found to be identical ($^1\text{H-NMR}$; IR; tlc) with an authentic sample of ethyl 3-(1',2'-dihydroxyethyl)-2,2-dimethylcyclopropane carboxylate. The use of aminium salt as received or a sample crystallised [from CH_2Cl_2 /ether 1 : 3; mp 141 °C dec. (sealed capillary) (lit.⁸ 141-142 °C dec.)] did not alter either the time of reaction or the nature of the product.
- Deketalisations of ketals with $\text{Et}_4\text{N}^+\text{SbCl}_6^-$ ⁹ were performed following the procedure described above.
- (a) Neumann, H. M. *J. Am. Chem. Soc.* **1954**, *76*, 2611; (b) Neumann, H. M.; Ramette, R. W. *J. Am. Chem. Soc.* **1956**, *78*, 1848; (c) Willis, S. B.; Neumann, H. M. *J. Am. Chem. Soc.* **1969**, *91*, 2924.
- The percentage of water in CD_3CN was determined by $^1\text{H-NMR}$ by comparison of the integral values of aromatic protons corresponding to a known concentration of Ph_2O (3 mg) in CD_3CN (1 mL) and those due to the water present.
- Whilst a reading of 1.59 was obtained with a pH meter for a solution of $\text{Et}_4\text{N}^+\text{SbCl}_6^-$ (6×10^{-3} M) in MeCN containing 0.1% water, a value of 0.83 was registered for $\text{Ar}_3\text{N}^+\text{SbCl}_6^-$, for the same concentration and in the same solvent system. In connection with a query from a reviewer, a seven-fold increase in the concentration of the said ammonium salt, which gave a reading of 0.83 in the pH meter, did in fact generate, as expected, the phenol **11** from **10**.
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