Direct Observation of Bicyclic α-Alkoxyoxonium Ions; Reductive Cleavage to Medium-ring Diethers

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1-Oxonia-5-oxabicyclo[4.3.0]nonane and 1-oxonia-6-oxabicyclo[5.3.0]decane ions differ in the extent of charge delocalisation between the two oxygen atoms as shown by ^{1}H and ^{13}C n.m.r. spectroscopy in SO_2 solution; trapping with triethylsilane leads to medium-ring diethers.

We report the first direct observation in solution of α-alkoxyoxonium ions, (**1**); these species are important because of the involvement of analogues in the mechanisms of formation and hydrolysis of acetals.[1] The extent of charge delocalisation and concomitant structural changes, (**1a**) ⟷ (**1b**), is of considerable interest. The degree of delocalisation in related neutral species ROCHRX (the generalised anomeric effect)[2] has been studied thoroughly[3] and the importance of stereoelectronic effects on this delocalisation debated extensively.[4,5] In the case of (**1a**) ⟷ (**1b**), no charge separation is involved in the resonance, so the contribution of canonical form (**1b**) is expected to be greater. On the other hand, it might be thought that the reverse anomeric effect[6] could apply to these ions.

Reaction of 2-(3-azidopropyl)-1,3-dioxolane† (**2**) with nitrosonium tetrafluoroborate in sulphur dioxide solution produces a solution which gives a ^{13}C n.m.r. spectrum with lines at δ 121.7 (C-6), 80.9, and 79.9 (C-2 and C-9), 67.0 (C-4), and 28.5, 21.6, and 20.0 (C-3, C-7, and C-8) which may be assigned to the 1-oxonia-5-oxabicyclo[4.3.0]nonane ion, (**3**). Similar reaction of 2-(3-azidopropyl)-1,3-dioxepane† (**4**) leads to the 1-oxonia-6-oxabicyclo[5.3.0]decane ion, (**5**), with ^{13}C n.m.r. lines at δ 145.5 (C-7), 80.1, 79.5, and 79.2 (C-2, C-5, C-10), and 30.4, 29.9, 25.4, and 25.2 (C-3, C-4, C-8, and C-9). Additional proof that these species are responsible for the spectra observed comes from the hydride-trapping experiments described later. It is remarkable that the chemical shift of the methine carbon in (**5**) is 23.8 p.p.m. downfield of that in (**3**). We ascribe the difference to a larger contribution from canonical form (**1b**) to the structure of (**5**) compared to (**3**).‡

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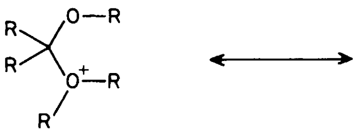
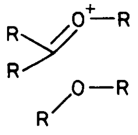
† Azides were prepared from the corresponding chlorides by heating with sodium azide for 2 h at 100 °C in DMF.

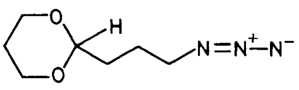
‡ The experimental evidence doe not exclude that both (**3**) and (**5**) are different equilibrium mixtures of discrete chemical structures corresponding to (**1a**) and (**1b**); we consider this possibility unlikely.



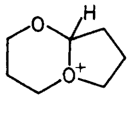
(1a)



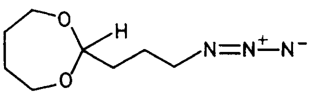
(1b)



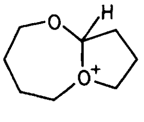
(2)



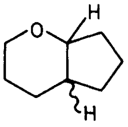
(3)



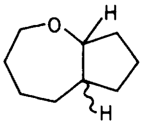
(4)



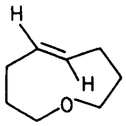
(5)



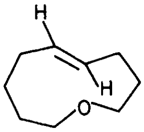
(6)



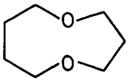
(7)



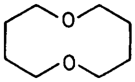
(8)



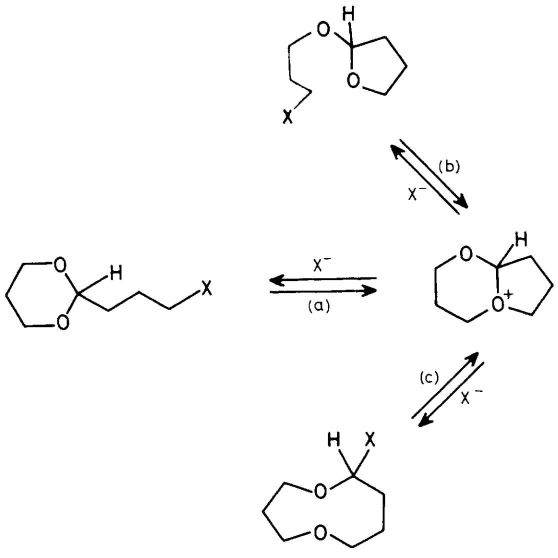
(9)



(10)



(11)



Scheme 1

The chemical shift of the methylene group next to the dico-ordinate oxygen atom also indicates that there is less positive charge on this oxygen atom in (**3**) than in (**5**). If the ions had structures which were entirely of the (**1b**) type, the chemical shift of the methine carbon would be expected to be about δ 250.[7] Estimation of the chemical shift to be expected from a non-delocalised (**1a**) structure is not easy. The chemical shifts of the methine carbon in the starting acetals (**2**) and (**4**) are δ 101.3 and 102.2 respectively, while triethyloxonium ion has a chemical shift which is about 20 p.p.m. downfield of that of diethyl ether.[8] Thus (**1a**) might have a chemical shift of about δ 120. Clearly these ions are more 'shut' than 'open' and this is in accord with calculations on the $HOCH(OH_2)^+$ ion.[9] In the ^1H n.m.r. spectra of (**3**) and (**5**), the methine hydrogen absorptions occur at δ 6.56 and 7.22 respectively; this is also in accord with a more 'open' structure for (**5**).

Why is (**5**) more 'open' than (**3**)? Kirby *et al.*[3] have correlated the extent of C–X bond breaking in a series of compounds ROCHRX with the electronegativity of X but this is not a variable here. Strain differences between the 'open' and 'shut' forms might be important in our case. We have tried to assess these by doing MM2[10] calculations on (**6**) and (**7**) as models for the closed forms of (**3**) and (**5**), and on (**8**) and (**9**) in conformations derived by least-motion ring-opening of the best conformations of (**6**) and (**7**) as models for the opened forms. The best conformation of (**6**) (both *cis* and *trans* ring junctions were considered; four conformations were calculated) is 26 kJ mol^{-1} less strained than (**8**) in the same conformation, but (**7**) (eighteen conformations calculated) is 19 kJ mol^{-1} more strained than (**9**). The preferred conformations of (**6**) and (**7**) lead to *trans*-isomers of (**8**) and (**9**) on ring opening, and it is the strain in the *trans*-alkene bond which is largely responsible for the differences between the two cases, with (**8**) having a calculated C–C=C–C torsion angle of 152° compared with 168° for (**9**). This suggests that unstrained α-alkoxyoxonium ions would resemble (**5**) rather than (**3**) in their properties.

The reaction of azides with nitrosonium salts to generate carbonium ions which we have used for generating (**3**) and (**5**) has been in the literature for some time[11] but has attracted little attention. In order to generate (**3**) and (**5**) it is imperative that their precursors are activated in a chemoselective way so that initial reaction occurs at the end-of-chain functionality and not directly at the acetal. Protic acids are clearly useless and many Lewis acids are likely to be little better; our first attempts to generate (**5**) used the reaction of 2-(3-chloropropyl)-1,3-dioxepane with silver tetrafluoroborate, but this gave, at best, only partial conversion to (**5**). We believe that the azide/nitrosonium ion reaction has wider application for the cycloalkylation of weakly nucleophilic centres.

In principle, ions such as (**3**) may be derived from three precursors, and give any of three products on trapping with nucleophiles, as shown in Scheme 1. We have attempted the generation of (**3**) by route (b) from 1-tetrahydrofuranyloxy-3-azidopropane, but without success. We have also tried without success to apply route (a) to generate analogous ions, for example from 2-(3-azidopropyl)-1,3-dioxane, 2-(4-azidobutyl)-1,3-dioxolane, and 4-azidobutanal dimethyl acetal. Thus even the azide/nitrosonium ion reaction has very limited scope for the preparation of these ions. Both the successful cases involve RO5 participation, which is known[12,13] to be the most favourable; the reaction of 2-(4-azidobutyl)-1,3-dioxane requires RO6 participation,[12] expected to be substantially less favourable. We do not understand the failure of 2-(3-azidopropyl)-1,3-dioxolane and 4-azidobutanal dimethyl acetal to yield observable α-alkoxyoxonium ions.

Finally, we have trapped ions (**3**) and (**5**) by reaction with triethylsilane[14] to give 1,5-dioxacyclononane (**10**) and 1,6-dioxacyclodecane[15] (**11**) in 40 and 51% yields respectively after distillation, thus providing simple syntheses of these interesting compounds. Clearly even (**3**) possesses enough electron deficiency at the CH group for attack of hydride to take place there rather than at the less sterically-hindered methylene groups. Synthesis was in fact the original motivation for this work; we had earlier[16,17] shown that the related hydridic cleavage of α-aminoammonium ions provides an extremely flexible route to medium-ring bicyclic diamines. Unfortunately, this method of making medium-ring diethers is at present very limited in scope, owing to the problems of ion generation.

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