Stable Oxonium Ions

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Taming the Highly Reactive Oxonium Ion**

*Michael M. Haley**

cage compounds · oxonium compounds · reactive species · ring strain · superacidic systems

On opening an introductory organic textbook the student reader sees that oxonium ions are invoked in numerous transformations—E1 reactions, S_N1 reactions, cleavage of ethers with strong acids, etc. In each of these instances, the positively charged trivalent oxygen ions are depicted as fleeting intermediates as part of the various reaction mechanisms. At a more advanced level, students learn that tertiary oxonium ions and their salts, while extremely reactive, are some of the most powerful and therefore useful electrophilic alkylating reagents in the laboratory setting. Commonly known as Meerwein salts,[1] salts of tertiary alkyl oxonium ions ($R_3O^+ X^-$) are stable, even isolable, so long as X^- is an inert, non-nucleophilic counterion such as BF_4^- or PF_6^-.[2] Not surprisingly, these salts are extremely reactive towards water and alcohols; thus, great care must be taken to exclude adventitious nucleophiles in solvents and reagents when tertiary oxonium ions are used.

Imagine then, my surprise and that of my students upon reading the recent communication by Mascal and co-workers disclosing the preparation of "extraordinary" oxonium ions (Figure 1), namely tricyclic oxatriquinane **1**, oxatriquinene **2**, and oxatriquinacene **3**.[3,4] New oxonium ions are reported on a somewhat regular basis, though admittedly half-cage compounds such as **1**–**3**, as well as cage compounds like oxaadamantane **4** recently reported by Olah et al.,[5] are quite rare. In fact, the only previously well-characterized bicyclic or tricyclic oxonium ion is **5**, described by Klages and Jung in 1965.[6] I initially approached the Mascal publication somewhat skeptically and kept thinking, "What makes cations **1**–**3** so extraordinary?" Call me a skeptic no more.

A comparison of the synthesis and reactivity of **1** versus **4** readily illustrates the differences between an ordinary oxonium ion (**4**) and an extraordinary one (**1**). The synthesis of cation **4** (Scheme 1), which started from known alcohol **6**,[7] could be accomplished either 1) by the ionization of haloethers **7** and **8** using HF/SbF_5 in SO_2ClF and $AgBF_4$ in SO_2, respectively, or 2) by the ionization of alcohol **6** under strongly acidic conditions ($CF_3SO_2H/(CF_3SO_2)_2O$). Oxonium ion **4** is stable in solution and the solid state "as long as moisture and other nucleophiles are excluded". X-ray-quality single crystals of **4** could be grown using the poorly nucleophilic carborane cluster $CB_{11}H_6Cl_6^-$ as the counterion.

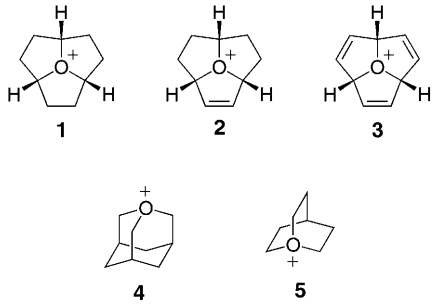
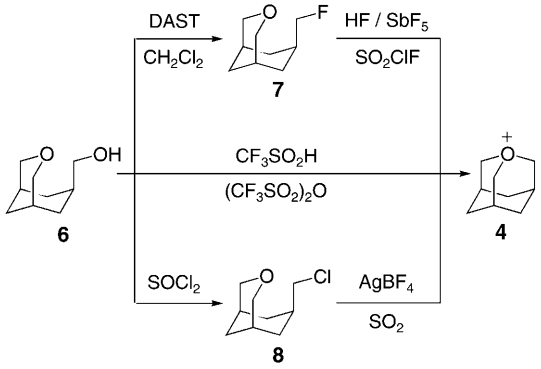


Figure 1. Bicyclic and tricyclic oxonium ions **1**–**5**.



Scheme 1. Synthesis of oxaadamantane **4** reported by Olah et al. DAST = (diethylamino)sulfur trifluoride.

The facile preparation of **1** is shown in Scheme 2. Starting from the known epoxide **9**,[8] reduction with $LiAlH_4$ in the presence of $ZnCl_2$ afforded dienol **10**. Iodoetherification with elemental iodine gave bicyclic ether **11**, which was subsequently dehalogenated using Raney nickel to yield **12**. Completion of the tricyclic skeleton was accomplished by treatment of **12** with HBr, furnishing **1** as its bromide salt in high yield. This last reaction already hints at the unusual behavior of **1**, as a typical trialkyloxonium ion would revert quickly back to the corresponding dialkyl ether and alkyl bromide.

X-ray-quality crystals of $\mathbf{1}^+Br^-$ could not be obtained, but anion exchange afforded suitable crystals of both the PF_6^- and SbF_6^- salts. While this transformation may seem routine at first, the fact that the exchange reaction was performed in a biphasic system using *aqueous* solutions of the salts yet *no*

[*] Prof. Dr. M. M. Haley
Department of Chemistry and the Material Science Institute
1253 University of Oregon, Eugene, OR 97403-1253 (USA)
Fax: (+1) 541-346-0487
E-mail: haley@uoregon.edu
Homepage: darkwing.uoregon.edu/~chem/haley.html

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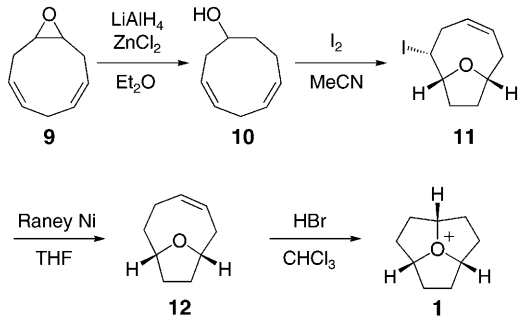


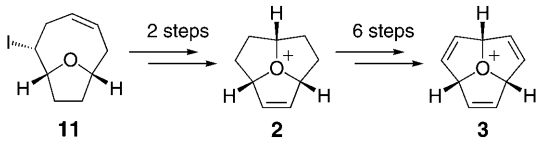
Scheme 2. Synthesis of oxatriquinane **1** reported by Mascal and co-workers.

decomposition was observed is a truly remarkable result. The authors demonstrated the high stability of **1** towards water by: 1) obtaining an NMR spectrum in D_2O, 2) recrystallizing it from water, 3) refluxing the SbF_6^- salt in water for 72 hours, and 4) chromatographing both salts on silica gel. Whereas a typical trialkyloxonium ion would have been instantly hydrolyzed under any of these conditions, **1** remained intact. Treatment with other weak nucleophiles such as alkanols, alkanethiols, and iodide ion also left **1** unchanged. This is, however, not to say that **1** is completely inert. S_N2-type nucleophiles such as OH^-, CN^- and N_3^- were all readily alkylated by **1**.

Iodoether **11** was the starting point for the synthesis of oxatriquinene **2** and subsequently oxatriquinacene **3** (Scheme 3). In both cases, a stronger acid possessing a weakly nucleophilic anion, namely CF_3SO_2H, was required for oxonium ion formation. As allylic congeners of **1**, these compounds might be expected to be more reactive toward nucleophiles, and this proved to be the case. Whereas cation **3** underwent facile ring-opening back to the immediate trienol precursor in the presence of water, its NMR spectrum could be obtained in CD_3CN; a typical Meerwein salt would have alkylated this solvent to generate a nitrilium ion. Not surprisingly, cation **2** exhibits reactivity intermediate between that of **1** and **3**.[9]

Examination of the NMR data shows the typical downfield shifts of protons and carbons immediately adjacent to the cationic oxygen center. For example, the methine protons of **1** show up at $\delta = 5.4$ ppm, whereas the α-methylene protons of **4** resonate at $\delta = 5.3$ ppm, which is comparable. The methine protons of **3** appear at $\delta = 6.8$ ppm, but the extra ca. 1.5 ppm downfield shift can be attributed to the doubly allylic nature of the position. The ^{13}C NMR shifts also do not exhibit major variances between **1**–**3** and **4**.

The X-ray structural data of **1** and **4** do reveal some differences between the two systems, and in comparison with other simple oxonium ions. For example, crystal data for $Me_3O^+AsF_6^-$ show C–O bond lengths of 1.47 Å and C-O-C bond angles of 113.1°.[10] For cation **4** the bonds are longer (1.51 Å) and bond angles more acute (average 110.5°). These differences are even more pronounced for **1** (1.54 Å and 109.8°, respectively). On a purely structural argument, one would predict that, with longer bonds and more acute angles, **4** should be more reactive, which is clearly not the case.



Scheme 3. Synthetic route to oxatriquinene **2** and oxatriquinacene **3**.

To what then do cations **1**–**3** owe their remarkable lack of reactivity? The most plausible explanation is also one of the simplest—ring strain. Nucleophilic attack on **1**–**3** opens the tricyclic core to afford a bicyclo[5.2.1]decane skeleton, which incorporates a higher-energy eight-membered ring. In contrast, nucleophilic attack on **4** generates a much more favorable bicyclo[3.3.1]nonane system, complete with two six-membered rings. This same argument may also explain why it is easier to collapse the bicyclo[5.2.1]decane skeleton of **12** with HBr to generate **1**, whereas closure of the bicyclo[3.3.1]nonane system of **6** to prepare **4** requires more stringent conditions such as $CF_3SO_2H/(CF_3SO_2)_2O$. Although not intentionally designed to do so, the incorporation of the trivalent oxygen atom as a structural element within the tricyclic core of **1**–**3** is what imparts the unprecedented kinetic stability for these trialkyloxonium ions.

Whereas oxonium ions are components of *basic* organic chemistry, to discover a new subset of these that show the unique properties reported in the Mascal paper is an impressive accomplishment. So how to top this feat? The authors rightly point out that the remaining lone pair of electrons on cation **1** is available for further reaction. Might it be possible to protonate or alkylate oxoniums of this type to generate detectable, even isolable, expanded-valence-shell species such as R_3OH^{2+} or R_4O^{2+}? The thought of possibly creating "stable" hypervalent species such as these, which have long been implicated as intermediates in numerous studies by Olah and his group,[11] is very intriguing. I for one look forward to seeing future reports on this fascinating subject.

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