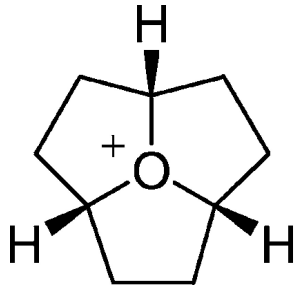
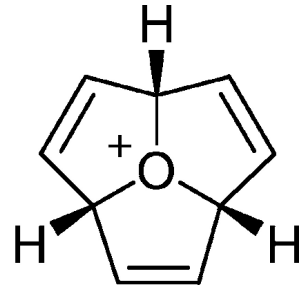
Communication

Oxatriquinane and Oxatriquinacene: Extraordinary Oxonium Ions

Mark Mascal, Nema Hafezi, Nabin K. Meher, and James C. Fettinger

J. Am. Chem. Soc., **2008**, 130 (41), 13532-13533 • DOI: 10.1021/ja805686u • Publication Date (Web): 18 September 2008





More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 1 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

View the Full Text HTML

J|A|C|S
COMMUNICATIONS

Published on Web 09/18/2008

Oxatriquinane and Oxatriquinacene: Extraordinary Oxonium Ions

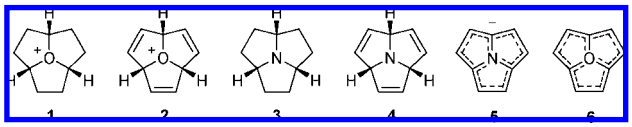
Mark Mascal,* Nema Hafezi, Nabin K. Meher, and James C. Fettinger

Department of Chemistry, University of California Davis, 1 Shields Avenue, Davis, California 95616

Received July 30, 2008; E-mail: mascal@chem.ucdavis.edu

The term "oxonium ion" is freighted with significance and evokes images of fleeting intermediates or highly reactive chemical reagents. Indeed, in terms of isolable oxonium species, trialkyloxonium salts with inert counterions (such as BF_4^- or PF_6^-) are the most powerful alkylating agents one is likely to encounter in the laboratory. In general, they are prepared either by the reaction of an epoxide with an ether in the presence of a Lewis acid,[1] from orthoformates and ethers via dialkoxy-carbenium salts,[2] by the reaction of diazoalkanes with ethers in the presence of an acid with a non-nucleophilic counterion,[3] or by simple alkylation of ethers with alkyl halides in the presence of Lewis acids or silver salts.[4] Herein, we report the synthesis of oxatriquinane (**1**) and oxatriquinacene (**2**), the rigid, tricyclic frameworks of which impart to them properties unheard of in alkyl oxonium ion chemistry.

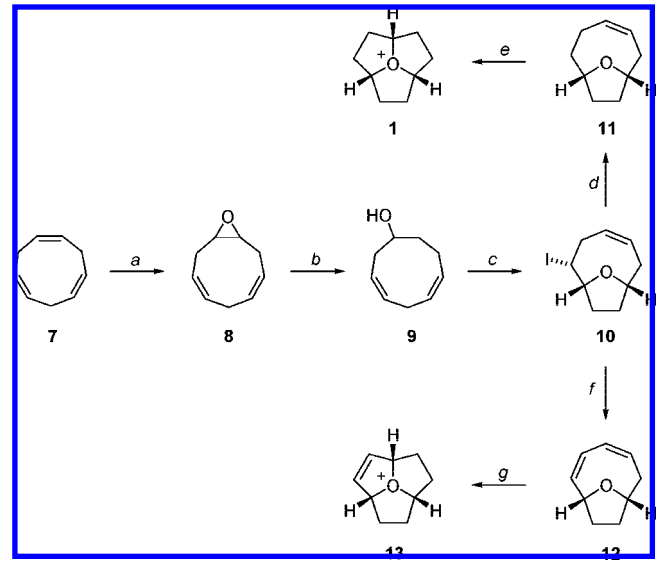
Our interest in this area proceeds from our work with the analogous azatriquinane and azatriquinacene tricycles **3** and **4**. The successful oxidation of **4** to the stable, bowl-shaped aromatic azaacepentalenide **5** led us to consider whether a neutral O-analogue of **5**, that is, **6**, could be produced. Theoretical modeling of **6** has suggested its aromaticity would surpass even that of **5**, which itself was predicted by NICS calculations[5] to be at least as aromatic as benzene.



The synthesis of **1** was accomplished as shown in Scheme 1. Thus, cyclononatriene (**7**) is treated with *m*-cpba to give the known monoepoxide **8** in high yield.[6] Reduction of **8** with $LiAlH_4$ in the presence of $ZnCl_2$ provided dienol **9**, which underwent facile iodoetherification to **10**. Reduction of the iodine in **10** without cleavage of the THF ring proved difficult but was eventually achieved in modest yield with Raney nickel. Remarkably, final ring closure to the tricycle **1** was most conveniently accomplished by treatment of **11** with hydrogen bromide, providing the Br^- salt of **1** in 94% yield. Ample evidence that the desired transformation had taken place was seen in the ^1H NMR spectrum of **1**, which was greatly simplified relative to **11** and showed a ca. 1 ppm downfield shift of the protons α to oxygen. Despite efforts, **1** Br^- could not be induced to crystallize, so we prepared the corresponding hexafluorophosphate and hexafluoroantimonate salts of **1** by simple ion exchange, both of which were white, high-melting crystalline solids.

It was at this point that we recognized that **1** possessed unusual stability for an alkyl oxonium ion. First, it appeared that the aforementioned anion exchanges could be done in a biphasic system using aqueous solutions of the salts without decomposition of the oxonium products. In fact, it turned out that an NMR spectrum of **1** could be recorded in D_2O and that it could even be recrystallized from water. Pushing this issue to the extreme, an aqueous solution

Scheme 1[a]



[a] Reagents and conditions: (a) *m*-cpba, CH_2Cl_2, 0 °C, 12 h, 85%; (b) $LiAlH_4$, $ZnCl_2$, ether, 2 h, 98%; (c) I_2, MeCN, 15 min, 80%; (d) Ra−Ni, THF, 20 min, 54%; (e) HBr, $CHCl_3$, 94%; (f) DBU, benzene, reflux, 12 h, 49% (from **9**); (g) TfOH, MeCN, 100%.

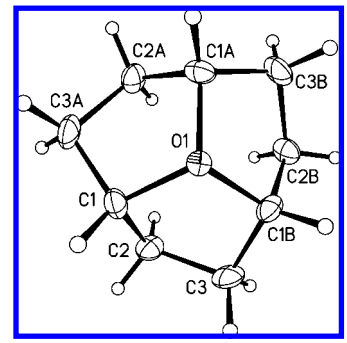


Figure 1. X-ray crystal structure of cation of **1** SbF_6^- showing thermal ellipsoids at the 50% probability level. The counterion and a minor disorder component are omitted for clarity.

of the SbF_6^- salt was heated at reflux in water and showed no evidence of decomposition after 72 h. Finally, it emerged that the PF_6^- and SbF_6^- salts of **1** could even be column chromatographed on silica gel.

X-ray quality crystals of **1** SbF_6^- were grown from CH_2Cl_2, and the crystal structure was determined (Figure 1). The structure distinguishes itself from those of other alkyl oxonium species in the Cambridge Structural Database both in its longer C−O bond distances (1.54 Å) and more acute C−O−C bond angles (109.8°). The most accurate published crystal structure of an alkyl oxonium salt is that of Me_3O^+ AsF_6^-, which has C−O bond lengths and

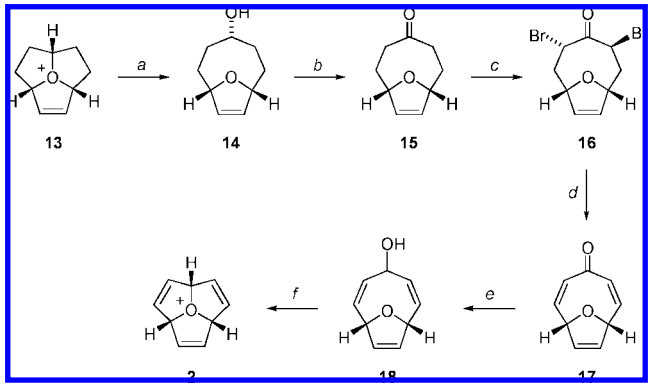
10.1021/ja805686u CCC: $40.75

C−O−C bond angles of 1.47 Å and 113.1°, respectively.[7] The acute bond angles in **1** are the result of the puckering that accompanies the trefoil fusion of three five-membered rings. The reason for the lengthening of the C−O bonds is less clear, although it is interesting to note that gas phase modeling of this cation at the B3LYP/6-31+(g,d) level of theory results in virtually identical bond lengths.[8]

Examining the reactivity of **1** against weak nucleophiles other than water showed that it was also inert at room temperature toward alkyl alcohols, alkyl thiols, and iodide ion. The sterically hindered base *N*,*N*-diisopropylethylamine also gave no evidence of reaction with **1**. However, S_N2-type nucleophiles such as CN^-, OH^-, and N_3^- were quickly alkylated by **1**, and it was a reaction of this type between hydroxide and the monounsaturated tricycle **13** that eventually led to the synthesis of oxatriquinacene **2**.

Triquinacenes of the kind described above are tricyclic, bowl-shaped trienes, the parent hydrocarbon analogue of which was first synthesized by Woodward in the 1960s in order to probe the concept of neutral homoaromaticity and as a potential precursor to dodecahedrane.[9] We were presented with an opportunity to prepare the oxygen analogue **2** when it was observed that the hydrolysis of oxatriquinene **13** proceeded not as expected, that is, at one of the allylic positions, but mainly by attack at the methine carbon opposite the C=C bond. As shown in Scheme 1, **13** could be obtained by branching off the synthesis of **1** via elimination product **12**. The hydrolysis product **14** was oxidized to the ketone **15** (Scheme 2), which could be brominated in the positions α to the carbonyl group in modest but workable yield by simple reaction with Br_2. Elimination to **17**[10] followed by Luche reduction gave dienol **18**, which closed down to the oxatriquinacene cation **2** on treatment with triflic acid.

Scheme 2[a]



[a] Reagents and conditions: (a) aq $NaHCO_3$, CH_2Cl_2, 64%; (b) CrO_3, pyridine, CH_2Cl_2, 30 min, 88%; (c) Br_2, $CHCl_3$, 0 °C→room temp, 4 h, 34%; (d) DBU, PhMe, 100 °C, 6 h, 65%; (e) $NaBH_4$, $CeCl_3$, MeOH, 3 h, 88%; (f) TfOH, MeCN, 87%.

Oxatriquinacene is formally a triply bis-allylic oxonium ion. Apart from **2** and **13**, no other stable allyl oxonium ions have been reported to our knowledge. Cation **2** is more reactive than **1**, and is rapidly opened back to **18** in water, although its NMR spectrum could be recorded in d_3-acetonitrile, which would be alkylated to the nitrilium salt by typical oxonium reagents. The protons in the α positions of **2** show evidence of their extreme environment, appearing at 6.80 ppm, which is downfield even of the olefinic hydrogens. Attempts to crystallize **2** TfO^- for the purposes of X-ray diffraction have thus far proved unsuccessful.

In conclusion, we describe in this preliminary communication the synthesis and some of the properties of novel cations **1**, **2**, and **13**, which among them represent a number of firsts in the area of alkyl oxonium chemistry: the first bromide salt, the first NMR spectrum recorded in D_2O, the first to be crystallized from water and to even survive reflux in water, the first to be chromatographed, and the first stable allylic representatives (**2** and **13**). Furthermore, the crystal structure of **1** reveals the longest C−O bond distances and most acute mean C−O−C bond angles of any published alkyl oxonium structure. The extraordinary stability of **1** in the face of conditions that would quickly degrade Meerwein-type salts can be rationalized both in its tricyclic construction and in the angle strain which accompanies the formation of medium rings (eight-membered in the case of nucleophilic attack on **1**).

Our intention at this point is to study in greater detail the properties and chemistry of **1** and **2**, with a particular eye to the oxidation of the latter to the aromatic oxaacepentalene **6**. We also note in passing that the structural correspondence between **1** and azatriquinane **3** may be significant in the sense that **3** has been described as the most basic, simple trialkyl amine known, the conjugate acid of which has a pK_a value ca. 0.5 pK_a units greater than that of quinuclidine.[11] This can be attributed in part to the acute pyramidalization of the apical nitrogen but also to the fact that the nitrogen cannot invert. The "availability" of the lone pair in **1** leads to the intriguing question of whether a persistent, valence shell expanded R_3OH^{2+} or R_4O^{2+} species could be observed, such as have long been implicated as intermediates in work by Olah and co-workers.[12] We will visit this possibility both in theory and experiment in a future report.

Acknowledgment. This work was financially supported by National Science Foundation grant CHE 0448976.

Supporting Information Available: Complete ref 8; ^1H and ^{13}C NMR spectra and experimental details for the preparation of compounds **1**, **2**, and **8**−**18**; crystal structure determination and refinement for **1** SbF_6^-. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Meerwein, H. *Org. Synth.* **1966**, *46*, 113. (b) Curphey, T. J. *Org. Synth.* **1971**, *51*, 142.
(2) Olah, G. A.; Olah, J. A.; Svoboda, J. J. *Synthesis* **1973**, 490.
(3) Helmkamp, G. K.; Pettitt, D. *J Org. Synth.* **1966**, *46*, 122.
(4) Meerwein, H.; Wunderlich, K. *Angew. Chem.* **1957**, *69*, 481.
(5) The calculated NICS(1) values are **5**, −9.64; **6**, −11.73; benzene, −10.22 ppm. Since **5** and **6** are nonplanar, the NICS(1) shifts are artificially high. Planarization of **5** and **6** gives values of −11.45 and −14.09 ppm, respectively, and the actual shifts probably lie between the planar and nonplanar values. See: Mascal, M. *J. Org. Chem.* **2007**, *72*, 4323.
(6) Thies, R. W.; Gasic, M.; Whalen, D.; Grutzner, J. B.; Sakai, M.; Johnson, B.; Winstein, S. *J. Am. Chem. Soc.* **1972**, *94*, 2262.
(7) Lork, E.; Gortler, B.; Knapp, C.; Mews, R. *Solid State Sci.* **2002**, *4*, 1403.
(8) Calculation performed using the Gaussian 03 program with default optimization parameters: Frisch, M. J.; et al. *Gaussian 03*, revision D.01; Gaussian, Inc.: Wallingford CT, 2004.
(9) Woodward, R. B.; Fukanaga, T.; Kelly, R. C. *J. Am. Chem. Soc.* **1964**, *86*, 3162.
(10) Compound **17** bears a close resemblance to a molecule synthesized over a decade ago by Prinzbach and co-workers. (Person, G.; Keller, M.; Prinzbach, H. *Liebigs Ann.* **1996**, 507. See also: Pleschke, A.; Geier, J.; Keller, M.; Wörth, J.; Knothe, L.; Prinzbach, H. *Eur. J. Org. Chem.* **2007**, 4867.) The only difference is a hydroxyl group α to the THF oxygen. This hemiacetal showed apparent C_s symmetry on the NMR time scale and thus could be considered a time-averaged oxatriquinacenium species. The synthesis of oxatriquinanes from this or related precursors in these papers does not appear to have been further investigated.
(11) Hext, N. M.; Hansen, J.; Blake, A. J.; Hibbs, D. E.; Hursthouse, M. B.; Shishkin, O. V.; Mascal, M. *J. Org. Chem.* **1998**, *63*, 6016.
(12) Olah, G. A.; Prakash, G. K. S.; Barzaghi, M.; Lammertsma, K.; Schleyer, P. v. R.; Pople, J. A. *J. Am. Chem. Soc.* **1986**, *108*, 1032.

JA805686U