DOI: 10.1002/ejoc.200800530

1-Oxoniaadamantane

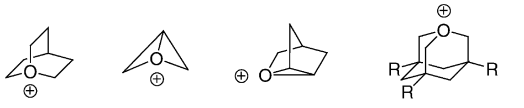
Markus Etzkorn,[a][‡] Robert Aniszfeld,[a] Tiejun Li,[a] Herwig Buchholz,[a] Golam Rasul,[a] G. K. Surya Prakash,*[a] and George A. Olah*[a]

Keywords: Tertiary cage oxonium ions / 1-Oxoniaadamantane / Bridgehead oxonium ions / Heteroadamantanes

The missing member of the heteroadamantane series, 1-oxoniaadamantane (**4a**), was prepared by the ionization of suitable bicyclic precursors under strongly acidic conditions. The ion **4a** was characterized by ^1H and ^{13}C NMR spectroscopy. The X-ray crystal structure of ion **4a** was also obtained with a $CB_{11}H_6Cl_6$ counter anion. DFT calculations were performed on 1-elementaadamantane cations for comparison.

Introduction

A broad variety of oxonium ions has been studied, and in particular tertiary alkyl oxonium ions are readily isolated as stable salts known as Meerwein salts, $R_3O^+BF_4^-$ (Scheme 1). Meerwein salts and related oxonium ions are of preparative interest as convenient and powerful electrophilic alkylating reagents.[1] In contrast, tertiary cage oxonium ions are rare and besides the characterized 1-oxoniabicyclo[2.2.2]octane **1**,[2] there is only indirect evidence for the involvement of 1-oxabicyclobutonium ion **2**[3] and the tricyclic ion **3**.[4] We were for long interested in the synthesis of 1-oxoniaadamantane **4a**, one of the two missing members in the series of second (B, N, C, O) and third row (Al, P, Si, S) 1-heteroadamantanes, respectively.[5] Earlier synthetic approaches toward the title compound by Klages et al., who prepared the analogous 1-thioniaadamantane, remained unsuccessful.[5f]



Scheme 1. Structures of cage oxonium ions and target **4**.

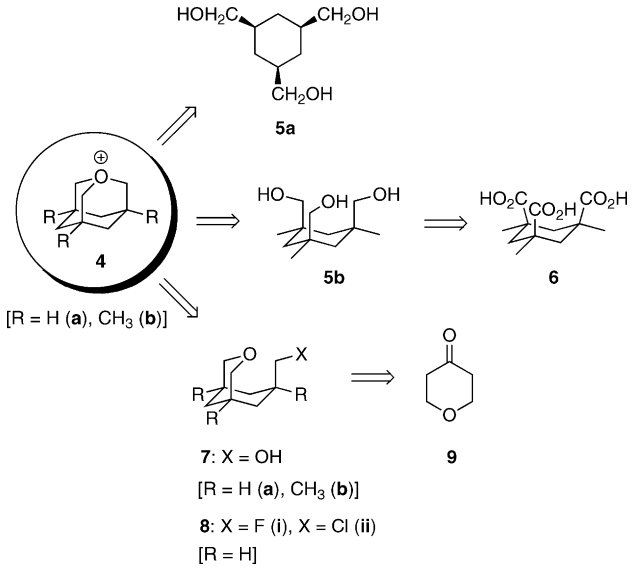
We now wish to report our results en route to 1-oxoniaadamantane **4**. We have synthesized various suitable precursors and used them to generate ion **4**. We have unequivocally characterized the target ion by spectroscopic and X-ray crystallographic evidence as well as computational studies.

Results and Discussion

The retrosynthesis of **4** or that of the trimethyl derivative thereof is shown in Scheme 2. A trisubstituted cyclohexane with its strategic functional groups all in axial positions leads back to Kemp's triacid **6**, either via the 1,3,5-trimethyl-1,3,5-tris(hydroxymethyl)cyclohexane (**5b**) or through some other intermediate.[6] The methyl substituents could eventually favor cage cyclization, although the hydroxymethyl groups in **5b** were shown to be equatorial in the solid state (X-ray crystallographic structural studies).[7] Alternatively, the bicyclic functionalized ether precursor **7a** with two axial "substituents" demands only one final cage formation step, but it has to be synthesized from tetrahydropyran-4-one (**9**) in a rather lengthy and tedious procedure.[8] The easily accessible *cis*,*cis*-tris(hydroxymethyl)cyclohexane (**5a**) is conformationally a rather poor precursor due to three equatorial substitutents.[9] The latter have to be reversed into the axial position by energetically unfavorable chair-chair inversion of the cyclohexane core to achieve cage formation, once again through a bicyclic ether intermediate.

We have synthesized the two triols **5a** and **5b** by following literature methods[9] and investigated the reduction of Kemp's triacid **6** with BH_3 reagents. The latter approach resulted in complex product mixtures and was not reproducible in a satisfactory manner. Since the equal functionalization of three identical substituents with three possible redox states and complex intramolecular reactivity of par-

[a] Loker Hydrocarbon Research Institute and Department of Chemistry, University of Southern California
837 Bloom Walk, Los Angeles, CA 90089
Fax: +1-213-740-6679
E-mail: gprakash@usc.edu
olah@usc.edu
[‡] Present address: The University of North Carolina at Charlotte, Department of Chemistry
9201 University City Blvd., Charlotte, NC 28223
Supporting information for this article is available on the WWW under http://www.eurjoc.org or from the author.

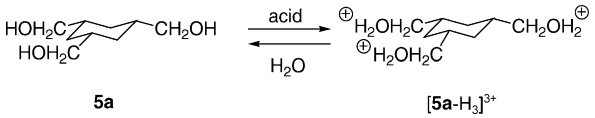


Scheme 2. Retrosynthesis of oxoniaadamantane.

tially reduced species (e.g. lactone or acetal formation) has been reported in the reverse approach, namely the oxidation of triol **5b**, the observed results were not surprising.[10]

Ether alcohol **7a** was synthesized in accordance with the literature procedure[8] and further functionalized. The liquid chloro ether **8i** was isolated in 95% yield by treating **7a** in excess thionyl chloride under reflux. Conversion of **7a** with (diethylamino)sulfur trifluoride (DAST) in dichloromethane under standard conditions yielded fluoro ether **8ii** in 85% yield as a colorless liquid. The new compounds are stable at room temperature, although **8ii** should be stored at –20 °C over extended periods of time. Both derivatives were fully characterized and reveal the typical NMR spectral pattern of the bicyclic ether skeleton. The NMR spectra of fluoro ether **8ii** are somewhat more complex because of the well observed fluorine–carbon and fluorine–hydrogen coupling.

Ionization reactions were attempted in neat superacids from H_2SO_4 to HF/SbF_5 (Scheme 3, Table 1) due to the limited solubility of **5a** in typical low-nucleophilicity solvents (SO_2, SO_2ClF). Thus, a small sample of alcohol **5a** (10 mg) was dissolved in acid (ca. 2 mL, NMR tube) at 0 °C and slowly warmed up to room temperature. The spectrum was measured against an external standard of [D_6]acetone. Under a variety of acidic conditions, threefold protonated trication [**5a**-H_3]$^{3+}$ was the only observed species as indicated by the ^{1}H and ^{13}C NMR spectral pattern (Table 1). Careful quenching of the reaction mixture resulted in the recovery of the starting material **5a**.



Scheme 3. Triple protonation of triacid **5a**.

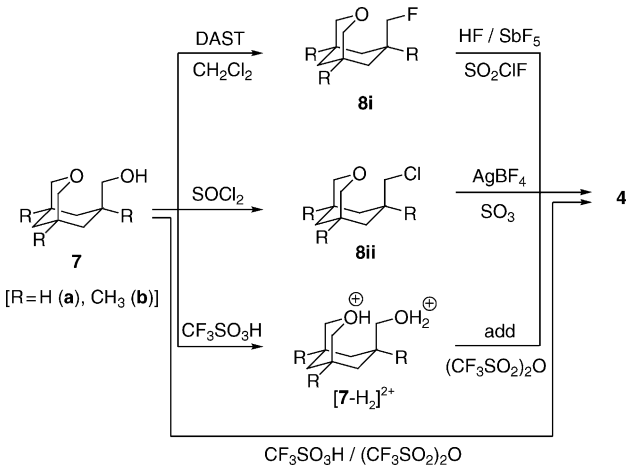
Table 1. ^{13}C NMR spectroscopic data (ppm).

Entry	Conditions	$CH_2OH_2^+$	CH	CH_2
1	conc. H_2SO_4	78.5	35.0	29.4
2	H_2SO_4 (30% SO_3)	78.3	35.0	29.4
3	CF_3sO_3H	76.0	35.0	28.6
4	FSO_3H	77.3	34.0	27.7
5	FSO_3H/SbF_5 (1:1)	79.1	33.6	27.0
6	HF/SbF_5 (4:1)	79.2	34.2	27.4
7	$CF_3SO_3H/(CF_3SO_2)_2O$	73.8	33.9	27.9

Similar experiments with the trimethylated triol **5b** resulted in an unidentified product with complete loss of symmetry, therefore ruling out threefold protonation to [**5b**-H_3]$^{3+}$, formation of the bicyclic diprotonated ether alcohol [**7b**-H_2]$^{2+}$, or trimethyl-1-oxoniaadamantane **4b**. The ^{13}C NMR spectrum obtained was not in accordance with any possible mixture of these species, either. Our initial ionization attempts of **7a** under the above conditions did not result in the expected 1-oxoniaadamantane **4a** but exclusively led to the formation of diprotonated ether alcohol [**7a**-H_2]$^{2+}$. This dication combines a primary and secondary oxonium ion in its structure and was characterized by ^{13}C NMR spectroscopy (see Experimental Section).

We then attempted two different strategies to achieve our target, 1-oxoniaadamantane **4a**. The first approach was the metathesis of the halo ethers **8i** or **8ii** by treatment with HF/SbF_5 in SO_2ClF or $AgBF_4$ in SO_2, respectively (Scheme 4). The second approach was the ionization of ether alcohol **7a** under more acidic conditions, by either adding triflic anhydride to the mixed bis(oxonium) ion [**7a**-H_2]$^{2+}$ in triflic acid or by dissolving the neutral precursor in a triflic acid/triflic anhydride mixture. With both these approaches, we succeeded in obtaining the target tertiary cage oxonium ion **4a**. The anticipated anchimeric assistance of the ether functionality indeed takes place in the formation of the oxonium ion and excludes any primary carbocation intermediate. In the case of ionization under acidic conditions, the increased acidity seems to be of crucial importance. The scavenging of water by triflic anhydride cannot be the determining factor, since the use of 30% oleum as an effective water scavenger should have resulted in the same conversion of **5a**.

The observed ^{1}H and ^{13}C NMR spectroscopic data (Figure 1) are in excellent agreement with the calculated DFT data (Table 2): The ^{1}H NMR spectrum shows the expected four sets of hydrogen; the methylene group neighboring the oxonium center at δ = 5.30 ppm, a broad multiplet for the bridgehead hydrogen at δ = 2.65 ppm, and two AB sets (between 2.52–2.65 ppm) for the remaining axial and equatorial methylene hydrogens. ^{13}C NMR spectroscopy, and in particular the proton-coupled spectrum, reveals a triplet for the methylene carbons in α-position to the oxonium oxygen center at δ (^{13}C NMR) = 94.6 ppm, another triplet at δ = 31.7 ppm for the cyclohexane methylene carbons and a doublet at δ = 28.2 ppm for the bridgehead carbons. In solution and in the crystalline state, **4a** is stable under ambient conditions as long as moisture and other nucleophiles are excluded. On the basis of the studies of the low-nucleo-



Scheme 4. Synthesis of 1-oxoniaadamantane **4**.

philicity carborane cluster $CB_{11}H_6Cl_6^-$ that has been used to stabilize various reactive cations,[11] we were able to grow single crystals of **4a**-$CB_{11}H_6Cl_6^-$ from dichloromethane and could resolve an X-ray crystallographic structure of a twin crystal at low temperature (Figure 2).[12] The salt crystallizes in the orthorhombic crystal system in the space group $P2_12_12_1$. No unusual bond features were observed. Salient bond lengths are shown in Table 3 along with the structural data of various 1-elementa-adamantane cations computed by using GIAO-DFT/B3LYP/6-311G* level calculations. The X-ray crystallographic structural data matches those from theory reasonable well.

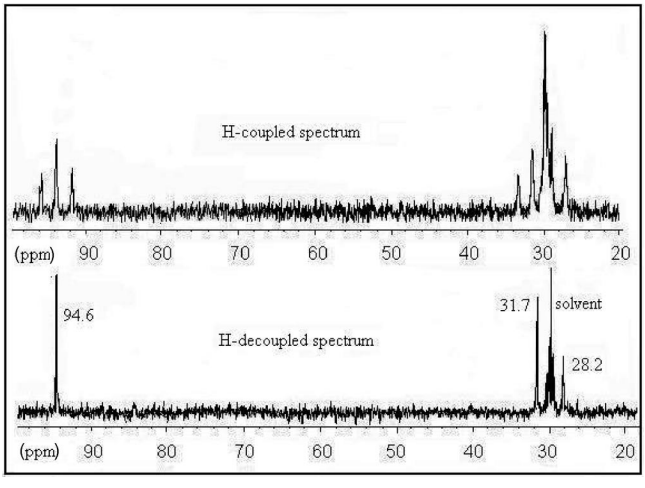


Figure 1. ^{13}C NMR spectrum (300 MHz, SO_2) of 1-oxoniaadamantane **4**.

Finally, we carried out ESI-MS studies on all alcohol precursors. It should be mentioned that the generation of cationic species of the alcohols **5a**, **5b**, and **7** under EI conditions did not result in a mass spectrum with any observable molecular ion peaks or the oxonium ion peak. Under ESI conditions, however, we were able to observe an oxonium ion mass fragment for all three alcohol precursors. By electron spray ionization of alcohol samples dissolved in methanol/water and by using the MS/MS capability of the instrument, we detected positively charged mass fragments that correspond to the respective oxonium ions; alternatively a primary ether alkyl cation cannot be excluded on the basis of the mass spectroscopic data alone.

Table 2. Selected GIAO-DFT/B3LYP/6-311G* calculated data and experimental data for the 1-elementa-adamantane cations **4a** and **4b**.

R	X	X–*C*H$_2$	*C*H$_2$	*C*R[a]	C–*C*H$_3$
H	C	71.4	41.4	102.3	N/A[a]
H	O	100.1	35.2	34.3	N/A[a]
Exp. (SO_2)		94.6	28.2	31.7	N/A[a]
H	S	49.0	35.6	29.6	N/A
CH_3	C	74.7	53.0	106.9	32.8
CH_3	O	100.9	48.9	38.8	24.1
CH_3	S	50.6	48.8	36.5	31.5

[a] For the parent systems there is no substituent present.

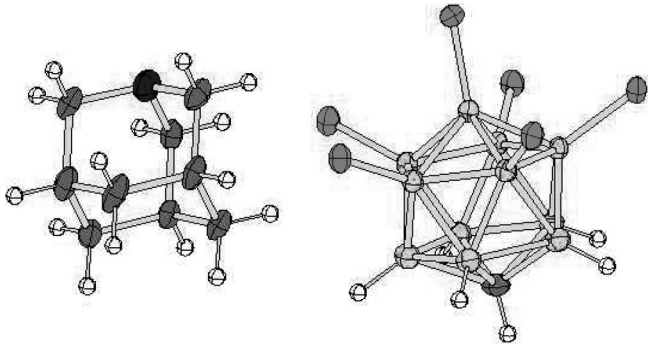


Figure 2. ORTEP depiction of the solid-state molecular structure of **4a**-$CB_{11}H_6Cl_6^-$. Selected bond lengths (Å): O1–C2, 1.508; C2–C3, 1.511; C3–C4, 1.536 (the atom numbers do not correspond to the crystallographic numbering of the compound).

Table 3. Selected GIAO-DFT/B3LYP/6-311G* calculated data and experimental data for structures of the 1-elementa-adamantane cations **4a** and **4b**.

R	X	$d_{X–C2}$ (Å)	$d_{C2–C3}$ (Å)	$d_{C3–C4}$ (Å)	Φ (°) C_3–C_2–X
H	C	1.455	1.627	1.534	99.0
H	O	1.513	1.522	1.544	108.3
X-ray cryst. data		1.508	1.511	1.536	109.6
H	S	1.846	1.534	1.542	112.0
CH_3	C	1.453	1.634	1.538	99.9
CH_3	O	1.509	1.525	1.547	109.2
CH_3	S	1.841	1.539	1.545	112.9

Conclusions

In summary we have successfully synthesized 1-oxoniaadamantane **4** by two different methodologies: We were able to obtain the bicyclic dication $[7a\text{-}H_2]^{2+}$ or the target 1-oxoniaadamantane **4** by ionization of the same precursor. The ionization is acidity-controlled. The new and readily available fluoro ether **8i** and chloro ether **8ii** are suitable precursors of **4** in a metathesis reaction. All these methods yielded the same oxonium ion, which was completely characterized by NMR spectroscopy and X-ray crystallographic

structure analysis with the low-nucleophilicity $CB_{11}H_6Cl_6$ anion.

Supporting Information (see footnote on the first page of this article): Experimental procedures, NMR spectroscopic data, and DFT computational data.

Acknowledgments

Support of our work by the Loker Hydrocarbon Research Institute and National Science Foundation is gratefully acknowledged.

[1] G. A. Olah, K. K. Laali,Q. Wang. G. K. S. Prakash, *Onium Ions*, J. Wiley and Sons, New York, **1998**.
[2] F. Klages, H. A. Jung, *Chem. Ber.* **1965**, *98*, 3757.
[3] M. M. Francl, G. Hansell, B. P. Patel, C. S. Swindell, *J. Am. Chem. Soc.* **1990**, *112*, 3535.
[4] W. Kirmse, U. Mrotzeck, *Chem. Ber.* **1988**, *121*, 485.
[5] a) B. M. Mikhailov, V. N. Smirnov, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1973**, *22*, 2165; b) B. M. Mikhailov, V. N. Smirnov, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1974**, *23*, 1137; c) W. N. Speckamp, J. Dijkink, H. O. Huisman, *J. Chem. Soc. C* **1970**, 197; d) C. A. Kapfer, P. Boudjouk, *J. Organomet. Chem.* **1978**, *144*, C6; e) H. E. Meeuwissen, Th. Kraap, F. Bickelhaupt, *Tetrahedron* **1983**, *39*, 4225; f) F. Klages, H.-U. Klages, *Chem. Ber.* **1963**, *96*, 2063.
[6] D. S. Kemp, K. S. Petrakis, *J. Org. Chem.* **1981**, *46*, 5140.
[7] H. A. Meyer, R. Fawzi, M. Steinmann, *Chem. Ber.* **1993**, *126*, 1341.
[8] J. A. Peters, B. van de Graaf, P. J. W. Schuyl, Th. M. Wortel, H. van Bekhum, *Tetrahedron* **1976**, *32*, 2735.
[9] A. T. Nielsen, S. L. Christia, D. W. Moore, R. D. Gilardi, C. F. George, *J. Org. Chem.* **1987**, *52*, 1656.
[10] a) H. Izumi, O. Setokuchi, Y. Shimizu, H. Tobita, H. Ogino, *J. Org. Chem.* **1997**, *62*, 1173; b) H. Izumi, S. Futamura, *J. Org. Chem.* **1999**, *64*, 4502.
[11] a) C. A. Reed, *Chem. Commun.* **2005**, *13*, 1669; b) Z. Xie, J. Manning, R. W. Reed, R. Mathur, P. D. W. Boyd, A. Benesi, C. A. Reed, *J. Am. Chem. Soc.* **1996**, *118*, 2922.
[12] Data were collected at 100 K with a Bruker Nonius Kappa CCD diffractometer by using Mo-K_α radiation (λ = 0.71073 Å, graphite monochromator). The structure was solved by direct methods and refined on F^2 by using full-matrix least-squares techniques. **4a**-$CB_{11}H_6Cl_6$: orthorhombic, $P2(1)2(1)2(1)$, a = 11.2548(10) Å, b = 11.2572(10) Å, c = 17.0915(15) Å, $\alpha = \beta = \gamma = 90°$, V = 2165(5) Å^3, Z = 4, R_1 = 0.0260 [$I > 2\sigma I$], wR_2 = 0.0721 (all data). CCDC-698336 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Received: June 1, 2008
Published Online: August 19, 2008

