no important π-interactions should be expected, and none were found. The major effect contributing to energy differences appeared to be lone-pair repulsion.

7. Calculations

The ab initio calculations were carried out using GAUSSIAN-86,[26] and the charge density analysis was performed using PROAIM.[27]

Acknowledgment. This investigation was supported by grants from the National Institutes of Health and the Exxon Educational Foundation.

Registry No. 1, 137695-67-1; **2**, 107-29-9; **3**, 5799-73-5; **4**, 6898-67-5; CH_3CHO, 75-07-0; NH_2F, 15861-05-9; NH_2OH, 7803-49-8; NH_2NH_2, 302-01-2; CH_3NH_2, 74-89-5.

Supplementary Material Available: Tables A–J listing the bond and atom properties of compounds **1–4** and the compounds from which they are formed (30 pages). Ordering information is given on any current masthead page.

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(26) Frisch, M. J.; Binkley, J. S.; Schlegel, H. B.; Raghavachari, K.; Melius, C. F.; Martin, R. L.; Stewart, J. J. P.; Bobrowicz, F. W.; Rohlfing, C. M.; Kahn, L. R.; Defrees, D. J.; Seeger, R. A.; Whiteside, R. A.; Fox, D. J.; Fluder, E. M.; Pople, J. A. Carnegie-Mellon Quantum Chemistry Publishing Unit, Pittsburgh, PA, 1984.

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Molecular Mechanical Investigations of the Properties of Oxocarbenium Ions. 1. Parameter Development[§]

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Contribution from the Laboratory for Molecular Modeling, Division of Medicinal Chemistry and Natural Products, School of Pharmacy, The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599, and Burroughs Wellcome Company, 3030 Cornwallis Road, Research Triangle Park, North Carolina 27709.

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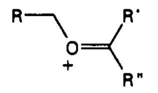
Abstract: The structural properties of a series of acyclic oxocarbenium ions containing the C—O=C atomic linkage have been investigated at the Hartree–Fock and Møller–Plesset ab initio levels with a variety of basis sets up to the 6-311++G** level. The results from the ab initio calculations provide insight into the extent of charge delocalization in these ions, and have been used to generate parameters for the MM2(87) molecular mechanics program. Two approaches to the incorporation of electrostatic interactions within a molecular mechanical framework are presented and evaluated. An application of the parameter set in the evaluation of the relative stabilities and heats of formation of several experimentally observed acyclic oxocarbenium ions is presented.

While oxocarbenium ions are believed to be reaction intermediates in the acid-catalyzed hydrolysis of glycosides,[2] and ketals in general,[3] the transient nature of these species has prevented their isolation. In the case of glycoside hydrolysis, the postulate that the rates of hydrolysis are related to the stabilities of the cyclic oxocarbenium ions has been generally accepted for over 30 years,[2,4] despite the lack of direct evidence that such a relationship exists. Recently, the importance of nonsteric interactions has been discussed by Toullec,[5] who reported that C–H acidities in acyclic oxocarbenium ions play a role in determining the rates of hydrolysis of the parent acetals. In contrast, Amyes and Jencks have reported that in the hydrolysis of certain acetals the lifetimes of the oxocarbenium ions may be too short to support the belief that these ions exist as discrete intermediates.[6]

In an effort to quantify the extent to which steric effects are related to oxocarbenium ion stabilities, we have examined the structural properties of a series of closely related oxocarbenium ions, applying computational methods. As we wished to be able to extend the calculational method to larger oxocarbenium ions, derived from oligosaccharides, we chose to treat the problem within a molecular mechanical framework, employing the program MM2(87).[7] This version of MM2 includes parameters necessary to describe the relationship between C–O–C–O torsion angles and C–O bond lengths as manifest by the anomeric effect.[8] Among the improvements present in MM2(87) is an ability to describe hydrogen bonding, a feature of particular relevance to carbohydrates. However, previous to this work, there were no MM2 parameters for species containing the C—O=C linkage, present

Chart I



1: $R = R' = R'' = H$
2: $R = R' = H$, $R'' = CH_3$
3: $R = R'' = H$, $R' = CH_3$
4: $R = H$, $R' = R'' = CH_3$
5: $R = R' = H$, $R'' = CH_2CH_3$
6: $R = R'' = H$, $R' = CH_2CH_3$
7: $R = CH_3$, $R' = R'' = H$
8: $R = CH_2CH_3$, $R' = R'' = H$
9: $R = CH_2OH$, $R' = R'' = H$
10: $R = R' = H$, $R'' = CH_2OH$
11: $R = CH_2OH$, $R' = H$, $R'' = CH_3$
12: $R = R' = H$, $R'' = CH_2CH_2OH$

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[§] Dedicated to Ernest Eliel on the ocassion of his 70th birthday.

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(5) Toullec, J. *J. Chem. Soc., Perkin Trans. 2* **1989**, 167–171.

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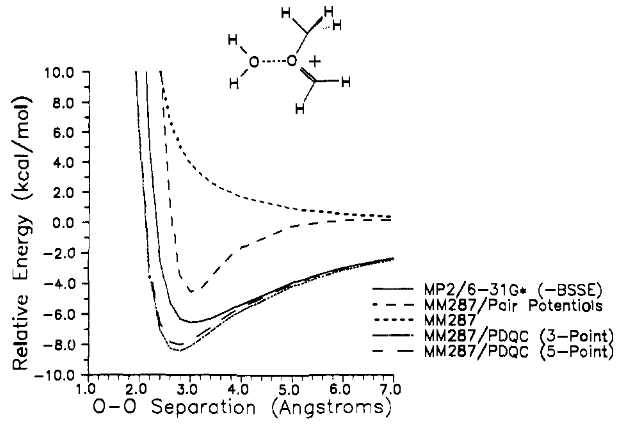

Figure 1. Calculated interaction energy between water and **1** along a front-attack pathway (see text for a description of the pathways).

in oxocarbenium ions. As there is a paucity of experimental structural data pertaining to oxocarbenium ions, a structural database was compiled from high-level ab initio molecular orbital calculations. Where possible the results have been compared to experimental data.

Method

We have performed ab initio calculations, using the Gaussian90 series of software packages,[9] to estimate the physical properties of a series of acyclic oxocarbenium ions containing from two to four carbon and one to two oxygen atoms, giving rise to twelve chemically unique ions. The geometries of these species were optimized with no constraints, unless otherwise noted, at both the restricted Hartree–Fock (RHF) and second-order Møller–Plesset (MP2) levels,[10] with basis sets of varying sophistication. All calculations were performed on either a CRAY-YMP or a Convex C220 computer.

Discussion

Basis Set Selection. The simplest cation containing the $\mathrm{C{-}O{=}C}$ linkage is *O*-methylformaldehydium ion (**1**),[11] a species that has been studied both experimentally, using solution NMR and mass spectroscopic techniques,[12] and theoretically at several levels of molecular orbital theory (see Chart I).[12b,c,13] The effects of basis set and electron correlation on the geometry and energy of **1** are summarized in Table I. The geometries calculated at the HF level appeared to be rather insensitive to the basis set, and the effect of adding diffuse functions was negligible. As previously observed,[12c] the value of the $\mathrm{C{-}O{=}C}$ bond angle exhibited a significant dependence on the effects arising from electron correlation. Notably, this angle appeared to become more acute at the MP2 level than at each of the corresponding HF levels, by as much as 3°. As expected, the $\mathrm{C{-}O}$ and $\mathrm{C{=}O}$ bond lengths were predicted to be longer than found for dimethyl ether and formaldehyde, respectively. A slight shortening of the $\mathrm{C{-}O}$ and $\mathrm{C{=}O}$ bond lengths, on performing the calculations at the MP2/6-311G** level,[14] relative to the results obtained at the MP2/6-31G* level,[15] was observed. Similar trends were predicted for each of the oxocarbenium ions. On the basis of these results, the subsequent geometry optimizations were performed at the MP2/6-311G** level. In the evaluation of torsional potentials, the calculations were performed at the MP2/6-31G* level. The use of the less extensive basis set resulted in little difference in the calculated conformational energies, relative to those at the MP2/6-311G** level, and was slightly more economical. The

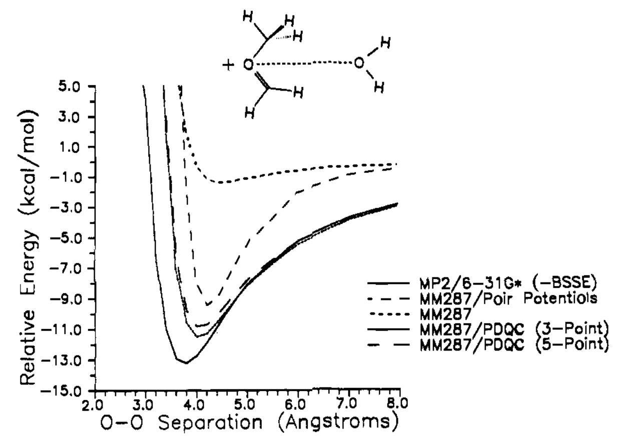

Figure 2. Calculated interaction energy between water and **1** along a back-attack pathway.

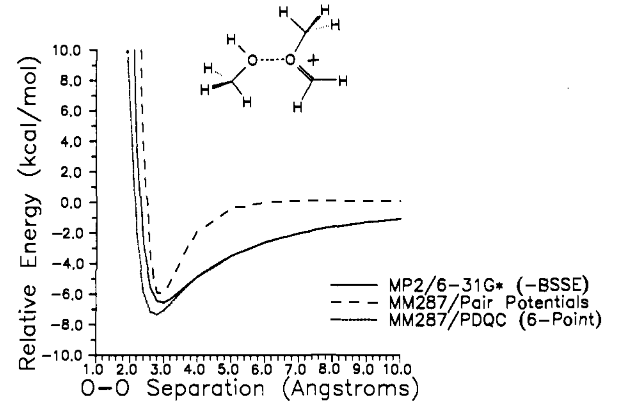

Figure 3. Calculated interaction energy between methanol and **1** along a front-attack pathway.

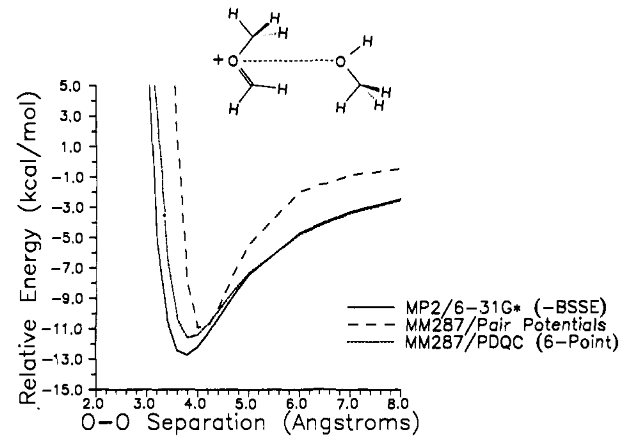

Figure 4. Calculated interaction energy between methanol and **1** along a back-attack pathway.

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(6) Amyes, T. L.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 7888–7900.

(7) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127–8134 and subsequent papers. The program MM2(87), which is an extended, but otherwise unchanged, version of MM2, is available from the Quantum Chemistry Program Exchange, Department of Chemistry, University of Indiana, Bloomington, IN 47401, and from Tripos Associates, 1699 Hanley Rd, Suite 303, St. Louis, MO 63144.

(8) For a discussion of the parameters as well as a summary of the anomeric effect, see: Nørskov-Lauritsen, L.; Allinger, N. L. *J. Comput. Chem.* **1984**, *5*, 326–335.

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(11) The nomenclature for the oxocarbenium ions is taken from Perst, H. *Oxonium Ions in Organic Chemistry*; Academic: New York, 1971; Chapter 2.

(12) See for example: (a) Lossing, F. P. *J. Am. Chem. Soc.* **1977**, *99*, 7526–7530. (b) Farcasiu, D.; Horsley, J. A. *Ibid.* **1980**, *102*, 4906–4911. (c) Cremer, D.; Gauss, J.; Childs, R. F.; Blackburn, C. *Ibid.* **1985**, *107*, 2435–2441.

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(14) Kirshnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650–654.

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Table I. Geometries[a] and Energies[b] for **1** Calculated at the ab Initio Level

parameter	HF 6-31G*	HF 6-311G**	HF 6-311++G**	MP2 6-31G*	MP2 6-311G**
		Bond Lengths			
C—O (1.410)[c]	1.478	1.479	1.479	1.493	1.486
C═O (1.208)[d]	1.219	1.215	1.215	1.148	1.240
CH_3—syn	1.078	1.079	1.080	1.089	1.089
CH_3—gauche	1.076	1.077	1.077	1.087	1.087
CH—cis	1.080	1.083	1.083	1.091	1.092
CH—trans	1.077	1.080	1.080	1.087	1.088
		Bond Angles			
C—O═C	124.5	124.3	124.3	121.9	121.3
H—C—O—syn	108.8	108.7	108.7	109.1	108.9
H—C—O—gauche	105.0	105.0	105.0	104.4	104.6
H—C═O—cis	121.5	121.6	121.6	121.4	121.4
H—C—O—trans	117.1	117.2	117.3	116.0	116.2
		Torsion Angles			
H—C—O═C—gauche	121.0	121.0	120.9	121.2	121.2
Total Energy	−153.20403	−153.24671	−153.24788	−153.63273	−153.77384

[a] Geometries in angstroms and degrees. [b] Energies in hartrees. [c] Experimental value for the C—O bond length in dimethyl ether taken from Blukis, U.; Kasai, P. H.; Meyers, R. J. *J. Chem. Phys.* **1963**, *38*, 2753–2760; see text. [d] Experimental value for the C═O bond length in formaldehyde taken from Takagi, K.; Oka, T. *J. Phys. Soc. Jpn.* **1963**, *18*, 1174; see text.

torsional energies were evaluated by constraining the relevant torsion angles for rotations from 0° to 180° in 30° increments.

Nonbonded Interactions. New atom types (O^+, type 70, and C^+, type 71)[16] were introduced, corresponding to the oxonium and carbenium atoms of the C—O═C fragment, respectively (see Table III). With the exception of two parameters, namely, one bending (O–C–C^+) and one torsion (O–C–C–C^+) term, all of the parameters associated with atom type C^+ were taken directly from those currently assigned in MM2(87) to carbonyl carbon atoms. The two exceptions are discussed in detail below. For atom type O^+ all of the necessary parameters were developed de novo.

A principal concern in the molecular modeling of charged species must be the ability of the model to reproduce nonbonded interactions. In an attempt to estimate the magnitude of the interactions between oxocarbenium ions and polar molecules, the interaction potential curves for the interaction between **1** and water or methanol were calculated at the MP2/6-31G* level. These molecules were chosen because, in the case of the former, the interaction provides insight into the energy of aqueous solvation of the oxocarbenium ion, while the latter serves to model both methanolic solvation and interactions involving hydroxyl substituents in the ion. The results of these calculations are presented in Figures 1–4.

The neutral species were constrained to approach the ion in the C—O═C plane, either from the side of the oxygen atom (front-attack) or from the side of the carbon atoms (back-attack). In both front- and back-attacks the approach geometry was defined such that the oxygen atom of the molecule was located along the bisector of the C—O═C angle, while the oxygen atom of the ion was constrained to lie along the bisector of the H—O—R (R = H, CH_3) angle. The geometry of each species was frozen at the MP2/6-31G* optimized structure. Corrections for basis set superposition errors (BSSE) were performed according to the counterpoise method.[17] At the minimum in each of the interaction potentials, the estimated values for the BSSE were 0.7 and 0.8 kcal/mol for the front-attack of water and methanol, respectively, and 1.6 and 1.8 kcal/mol for the back-attack of water and methanol, respectively.

An examination of Figures 1–4 indicated that both water and methanol formed very stable charge–dipole complexes, with O···O separations of approximately 3.0 and 3.8 Å for front- and back-attacks, respectively. Moreover, for both water and methanol, the complexes arising from back-attack were predicted to be more stable than those from front-attack, by a factor of approximately 2. This observation implied that a description of the oxocarbenium ion as a positive charge localized on the oxygen atom was inaccurate. Moreover, it indicated that charge delocalization extended to include the methyl group of the ion.

Ideally a molecular mechanical force field should be able to reproduce these interaction potentials. However, it should be noted that the interaction energy is composed of contributions from several sources,[18] not all of which have classical counterparts. We chose to explore the modeling of the nonbonded interactions from two approaches. Firstly, we sought to reproduce the curves through a simple model for the electrostatic component of the interaction energy. This component has been shown to be the predominant contributor to the stabilization energy.[18] Within the framework of Allinger's MM2 series of programs, the electrostatic interactions between polar molecules are approximated by calculating the interaction energy between pairs of bond moments. Similarly, the electrostatic interactions between a polar molecule and an ion could be approximated by calculating the interactions between the bond moments of the molecule and the charges on each of the atoms of the ion. This method would require that the charge distribution over the atoms in the ion be determined in some "reasonable"[19] manner and that attention be paid to the method used to determine the bond moments, so as to ensure a balanced interaction between the moments and the charges. While the option of invoking this method exists in the recently released molecular mechanics program, MM3,[20] it is not present in MM2(87). Moreover, the extensive parameter compilation existing for use with MM2(87) is not transferable to MM3.[21]

The interaction potentials generated from bond moments alone resulted in an extremely poor reproduction of the ab initio potentials. In the case of front-attack a bond moment model resulted in a purely repulsive curve that clearly indicated the need for explicit consideration of the charge (see Figures 1 and 2).

We chose to replace the bond moments in favor of net atomic charges. This approach allowed the electrostatic interactions to

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(16) (a) Our parameters for C^+ are for carbenium ions and should not be confused with the MM2(87) parameters for carbonium ions (C^+, atom type 30). (b) In the development of these parameters, the stretch–bend term for the C—O═C fragment was defined as zero. In MM2(91) this parameter has been set to 0.12.

(17) Boys, S. F.; Bernardi, F. *Mol. Phys.* **1970**, *19*, 553–566.

(18) Umeyama, H.; Morokuma, K. *J. Am. Chem. Soc.* **1977**, *99*, 1316–1332.

(19) Net atomic charges are not physical observables, and hence are not uniquely defined. Thus, one may select from a variety of more or less reasonable charge partitioning methods.

(20) (a) Allinger, N. L.; Yuh, L. H.; Lii, J.-H. *J. Am. Chem. Soc.* **1989**, *111*, 8551–8566. (b) Lii, J.-H.; Allinger, N. L. *J. Ibid.* **1989**, *111*, 8566–8575. (c) Lii, J.-H.; Allinger, N. L. *Ibid.* **1989**, *111*, 8576–8582. The MM3 program is available from the Technical Utilization Corp., Inc., 235 Glen Village Ct, Powell, OH 43065, and from Molecular Design Ltd., 2132 Farallon Dr, San Leandro, CA 94577.

(21) Allinger, N. L., The University of Georgia, personal communication, 1991.

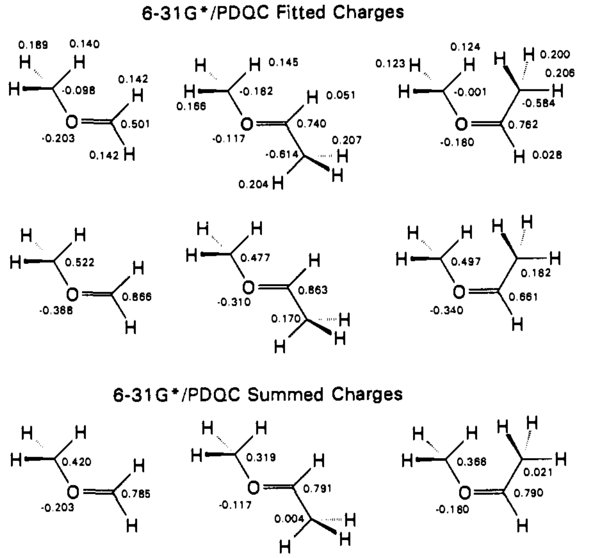

Figure 5. Net atomic charges derived from a fitting to the HF/6-31G* electrostatic potentials for **1–3**.

be calculated as charge–charge interactions, an option present in MM2(87). The net atomic charges were determined in such a way that they best reproduced the molecular electrostatic potential calculated at the HF/6-31G* level. While several programs are available that make use of this method to generate net atomic charges,[22] we chose to use the program PDQC.[22d] Not only do charges determined in this manner reproduce the molecular electrostatic potential, but also the ab initio dipole moment. Charges of this type have been reported for a variety of molecules including nucleic acids,[22a] carbohydrates,[22a,d] and amino acids.[22d,23] The net atomic charges determined for **1–3** are presented in Figure 5.

It is noteworthy that, in agreement with the conclusions based on the ab initio interaction potentials, the oxygen atom in the ion does not carry a positive charge, but rather, the positive charge is delocalized over the whole atomic framework. The highly polar nature of the C–H bonds in the methyl groups has been reported previously for neutral species,[22] and it has been suggested that it is more consistent to consider the charge on the methyl group as a point charge on the carbon atom equal to the sum of the individual charges.[22d] The summed atomic charges for the ions indicated that the positive charge was delocalized over both of the carbon atoms geminal to the oxygen atom, but was not spread beyond that region to other methyl groups. Atomic charges derived from fitting the charges only to the non-hydrogen atoms showed qualitatively similar distributions, although the bonds tended to be slightly more polar. A comparison of the summed charges on the C—O═C fragment with those calculated for dimethyl ether ($Q(CH_3) = 0.153$ au, $Q(O) = -0.310$ au)[22c] and formaldehyde ($Q(CH_2) = 0.455$ au, $Q(O) = -0.456$ au)[22c] indicated that, in the case of the ion, the positive charge resulted in an approximately 2-fold increase in the charge on each of the carbon atoms and a similar decrease in the charge on the oxygen atom, relative to the corresponding neutral species. This short-range charge delocalization allows a model for the charge distribution in the ions to be proposed that may be relatively independent of the structure of the ion, in which the positive charge of the oxocarbenium ion is described as being localized on the atoms of the C—O═C fragment.

The bond moments for the C═O and C—O bonds were calculated to be approximately 2.80 and 1.90 D, respectively,[24] on the basis of the summed atomic charges. These values may be compared to bond dipoles reported for the C═O bonds in formaldehyde (2.66 D), acetaldehyde (3.08 D), and acetone (3.52 D), and for the C—O bonds in methanol (2.00 D) and dimethyl ether (1.16 D).[22c]

The interaction potentials presented in Figures 1–4 illustrate the effectiveness of a simple coulombic model. A bulk dielectric constant of unity was used in each of the calculations. Included for comparison in Figures 1 and 2 are the results for two charge arrangements. While a point-charge model for water in which the lone pairs were assigned partial negative charges has been shown to result in a better fitting of the electrostatic potential,[22a] it was found here to be of no advantage over a three-point model, in which the lone pairs were assigned zero charge.[25]

In the case of front-attack, by either water or methanol, the coulombic model led to deeper potential energy wells, and shorter O···O separations in the complex, than predicted at the ab initio level, by approximately 1.5 kcal/mol, and 0.2 Å, respectively. This overstabilization likely arose from the inability of the classical model to mimic the destabilizing interactions attributable to the exchange repulsion energy.[18] Recently, in a calculational study of the hydrogen bonding between N—H and C═O functional groups, the exchange repulsion energy was modeled by an atom–atom exponential repulsion term.[26] However, for ease of incorporation into the MM2 framework we chose to approximate the electrostatic interactions by employing net atomic charges, without the inclusion of an exchange repulsion correction term. In the complexes arising from back-attack by water or methanol, the coulombic model predicted lower interaction energies than found at the ab initio level, by 1–2 kcal/mol. Furthermore, back-attack by water led to a complex in which the O···O separation was found to be longer than that predicted at the ab initio level, by approximately 0.2 Å. The lengthening of the O···O separation in the latter situation may arise from an overestimation of the van der Waals repulsions between hydrogen atoms.

The second approach to the incorporation of nonbonded interactions involved the use of atomic pair potentials. Modified Buckingham pair potential functions, of the forms shown in eqs 1 and 2, are used in MM2(87) to describe the interactions associated with hydrogen bonding, a phenomenon that is not fully described by dipole–dipole interactions.[7] If $r_{ik}/R_{ik} \leq 3.311$

$$E_{ik} = (\epsilon_{ik})^{1/2}((2.9 \times 10^5)e^{-12.5(R_{ik}/r_{ik})} - 2.25(r_{ik}/R_{ik})^6) \quad (1)$$

or if $r_{ik}/R_{ik} > 3.311$

$$E_{ik} = 336.176(\epsilon_{ik})^{1/2}(r_{ik}/R_{ik})^2 \quad (2)$$

where R_{ik} is the internuclear separation of atoms i and k, r_{ik} corresponds to the internuclear separation at the minimum in the potential energy well, and ϵ_{ik} is related to the depth of the well and the steepness of the repulsion curve (or atomic "hardness"). In the case of hydrogen bonding, r_{ik} is smaller than the sum of the van der Waals radii for atoms i and k, allowing a closer approach between the atoms, and ϵ_{ik} is larger than the sum of the individual atomic values, reflecting an increased interaction energy.

In the case of oxocarbenium ions, one would anticipate the presence of attractions between electronegative atoms and the atoms of the ion that carry partial positive charges. In the specific case of interactions between oxocarbenium ions and hydroxyl oxygen atoms, we investigated the simultaneous application of two "hydrogen bonding" potential functions. The first function described the interaction between the carbon atom of the methyl group of the ion and the hydroxyl oxygen atom ($\epsilon_{C,O}$ and $r_{C,O}$), while the second described that between the carbenium atom of the ion and the hydroxyl oxygen atom ($\epsilon_{C^+,O}$ and $r_{C^+,O}$).

A comparison of the well depths in Figures 1–4 indicated that the values of ϵ and r for the pair potentials could be chosen such

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[22] See for example: (a) Singh, U. C.; Kollman, P. A. *J. Comput. Chem.* **1984**, *5*, 129–145. (b) Chirlian, L. E.; Francl, M. M. *Ibid.* **1987**, *8*, 894–905. (c) Williams, D. E. *Ibid.* **1988**, *9*, 745–763. (d) Woods, R. J.; Khalil, M.; Pell, W.; Moffat, S. H.; Smith, V. H., Jr. *Ibid.* **1990**, *11*, 297–310.

[23] Gruschus, J. M.; Kuki, A. *J. Comput. Chem.* **1990**, *11*, 978–993.

[24] Hopfinger, A. J.; Pearlstein, R. A. *J. Comput. Chem.* **1984**, *5*, 486–499.

[25] In order to be consistent with the MM2 approach, lone pairs were added to the MP2/6-31G* geometry with their locations defined as described in ref 6.

[26] Mitchell, J. B. O.; Price, S. L. *J. Comput. Chem.* **1990**, *11*, 1217–1233.

Table II. Values for Selected Oxocarbenium Ion Structural Features Calculated at the MP2/6-311G** ab Initio Level and by MM2(87) (in Parentheses)

ion	C—O+	C=O+	C—C+	C—O=C	C—C—O+	C—C=O+	O=C—H
1[a]	1.486	1.240		121.3			121.4,[b] 116.2[c]
	(1.488)	(1.239)		(121.3)			(121.6),[b] (116.4)[c]
2[d]	1.479	1.251	1.462	121.0		120.4	118.4
	(1.488)	(1.252)	(1.472)	(121.6)		(120.5)	(119.2)
2[e]	1.487	1.252	1.462	119.9		120.4	118.5
	(1.488)	(1.252)	(1.472)	(121.6)		(119.8)	(119.3)
3[e]	1.481	1.252	1.466	122.5		127.8	112.3
	(1.484)	(1.252)	(1.474)	(122.6)		(127.5)	(112.8)
4[f]	1.474	1.264	1.476,[b] 1.483[c]	123.0		124.5,[b] 114.8[c]	
	(1.484)	(1.263)	(1.476),[b] (1.476)[c]	(123.5)		(124.5),[b] (114.8)[c]	
5[g]	1.486	1.253	1.473	119.7		120.2	118.1
	(1.486)	(1.253)	(1.475)	(120.2)		(120.2)	(118.3)
6[g]	1.476	1.255	1.474	121.3		126.2	112.2
	(1.485)	(1.253)	(1.476)	(122.0)		(126.0)	(113.1)
6[h]	1.482	1.254	1.472	126.0		132.6	110.9
	(1.478)	(1.252)	(1.479)	(125.6)		(132.7)	(109.7)
7[g]	1.530	1.239		120.1	106.8		121.3,[b] 116.6[c]
	(1.520)	(1.239)		(119.9)	(106.1)		(120.7),[b] (116.9)[c]
8[g]	1.531	1.239		120.1	107.4		121.3,[b] 116.6[c]
	(1.520)	(1.239)		(120.1)	(108.9)		(120.7),[b] (116.8)[c]
9[g]	1.509	1.240		120.1	107.1		121.2,[b] 116.4[c]
	(1.519)	(1.239)		(119.6)	(105.4)		(120.7),[b] (116.9)[c]
10[g]	1.490	1.248	1.482	119.7		120.2	120.5
	(1.486)	(1.253)	(1.478)	(120.0)		(119.0)	(118.5)
11[g]	1.498	1.251	1.463	119.5	107.0	120.6	118.3
	(1.519)	(1.252)	(1.471)	(119.9)	(105.5)	(120.8)	(118.3)
12[g]	1.486	1.254	1.457	119.6		120.9	118.3
	(1.488)	(1.253)	(1.475)	(121.6)		(120.0)	(119.0)

[a] O–CH_3—syn. [b] Cis configuration. [c] Trans configuration. [d] O–CH_3—syn, C–CH_3—syn. [e] O–CH_3—anti, C–CH_3—syn. [f] O–CH_3—anti, C–CH_3—syn, trans—C–CH_3—anti. [g] All anti conformation. [h] O–CH_3—anti, C–CH_2—syn, CH_2–CH_3—anti.

that the complexes arising from back-attack were approximately twice as stable as those arising from front-attack. However, it was not possible to find a set of parameters that reproduced the values for the O···O separations in both front- and back-attacks. In determining the final values for ϵ and r, the front-attack model was given priority over that of back-attack as it was believed that the potential associated with the former trajectory more accurately reflected the contributions arising directly from the pair potentials. Moreover, as the values of ϵ were adjusted to increase the depth of the well, the position corresponding to that of complex formation shifted toward longer O···O separations. Thus, the final values for the pair potential parameters ($\epsilon_{C,O}$ = 3.125 kcal/mol, $\epsilon_{C^+,O}$ = 5.0 kcal/mol, $r_{C^+,O}$ = 3.6 Å, and $r_{C,O}$ = 3.6 Å) represented a compromise between well depth and location. In general, each of the interactions modeled by pair potentials arose too quickly toward the asymptotic limit, with increasing O···O separations, and exhibited excessive repulsions at shorter separations. While the pair potential model did not reproduce the ab initio data as accurately as did the coulombic model, it had the advantage of being applicable to systems for which charges are not available. An improved reproduction of the potentials would be expected to occur on extending the number of pair potentials to include interactions between each atom. However, the optimization of the parameters would require a more complicated approach.

The van der Waals parameters for O^+ were determined by probing **1** with H_2 (a molecule that minimizes other energetic contributions, for example, dipole–charge interactions). The interaction energy was determined at the MP2/6-31G** level for a front-attack of H_2. The resulting interaction curve was employed to determine values of the "hardness", ϵ_{O^+}, and the van der Waals radius, r_{O^+}, that allowed the best reproduction of the ab initio data (see Figure 6). While a decrease in the van der Waals radius of O^+ relative to that of the neutral atom might have been anticipated, the best values of ϵ_{O^+} and r_{O^+} were found to be approximately 0.066 kcal/mol and 1.740 Å, respectively, in agreement with current values in MM2(87) for carbonyl oxygen atoms. In light of the charge distribution discussed above, this result is not unreasonable.

Bonded Interactions. Preliminary values for the bond stretching and angle bending force constants were determined using the standard procedure described by Hopfinger and Pearlstein.[24] Following this method, suitable model compounds were chosen and the geometric parameters of interest were distorted from their equilibrium values to generate distortion energy curves. Using a nonlinear least-squares curve-fitting algorithm, and incorporating the relevant analytical forms of the energy functions, force constants were derived for the distortion curves. However, these curves may contain energetic contributions attributable to more than one source, and consequently, the derived force constants and equilibrium parameter values are not always ideal. Consequently, we performed a refinement of these preliminary values in an iterative manner so as to best reproduce the structures of each ion. The ions chosen for examination were selected in order to provide all of the parameters necessary for performing MM2(87) calculations on cyclic oxocarbenium ions, derived from carbohydrates, as well as for a variety of simple acyclic ions. Selected bond lengths and angles predicted by ab initio and MM2(87) calculations for each of the following oxocarbenium ions are presented in Table II: **1**, *trans*-*O*-methylacetaldehydium (**2**), *cis*-*O*-methylacetaldehydium (**3**), *O*-methylacetonium (**4**), *trans*-*O*-methyl-*n*-propionaldehydium (**5**), *cis*-*O*-methyl-*n*-propionaldehydium (**6**), *O*-ethylform-

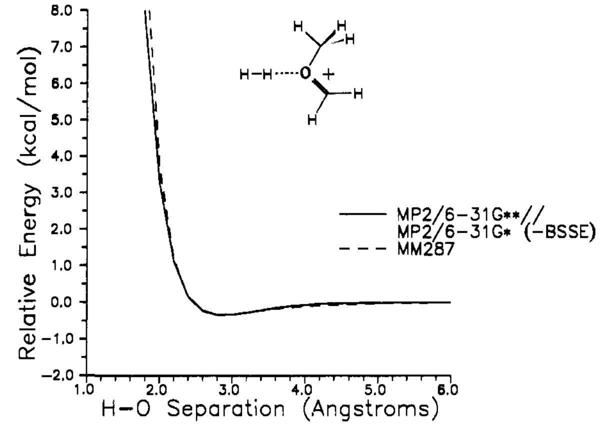

Figure 6. Calculated interaction energy between hydrogen and **1** along a front-attack pathway.

aldehydium (**7**), *O*-*n*-propylformaldehydium (**8**), *O*-(2-hydroxyethyl)formaldehydium (**9**), *trans*-*O*-methyl-2-hydroxyacetaldehydium (**10**), *trans*-*O*-(2-hydroxyethyl)acetaldehydium (**11**), and *trans*-*O*-methyl-3-hydroxypropionaldehydium (**12**); see Chart I.

An examination of the ab initio geometries presented in Table II indicated that the values of the C—C$^+$, C=O$^+$, and C—O$^+$ bond lengths depended to some extent on the degree of substitution at each end of the C=O$^+$ bond. For example, replacement of one hydrogen atom, at the carbon terminus of the C=O$^+$ bond in **1**, by a methyl group, increased the C=O$^+$ bond length, by approximately 0.012 Å. Furthermore, the transformation from **2** to **4** increased the C=O$^+$ bond length by approximately the same amount. These variations were incorporated into the MM2(87) force field through the use of an electronegativity correction term (see Table III).[27] A similar correction term was introduced for the C—O$^+$ bond, which appeared to be larger in the *O*-ethyl than in the *O*-methyl ions, by approximately 0.040 Å. Decreases in the C—C bond lengths, relative to the standard MM2(87) values, were observed in ions containing C—C—O$^+$ or C—C=O$^+$ linkages, of approximately 0.029 and 0.040 Å, respectively. Electronegativity correction terms were included in these cases. For both the C=O$^+$ and C—O$^+$ bond types, the equilibrium bond lengths (1.236 and 1.480 Å, respectively) were longer than for the corresponding C=O and C—O neutral bond types (1.208 and 1.402 Å),[7] while the stretching force constants (3.00 and 10.00 mdyn/Å, respectively) were somewhat smaller than those for the neutral bond types (5.36 and 10.80 mdyn/Å).[7]

The data in Table II indicated that the C—C=O$^+$ bond angle exhibited a rather extreme dependence on the configuration of the C=O$^+$ bond, varying from a value of approximately 120°, in trans isomers, to approximately 126° in cis isomers. Moreover, this angle appeared to be capable of further distortion depending on the orientation of the substituents in the cis conformers. This feature is illustrated in the case of the syn conformation of **6** in which the C—C=O$^+$ angle was predicted to be approximately 133°. Complementary changes in the value of the H—C=O$^+$ bond angle were observed.

The O-C-C$^+$ bond angle in **10** was predicted to have a value of approximately 105° at the MP2/6-311G** level. Whether similar angles in neutral carbonyl compounds are equally acute was not examined; however, it seems likely that in **10** electrostatic attractions are responsible for the observed value. In order to more accurately model this angle, the equilibrium value for this angle was lowered to 103° from that of 109.5°, present in MM2(87) for the corresponding angle in neutral species, while a force constant of 0.7 mdyn/Å was maintained. The new MM2(87) bending parameters led to a predicted value for this angle of approximately 106°.

The C—O=C bond angle showed relatively little variation among the oxocarbenium ions. However, the value of the O-C-C bond angle, present in ions **9** and **11**, appeared to depend on the value of the O-C-C-O$^+$ torsion angle. A torsion angle of 180° (anti) gave rise to a decrease in the value of the O-C-C bond angle, compared to conformations in which this torsion angle was 60° (gauche), of approximately 6°. In the case of the anti conformation the small value for the O-C-C angle may arise from an electrostatic attraction between the hydroxyl oxygen atom and the nearest carbon atom of the C—O=C fragment, whereas in the gauche conformation a repulsive interaction between the two oxygen atoms may be present. A torsion-bend coupling term does not exist in either MM2(87) or MM3, and consequently this angular variation has not been completely modeled.

Oxocarbenium ions exhibit a well-known coupling between the R—O=C—R′ (R, R′ = H, CH$_3$) torsion angle and the R—O=C bond angle. This feature has led to some question as to the nature of the mechanism through which the cis-trans isomerization about the C=O$^+$ bond occurs.[12b,c,13] An experimental barrier to rotation for the C=O$^+$ bond in **1** (11.9 kcal/mol),[28] determined by solution NMR, is in good agreement with an ab initio value of 12 kcal/mol, calculated at the HF/4-31G//4-31G level, for an inversion mechanism.[12b] A more extensive theoretical examination at the HF/6-31G*//MP2/6-31G* level led also to the conclusion that the stereomutation in the gas phase proceeded via inversion.[12c]

Table III. MM2(87) Force Field Parameters[a] for Oxocarbenium Ions[16]

Torsion

atom types				V_1	V_2	V_3	atoms
1	1	1	71	0.129	−0.650	0.817	C—C—C—O$^+$
6	1	1	71	−5.500	−2.500	2.000	O—C—C—O$^+$
6	1	1	70	−7.250	0.000	0.740	O—C—C—C$^+$
6	1	70	71	−3.870	5.700	0.000	O—C—C=O$^+$
1	1	71	70	−1.340	1.020	−0.900	C—C—O=C$^+$
1	1	70	71	−0.250	0.200	0.000	C—C—C=O$^+$
1	70	71	1	0.000	10.56	0.000	C—C=O—C
5	1	1	71	0.004	0.000	0.427	H—C—C—O$^+$
5	1	70	71	0.000	0.000	−0.270	H—C—C=O$^+$
5	1	71	70	0.000	0.000	−0.620	H—C—O=C
5	70	71	1	0.000	9.070	0.000	H—C=O—C

Stretching

atom types		K_s	r_0	atoms
1	71	3.0	1.480	C—O$^+$
70	71	10.0	1.236	C=O$^+$

Electronegativity Corrections

atom types				Δr_0	
1	71	1	1	0.030	(C)C—O$^+$
1	1	1	71	−0.029	(O+)C—C
70	71	70	1	0.013	(C)C=O$^+$
1	70	70	71	−0.040	C—C$^+$(O$^+$)

Bond Moments

atom types		BM	
1	71	1.900	C—O
70	71	2.800	C=O

van der Waals

atom type	ϵ	r^*	
71	0.066	1.740	O$^+$

Bending

atom types			K_b	θ_0	J^b	
6	1	70	0.700	103.0	0	O—C—C$^+$
1	1	71	0.700	104.0	0	C—C—O$^+$
1	71	70	0.800	116.0	0	C—O=C$^+$
1	70	71	0.520	113.0	1	C—C(C)=O$^+$
1	70	71	0.520	116.5	2	C—C(H)=O$^+$
5	70	71	0.710	111.0	1	H—C(C)=O$^+$
5	70	71	0.360	117.0	2	H—C(H)=O$^+$
5	1	71	0.350	102.8	0	H—C—O$^+$

Out-of-Plane Bending

atom types		K_{oop}	
70	71	1.569	C=O$^+$

Heat of Formation

atom types		BE	
1	71	56.84	C—O$^+$
70	71	113.69	C=O$^+$

[a] Units are as follows: bond lengths (Å), angles (deg), K_s (mdyn/Å), K_b and K_{oop} (mdyn/(Å rad^2)), BM (D), ϵ (kcal/mol)^2, BE (kcal/mol). [b] For positive "*J*" values *J* − 1 indicates the number of hydrogen atoms attached to the central atom; if *J* = 0, the bending constants are applied to all of the relevant angles, regardless of the degree of substitution; see ref 7.

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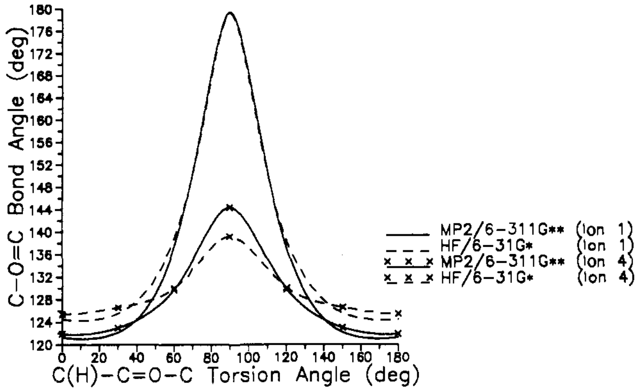

Figure 7. Variation in the C—O═C angle as a function of rotation about the C═O bond in **1** and **4**.

However, in the latter study the calculated barrier to inversion (17.5 kcal/mol) was in poor agreement with the experimental values (10–14 kcal/mol), and it was noted that the experimental value exhibited a significant dependence on the composition of the solution medium. Furthermore, those researchers concluded that solvation effects would act to lower the barrier to rotation and raise the barrier to inversion, and that in the solution phase the stereomutation would occur via rotation. Our results for the stereomutation of **1–4** indicated that the extent to which the C—O═C angle distorted toward linearity depended on the degree of substitution at the carbon terminus of the $C{=}O^+$ bond. In agreement with previous results,[12] the stereomutation of **1** was predicted to proceed through a linear transition state (see Figure 7). However, the transition states for the stereomutation of **2** or **3** and **4** displayed increasingly nonlinear C—O═C angles having values of 177.4°, 177.4°, and 144.3°, respectively. On the basis of these results, it appeared that a mechanism, intermediate between that of rotation and inversion, was favored in the gas phase for larger oxocarbenium ions.[29] Moreover, the solution-phase reaction may be expected to proceed through a rotational mechanism.[12c] It is noteworthy that similar energy barriers were predicted for the stereomutations of **1–4**. The geometries of **1–4** were optimized at the MP2/6-311G** level, and conformational relative energies were evaluated at the same level as well as at the HF/6-311++G** level. The barriers to the stereomutation of **1–4** calculated at the MP2 level (22.3, 21.5, 24.0, and 22.9 kcal/mol, respectively) were higher, by approximately 5 kcal/mol, than those calculated at the HF level (17.4, 17.0, 19.7, and 18.0 kcal/mol, respectively). As noted,[12c] the MP2 approximation overestimates the stabilization arising from π-interactions, and consequently, may be expected to lead to excessive barriers to stereomutation about the $C{=}O^+$ bond. We chose to derive parameters for the C—O═C—R (R = H, CH_3) torsion angles based on the HF results (see Figure 7).

Despite the successful application of semiempirical molecular orbital methods in the evaluation of structural and electronic properties of both neutral and protonated sugars,[30] neither the angular nor the energetic variations associated with the stereomutation were accurately reproduced at the AM1 semiempirical level.[31] The values for the C—O═C angles and the associated activation energies as predicted by AM1 for the stereomutations of **1–4** were the following: **1** (131.5°, 26.5 kcal/mol), **2** (122.4°, 22.0 kcal/mol), **3** (122.4°, 22.3 kcal/mol), **4** (120.0°, 20.0 kcal/mol).

As discussed above, a torsion-bend coupling term is lacking in the MM2(87) force field, and consequently, a strictly rotational model for the mechanism of stereomutation is predicted by MM2(87). However, in cyclic oxocarbenium ions derived from carbohydrate systems, the R—O═C—R′ torsion angle is constrained by the ring to a narrow range of allowable values. Moreover, an examination of Figure 7 indicated that torsional deviations of up to 60° may occur with little distortion of the C—O═C angle.

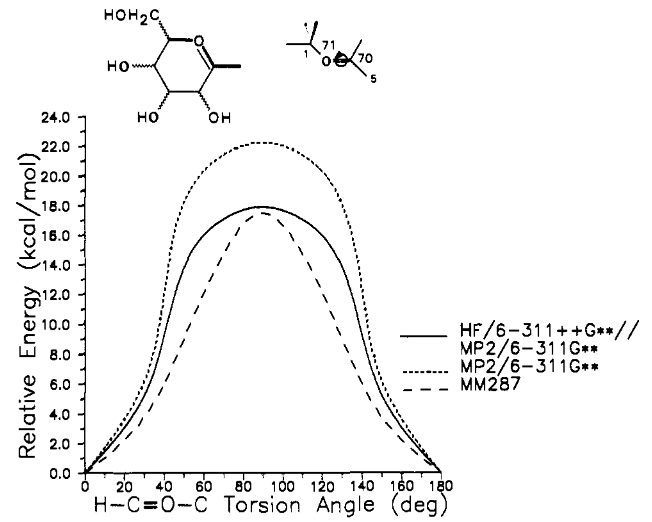

Figure 8. Potential energy as a function of rotation about the H—C═O—C torsion angle in **1**.

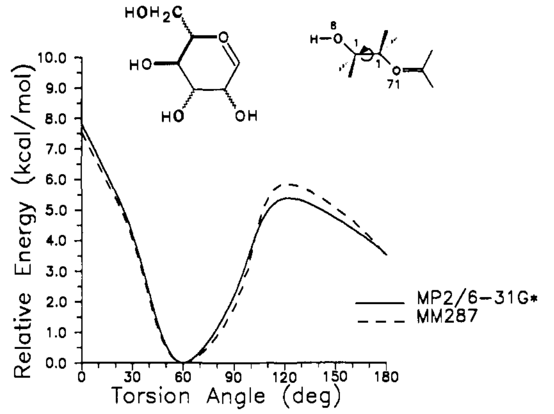

Figure 9. Potential energy as a function of rotation about the O–C–C–O^+ torsion angle in **9**.

In most molecular mechanical calculations,[32] torsional potentials are modeled by parameters acting on the 1–4 relationship between the atoms defining the torsion angle.[33] In the development of a force field for cyclic oxocarbenium ions derived from carbohydrates, it was necessary to provide a means through which the interactions between hydroxyl groups located on carbon atoms C-2, C-3, and C-4 of the oxocarbenium ring and the atoms carrying the positive charge could be reproduced. We have discussed above two methods for modeling similar nonbonded interactions. Such methods could in principle be employed in the case of atoms that bear a 1–4 relationship to one another. However, in the case of hydroxyl substituents on C-2, C-3, or C-4, the interactions could be modeled through the incorporation of parameters for three types of linkages, namely, for the O—C—C—O^+, O—C—C═O^+, and O—C—C—C^+ torsion angles. The former approach has one noteworthy disadvantage. Within the MM2 series of programs, 1–3 nonbonded interactions (Urey-Bradley terms) are not included.[34] The omission of such terms,

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(30) (a) Woods, R. J.; Szarek, W. A.; Smith, V. H., Jr. *J. Chem. Soc., Chem. Commun.* **1991**, 334–337. (b) Fraser-Reid, B.; Wu, Z.; Andrews, C. W.; Skowronski, E.; Bowen, J. P. *J. Am. Chem. Soc.* **1991**, *113*, 1434–1435.

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(32) For a recent example of a nonbonded approach to the incorporation of 1–4 interactions in molecular mechanical calculations, see: Dinur, U.; Hagler, A. T. *J. Comput. Chem.* **1990**, *11*, 1234–1246.

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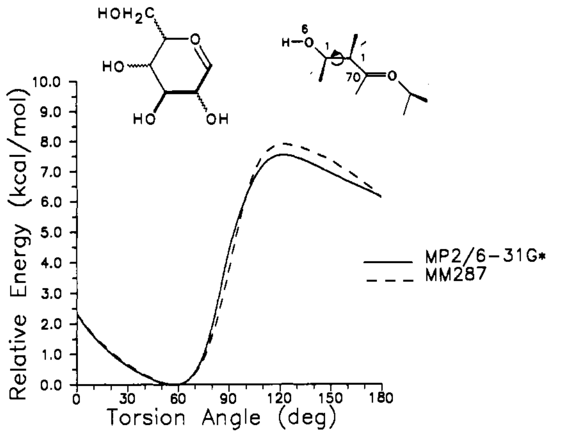

Figure 10. Potential energy as a function of rotation about the O–C–C–C^+ torsion angle in **12**.

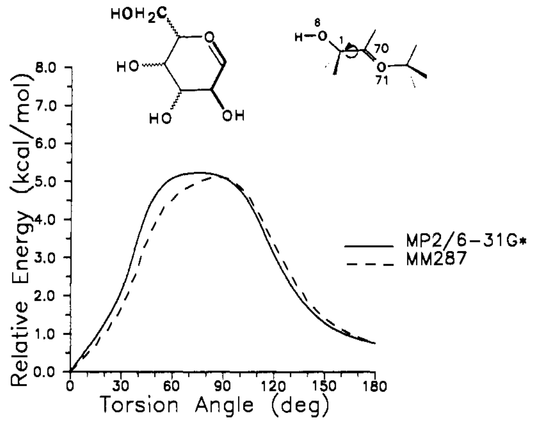

Figure 11. Potential energy as a function of rotation about the O—C—C=O^+ torsion angle in **10**.

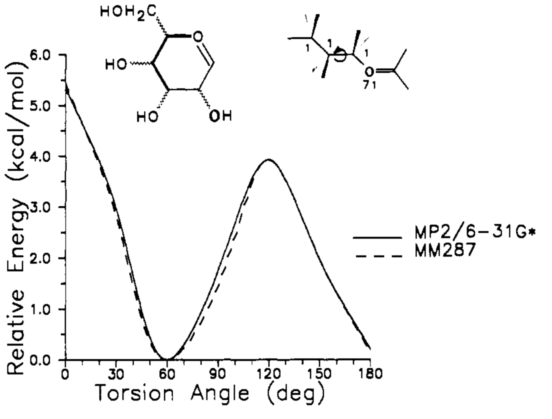

Figure 12. Potential energy as a function of rotation about the C–C–C–O^+ torsion angle in **8**.

in this case, would lead to the omission of certain significant stabilizing interactions. Specifically, the interaction between the hydroxyl oxygen atom at C-2 and the carbonyl-type carbon atom (C-1) would not be calculated, whereas the analogous interactions involving hydroxyl substituents at C-3 or C-4 would be included. In order to avoid these complications, we chose to include parameters for the O—C—C—O^+, O—C—C=O^+, and O—C—C—C^+ angles.

The torsional parameters were determined through an iterative fitting of the MM2(87) parameters to the rotational barriers determined at the MP2/6-31G* level for the relevant torsion angles in each of **1**–**12**. The ab initio and MM2(87) results for several torsion angles are illustrated in Figures 8–14. In agreement with previous calculations,[11b] *O*-methyl group rotation was predicted to lead to significant differences in the energies of the conformers, with the syn orientation being preferred over the gauche, by approximately 1.1 kcal/mol. Similar rotational energy profiles were found for methyl groups attached to the carbon terminus of the C=O^+ bond, with the syn orientation being preferred over the gauche, by approximately 1.6 kcal/mol.

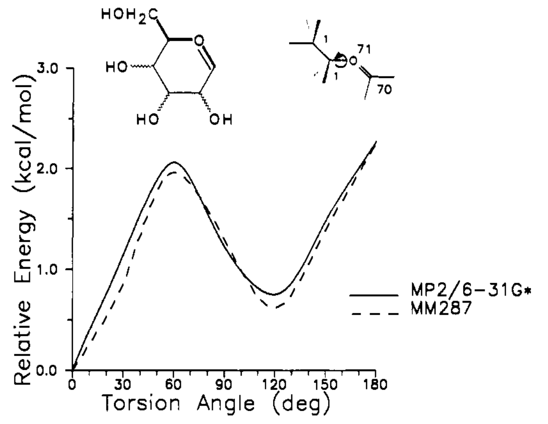

Figure 13. Potential energy as a function of rotation about the C—C—O=C^+ torsion angle in **7**.

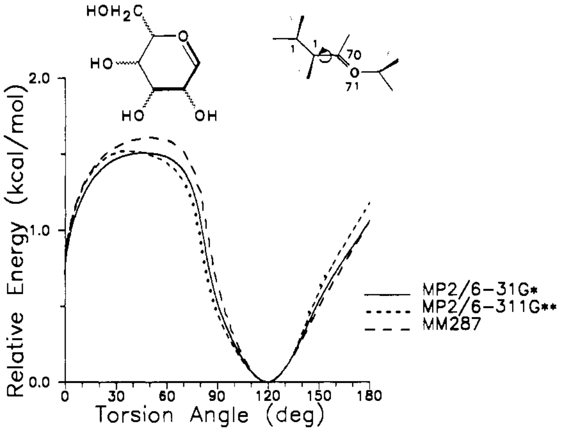

Figure 14. Potential energy as a function of rotation about the C—C—C=O^+ torsion angle in **5**.

Rotation about the C—C^+ bond in **5** indicated the presence of minima corresponding to C—C—C=O^+ torsion angles of 0° and 120°, with the latter favored over the former, by approximately 0.75 kcal/mol (see Figure 14). An analogous result was obtained for rotation about the C—O^+ bond in **7** (see Figure 13). However, in **7** the C—C—O=C^+ torsion angle preferred the 0° orientation over that at 120°, by approximately 0.75 kcal/mol. These results may be compared to the corresponding torsional preferences for ketones and aldehydes, where the C—C—C=O torsion angle exhibits energy minima at 0° and 120°, with the syn orientation being favored by approximately 1.0 kcal/mol.[35] Extension of the hydrocarbon chain of **5** to generate **8** led to a structure in which minimum energy orientations of the C—C—C—O^+ torsion angle were found at 60° and 180°, with only a slight preference for the former.

As discussed above, the rotational energy profiles for torsion angles O—C—C—O^+, O—C—C—C^+, and O—C—C=O^+, in **9**, **12**, and **10**, respectively, were parametrized with no explicit inclusion of electrostatic effects. The ab initio potentials for rotation about these angles are presented in Figures 9–11. The rotational energy profile for **9** indicated that the O—C—C—O^+ torsion angle preferred a gauche over an anti orientation, by approximately 3.5 kcal/mol. This value represented an enhancement of the gauche effect,[36] observed in molecules containing the O—C—C—O linkage, of approximately 2.5 kcal/mol.[37] As

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Table IV. MM2(87) and Experimental Heats of Formation[a] for **1–8**

oxonium ion	MM2(87) total energy	MM2(87) ΔH_f	exptl ΔH_f
1	1.09	158	158[c]
2[b]	2.31	149	133,[c] 150[d]
3[b]	4.81	151	133,[c] 150[d]
4	6.66	142	114,[c] 140[e]
5[b]	4.14	142	141[e]
6[b]	6.50	145	141[e]
7	1.22	151	144,[c] 153,[d] 148[e]
8	1.75	145	143[e]

[a] kcal/mol. [b] Experimental values did not differentiate between the cis and trans isomers. [c] See ref 12a. [d] See ref 39. [e] See ref 40.

the magnitude of the gauche effect increases proportionally with the electronegativity of the heteroatoms, the enhancement observed for the ionic species may arise largely from electrostatic interactions.

The O–C–C–C$^+$ torsion angle in **12** displayed an analogous preference for a gauche orientation. However, in the case of **12**, the gauche was preferred over the anti orientation, by approximately 7.5 kcal/mol. Presumably, the higher stabilization of the gauche orientation in **12** arises from an enhanced electostatic interaction between the oxygen and carbonyl-type carbon atom. Furthermore, it is noteworthy that the syn orientation of the O–C–C–C$^+$ torsion angle in **12** is more stable than the corresponding orientation of the O–C–C–O$^+$ angle in **9**, by approximately 5 kcal/mol.

In the case of **10**, the minima predicted for the syn and anti orientations of the O—C—C=O$^+$ torsion angle were separated by a 2-fold barrier to rotation of approximately 5 kcal/mol, with the former conformation predicted to be more stable than the latter, by approximately 0.75 kcal/mol. A 2-fold barrier to rotation indicated the presence of hyperconjugation between the hydroxyl oxygen atom and the carbonyl-type carbon atom, in agreement with the charge distributions discussed above. In the related species (hydroxyethyl)carbenium ion, hyperconjugation has been reported to lead to a similar rotational profile, with a barrier height of 7.67 kcal/mol.[38]

Heats of Formation. Much of the experimental evidence for oxocarbenium ions arises from the results of mass spectroscopic investigations, and in many cases, the ionic heats of formation have been reported.[12a,39,40] Within MM2(87) a heat of formation calculation may be performed by assigning enthalpy corrections to bond types (BE's) or functional groups, and by applying an additivity rule of the type shown in eq 3, where E_s is the total steric energy, POP and TOR are population and torsional correction terms that approximate the effects arising from the presence of higher energy conformers, and TR is a constant representing the combined translational and rotational energy contributions.[41] An enthalpy correction term for the C—O=C fragment was derived in such a way that the calculated heat of formation of **1** reproduced the experimental value (158 kcal/mol).[12a] As it is not possible to incorporate new functional group heats of formation into MM2(87), the enthalpy correction term was divided arbitrarily between the C—O$^+$ and C=O$^+$ bonds. Both POP and TOR were assigned values of zero. The calculated and experimental heats of formation for ions **1–8** are presented in Table IV. The overall agreement between the calculated and experimental values is within approximately 4 kcal/mol. It is noteworthy that, in the cases of ions **2–4**, where several different experimental values have been reported, the MM2(87) value is in close agreement with only one of the experimental values. In mass spectroscopic experiments it is not always possible to determine whether the ion has undergone a rearrangement prior to being detected, and this may lead to incorrect assignments. It is hoped that the new heat of formation parameters for MM2(87) may be of assistance in such circumstances.

$$\Delta H_f = E_s + \sum \mathrm{BE} + \mathrm{POP} + \mathrm{TOR} + \mathrm{TR} \qquad (3)$$

Conclusions

The MM2(87) force field has been extended to include parameters that reproduce the structural features and conformational preferences, as predicted by high-level ab initio calculations, of a series of acyclic oxocarbenium ions. Heat of formation parameters for these ions have been introduced, and the calculated heats of formation have been compared to experimental values. We have shown that the effects of nonbonded electrostatic interactions, between electronegative substituents, and the atoms carrying partial positive charges in the ions, may be incorporated implicitly into torsional parameters. Moreover, alternative methods for the explicit incorporation of nonbonded interactions between solvent molecules and oxocarbenium ions have been proposed and evaluated.

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