

Negative Chemical Ionization of Alcohols

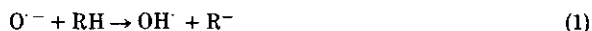
by R. Houriet,* D. Stahl,* and F. J. Winkler†

Reactions of the oxygen radical anion at low pressure (ICR conditions) with aliphatic alcohols are seen to give a limited number of product anions which allows for unambiguous determination of the structure of the neutral. The reactions of OH^- are also investigated and mechanisms of reactions are discussed. Analytical application of NCI is also considered.

OH^- negative chemical ionization mass spectra, negative metastable ion spectra, and negative collisional activation spectra (negative product from negative precursor ions) have been applied to stereochemical problems of cyclic diols. The spectra of the *cis* and *trans* isomers of 1,3- and 1,4-cyclohexanediols and 1,2-cyclopentanediols show substantial and characteristic differences. The $(\text{M-H})^-$ alkoxide anions produced by OH^- reagent ions are stabilized for the *cis* isomers by formation of an intramolecular hydrogen bridge involving both oxygen functions. However, *trans* geometry of the $(\text{M-H})^-$ ions is indicated by abundant $(\text{M-H}_2)^-$ and/or $(\text{M-H-H}_2\text{O})$ fragment ions. The stereospecificity increases with ion internal energy (high temperature, collisional activation) or especially with ion life times (metastable ions). It is shown that in F^- negative chemical ionization the relative intensities of the fluoride attachment ions MF^- and of the proton abstraction ions $(\text{M-H})^-$ reflect the stereochemistry of the cyclic diols. The results demonstrate the potential of negative ion mass spectrometry for stereochemical investigations.

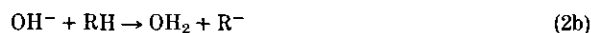
ICR Study of the Negative Chemical Ionization of Alcohols

Negative chemical ionization (NCI) is a fast growing technique in the field of analytical mass spectrometry (1). In a recent publication by Smit and Field (2), the potential use of high pressure NCI in analytical chemistry has been demonstrated. In these studies, mixtures of N_2O with various bath gases were used to generate the O^- and OH^- reactant ions. The oxygen radical anion is easily formed by dissociative electron attachment to neutrals such as N_2O , O_2 , CO_2 , (1). O^- may react with the appropriate neutral RH in a proton transfer process, [Eq. (1)]:



or by hydrogen atom transfer to form the hydroxyl anion that can in turn react with the RH

molecule in a proton transfer process [Eq. (2)]:



The use of O^- (and consequently of OH^-) as reactant ion is dictated by the relative ease of its formation from N_2O and also because of its relatively high proton affinity [$\text{PA}(\text{O}^-) = 1594 \text{ kJ/mole}$ and $\text{PA}(\text{OH}^-) = 1628 \text{ kJ/mole}$], thus resulting in efficient proton transfer reaction from most organic molecules. It was of interest to us that the O^- and OH^- ions react with alcohols to form a limited number of specific product anions (2). This is in contrast to the positive ion chemistry of alcohols in which most of the structural information related to the original molecule is lost in the course of either the unimolecular or the bimolecular reactions of ions derived from alcohols; typical examples will be briefly enumerated here.

In the positive ion mass spectra, the hydrocarbon ions predominate as the chain length increases, thus obscuring the typical alcohol fragmentation behavior (3). The intensity of the

* Institut de chimie physique, EPFL, CH-1015 Lausanne, Switzerland.

† Institut für Chemie Weihenstephan, TU München, D-8050 Freising, Federal Republic of Germany.

molecular ion is always low or not detectable in tertiary alcohols.

In positive ion CI conditions (4), the first reaction step is a proton transfer to the alcohol followed by rapid loss of a water molecule to form an alkyl ion. The decomposition reactions of the latter involves a substantial scrambling of the hydrogen and of the carbon atoms (5), in which the structural information on the original molecule is lost. Partial information on the structure of aliphatic alcohols may be obtained in more sophisticated CI experiments with protonated acetone and protonated acetaldehyde (6) or NO^+ (7) as reagent ions.

In this work, we have used ion cyclotron resonance (ICR) to study the details of the reactions occurring between aliphatic alcohols and the ions present in the NCI conditions. ICR has been proven to be a powerful tool for simulating the high-pressure conditions (8, 9); moreover, the use of double resonance techniques permits to identify the reaction sequences and product distribution resulting from the different reactant ions. A number of deuterated alcohols were also used.

Experimental

The ICR spectrometer used in this study was equipped with a four-section cell and marginal oscillator detection (5).

Formation of OH^- . The hydroxylanion was formed from water by dissociative attachment of electrons accelerated at about 6.5 V (uncalibrated value), which in a first step produces H^- that rapidly reacts with water (10), according to the reaction sequence (3):

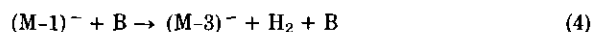


Formation of O^- . The oxygen radical anion was formed from pure N_2O under the conditions described above. It is known that under these conditions, O^- is formed with an average 0.38 eV kinetic energy (11). In all experiments, the electrons were ejected from the reaction region of the ICR cell by applying a continuous radiofrequency of about 8MHz.

Samples. Mixtures of the alcohol with either H_2O or N_2O were introduced via the dual inlet system at a total pressure between 10^{-5} and 10^{-4} Torr (uncorrected reading). The following deuterated alcohols were used: methanol- d_1 , 1-butanol-1- d_2 ; 1-butanol-3,4- d_5 ; 2-propanol-1,3- d_6 , 2-butanol-2- d_1 , and 2-butanol-1,3- d_5 .

Results and Discussion

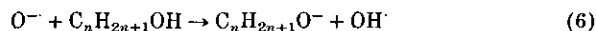
Reaction of OH^- . The reaction of OH^- with an aliphatic alcohol is known to consist of a proton transfer to the hydroxyl anion to form an alkoxide anion (12). When OH^- was formed according to reaction (3) and made to react with alcohols (M), we found that in addition to the alkoxide anion product $(\text{M} - 1)^-$, a $(\text{M} - 3)^-$ product was also formed. These results are reported in Table 1. From thermochemical data (13-15), it can be deduced that the loss of H_2 from an alkoxide anion is a quite endothermic process ($\Delta H_f = 35 - 40$ kJ/mole). On the other hand, the proton affinities of alkoxide anions lie at 1560 ± 5 kJ/mole. Therefore the formation of alkoxide anions by reaction of OH^- with alcohols is exothermic by about 68 kJ/mole. Part of this excess energy may be available to drive the endothermic loss of molecular hydrogen. The present results indicate that the $(\text{M} - 3)^-$ formation is quite a specific process involving the loss of one hydrogen atom from the α and one hydrogen atom from the β position with respect to the hydroxyl group. Pressure and time dependence experiments now in progress indicate that the formation of $(\text{M} - 3)^-$ is a collisionally induced decomposition of the alkoxide anion according to reaction (4):



Reaction of O^- . The reaction of O^- with primary alcohols yields three types of ions (Table 2). Firstly OH^- is formed in an abstraction reaction from the hydroxylic hydrogen atom:



The second reaction is a proton transfer reaction (6):



The formation of the alkoxide anion involves the transfer of the hydroxylic proton to O^- as indicated by the results of the labeling. Reaction

Table 1. Product distribution in the reaction of OH^- with alcohols (M).

M	$(\text{M} - 1)^-$	$(\text{M} - 3)^-$	$(\text{M} - 4)^-$
$\text{C}_4\text{H}_9\text{OH}$	100	6	
<i>i</i> - $\text{C}_4\text{H}_9\text{OH}$	100	5	
$\text{C}_2\text{H}_5\text{CHOHCH}_3$	100	6	
$\text{CH}_3\text{CD}_2\text{CHOHCD}_3$	100		12
$\text{C}_2\text{H}_5\text{CDOHCH}_3$	100		6
<i>t</i> - $\text{C}_4\text{H}_9\text{OH}$	100		
$\text{C}_3\text{H}_7\text{COH}(\text{CH}_3)\text{C}_2\text{H}_5$	100		

Table 2. Product distribution in the reaction of O^- with primary alcohols (M).

M	(M-1) ⁻	(M-2) ⁻	(M-3) ⁻	(M-4) ⁻
CH ₃ OD		100		
C ₄ H ₉ OH	100		37	
<i>i</i> -C ₄ H ₉ OH	100		43	
C ₃ H ₇ CD ₂ OH	100			58
C ₂ D ₅ C ₂ H ₄ OH	100		72	

(6) is the predominant process with all primary alcohols.

A third product, (M - 3)⁻, is formed from all alcohols except from methanol. The labeled compounds show that the formation of this ion involves the loss of two hydrogen atoms from the alkoxide anion, viz. one H from the α and one H from the β position with respect to the hydroxyl group.

O^- reacts with secondary alcohols (Table 3) to form the same type of ions as with primary alcohols. Besides the (M - 3)⁻ ion, a series of lower homologs (M - 17)⁻, (M - 31)⁻, etc., is observed, where it is now the alkyl group in the α position which is lost along with one H atom in the β position. This is substantiated by the results obtained both with the deuterated samples of butanol-2 and with the 3,3-dimethylbutanol-2, in which no (M - 17)⁻ product is formed due to the absence of an H atom in the β position of the *tert*-butyl group.

The formation of the $C_nH_{2n-1}O^-$ product is not observed with the tertiary alcohols (Table 4) since no α hydrogen atom is available, but a large increase in the intensity of lower homolog ions is observed.

Reaction Mechanism

The most striking difference in the reaction of O^- with aliphatic alcohols as compared to the reaction of OH^- , is the formation of fragment ions. Given the fact that the formation of the alkoxide anion is more exothermic by about 33 kJ/mole when OH^- rather than O^- reacts with the alcohol

(13-15), these facts seem difficult to reconcile. An explanation is provided by the reaction mechanism proposed in the scheme shown as Eq. (7). The first step of the reaction consists of the addition of the reacting base to the hydroxylic group of the alcohol to form the addition complex I. Following an internal shift of a hydrogen atom which results in a significant gain in internal energy, the resulting intermediate II decomposes by losing a hydrogen atom (or an alkyl radical) and a water molecule to form the $C_nH_{2n-1}O^-$ ($C_kH_{2k-1}O^-$) product ($k < n$). The overall reaction results in the elimination of the hydroxyl and the hydrogen atoms to form water and the loss of an α hydrogen atom (or an alkyl group), in accordance with our labeling experiments. On the other hand, when OH^- adds to alcohol to form the intermediate I' [Eq. (8)] the latter can only lose a water molecule to form the alkoxide anion.

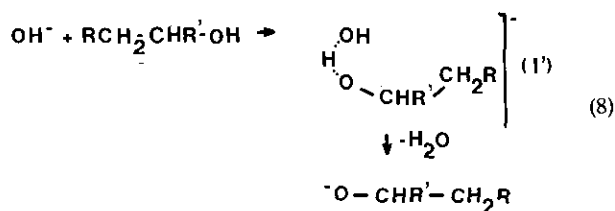
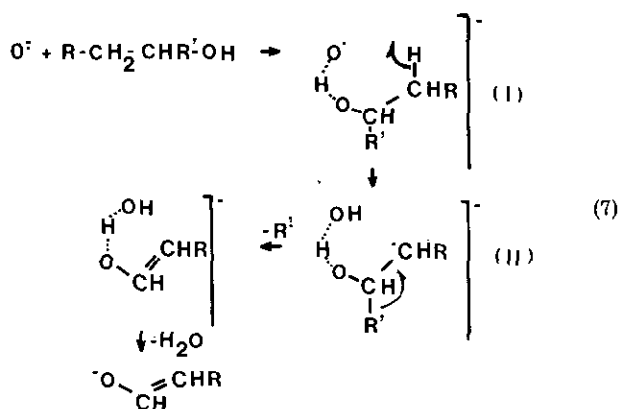


Table 3. Product distribution in the reaction of O^- with secondary alcohols M.

M	(M-1) ⁻	(M-3) ⁻	(M-4) ⁻	(M-6) ⁻	(M-17) ⁻	(M-19) ⁻	(M-21) ⁻	(M-31) ⁻	(M-34) ⁻	(M-45) ⁻	(M-59) ⁻
CH ₃ CHOHCH ₃	100	21	2		34	1					
C ₂ H ₅ CHOHCH ₃	100	27			23				58		
<i>i</i> -C ₃ H ₇ CHOHCH ₃	100	13			22					48	
<i>t</i> -C ₄ H ₉ CHOHCH ₃	100	26									14
CD ₃ CHOHCD ₃	100		22	2			32				
C ₂ H ₅ CDOHCH ₃	100		36		41			59			
CD ₃ CD ₂ CHOHCD ₃	100		21				26		29		

Table 4. Product distribution in the reaction of O^- with tertiary alcohols M.

M	(M-1) ⁻	(M-17) ⁻	(M-31) ⁻	(M-45) ⁻
<i>t</i> -C ₄ H ₉ OH	59	100		
C ₃ H ₇ COH(CH ₃)C ₂ H ₅	77	79	100	87

Analytical Application

The present work shows that NCI conditions are especially well suited to the problem of identification of alcohols. On one hand, the OH^- reactant ion yields essentially the $(M-1)^-$ product ion thus permitting the analysis of mixtures of alcohols. On the other hand, the O^- reactant ion yields $(M-1)^-$ ion and fragment ions which allow for the structural elucidation of alcohols. From our results we can establish a set of simple rules: (1) Primary alcohols form the $(M-1)^-$ and the $(M-3)^-$ ions. (2) Secondary alcohols $R_1-CH_2-CHOH-CH_2-R_2$ form $(M-1)^-$, $(M-3)^-$, $R_1-CH=CHO^-$ and $R_2-CH=CHO^-$ ions. The formation of the latter two ions requires the presence of a hydrogen atom in the β position with respect to the hydroxyl group. (3) Tertiary alcohols differ from secondary alcohols only by the absence of the $(M-3)^-$ product.

Some limitations to this analytical approach can be foreseen, as for instance its inability to distinguish between, e.g., *n*-propyl and isopropyl groups. This work emphasizes the use of NCI as an analytical technique for a wide range of classes of organic compounds (1).

Stereochemical Effects on Anion Mass Spectra of Cyclic Diols

From the above section it is seen that gaseous alkoxide anions can provide conclusive mass spectrometric molecular weight and structural information in the alcohol series.

In contrast to the importance of stereo-chemis-

try in positive ion mass spectrometry (16-18), there are no detailed and systematic investigations on the stereochemistry of gas phase anions (19). This also applies to the class of cyclic alcohols, especially diols, which are model compounds of natural products. The observations of dimeric $(M_2-H)^-$ alkoxide ions (20-22) indicated to us that stereochemical studies, based on intramolecular hydrogen bridge effects in diol mass spectra (23-28), might be extended from the cationic species MH^+ and M^+ to the anionic species $(M-H)^-$. Gas phase anion techniques have been used to screen for stereochemical effects in the series of cyclohexane diols and related compounds.

Experimental

The spectra were recorded on a ZAB-2F double focusing, reverse geometry instrument equipped with a combination EI/CI source. A N_2O/CH_4 mixture was used to generate OH^- reagent ions (2). The reagent gas pressure was 0.5 Torr. At ~3% N_2O in CH_4 , the optimum yield of OH^- was was was was was obtained (70% OH^- , 30% O^-). The diol spectra seemed to be insensitive to the O^- reactant ions constantly present under our conditions. Negative collisional activation (NCA) spectra, corrected for negative metastable ion (NMI) contributions, were obtained at a helium pressure which reduced the precursor ion intensity to one third of its original value.

OH^- Negative Chemical Ionization. The spectra of configurational isomers of cyclic diols show substantial and characteristic differences (Table 5). The alcoholate anions, $(M-H)^-$, are stabilized for *cis* isomers by intramolecular hydrogen bridge formation (*cis* I to *cis* III). However, *trans* geometry of the $(M-H)^-$ ions does not permit transannular hydroxyl interaction and consequently is indicated by abundant $(M-H_3)^-$ [and/or $(M-H-H_2O)^-$] fragment ions, decomposition products typical of anion mass spectra of primary and secondary monoalcohols. A similar hydrogen bridge stabilization effect is well known for the

Table 5. Partial OH^- NCI spectra of cyclic diols (% Σ_{40}).

M ^a	80-140°C			210-240°C		
	(M-H) ⁻	(M-H ₃) ⁻	(M-H-H ₂₀) ⁻	(M-H) ⁻	(M-H ₃) ⁻	(M-H-H ₂₀) ⁻
<i>cis</i> -I	94	0.9	1.2	95	0.7	1.5
<i>trans</i> -I	68	24	0.9	34	57	0.6
<i>cis</i> -II	81	7	2	82	4	4
<i>trans</i> -II	61	6	12	50	11	20
<i>cis</i> -III				82	3	
<i>trans</i> -III				37	56	

^a I = 1, 3-cyclohexanediol; II = 1, 4-cyclohexanediol; III = 1, 2-cyclopentanediol.

Table 6. Partial NCA and NMI spectra of (M-H)⁻ ions from cyclic diols.

	NCA (% Σ_{40})			NMI (% Σ_{40})	
	(M-H) ⁻	(M-H ₃) ⁻	(M-H-H ₂₀) ⁻	(M-H) ⁻	(M-H ₃) ⁻
<i>cis</i> -I	96.5	0.06	3.1	99.0	0.02
<i>trans</i> -I	89.4	8.2	1.2	96.1	3.8

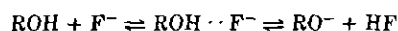
MH⁺ species in positive CI spectra of cyclic *cis*-amino alcohols (24) and *cis*-diols (25).

In NCI, high ion source temperatures around 220°C are obviously more favorable for assignment of the diol configuration than lower temperatures, contrary to positive CI. Thus NCI seems to be promising for stereochemical analysis of natural products which show excessive fragmentation in positive CI spectra.

Negative Collisional Activation (NCA). The difference for the configurational isomers (Table 6) is increased strongly regarding the ratio for the (M-H₃)⁻ product peaks, even compared to the high temperature NCI spectra. Additional peaks with structural information also become more significant.

Negative Metastable Ion (NMI) Spectra. Metastable (M-H)⁻ parent ions with little excess energy are highly sensitive to stereospecific reactions having low activation energy requirements. The intramolecular hydrogen bridge stabilization effect in the spectra of the *cis* isomers becomes maximized (Table 6).

F⁻ Negative Chemical Ionization (NCI). Fluoride F⁻ reactant ions were produced by using CHF₃ reagent gas. The reaction scheme for ROH substrates is:



The gas phase proton affinities of F⁻ (1548 kJ/mole) and secondary alcoholate anions (e.g., Me₂HCO⁻, 1565 kJ/mole) are nearly the same. Thus for the *trans* isomers of cyclic diols (Table 7), the base peak is formed by fluoride attachment ions, MF⁻. However, *cis* isomers with higher acidity due to intramolecular anion solvation, give (M-H)⁻ proton abstraction ions as base peak. In

Table 7. Partial F⁻ NCI spectra of cyclic diols. (% Σ_{40} ; 140°C).

	(M-H) ⁻	MF ⁻	(M ₂ -H) ⁻	M ₂ F ⁻
<i>cis</i> -I	59	7	28	0.6
<i>trans</i> -I	24	47	15	3
<i>cis</i> -II	90	7	2	
<i>trans</i> -II	33	56	6	0.7

this approach proton transfer equilibria are used to probe alcohol acidities related to the diol geometry. (In any of the dimeric M₂F⁻ ions, independent of stereochemistry, intermolecular anion solvation supports proton transfer).

These examples demonstrate the potential of negative ion mass spectrometry for the identification of stereoisomers. A larger variety of compounds has to be investigated to obtain more information about the analytical utility of stereochemical effects on anion mass spectra.

The financial support of the Fonds National Suisse de la Recherche Scientifique is gratefully acknowledged.

REFERENCES

- Jennings, K. R. Negative chemical ionization mass spectrometry. In: Mass Spectrometry (Specialist Periodical Reports, vol. 4), R. A. W. Johnstone, Ed., The Chemical Society London (1977).
- Smit, A. L. C., and Field, F. H. Gaseous anion chemistry. Formation and reactions of OH⁻; reactions of anions with N₂O; OH⁻ negative chemical ionization. J. Am. Chem. Soc. 99: 6471 (1977).
- Budzikiewicz, H., Djerassi, C., and Williams, D. H. Mass Spectrometry of Organic Molecules, Holden-Day, San Francisco, 1967.
- Field, F. H. Chemical ionization mass spectrometry. XII Alcohols. J. Am. Chem. Soc. 92: 2672 (1970).
- Houiet, R. and Gäumann, T. An ICR study of the reactions of CH₅⁺ and C₂H₅⁺ with *n*-hexane labelled with ¹³C. Int. J. Mass Spectrom. Ion Phys. 28: 93 (1978).
- Hunt, D. F., and Ryan III, F. J. Chemical ionization mass spectrometry studies. I. Identification of alcohols. Tetrahedron Letters, 1971. 4535
- Hunt, D. F., and Sethi, S. K. Analytical applications of positive and negative ion chemical ionization mass spectrometry. In: High Performance Mass Spectrometry: Chemical Applications. M. L. Gross, Ed., American Chemical Society, Washington, D.C., 1978.
- Hunter, R. L., and McIver, R. T. Mechanism of low-pressure chemical ionization mass spectrometry. Anal. Chem. 51: 699 (1979).
- Houiet, R., and Gäumann, T. Studies in the chemical ionization of hydrocarbons. In: Ion Cyclotron Resonance Spectrometry, H. Hartmann and K. P. Wanczek, Eds., Springer Verlag, 1978.
- Stockdale, J. A. D., Compton, R. N., and Reinhardt, P. W. Studies of negative-ion-molecule reactions in the energy region from 0 to 3 eV. Phys. Rev. 184: 81 (1969).
- Chantry, P. J. Temperature dependence of dissociative attachment in N₂O. J. Chem. Phys. 51: 3369 (1969).
- Braumann, J. I., and Blair, L. K. Gas phase acidities of alcohols. J. Am. Chem. Soc. 92: 5986 (1970).
- Hotop, H., and Lineberger, W. C. Binding energies in atomic negative ions. J. Phys. Chem. Ref. Data 4: 539 (1975).
- Bowers, M. T., Ed. Gas phase ion chemistry. Academic Press, New York, 1979.
- Rosenstock, H. M., Draxl, K., Steiner, B. W., and Herron, J. T. Energetics of gaseous ions. J Phys. Chem. Ref. Data, 6:786 (1977).
- Green, M. M. Mass spectrometry and stereochemistry of organic molecules. Topics Stereochem. 9: 35 (1976).

17. Mandelbaum, A. D. In: *Handbook of Stereochemistry*, H. Kagan, Ed. Thieme Verlag, Stuttgart, 1977.
18. Zaretskii, Z. v. *Mass Spectrometry of Steroids*. Halsted Press, Wiley, New York, 1976.
19. Baltina, L. A., Falko, V. S., Khvostenko, V. I., and Tolstikov, G. A. Mass spectrometry of negative ions and the stereochemistry of organic compounds. III. Methyl pentose and hexo-pyranoside methyl ethers. *Zh. Obshch. Khim. SSSR*. 47: 2379 (1977).
20. von Ardenne, M., Steinfelder, K., and Tümmeler, R. Elektronen-anlagerungsmassenspektrographische Untersuchungen von höheren Alkoholen und Fettsäuren, *Z. Physik. Chem.* 220: 105 (1962).
21. von Ardenne, M., Steinfelder, K., and Tümmeler, R. Erweiterung der EA-massenspektrographischen Methode durch den Mechanismus der Anlagerung negativer Ionen an Moleküle, *Z. Physik. Chem. (Leipzig)* 221: 240 (1963).
22. Cumming, J. B., French, M. A., and Kebarle, P. Effects of charge delocalization on hydrogen bonding to negative ions and solvation of negative ions. Substituted phenols and phenoxide anions. *J. Am. Chem. Soc.* 99: 6999 (1977).
23. Kim, J. K., Findley, M. C., Henderson, W. G., and Caserio, M. C. Ion cyclotron resonance spectroscopy. Neighboring group effects in the gas-phase ionization of β -substituted alcohols. *J. Am. Chem. Soc.* 95: 2184 (1973).
24. Longevialle, P., Milne, G. W. A., and Fales, H. M. Chemical ionization mass spectrometry of complex molecules. XI. Stereochemical and conformational effects in the isobutane chemical ionization mass spectra of some stereoidal amino alcohols. *J. Am. Chem. Soc.* 95: 6666 (1973).
25. Winkler, F. J., and McLafferty, F. W. Stereochemical effects in the chemical ionization mass spectra of cyclic diols. *Tetrahedron* 30: 2971 (1974).
26. Van de Sande, C. C., van Gaever, F., Hanselaer, R., and Vandewalle, M. Correlations between the stereochemistry and the chemical ionization spectra of epimeric 3,4-dimethyl-1,2-cyclopentane diols, *Z. Naturforsch. B32*: 810 (1977).
27. Claeys, M., and Van Haver, D. Conformational effects in the chemical ionization spectra of derivatives of isomeric 2,3-dimethyl-1-1,4-cyclopentane diols. *Org. Mass Spectr.* 12: 531 (1977).
28. Winkler, F. J., and Robertson, A. V. Wasserstoffbrückeneffekte in der Massenspektren der 5-Methyl-1,3-cyclohexendiole. *Chem. Ber.* 109: 633 (1976).