Methoxymethyl formate was prepared by the reaction of chloromethyl methyl ether[22] (doubly distilled) with sodium formate and 0.05 mol% tetra-*n*-butylammonium hydrogen sulfate. The reactants were refluxed at 100 °C for 2 h.[23] The product, bp 100–103 °C (103 °C[24]) had the following ^{1}H NMR (10% $CDCl_3$): δ 8.05 (8.15[24]) (s, 1), 5.22 (5.34[9]) (s, 2), 3.42 (3.50[9]) (s, 3).

The trideuterio analog was prepared similarly, using CD_3OCH_2Cl. ^{1}H NMR (10% $CDCl_3$) showed δ 8.1 (s, 1) and 5.2 (s, 2). Methyl glyoxylate was prepared by heating glyoxylic acid (Aldrich) with the appropriate labeled or unlabeled methanol in sealed tubes and also by the $Pb(OAC)_4$ oxidation of trimethyl L-tartrate using the procedure of Wolf and Weijland.[25] Oxirane was purchased from Matheson Gas Products (Canada).

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Registry No. 1, 36505-03-0; **4**, 57062-76-7; **5**, 72192-21-3; **6**, 72192-22-4; **8**, 57239-63-1; CD_3OCH_2Cl, 54716-95-9; ionized methyl glyoxylate, 110661-93-3; ionized 1,3-dioxolane, 81027-69-2; ionized methoxymethyl formate, 110661-94-4; ionized ethylene carbonate, 110661-95-5; ionized methoxymethyl formate-d_3, 110661-96-6; oxirane, 75-21-8; methoxymethyl formate-d_3, 110661-97-7; acetaldehyde, 75-07-0; cyclobutanol, 2919-23-5; 1,3-dioxolane, 646-06-0; ethylene carbonate, 96-49-1; methyl glyoxylate, 922-68-9; methoxy methyl formate, 4382-75-6; chloromethyl methyl ether, 107-30-2; sodium formate, 141-53-7.

Propellanes. 91.[1] Fragmentation Mechanism of Alcohols under Isobutane Chemical Ionization. Highly Stereospecific Formation of $[M - OH]^+$ Ions from [4.3.3]Propellane-8,11-diols

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Abstract: The stereoisomeric title diols afford different isobutane chemical ionization mass spectra: the anti,anti diol affords an abundant MH^+ ion while the syn,syn and syn,anti isomers give very abundant $[M - OH]^+$ ions. A stereospecific ^{18}O-labeling study shows that the *syn*-hydroxyl group is preferentially lost in the syn,anti diol. This high syn specificity indicates that the mechanism of formation of the $[M - OH]^+$ ions involves a reversible interaction of the diol molecules with the t-$C_4H_9^+$ ions followed by loss of *tert*-butyl alcohol rather than elimination of H_2O from the MH^+ ions. This conclusion is supported by the low stereospecificity of this process under propane CI conditions.

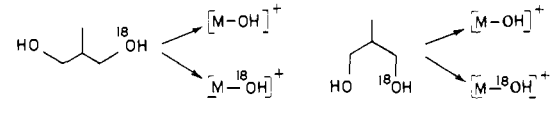
Two general features of isobutane CI mass spectra of alcohols containing more than four carbon atoms are the instability of MH^+ and the very high abundance of $[M - OH]^+$ ions.[2] The formation of the $[M - OH]^+$ ions has been often described in terms of H_2O elimination from MH^+ (eq 1). If a *second* functional group is

$$ROH \xrightarrow{t\text{-}C_4H_9^+} \underset{\text{unstable}}{ROH_2^+} \rightarrow R^+ + H_2O \qquad (1)$$

present in a configuration which allows formation of *intramolecular* hydrogen bridging, the MH^+ ion is greatly stabilized.[3,4] In several β-amino alcohols where such bridging was possible, no elimination of H_2O was observed.[5] In other amino alcohols in which the interfunctional distance was increased, the elimination of H_2O appeared, and its extent was correlated to the distance between the OH and amino groups. The loss of H_2O in the latter was assumed to occur from those ions which had been protonated at the hydroxyl (eq 2); moreover, it has been suggested that the

$$R_2N\text{—}X\text{—}OH \xrightarrow{t\text{-}C_4H_9^+} \begin{cases} R_2\overset{+}{N}H\text{—}X\text{—}OH \\ \text{stable } MH^+ \\ R_2N\text{—}X\text{—}\overset{+}{O}H_2 \rightarrow [MH - H_2O]^+ \end{cases} \qquad (2)$$

Scheme I



1a 3a

abundance ratio be used as a quantitative measure of the oxygen–nitrogen protonation ratio.[5] We report herein isobutane CI results of stereoisomeric propellane diols which cast new light on the formation of $[M - OH]^+$ ions.

Results and Discussion

The stereoisomeric propellane diols **1–3** exhibit pronounced stereospecificity under isobutane CI (Figure 1). Only the anti,anti isomer **3**, which is capable of internal hydrogen bridging, gives

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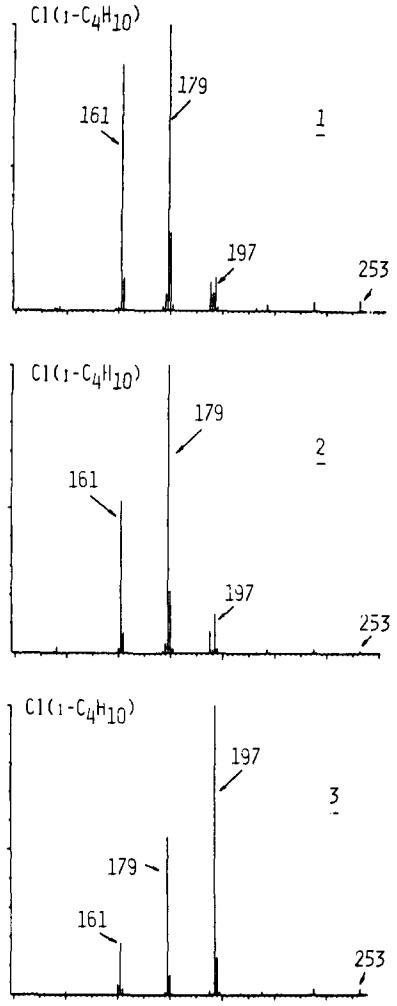
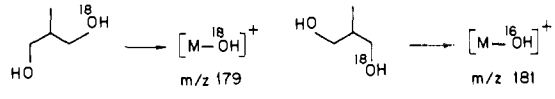


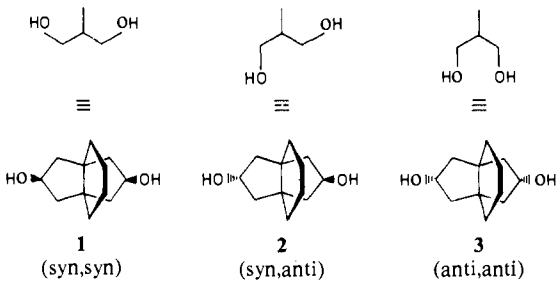
Figure 1. i-C_4H_{10} CI mass spectra of *syn,syn*, *syn,anti*, and *anti,anti* [4.3.3]propellane-8,11-diols (**1**, **2**, and **3**).

Scheme II



2a 2b

rise to a very abundant MH^+ ion. However, the two other stereoisomers **1** and **2** exhibit very abundant $[M - OH]^+$ and $[M - OH - H_2O]^+$ ions and, in much smaller proportion, $[M - H]^+$. The abundance of $[M - OH - H_2O]^+$ is reduced on lowering ion source temperature. The abundance of MH^+ ions is very low in these isomers under any conditions.



1 (syn,syn) **2** (syn,anti) **3** (anti,anti)

The ^{18}O-labeled syn,syn and anti,anti diols **1a** and **3a** give rise to both m/z 181 $[M - {}^{16}OH]^+$ and m/z 179 $[M - {}^{18}OH]^+$ ions (Figure 2, Scheme I). The abundances of these ions correspond to a similar extent of elimination of ^{16}OH and ^{18}OH in both isomers.[6]

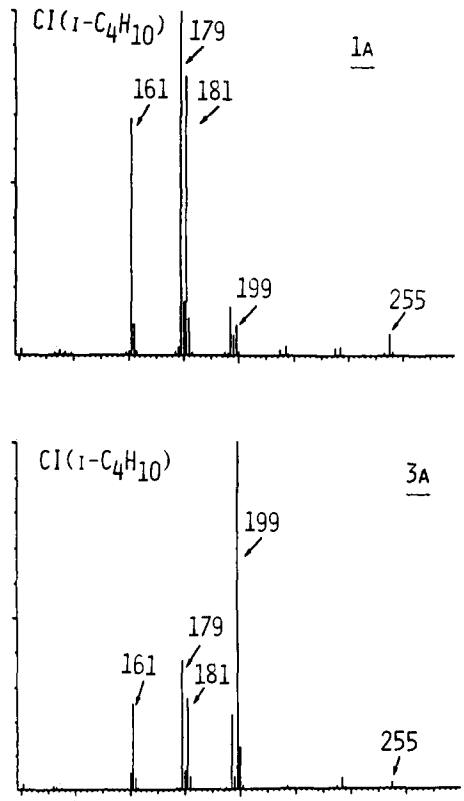


Figure 2. i-C_4H_{10} CI mass spectra of *syn,syn* and *anti,anti* [8-^{18}O]-[4.3.3]propellane-8,11-diols (**1a** and **3a**).

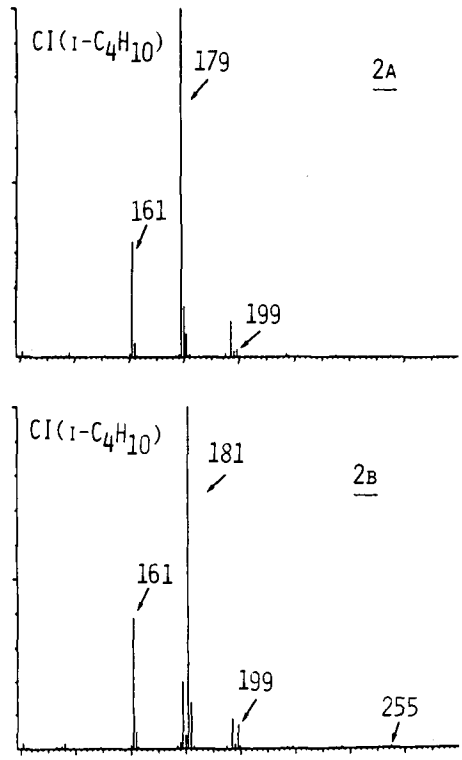
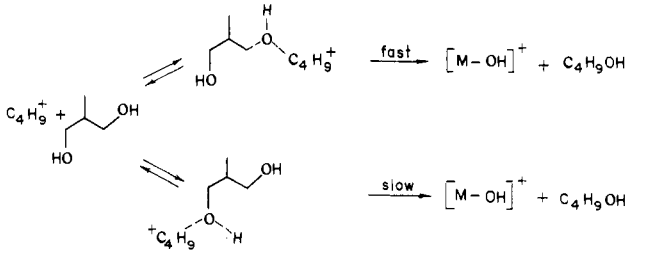


Figure 3. i-C_4H_{10} CI mass spectra of [8-^{18}O][4.3.3]propellane-8-*syn*,11-*anti*-diol (**2a**) and [8-^{18}O][4.3.3]propellane-8-*anti*,11-*syn*-diol (**2b**).

A highly stereospecific process takes place in the two syn,anti stereoisotopomers **2a** and **2b** (Figure 3). Diol **2a** with a syn ^{18}O-hydroxyl group gives rise to 93% $[M - {}^{18}OH]^+$ (corrected for

(6) The excess abundance of the m/z 179 ion in the mass spectra (Figure 2) is due to the presence of the unlabeled diols (estimated as ca. 10% from the $[M + C_4H_9]^+$ adduct ions at m/z 253 and 255).

Scheme III



the presence of the unlabeled analogue) vs. 7% $[M - {}^{16}OH]^+$, while **2b** with an anti ^{18}O-hydroxyl shows the reverse behavior (91% $[M - {}^{16}OH]^+$ vs. 9% $[M - {}^{18}OH]^+$, Scheme II).

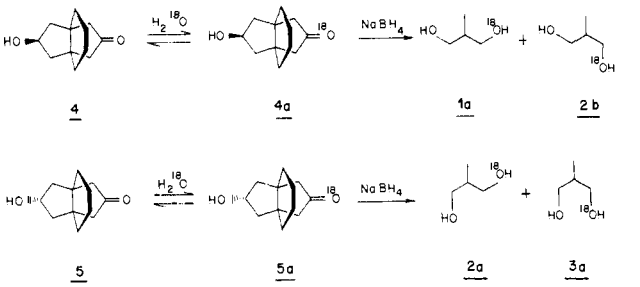
The high preference of elimination involving the *syn*-hydroxyl in **2a** and **2b** cannot be explained satisfactorily by the protonation scheme at different functions as in eq 2. There is no reason to assume highly preferred protonation at the *syn*-OH group which would be followed by an anchimerically assisted loss of H_2O (i.e., $H_2{}^{18}O$ in **2a** and $H_2{}^{16}O$ in **2b**). Protonation at the *anti*-OH group would, of course, cause elimination of water involving the *anti*-hydroxyl. Subsequent simple proton transfer from the *anti*- to the finally eliminated *syn*-OH group is *not* possible in the syn,anti configuration. Rearrangements, leading to the same effect, are excluded by the highly stereospecific behavior of the four stereoisomers.

We believe that the high *syn* specificity of both **2a** and **2b** indicates that the formation of the $[M - OH]^+$ ions is the result of a *reversible* interaction with the chemical ionization reagent. Proton transfer from t-$C_4H_9^+$ to alcohols is endothermic, and therefore $[M - OH]^+$ ions should be formed by direct reaction with t-$C_4H_9^+$ rather than by elimination of H_2O from an MH^+ intermediate.[7] As mentioned above, the abundance of MH^+ is very low in the isobutane CI mass spectra of these isomers, and it may be formed from the $[M + C_4H_9]^+$ ion[8] and/or by direct protonation with excited $C_4H_9^+$ ions.[2] We suggest (Scheme III) that an interaction of **2a** and **2b** with t-$C_4H_9^+$ ions may take place reversibly at both OH groups. At the *syn*-OH group, however, such a reaction will result in highly enhanced elimination of t-C_4H_9OH via a low-energy channel owing to a stereoelectronic effect exerted by the *anti*-OH group. In the absence of such an effect, elimination of *tert*-butyl alcohol from the product of interaction at the *anti*-OH group would require higher energy, and would consequently be suppressed.

It should be noted that under propane CI conditions the stereospecificity of formation of the $[M - OH]^+$ ions from **2a** and **2b** was strongly reduced. The abundance ratio of $[M - syn\text{-}OH]^+$ to $[M - anti\text{-}OH]^+$ was 60:40 in both isotopomers (93:7 in isobutane CI). This effect may be explained by the higher gas-phase acidity of the CI reagent (proton affinity values are 179.5 kcal/mol for propene and 195.9 kcal/mol for isobutene[9]), possibly resulting in exothermic protonation of alcohols (proton affinity $\sim$ 191 kcal/mol[9]). Such protonation should occur to a comparable extent on either hydroxyl group and thus reduce the stereospecificity of the elimination. If reaction partially takes place via removal of the hydroxyl group by the i-$C_3H_7^+$ ions, their relatively high hydroxyl affinity (higher by 16 kcal/mol than that of t-$C_4H_9^+$ ions) should have a negative effect on the reversibility of the adduct-formation step of Scheme III, again reducing stereospecificity.

The suggested mechanism for the formation of the $[M - OH]^+$ ions under isobutane CI could also apply to the β-amino alcohols mentioned above. The high abundance of the $[M - OH]^+$ ion in those compounds with unfavorable bridging geometries could be explained similarly by lower energy channels of t-C_4H_9OH elimination due to anchimeric assistance by the amino function, rather than primary protonation of the OH group by t-$C_4H_9^+$ (endothermic process) in the presence of an amino function in the molecule.

Scheme IV



Synthesis of ^{18}O-Labeled Stereoisomers

Labeling with ^{18}O was performed by exchange of the carbonyl oxygen of syn and anti ketols **4** and **5** with $H_2{}^{18}O$, followed by reduction. The pairs of stereoisomeric diols were separated in each case by preparative TLC. The synthesis is shown in Scheme IV.

The exchange of carbonyl oxygen for ^{18}O from $[^{18}O]$ water is usually accomplished by refluxing the ketone with sodium hydroxide–$[^{18}O]$ water solution.[10] However, in our case, the low solubility of the ketols in water and the side reactions that occur during reflux in aqueous NaOH precluded such approach for ^{18}O incorporation. We were able to obtain high incorporation of ^{18}O by using methanol as a mutual solvent.

Experimental Section

Mass Spectral Measurements. The stereoisomeric diols were analyzed by evaporation from a commercial DCI probe directly into the CI plasma, applying slow heating rates. CI conditions were 0.4 torr of isobutane or 0.35 torr of propane reagent gas (Carbagas, both 99.95% purity), 110° ion source temperature. A Finnigan MAT TSQ 45 triple quadrupole mass spectrometer was used in the Q-3 scan mode for recording CI spectra (average of $\sim$10 scans).

8-[^{18}O]Oxo[4.3.3]propellane-11-*syn*-ol (4a). To a solution of the ketol[11] **4** (96 mg, 0.5 mmol) in 2 mL of dry methanol were added 0.1 mL of a solution of NaOMe in MeOH (ca. 0.06 mmol, prepared by dissolving Na (80 mg) in 6 mL of MeOH) and $H_2{}^{18}O$ (0.5 mL, ca. 25 mmol, 98 atom % ^{18}O, purchased from Yeda-Stable Isotopes, Israel). The solution was heated under reflux for 5 h and evaporated to dryness to give yellowish crystalline material (98 mg, 100%) whose TLC was identical with that of the starting ketol.

8-[^{18}O]Oxo[4.3.3]propellane-11-*anti*-ol (5a) was prepared from the anti ketol **5** as described for the syn isomer.

Reduction of 4a. The labeled ketol **4a** (33 mg, 0.17 mmol) in 5 mL of methanol was stirred overnight at room temperature with sodium borohydride (50 mg, 1.35 mmol). Conventional workup was followed by chromatography on thick-layer silica gel plates (ether:hexane 1:1) to yield [8-^{18}O][4.3.3]propellane-8-*syn*,11-*syn*-diol (**1a**) (14 mg, 42%), mp 164–165 °C (isopropyl ether) and [8-^{18}O][4.3.3]propellane-8-*anti*,11-*syn*-*diol* (**2b**) (19 mg; 58%), mp 136–137 °C (isopropyl ether).

Reduction of 5a. **5a** (90 mg, 0.45 mmol) in 10 mL of methanol was stirred overnight at room temperature with sodium borohydride (100 mg, 2.7 mmol). Workup followed by silica gel chromatography as above yielded [8-^{18}O][4.3.3]propellane-8-*syn*,11-*anti*-diol (**2a**) (28 mg, 31%), mp 144–145 °C (isopropyl ether) and [8-^{18}O][4.3.3]propellane-8-*anti*,11-*anti*-diol (**3a**) (63 mg, 69%), mp 126–127 °C (isopropyl ether).

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Registry No. 1, 82343-97-3; **1a**, 110773-27-8; **2**, 82373-88-4; **2a**, 110849-50-8; **2b**, 110849-49-5; **3**, 82373-89-5; **3a**, 110849-51-9; **4a**, 110773-26-7; **5a**, 110849-48-4.

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