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PROPELLANES. XCVI.[1] UNAMBIGUOUS CHEMICAL IONIZATION MASS SPECTRAL ASSIGNMENT OF CONFIGURATIONS TO THE DIOLS OBTAINED BY REDUCTION OF [n.3.3]PROPELLANEDIONES AND HPLC PURIFICATION

By YOCHANAN KLOPSTOCK,[a] PNINA ASHKENAZI[a], ASHER MANDELBAUM,[a]
D. MÜLLER,[b] WILHELM J. RICHTER,[b] AND DAVID GINSBURG.[a#]

a) Department of Chemistry, Israel Institute of Technology,
Haifa 32000, Israel.
b) Central Function Research, Ciba-Geigy AG, CH-4002 Basel, Switzerland.

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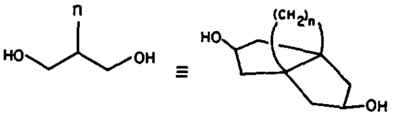
Abstract.- i-Butane chemical ionization mass spectrometry (CIMS) enables unambiguous configurational assignment of anti,anti[n.3.3]propellane diols which give rise to abundant $[M+H]^+$ ions in contrast to the syn,syn- and syn,anti-isomers. The syn,syn- and syn,anti-isomers may be differentiated by the relative abundance of the $[M+C_4H_9-2H_2O]^+$ ions under i-C_4H_9-CIMS conditions.

Introduction. - Chemical ionization mass spectrometry (CIMS) has been shown to be sensitive to the configuration of some epimeric alicyclic diols.[2] The abundance of the $[M+H]^+$ ions under isobutane chemical ionization conditions is much higher in stereoisomers which enable intramolecular H-bridging between the two hydroxyl groups.[2]

We had a problem in which we had the three isomeric propellane diols 1-3 (n=22), and we based their structure upon analogy to the chromatographic behavior of the three reduction products of [4.3.3]propellane-8,11-dione.[3] This analogy turned out to be a mistaken one and formed the raison d'etre for the CIMS results herein. Our attention was drawn by Prof. C.N. Sukenik of Case Western Reserve University to the necessity of reversing the configurations of our syn,syn- and anti,anti-isomer, n=22.[4]

Sukenik et al[4] had excellent HPLC-separated 1-3, n=10,12,22 as well as X-ray results supporting their reversal of the configurations of 1 and 3. We subjected all of their products to mass spectrometry as well as ours. The CIMS measurements provide an easy and reliable way way to determine the configuration of the anti,anti-diols 3.



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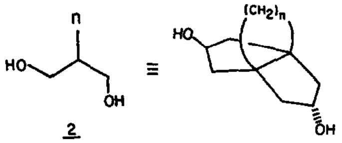

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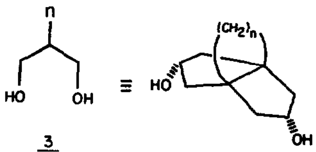

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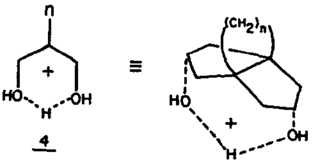

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Discussion and Results. - The diols 1-3 obtained by lithium aluminum hydride reduction of the corresponding [n.3.3]propellane diones were separated by HPLC. The analytical data for the [20.3.3], [28.3.3], and [38.3.3] triads of diols is given in Table 1. The components of the

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[#] Deceased March 9, 1988.

[20.3.3] diol mixture were not separated by ordinary HPLC and purification had to be conducted by reverse phase HPLC (*cf.* footnote in Table 1). From the data shown in Table 1 as well as from that of Sukenik it may be concluded that the order of elution of triad members is AA, SA, SS for the configurational isomers 1, 2, and 3 for large values of $n(n > 10)$. For $n=4$ it has been shown before that the order of elution from a liquid chromatography column is SS, SA, AA.

Table 1

Substrate	Order of elution	Composition %
[20.3.3]*	SS	15.7
	SA	49.9
	AA	35.4
[28.3.3]	AA	46.0
	SS	11.6
	SA	42.4
[38.3.3]	AA	46.9
	SS	18.4
	SA	34.7

* Reverse phase HPLC.

The relevant isobutane-CI mass spectral data of the stereoisomeric diols 1-3 are listed in Table 2.

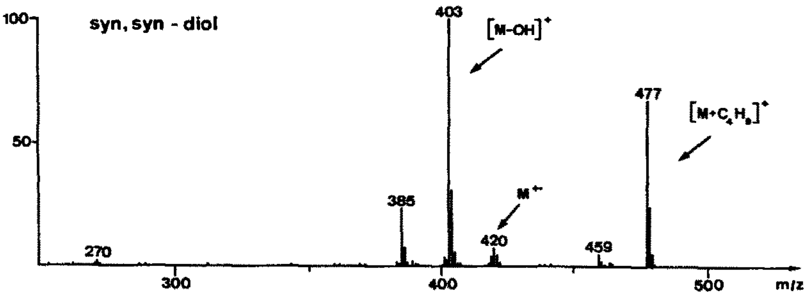
Table 2

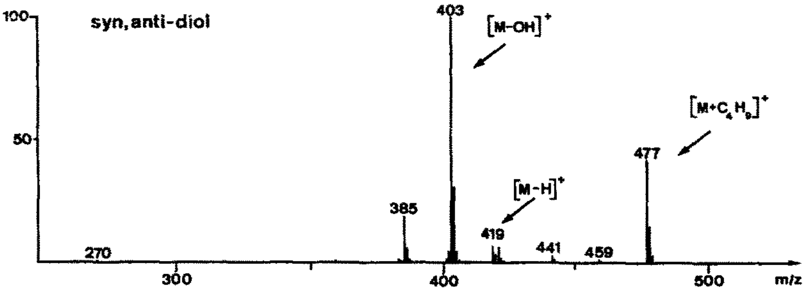
Relative Abundances of Selected Ions

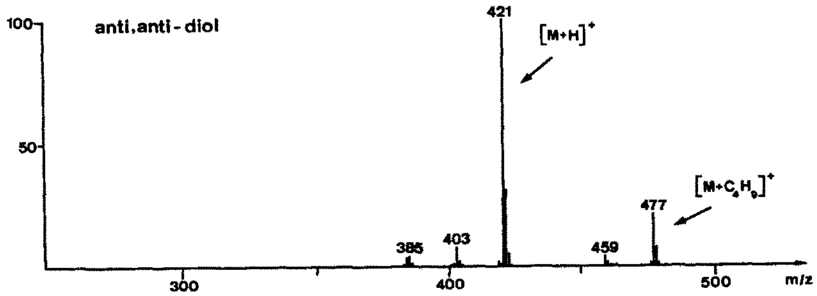
n in [n.3.3]	Configuration	$[M+H]^+$	$[M-OH]^+$	$[M+C_4H_9]^+$	$[M+C_4H_9-2H_2O]^+$
10	AA	100.0	15.6	11.1[1]	0.1
	SA	3.2	100.0	5.9	1.7
	SS	2.2	100.0	21.4	<1.1[2]
12	AA	100.0	24.7	11.5	0.1
	SA	2.2	100.0	9.2	1.7
	SS	0.8	100.0	17.9	0.3
20	AA	100.0	7.6	20.8	—
	SA	6.0	100.0	42.8	3.2
	SS	2.0	100.0	47.4	—
22	AA	100.0	14.1	13.6	—
	SA	2.2	100.0	22.7	1.8
	SS	0.3	100.0	32.8	—
28	AA	100.0	4.9	21.8	—
	SA	2.3	100.0	69.5	3.1
	SS	1.2	100.0	81.2	—
38	AA	100.0	2.0	26.6	—
	SA	1.8	100.0	58.3	2.5
	SS	2.7	100.0	73.3	—

[1] $[M+C_4H_9]^+/[M+H]^+$ ratios show strong dependence on the reagent gas pressure. Isobutane pressure (indicated) was 0.80 Torr for the analyses of the triads n = 10, 12 and 22, but 0.48 Torr for the triads n = 20, 28 and 38.

[2] Contains background contribution.







In all three AA isomers 1,2 and 3, n=20,28,38, the most abundant ion was $[M+H]^+$, respectively, as was the case in Sukenik's samples 1,2,3, n=10,12,22.[4] Here too the AA isomer may be unambiguously chosen on the basis of the relatively much stronger $[M+H]^+$ peaks. The high abundance of the $[M+H]^+$ ion is explained by intramolecular hydrogen bond as shown in structure 4. The abundance of $[M+H]^+$ ion is extremely low in the CI mass spectra of the SS and SA isomers, while $[M-OH]^+$ ions are of highest abundance. The origin of the latter ions has been discussed in detail in a previous publication.[5]

Another nice criterion for assignment of the choice between the SS and SA isomers throughout is apparent from the relative ease of elimination of two H_2O molecules from the respective $[M+C_4H_9]^+$ ions (see Table 2). This is greatest for the SA configuration as compared to that of the SS and AA isomers. The origin of this difference in the abundance of the $[M+C_4H_9-2H_2O]^+$ ions is not clear.

In summary, HPLC separation of the three isomeric diols in each n-triad allows one to obtain the quantitative ratio of each in the reaction mixture. CI mass spectrometry then allows unambiguous choice of configuration of each N-triad member: SS, SA or AA. The NMR data is comparable for the AA and SS symmetric isomers in each triad though consistent relative shifts exist. The CIMS behavior allows unequivocal assignment of the AA isomer even it alone is available.

CI mass spectra are available to the interested reader by writing either to Basel (W.J.R.) or to Haifa (A.M.) but because of the importance of the [20.3.3] diol triad to our further work we reproduce herein the CI mass spectra of the AA, SA, and SS isomer as a specific example for the generalizations made above. The material attached herein to the (major) CIMS work as to our HPLC and NMR results may be obtained by writing to P.A.

EXPERIMENTAL

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^o 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 ~ 10 scans).

Mixtures for separations were obtained by reduction of the respective diones with excess LAH using [20.3.3] dione (250 mg), anhyd. ether (100 ml) for 6 days under reflux; [28.3.3] dione (247 mg), LAH (865 mg), anhyd. ether (100 ml) for 6 days; [38.3.3]dione (224 mg), NaOH, NaBH$_4$/aq. hexacetyltrimethyl ammonium bromide^6 followed by the usual workup.

The crude diols were purified from starting diones + ketols before being subjected to HPLC; the [20.3.3]diols by crystallization from hexane, [28.3.3]diols by chromatography on a silica column, elution with CHCl$_3$:EtOAc 1:1, Vol. %, [38.3.3] diols by silica column, elution with EtOAc:Hexane 3:7.

HPLC separations of [20.3.3], [28.3.3], and [38.3.3]propellane diols respectively, were performed using Spectra Physics model 740B with RID.

Column for [20.3.3]: Supelcosil PLC-18, 25 cm x 4.6 mm. Eluent: MeOH (95): H$_2$O(5); 25ml/min. Sample size: 100 1. Separation: 1, SS, 15.7%, 2, SA, 49.9%, 3, AA (35.4%). Column for [28.3.3]: Supelcosil PLC-Si, 25 cm x 4.6 mm. Eluent: n-hexane (90): Acetone (9.8): i-PrOH (0.2) Vol. % ~ 1.5 ml/min. Sample size: 200μl. Separation: 1, AA, 46.0%; 2, SS, 11.6%; 3, SA, 42.4%. Column for [38.3.3] as for [28.3.3]. Eluent: n-hexane (87.4); acetone (12.4): i-PrOH (0.2) ~ 1 ml/min. Sample size 100μ l. Separation: 1, AA, 46.9%; 2, SS, 18.4%; 3, SA, 34.7%.

After HPLC all the diols were crystallized from i-Pr ethane-hexane. M.p's [20.3.3], AA, 122-123^o; SA, 138-140^{o}C; SS, 124-125^{o}C. M.p.'s [28.3.3] AA, 111-112^{o}C; SA, 106-108^{o}C; SS, 103-104^{o}C. M.p.'s [38.3.3], AA, 114-114.5^{o}C; SA, 109.5-110^{o}C; SS, 116-117^{o}C. All of these pure diols exhibit their OH IR band at 3600 cm^{-1} (CHCl$_3$).

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