C, 74.47; H, 3.47. Found: C, 74.37; H, 3.41.

3-(2-Carboxypyrenyl)propionic acid (19): mp 235 °C dec; ^{1}H NMR (DMSO-d_6) δ 2.81 (t, 2 H, $CH_2CH_2CO_2$, $J_{2,3}$ = 6.5 Hz), 3.77 (t, 2 H, $CH_2CH_2CO_2$, $J_{2,3}$ = 6.5 Hz), 8.15–8.38 (m, 7 H, Ar), 8.49 (s, 1 H, H_3); MS m/e (relative intensity) 318 (M^+, 100), 300 (15), 272 (34), 259 (79), 200 (38). Anal. Calcd for $C_{20}H_{14}O_4$: C, 74.54; H, 4.44. Found: C, 75.47; H, 4.38.

1,2,3,4-Naphthalenetetrone (3): mp 132 °C (lit.[27] mp 130–131 °C); ^{1}H NMR ($CDCl_3$) δ 7.63–7.82 (m, 2 H, $H_{6,7}$), 8.05–8.24 (m, 2 H, $H_{5,8}$); MS (positive chemical ionization, CH_4) m/e (relative intensity) 216 (M + 28, 19), 188 (M^+, 100).

1,2,3,4-Chrysenetetrone (16): mp 224–226 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.70–7.78 (m, 2 H, $H_{8,9}$), 7.95–8.00 (m, 2 H, $H_{7,10}$), 8.05 (d, 1 H, H_6, $J_{5,6}$ = 8.5 Hz), 8.72 (d, 1 H, H_{11}, $J_{11,12}$ = 7.9 Hz), 8.91 (d, 1 H, H_5, $J_{5,6}$ = 8.5 Hz), 9.03 (d, 1 H, H_{12}, $J_{11,12}$ = 7.9 Hz); MS (positive chemical ionization, CH_4) m/e (relative intensity) 316 (M + 28, 22), 288 (M^+, 100). Anal. Calcd for $C_{18}H_8O_4$ (unstable compound): C, 74.99; H, 2.80. Found: C, 74.05; H, 2.75.

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Conformations of [*m*.3.3]Propellane Ketones and Alcohols†

Anand Natrajan, Joseph D. Ferrara, John D. Hays, Mahesh Khot, Jennifer Colonell, Wiley J. Youngs, and Chaim N. Sukenik*,[1]

Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106

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We have prepared a series of [*m*.3.3]propellanediones (*m* = 3, 4, 10, 12, 22) and have studied various structural aspects of these diones and their ketol and diol reduction products. We have used X-ray crystallography to establish stereochemistry and to explore cyclopentyl ring conformations. The ^{1}H NMR spectra of the ketols and diols have also been used to probe their conformations. They provide evidence for intramolecular hydrogen bonding between the OH groups of some of the anti,anti (aa) diols. The folding needed for this interaction is also seen in the gas phase in the *i*-C_4H_{10} CIMS. For an aa diol, this leads to a bridged $[M + 1]^+$ ion. For an anti ketol, it promotes an intramolecular proton transfer leading to H_2O elimination from the $[M + 1]^+$ ion. This results in unusual stability for the protonated parent ion of an aa diol and enhanced fragmentation of the parent ion of an anti ketol, relative to their stereoisomers. The ease of the molecular puckering that is the key observation of both the NMR and CIMS work, is shown to be dependent on the size of the propellane polymethylene bridge.

As part of a research program on micelle-induced perturbations of organic reactions,[2] we have synthesized and determined the stereochemistry of the ketols and diols of some [*m*.3.3]propellanes (*m* = 3, 4, 10, 12, 22; Scheme I).[3] The structural work done to assign those propellane configurations prompted the following study of the conformations of the fused cyclopentyl rings of the [*m*.3.3]propellanes. We have determined the X-ray crystal structure of the [12.3.3]propellanedione to provide the first direct evidence for the conformation of such fused cyclopentanone rings. We have used ^{1}H NMR coupling constants to probe the solution conformations of the cyclopentanol rings. And, we have explored the ability of the two oxygen atoms in the anti,anti (aa) diols and the anti ketols to approach each other, by studying the solvent dependence of their ^{1}H NMR spectra and by obtaining their chemical ionization mass spectra (CIMS).

Results and Discussion

X-ray Crystallography. The single-crystal X-ray structures of the three [4.3.3]propellanediols have been reported by Kapon et al.[4] We have reported the structure of the [10.3.3] syn,syn (ss) diol.[3a] Comparison of these showed that, while *m* = 4 diols had relatively planar cyclopentanol rings, the *m* = 10 diol had puckered cyclopentanols whose OH-bearing carbons were bent down (away from the polymethylene ring) by 37°. Since no crystallographic data were available on any carbonyl-containing [*m*.3.3]propellanes, we solved the structure of a propellanedione.

The structure of [12.3.3]propellane-16,19-dione was determined by standard X-ray analysis. The molecular structure is shown in Figures 1 and 2. The five-membered rings are nearly planar with the root-mean-square deviation (rms dev) for the atoms defining the cyclopentanone plane for C(01), C(14), C(15), C(16), C(17), and O(01) at 0.134 (2) Å and C(01), C(14), C(18), C(19), C(20), and O(02) at 0.128 (2) Å. The rms deviation from the mean plane of

† This paper is dedicated to the memory of Professor David Ginsburg of the Chemistry Department at the Technion-Israel Institute of Technology, Haifa, Israel.

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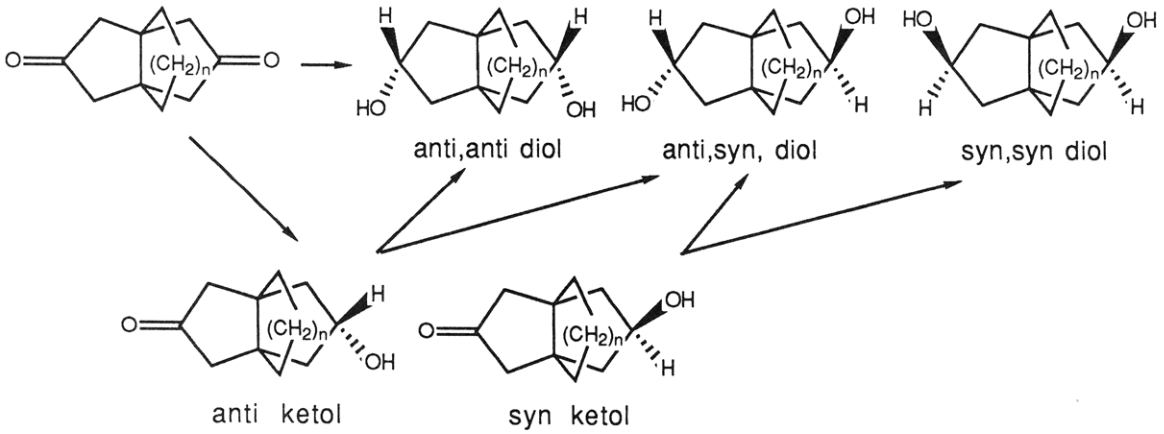
Scheme I. [m.3.3]Propellane Dione, Ketols, and Diols (m = n + 2)



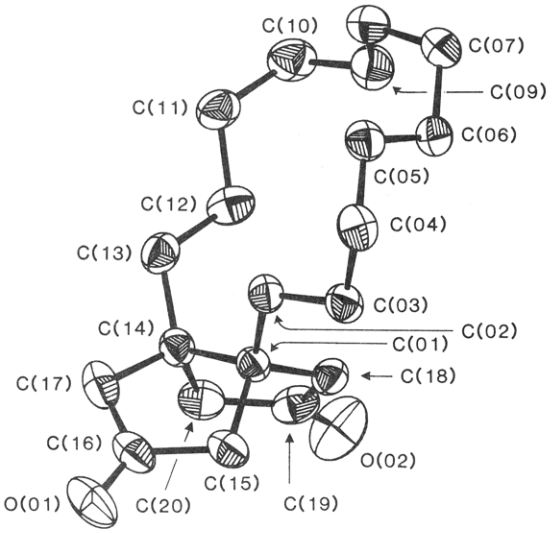


Figure 1. ORTEP of [12.3.3]propellane-16,19-dione.

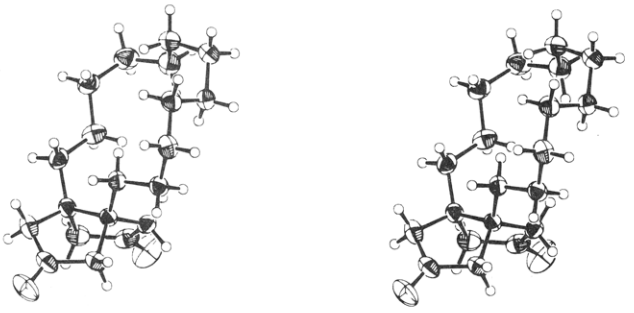


Figure 2. Stereoview of [12.3.3]propellane-16,19-dione.

the 14-membered ring is 0.483 (2) Å. The dione is less eclipsed about the bond between the two quaternary carbons than the previously described [10.3.3]propellane-14,17-*syn*,*syn*-diol[3a]. The mean torsion angle for C(02)–C(01)–C(14)–C(13), C(15)–C(01)–C(14)–C(17), and C(18)–C(01)–C(14)–C(20) is 33 (2)°, whereas in the [10.3.3] diol this angle ranges from 10.6 (4)° to 15.4 (5)°. The planes defined by C(01), C(14), C(16), and O(01) and C(01), C(14), C(19), and O(02) have rms deviations of 0.0003 and 0.010 Å, respectively. The methylene carbons of the five-membered rings are above and below these planes with the C(01)–C(14) and C=O bonds in the planes. The bond between the quaternary carbons is lengthened to 1.580 (3) Å. The mean bond lengths and angles are as expected for the 14-membered ring (1.53 (1) Å and 114.4 (12)°). For the five-membered ring the mean methylene to bridgehead C–C bond length is 1.538 (9) Å, and the mean methylene

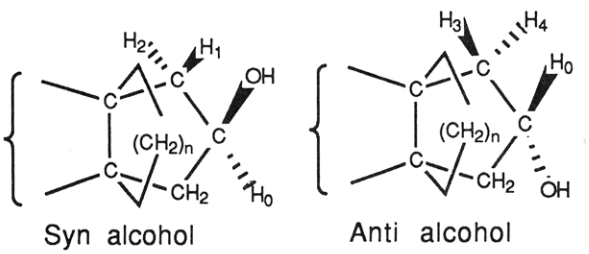


Figure 3. Numbering scheme for protons on the OH-bearing ring.

to carbonyl C–C bond length is 1.497 (5) Å. The mean angle around the aliphatic carbons in those rings is 105.0 (16)° while the C–C–C angle for the carbonyl is 109.8 (7)°. The mean C—C=O angle is 124.3 (2)° with a mean C=O bond length of 1.213 (3) Å.

The preference for planar cyclopentanone rings was confirmed with MM2 calculations.[5] By starting with the crystallographically determined coordinates of the [12.3.3] dione, we obtained an MM2 optimized structure with the same, nearly planar, cyclopentanones as the crystallographic structure. Similarly, the lowest energy conformation of the [4.3.3] dione has nearly planar cyclopentanones, with a puckered local minimum conformation approximately 5 kcal/mol higher in energy. Clearly, any significant cyclopentanone ring puckering is energetically unfavorable.

^{1}H NMR Studies. The ^{1}H NMR spectra of the ketols and diols in $CDCl_3$ had been obtained as part of our initial assignment of their configurational stereochemistry.[3,6] For purposes of this study, we focused on the coupling of the H on the OH-bearing carbon (H_O) to the β-H's (those on the adjacent carbons, Figure 3). Any interpretation of these couplings depends on having the correct assignment of the chemical shifts of the β-H's. Askani[7] suggested that β-H's cis to the OH (H_1, H_4) are relatively further *downfield* than those trans to the OH (H_2, H_3). Between our crystallography[3a] of the m = 10 ss diol and that of Kapon et al.[4] on the m = 4 diols, we assigned H's cis to the OH group as being *upfield*. This was done by comparing the crystallographically determined dihedral angles to those derived from the observed coupling constants using the

(5) (a) MM2 calculations were done using the Macromodel program (Version 2.0) of Still et al. and the parameters supplied therein. (b) Burkert, U.; Allinger, N. L. *Molecular Mechanics*; ACS Monograph Series; American Chemical Society: Washington, DC, 1982. (c) Some computational work on the m = 4 diols is reported in ref 4, and a conformational analysis of the [2.3.3], [3.3.3], and [4.3.3] hydrocarbons can be found in: Dodziuk, H. *J. Comput. Chem.* **1984**, *5*, 571.

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Table I. Assignment of β-H Chemical Shifts by Correlating Observed J Values with X-ray-Determined Dihedral Angles for Three [4.3.3] Diols and [10.3.3] ss Diol

substrate	β-H	average[a] dihedral angle with H_O	J,[b] Hz (cal.)	J, Hz (obs.)	δ
[4.3.3] aa diol	H_4	126	4.1	4.4	1.84
	H_3	17	8.1	7.9	2.11
[4.3.3] ss diol[c]	H_2	14	8.4	7.7	1.90
	H_1	126	4.1	5.1	1.64
[4.3.3] ss diol[d]	H_2	13	8.5	7.7	1.90
	H_1	120	3.2	5.1	1.64
[4.3.3] sa diol	H_4	117	2.8	5.1	1.67
	H_3	13	8.5	7.7	2.16
	H_2	11	8.7	8.0	2.04
	H_1	124	3.7	5.8	1.51
[10.3.3] ss diol	H_2	40	7.1	7.1	1.82
	H_1	161	9.9	9.3	1.52

[a] [4.3.3] crystallography data from Kapon (ref 4); [10.3.3] data from ref 3a. [b] Calculated as per ref 8. [c] Form A (ref 4). [d] Form B (ref 4).

Karplus relationship.[8] This correlation is shown in Table I.

To generalize such an assignment, we obtained ^1H NMR spectra of all five sets of ketols and diols in CD_3OD, $CDCl_3$, and C_6D_6. Tabulations of the chemical shifts and coupling constants for the pairs of symmetric diols are listed in Tables II and III. Spectra of the isomeric ketol pairs in $CDCl_3$ have either been reported[3a] or are included in the Experimental Section of this paper. Ketol spectra taken in all three solvents showed only small differences in chemical shifts (up to 0.4 ppm), even smaller changes in the $\Delta\delta$ between the pairs of β-H's (up to 0.1 ppm), and no changes (<0.4 Hz) in J values.

The spectra of the syn and anti ketols and the ss diols all showed distinct eight-line patterns for the β-H's and could be sensibly assigned (based on a Karplus relationship) with the β-H cis to the OH (H_1 or H_4) being relatively upfield. The aa diols, however, were different. Firstly, the coupling constants for the m = 10, 12, 22 aa diols showed a solvent dependence (CD_3OD versus $CDCl_3/C_6D_6$). Secondly, whereas all the other vicinal couplings were at least 3.9 Hz, the pairs of J values for these compounds in $CDCl_3/C_6D_6$ each included one $J < 2$ Hz and one $J \sim 6.5$ Hz.

While the fluxional nature of such cyclopentanols may complicate conformational assignments, the solvent-dependent change in J values for the large ring aa diols signals a change in ring conformation. Moreover, the only way that an aa diol can achieve a conformation with an H–H dihedral angle consistent with such a small J value, while keeping the other dihedral angle near a value permitted by a J of 6.5 Hz, is to severely pucker the hydroxyl-bearing carbon down, away from the polymethylene ring. This allows the H_4–H_O dihedral angle to a be nearly 90° with an H_3–H_O dihedral angle of ~30°. Consistent with the observation that such a puckered conformation is absent in CD_3OD but is present in $CDCl_3/C_6D_6$, we propose that the puckering of these diols is due to the formation of an intramolecular hydrogen bond (Figure 4).

The feasibility of the intramolecular hydrogen bond suggested for the aa diols is confirmed by MM2 calculations for the m = 12 aa diol. Using the [12.3.3] dione coordinates and changing the carbonyls to OH's with appropriate stereochemistry, we find a series of energetically similar minima. Some have the OH groups splayed out away from each other with an oxygen–oxygen distance as large as 6 Å. Others fold the rings down and bring the oxygens within 3 Å of each other and show an O–H–O angle >160°. In methanol there would be strong solvation and, therefore, minimal benefit from intramolecular H-bonding. However, in less polar solvents, such as chloroform and benzene, intramolecular H-bonding of the m = 10, 12, 22 diols compensates energetically for the puckering needed to achieve the required, shorter, oxygen–oxygen distance. The lack of such a puckered conformation in the [3.3.3] and [4.3.3] diols presumably reflects the short, rigid, polymethylene chains of these systems making such a folding too energetically costly. Such a dependence of ring folding on the length of the polymethylene chain is consistent with the crystallographic contrast between the relatively flat m = 4 ss diol[4] and the puckered m = 10 ss diol.[3a]

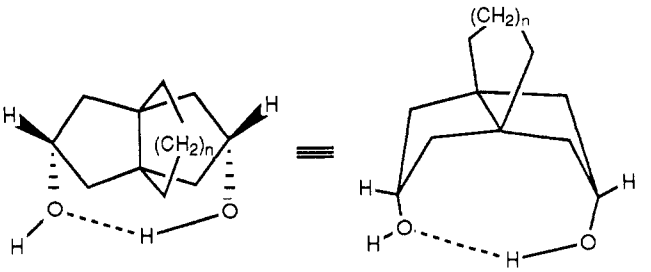

Figure 4. Intramolecular hydrogen bonding of *anti,anti*-Propellanediol.

A second consequence of this intramolecular hydrogen bonding is that the relative chemical shift assignments of the β-H's are now reversed. We had assigned protons cis to the OH group to be relatively upfield. This assignment fit all ketol and diol spectra in CD_3OD and the ketol and ss diol spectra in all solvents. In the m = 10, 12, 22 aa diols, in both C_6D_6 and in $CDCl_3$, $\Delta\delta \leq 0$ (Table III); i.e., the chemical shift of the β-H cis to the OH is now downfield relative to the trans β-H. This change in relative chemical shift (as well as our original chemical shift assignment) was corroborated by a difference NOE experiment on the [10.3.3] aa diol. Irradiation of the upfield polymethylene signal (particularly the CH_2 groups near the quaternary carbons) in CD_3OD enhanced by 10% the intensity of the proton at δ 2.00 relative to the signal at δ 1.89; i.e., the *downfield* signal is nearer to the polymethylene ring. In C_6D_6, this irradiation enhanced by 10% the intensity of the signal at δ 1.75 relative to the signal at δ 1.95; i.e., the *upfield* signal is nearer to the polymethylene. Perhaps the involvement of the otherwise unshared pairs of electrons around the oxygen in an intramolecular hydrogen bond lessens their ability to influence the effective magnetic field of the cis β-H's and is responsible for this change in relative chemical shift.

An interesting corroboration of the difference in behavior between the m = 3, 4 diols and the m = 10, 12, 22 diols is seen in their chromatographic behavior.[3,6,9b] The pairs of symmetric diols can each be separated on silica gel using the same 45:50:5 mix of hexane/EtOAc/*i*-PrOH. For m = 3, 4 the aa diol has a lower R_f than the ss diol; for m = 10, 12, 22 the ss diol has a lower R_f than the aa diol. This is consistent with the intramolecular hydrogen

(8) Angles or J values were calculated using the generalized Karplus equation (Haasnoot, C. A. G.; De Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783) as implemented in the MACROMODEL program (Version 2.0) of Still et al. Qualitative trends were consistent with standard Karplus curves.

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Table II. Chemical Shifts and Vicinal Coupling Constants of Syn,Syn Propellanediols

	CD_3OD		$CDCl_3$		C_6D_6		$\Delta\delta$ H_2–H_1		
ss, diol m =	δH_2 (J)	δH_1 (J)	δH_2 (J)	δH_1 (J)	δH_2 (J)	δH_1 (J)	CD_3OD	$CDCl_3$	C_6D_6
3	1.75 (5.5)	1.56 (6.4)	1.79 (5.4)	1.54 (6.3)	1.74 (5.5)	1.55 (6.3)	0.19	0.25	0.19
4			1.90 (7.7)	1.64 (5.1)				0.26	
10	1.66 (6.8)	1.45 (9.2)	1.82 (6.9)	1.51 (9.2)			0.21	0.31	
12	1.77 (7.0)	1.52 (9.5)	1.82 (7.1)	1.52 (9.3)	1.61 (6.8)	1.43 (9.5)	0.25	0.30	0.18
22			1.87 (6.6)	1.43 (9.3)				0.44	

Table III. Chemical Shifts and Vicinal Coupling Constants of Anti,Anti Propellanediols

	CD_3OD		$CDCl_3$		C_6D_6		$\Delta\delta$ H_3–H_4		
aa-diol m =	δH_4 (J)	δH_3 (J)	δH_4 (J)	δH_3 (J)	δH_4 (J)	δH_3 (J)	CD_3OD	$CDCl_3$	C_6D_6
3			1.78 (5.4)	1.91 (5.6)	1.55 (5.4)	1.83 (5.5)		0.13	0.28
4	1.81 (5.7)	2.06 (8.3)	1.84 (4.4)	2.11 (7.9)	1.89 (4.4)	1.91 (7.9)[a]	0.25	0.27	0.02
10	1.89 (4.8)	2.00 (7.0)	1.98 (1.8)	1.98 (6.8)[a]	1.95 (1.2)	1.75 (6.4)	0.11	0.0	−0.20
12	1.91 (4.5)	2.05 (7.5)	2.01 (1.2)	1.99 (6.4)[a]	1.99 (1.9)	1.83 (6.8)	0.14	−0.02	−0.16
22	1.93 (3.9)	1.93 (7.3)[a]	2.02 (0.0)	1.90 (6.1)	2.03 (0.0)	1.73 (6.5)	0.0	−0.12	−0.30

[a] Values determined by computer fitting to actual spectra.

bond of the larger ring aa diols giving them a lower effective polarity (hence a higher R_f) than the corresponding ss diols. Since this interaction is absent in the smaller ring systems, the (presumably) larger molecular dipole of the aa diol is manifest in its relatively lower R_f value.

Isobutane Chemical Ionization Mass Spectrometry (CIMS). The CIMS of the m = 4 diols shows a prominent $[M + 1]^+$ peak for only the aa isomer of the diol triad;[9a] the spectra of both the ss and sa diols are dominated instead by the loss of one or two molecules of water; they show little or no $[M + 1]^+$. A bridged ion, resembling a protonated form of our intramolecular hydrogen-bonded species, was proposed to account for the stable $[M + 1]^+$ seen in the CIMS of the aa diols. Using diol triads where m = 10, 12, 20, 22, this specificity has been extended[9b] to a general test for diol stereochemistry.

Taken in combination with our NMR study, this work raised two questions. Would the m = 3 bridge prevent the formation of a stabilized bridged ion in the m = 3 aa diol? NMR had shown no intramolecular hydrogen bond in solutions of the m = 4 aa diol, and yet a bridged ion was observed in its CIMS.[9a] Secondly, MM2 calculations show that the large ring aa diols had available conformations which put the two oxygens approximately 3 Å apart. For the m = 12 anti ketol, similar calculations revealed that the oxygens can approach within 3.4 Å of each other. While they did not evidence any intramolecular hydrogen bonding in solution, could a bridging-dependent phenomenon, analogous to that seen in the diols, be identified in the CIMS of the ketols?

The extension of the diol CIMS behavior to the m = 3 series was straightforward. Both the ss and sa m = 3 diols showed prominent peaks at 165 and 147 (loss of one and two molecules of water, respectively), with no detectable 183 $[M + 1]^+$ peak. For the aa diol, the prominence of $[M + 1]^+$, relative to the two water loss peaks (relative intensities of 10:3:1), resembles what we see for the m = 10, 12, 22 diols under comparable conditions.

We then explored the CIMS of the syn and anti ketols (m = 3, 10, 22). For all three systems, the syn ketols showed a dominant $[M + 1]^+$, with a small water loss peak. The anti ketols always showed a major $[(M + 1) - H_2O]^+$ peak. Interestingly, the relative intensity of these ions (particularly for the anti ketols) varied as a function of source temperature (Table IV). Throughout, the only significant peaks in the spectra are those for $[M + 1]^+$ and $[M - 17]^+$. Over a wide range of source temperatures, loss of water for anti ketols persists, while little water loss is observed for syn ketols.

Table IV. Relative Ion Intensities in the Isobutane CIMS of Propellane Ketols

sample	source temp, °C	$[M + 1]^+$	$[M - 17]^+$
m = 3 anti ketol	<150[a]	100	28
	150	100	68
	200	78	100
m = 3 syn ketol	<150[a]	100	4
	150	100	7
	200	100	9
m = 10 anti ketol	<150[a]	100	16
	150	100	51
	200	13	100
m = 10 syn ketol	<150[a]	100	4
	150	100	5
	200	100	13
m = 22 anti ketol	150	100	71
	200	13	100
m = 22 syn ketol	150	100	5
	200	100	9

[a] Signifies coldest source available (uncalibrated).

The results of the sa and ss diol CIMS require that any protonated OH group, not stabilized by bridging, preferentially loses water.[10] However, very little water loss is seen in the syn ketol spectra. Clearly, the >5-kcal/mol higher gas-phase proton affinity of ketones versus alcohols[11] leads to a kinetic preference for carbonyl protonation and/or such a small concentration of protonated hydroxyl that water loss is strongly disfavored. Ketol spectra dominated by the $[M + 1]^+$ ion would result from predominant carbonyl protonation. Where the syn and anti ketols diverge is in the anti ketol's potential for bridging. This allows for the protonated carbonyl to effect an intramolecular proton transfer leading to a protonated hydroxyl and subsequent loss of water (Figure 5).[12]

The strong dependence of anti ketol water loss on source temperature suggests that the bridging required to effect intramolecular proton transfer is a thermally activated process. To the extent that the $[M + 1]^+$ ion can be prominent even in the anti ketol spectrum, the contribu-

(10) (a) Field, F. H. *J. Am. Chem. Soc.* **1970**, *92*, 2672. (b) Despite the discussion of the roles of *tert*-butyl cation and/or protons in propellanediol water loss (ref 9), for clarity we have dealt only with protonation phenomena. If involved, OH abstraction by *tert*-butyl cation would favor water loss from the syn ketol, not the observed anti ketol water loss.

(11) Lias, S. G.; Liebman, J. F.; Levin, R. D. *J. Phys. Chem. Ref. Data* **1984**, *13*, 695.

(12) A referee suggested that a bridging hemiketal may be responsible for enhanced anti ketol water loss. We enriched the carbonyl oxygen of the [10.3.3] ketols with ^{18}O (Risley, J. M.; Van Etten, R. L. *J. Am. Chem. soc.* **1980**, *102*, 6699) and found no evidence for the loss of $H_2{}^{18}O$.

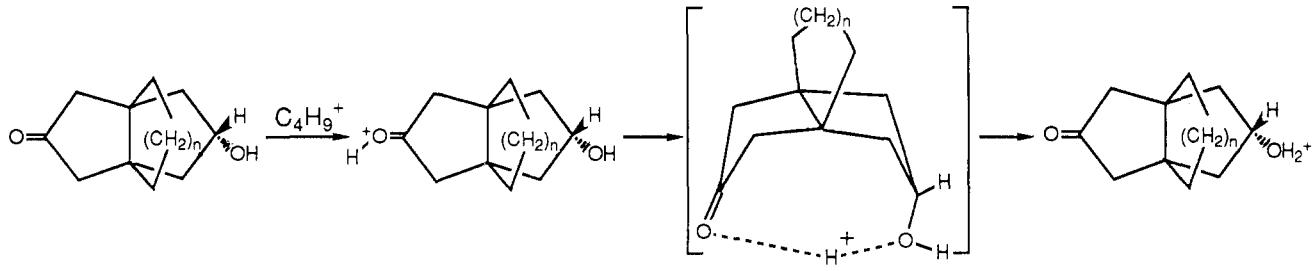

Figure 5. Bridged ion (proton transfer) in anti ketol CIMS.

tion of a bridged ion versus that of an ion that is protonated exclusively on the carbonyl oxygen, cannot be differentiated, and the question of whether such a bridged ion is an intermediate or simply a transition state for proton transfer cannot be addressed. It is clear, however, that whereas the bridging interaction in the aa diol provides the stabilization for an $[M + 1]^+$ ion to persist, in the anti ketol it is the opportunity for a bridging proton transfer that provides a unique pathway for the loss of water.

Conclusions. The following picture of the conformations of [*m*.3.3]propellanes emerges. Ketone-containing rings are relatively flat, as suggested by the $m = 12$ dione crystallography and confirmed by MM2 calculations. Alcohol containing rings can be either flat or puckered. The energetic benefit of intramolecular bridging interactions between the two oxygens can be important both in solution and in the gas phase. Finally, the ease of cyclopentanol puckering is a function of the size of the fused polymethylene ring. Rings were $n \geq 8$ ($m \geq 10$) readily accomodate a range of conformations in the cyclopentanols. When the polymethylene is only three or four carbons long, the resulting fused cyclopentane or cyclohexane influences the conformational flexibility of the two oxygen-bearing rings. The effect of polymethylene rings where $4 < m < 10$, the source of the constraint imposed by the C3 and C4 bridges, and the question of whether an appropriate medium or functionality can induce puckering and/or bridging in the neutral $m = 3, 4$ systems are subjects of ongoing research.

Experimental Section

General. NMR spectra are reported in units δ and were recorded on a Varian XL-200 spectrometer in $CDCl_3$ solvent (unless otherwise indicated). ^1H NMR spectra (200 MHz) are referenced to $CHCl_3$ at 7.24 ppm, and ^{13}C NMR spectra (50 MHz) are referenced to the center of the solvent triplet at 77.00 ppm. NMR's in CD_3OD (Aldrich) are referenced to CH_3 at 3.3 ppm and in benzene-d_6 (Norell) to TMS at 0 ppm. Where needed for spectral interpretation, the spin simulation program provided by Varian with the XL-200 was used to obtain both chemical shift and coupling information. The difference NOE experiments were done on a GE QE-300 spectrometer. IR spectra were recorded on a Mattson Cygnus 25 FT-IR equipped with a water-cooled source and a TGS detector, operating at a resolution of 4 cm^{-1}. HPLC was done on a Waters 590 pump equipped with a Rheodyne 7125 injector and a Waters 401 refractometer. TLC was done on aluminum-backed 0.2-mm 60F254 plates from EM Science and used phosphomolybdic acid as visualization agent. Column chromatography (flash) was done with silica gel from Aldrich (230–400 mesh). Melting points were obtained on a Mel-Temp apparatus and are uncorrected. Electron impact mass spectra (70 eV) were recorded at the Midwest Center for Mass Spectrometry, Lincoln, NE. DMSO (Fisher) was fractionally distilled under vacuum. Toluene (Fisher) was distilled under N_2. Chlorotrimethylsilane (Aldrich) was treated with a small quantity of water and distilled from CaH_2 under N_2. 2-Propanol (Fisher) was dried over active 4-Å molecular sieves. Water was doubly distilled, and all other solvents ($CHCl_3$, hexane, EtOAc, and CH_3OH) were Fisher HPLC grade (used as received). Dimethyl ketoglutarate, CaH_2, $NaBH_4$, and 1,14-tetradecanedioic acid diethyl ester (Aldrich) were used as received.

Propellanes. Synthesis and characterizations of the diones, ketols, and diols of the $m = 4, 10, 22$ systems have been reported.[3] The [3.3.3]propellane-7,10-dione was generously provided by Professor James Cook. The synthesis of [12.3.3]propellane-16,19-dione was accomplished as follows.

1. 2-Oxocyclotetradecanol. In a flame-dried, three-neck, 1-L flask equipped with a mechanical stirrer, reflux condenser with a N_2 inlet, and a 500-mL pressure equalized addition funnel, was placed 350 mL of toluene. The addition funnel was charged with a solution of 1,14-diethyl tetradecanedioate (5.5 g, 0.0175 mol) and TMSCl (55.5 mL, 0.438 mol) in 100 mL of dry toluene. Sodium (1.6 g, 0.07 mol) was introduced into the flask and the toluene was brought to a reflux. The molten sodium was dispersed by stirring at high speed for a few minutes. The stirring rate was then reduced and the solution in the addition funnel was added over a period of 8 h. After the addition was complete, the reaction was refluxed for an additional hour and then cooled to 0 °C. This cold solution was filtered quickly under a stream of argon. (*Caution*: The finely dispersed sodium metal in the filter funnel is pyrophoric and should be quenched carefully with dry 2-propanol). The filtrate was concentrated under reduced pressure, and to the residue were added 150 mL of THF and 10 mL of 1 N HCl. The solution was stirred at room temperature for 1.5 h. The reaction was then neutralized with $NaHCO_3$, and the THF was removed under reduced pressure. The remaining suspension was diluted with H_2O (100 mL) and extracted with $CHCl_3$ (3 × 75 mL). The combined $CHCl_3$ extracts were washed with brine, dried over $MgSO_4$, and concentrated under vacuum. The crude acyloin was purified by flash chromatography (20:80 EtOAc/hexane) and isolated as a white solid, yield 2.674 g (67%), mp 74–76 °C; ^1H NMR 1.30 (s, 20 H), 1.81–1.87 (m, 2 H), 2.26 (m, 1 H), 2.73 (m, 1 H), 3.60 (d, 1 H, $J = 4.4$ Hz), 4.30 (m, 1 H); ^{13}C NMR 212.26, 75.89, 35.18, 33.10, 26.33, 26.21, 25.75, 25.60, 24.55, 24.33, 24.07, 23.93, 20.62, 20.26; IR ($CDCl_3$) 3485, 2932, 2860, 1708.

2. Cyclotetradecane-1,2-dione. In a 100-mL two-neck flask with a magnetic stirring bar and N_2 inlet, were placed the acyloin (2.467 g, 0.011mol), 30 mL of dry Me_2SO, and 20 mL of acetic anhydride. The solution was stirred at room temperature for 16 h and then poured into an Erlenmeyer flask with 200 mL of a 1:1 mixture of EtOAc and saturated $NaHCO_3$ solution. More solid $NaHCO_3$ was added until the evolution of CO_2 ceased. The EtOAc layer was separated, washed with aqueous $NaHCO_3$ (×3) and H_2O (×4), dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude diketone was purified by flash chromatography (5% *tert*-butyl methyl ether, 95% hexane) and isolated as a yellow wax, yield 2.047 g (85%); ^1H NMR 1.22 (m, 16 H), 1.67 (m, 4 H), 2.74 (m, 4 H); ^{13}C NMR 199.85, 34.91, 25.60, 25.35, 25.24, 23.89, 22.47; IR ($CDCl_3$) 2930, 2857, 1711.

3. [12.3.3]Propellane-16,19-dione. To a solution of cyclotetradecane-1,2-dione (1.6 g, 7.1 mmol) in 30 mL of MeOH in a 100-mL two-neck flask was added a citrate–phosphate buffer,[13] dropwise, until the solution turned turbid. Additional MeOH (2 mL) was added to clarify the solution. To this solution was added dimethyl ketoglutarate (3.71 g, 21.3 mmol) in one portion. The reaction mixture was stirred at room temperature for 6 days. The MeOH was removed under vacuum, and the aqueous suspension was partitioned between EtOAc and H_2O. The EtOAc layer was

(13) Cook, J. M.; Yang, S. *J. Org. Chem.* **1976**, *41*, 1903.

separated, dried over $MgSO_4$, and concentrated under vacuum. The oily residue was subjected to Kugelrohr distillation to remove unreacted dimethyl ketoglutarate. The residue (3.77 g) was refluxed in 40 mL of 6 N HCl for 6 h. This mixture was cooled to room temperature and extracted with EtOAc. The EtOAc extract was washed with H_2O, aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude dione was purified (flash chromatography: 25% EtOAc, 75% hexane) and isolated as white crystals, yield 1.4 g (70%), mp 94–96 °C; ^1H NMR 1.35 (s, 20 H), 1.52 (m, 4 H), 2.25 and 2.43 (ABq, 8 H, J = 19.3 Hz); ^{13}C NMR 216.55, 50.35, 48.85, 33.83, 26.81, 25.61, 24.95, 23.42, 21.43; IR ($CDCl_3$) 2933, 2855, 1738.

The ketols and diols of both the m = 3 and m = 12 systems were obtained as described previously for the m = 4, 10, 22 systems.[3]

HPLC of Propellane Ketols. Preparative separations of propellane ketols used a Whatman Partisil Magnum-9 (10 μ) 9.4 mm × 50 cm column with a hexane/EtOAc/*i*-PrOH solvent and a flow of 8.3 mL/min. Separation of m = 3 used a 57:38:5 solvent and gave retention times (in minutes) of 5.8 (dione), 8 (anti ketol), and 10 (syn ketol). Separation of m = 12 used a 75:20:5 solvent and gave retention times (in minutes) of 7 (dione), 10.4 (anti ketol), and 12.4 (syn ketol).

Characterization of the individual ketol isomers from each propellane substrate is based on the following data.

7-Keto[3.3.3]propellane-10-*anti*-ol: mp 171–172 °C; ^1H NMR 1.54 (m, 6 H), 1.82 (m, 4 H), 2.31 and 2.62 (ABq, 4 H, J = 18.4 Hz), 4.43 (m, 1 H); IR (CCl_4) 3500–3200, 2920, 1738. 7-Keto-[3.3.3]propellane-10-*syn*-ol: mp 151–152 °C; ^1H NMR 1.33–1.95 (m, 6 H), 1.59 (dd, 2 H, proton syn to OH, J_{vic} = 9.0 Hz, J_{gem} = 12.8 Hz), 2.03 (dd, 2 H, protons anti to OH, J_{vic} = 5.9 Hz), 2.27 and 2.37 (ABq, 4 H, J = 18.6 Hz), 4.25 (tt, 1 H); IR (CCl_4) 3550–3320, 2922, 1740. 16-Keto[12.3.3]propellane-19-*anti*-ol: mp 68–70 °C; ^1H NMR 1.29 (m, 24 H), 1.70 (dd, 2 H, protons syn to OH, J_{vic} = 3.9 Hz), 2.24 (dd, 2 H, protons anti to OH, J_{vic} = 8.1 Hz, J_{gem} = 14.8 Hz), 2.29 and 2.52 (ABq, 4 H, J = 19.5 Hz), 4.49 (tt, 1 H); IR (CCl_4) 3590–3303, 2928, 1737. 16-Keto[12.3.3]-propellane-19-*syn*-ol: mp 82–83 °C; ^1H NMR 1.38 (m, 24 H), 1.81 (dd, 2 H, protons syn to OH, J_{vic} = 5.5 Hz, J_{gem} = 14.3 Hz), 2.06 (dd, 2 H, protons anti to OH, J_{vic} = 7.8 Hz), 2.13 and 2.29 (ABq, 4 H, J = 18.8 Hz), 4.45 (tt, 1 H); IR (CCl_4) 3590–3303, 2928, 1737.

Diol isomers from each propellane substrate were isolated by HPLC using an IBM ODS (5 μ) 10.0 mm × 25 cm column at 5 mL/min. Separation of the m = 3 diols used MeOH/H_2O 40:60 and gave retention times of 15 (aa diol), 8 (sa diol), and 7 (ss diol). Separation of the m = 12 diols used MeOH/H_2O 85:15 and gave retention times of 15.8 (aa diol), 10 (sa diol), and 7.9 (ss diol).

Characterization of diol isomers is based on the following data. [3.3.3]Propellane-7,10-*anti,anti*-diol: mp 153–155 °C; ^1H NMR 1.45 (m, 6 H), 1.78 (dd, 4 H, J_{vic} = 5.4 Hz), 1.91 (dd, 4 H, J_{vic} = 5.6 Hz, J_{gem} = 13.0 Hz), 4.32 (m, 2 H); IR ($CDCl_3$) 3556–3214, 2937, 1249, 1193, 1046. [3.3.3]Propellane-7,10-*syn,anti*-diol: mp 139–141 °C; ^1H NMR 1.30 (m, 6 H), 1.68 (m, 2 H), 1.73 (m, 2 H), 1.99 (m, 2 H), 2.06 (m, 2 H), 4.09 (m, 1 H), 4.23 (m, 1 H); IR ($CDCl_3$) 3518–3304, 2944, 1240, 1112, 1050. [3.3.3]Propellane-7,10-*syn,-syn*-diol: mp 178–180 °C; ^1H NMR 1.69 (m, 6 H), 1.57 (dd, 4 H, J_{vic} = 6.3 Hz, J_{gem} = 13.0 Hz), 1.79 (dd, 4 H, J_{vic} = 5.4 Hz), 4.19 (m, 2 H); IR ($CDCl_3$) 3357–3071, 2931, 1241, 1114, 1052. [12.3.3]Propellane-16,19-*anti,anti*-diol: mp 170–171 °C; ^1H NMR 1.27 (m, 24 H), 2.0 (m, 8 H), 4.32 (m, 2 H); IR ($CDCl_3$) 3500–3295, 2940, 1233, 1134, 1046. [12.3.3]Propellane-16,19-*syn,anti*-diol: mp 149–151 °C; ^1H NMR 1.32 (m, 24 H), 1.48 (m, 2 H), 1.58 (m, 2 H), 1.99 (m, 2 H), 2.07 (m, 2 H), 4.26 (m, 1 H), 4.55 (m, 1 H); IR ($CDCl_3$) 3500–3250, 2943, 1262, 1101, 1044. [12.3.3]Propellane-16,19-*syn,syn*-diol: mp 154–155 °C; ^1H NMR 1.31 (m, 24 H) 1.52 (dd, 4 H, J_{vic} = 9.3 Hz, J_{gem} = 13.1 Hz), 1.82 (dd, 4 H, J_{vic} = 7.1 Hz), 4.18 (m, 2 H); IR ($CDCl_3$) 3536–3313, 2939, 1266, 1046.

Final corroboration of the stereochemistry of the m = 12 anti,anti diol was obtained by synthesis of its cyclic oxalate as follows. A 50-mL single-neck flask equipped with a magnetic stirring bar, Dean-Stark trap, and a reflux condenser was charged with 20 mL of dry benzene, [12.3.3]propellane-16,19-*anti,anti*-diol (16 mg, 0.052 mmol), anhydrous oxalic acid (4.7 mg, 0.052 mmol), and *p*-toluenesulfonic acid (1 mg, 0.013 mmol). The solution was heated at reflux for 48 h and cooled to room temperature; the benzene was removed under vacuum, and the residue was partitioned between $CHCl_3$ and H_2O (50 mL, 1:1). The $CHCl_3$ layer was separated, washed with H_2O, and dried over $MgSO_4$. Evaporation of the solvent yielded a waxy solid which was chromatographed (silica; 20:80 EtOAc/hexane) to yield 8 mg (42%) of the oxalate. ^1H NMR 1.27 (m, 24 H), 2.01 (dd, 4 H, J_{vic} = 3.3 H and J_{gem} = 15.4 Hz), 2.27 (dd, 4 H, J_{vic} = 8.4 Hz), 5.36 (m, 2 H); IR ($CDCl_3$) 1756, 1732, 1261, 1194; MS (70 eV) no M+ detected, 319.98 (1%, M − CO_2), 290.2606 (40% M − C_2O_3), 272.2490 (7%), 245.2246 (1%).

X-ray Crystallography. A large single crystal of monoclinic habit (2.0 cm × 0.5 cm × 0.5 cm) of [12.3.3]propellane-16,19-dione was grown from ethyl acetate. An approximately spherically shaped sample was cut from this larger crystal and was mounted on a Syntex $P2_1$ diffractometer. The Laue symmetry ($2/m$) and the systematic absences ($h0l$, $h + l = 2n + 1$; $0k0$, $k = 2n + 1$) unambigously define the space group $P2_1/n$ (no. 14, 2nd setting).[14] The unit cell was determined by the least-squares refinement of 15 independent reflections 20.0° ≤ 2θ ≤ 30.0° giving a = 15.865 (5) Å, b = 7.821 (2) Å, c = 16.496 (6) Å, β = 118.14 (2)®, V = 1804.7 (9) Å^3, Z = 4. The data were collected at room temperature from 3.0° ≤ 2θ ≤ 55.0°. The intensity of three check reflections were monitored for decay and with no apparent change over the course of data collection. The density of the crystal determined by flotation in aqueous NaCl solution is 1.12 (1) g cm^{-3}.

The structure was solved by direct methods and refined by Fourier, difference Fourier, and least-squares methods.[15] Hydrogens were calculated at the ideal positions (d = 0.95 Å) and thermal parameters (+1 of the attached carbon). Anisotropic refinement of the nonhydrogen atoms with all the hydrogens "riding" the carbons gave final agreement factors $R(F)$ = 0.054 and $R_w(F)$ = 0.064 for $I \geq 3\sigma(I)$ (1994 data) and $R(F)$ = 0.100 and $R_w(F)$ = 0.074 for data $I \geq 0$ (3570 data).

Chemical Ionization Mass Spectrometry (CIMS). HPLC purified samples of the indicated propellane diols and ketols were introduced into a Kratos MS-25RFA mass spectrometer via the solid inlet probe. The source pressure was kept at 0.4 Torr of isobutane. The source temperature was set at the lowest temperature the instrument could deliver (indicated as <150 °C), at 150 °C or at 200 °C. Generation of the chemical ionization reagent ions was done at 30–100 eV with no significant variation in results. The probe temperature was adjusted, as needed, to volatilize samples: m = 3, 40–50 °C; m = 10, 100–150 °C; and m = 22, 200 °C (higher probe temperature induced sample decomposition).

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Supplementary Material Available: Tables listing the crystallographic data collection details, data reduction and refinement procedures, bond lengths, bond angles, positional parameters, and thermal parameters of the [12.3.3]propellanedione (6 pages); tables of calculated and observed structure factors (17 pages). Ordering information is given on any current masthead page.

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