"zero the block"; therefore the times for spectral acquisition were determined by manually timing the events. The spectrometer began acquiring data approximately 1 min after the sample was introduced into the probe. The first two spectra of each run were discarded to allow the sample to warm to 10 °C. Spectra in which the χ of **3** or **3d4** was below 0.20 were discarded due to the difficulty of accurately integrating small peaks.

Acknowledgment. We thank the NSF for financial support of this work and R. Addleman (Indiana University) for modifications to the NMR spectrometer.

Appendix. See Tables I and II.

Registry No. 1, 16177-46-1; **3**, 2984-58-9; **3d4**, 124200-42-6; **4**, 7161-35-5; **4d4**, 124200-43-7; *cis*-**5**, 826-34-6; *trans*-**5**, 826-35-7; *cis*-**6**, 2345-68-8; *trans*-**6**, 2345-75-7; **7**, 124200-36-8; **9**, 124200-37-9; **10**, 124200-38-0; **11**, 124200-39-1; **12**, 124200-44-8; **13**, 15135-97-4; **14**, 124200-40-4; **15**, 22823-00-3; **16**, 124200-41-5; methyl acrylate, 96-33-3; methyl chloroacetate, 96-34-4; cyclohexanone, 108-94-1; pyridinium chlorochromate, 26299-14-9; deuterium, 7782-39-0.

Thermochemical Studies of Carbonyl Reactions. 4. Enthalpies of Hydrolysis of Norbornyl Ketals

Kenneth B. Wiberg* and Wells C. Cunningham, Jr.

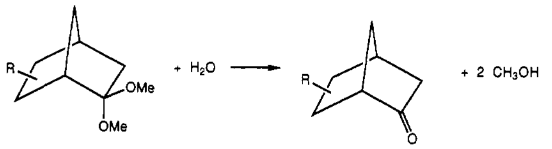
Department of Chemistry, Yale University, New Haven, Connecticut 06511

Received June 12, 1989

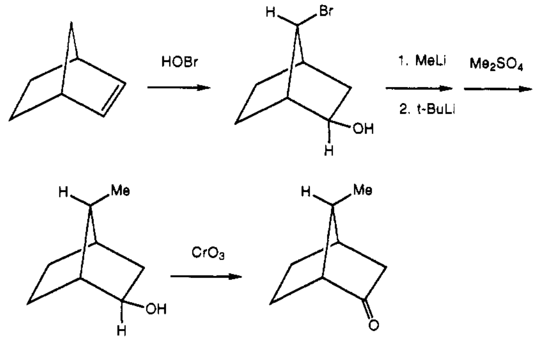
The dimethyl ketals of norbornanone and of eight methyl-substituted norbornanones were prepared, and the enthalpies of hydrolysis were determined. The compounds were chosen to provide a variety of steric interactions between the methyl substituents and the ketal group, much of which would be relieved on going to the ketone. The enthalpies of reaction varied by over 4 kcal/mol. The experimental data were modeled by molecular mechanics (MM2), and although a good correlation was found for the less substituted compounds, the ketal of camphor fell off the slope = 1 correlation line. The free energy changes were determined, and were found not to be well correlated with the enthalpy changes.

Steric effects are commonly associated with the conversion of a trigonal carbon to tetrahedral, as in ester hydrolysis,[1] semicarbazone formation,[2] and a wide variety of related processes. The free energies of activation for many of these reactions may be satisfactorily correlated with Taft's E_s values.[3] In order to gain further information concerning the origin of steric effects, we have measured via calorimetry the effect of alkyl substituents on the difference in energy between aldehydes and acetals,[4] ketones and ketals,[5] and esters and orthoesters.[6] Here, the enthalpy changes did not correlate with the free energy changes, and for the smaller alkyl groups, entropy changes were the dominant component of the free energy terms.

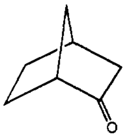
The conformational freedom characteristic of these open-chain compounds makes it difficult to study them via semiempirical methods such as molecular mechanics.[7] Therefore, we have now examined the heats of hydrolysis of methyl-substituted 2,2-dimethoxynorbornanes. Here, it is possible to introduce one or more methyl groups in different orientations with regard to the ketal function. The ring system is relatively rigid, and the use of methyl groups minimizes conformational problems.



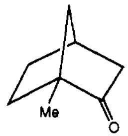
Scheme I



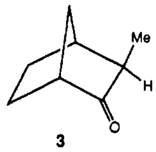
The ketones were obtained from commercial sources (**1**, **9**), prepared via literature procedures or modifications thereof (**2**, **3**, **4**, **5**, **8**), or prepared via a procedure developed in this work (Scheme I, **6**). All of the ketones were carefully purified and converted to their dimethyl ketals using methyl orthoformate. This reaction proceeded well



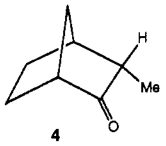
1



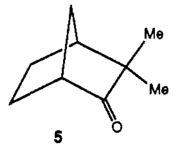
2



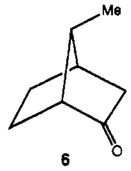
3



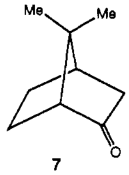
4



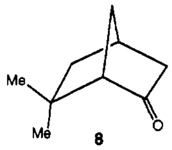
5



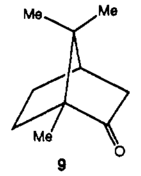
6



7



8



9

---

(1) Ingold, C. K. *J. Chem. Soc.* **1930**, 1032.

(2) Price, F. P., Jr.; Hammett, L. P. *J. Am. Chem. Soc.* **1941**, *63*, 2387.

(3) Taft, R. W., Jr. *Steric Effect in Organic Chemistry*; Newman, M., Ed., Wiley: New York, 1956.

(4) Wiberg, K. B.; Squires, R. R. *J. Am. Chem. Soc.* **1981**, *103*, 4473.

(5) Wiberg, K. B.; Squires, R. R. *J. Am. Chem. Soc.* **1979**, *101*, 5512.

(6) Wiberg, K. B.; Martin, E. J.; Squires, R. R. *J. Org. Chem.* **1985**, *50*, 4717.

(7) Burkert, U.; Allinger, N. L. *Molecular Mechanics*; American Chemical Society: Washington, DC, 1980.

0022-3263/90/1955-0679$02.50/0

Table I. Enthalpy of Hydrolysis of 2,2-Dimethoxynorbornane

run	wt, g	mmol	ΔT, °C	ϵ	ΔH_r, cal/mol
		a. ΔH_r, Dimethoxynorbornane			
1	0.191268	1.22515	-0.09417	80.793	6210
2	0.314582	2.01503	-0.15411	81.364	6223
3	0.280182	1.79468	-0.13712	81.240	6207
4	0.289430	1.85392	-0.14078	81.267	6171
5	0.377417	2.41751	-0.18440	81.316	6202
6	0.262819	1.68346	-0.12882	81.372	6227
				av	6207 ± 13[a]
		b. ΔH_{soln}, Norbornanone			
1	0.209006	1.89876	-0.03619	80.822	1540
2	0.177875	1.61594	-0.03065	80.743	1532
3	0.216876	1.97026	-0.03759	81.032	1546
4	0.247275	2.24642	-0.04284	80.833	1542
5	0.250398	2.27479	-0.04329	80.534	1533
				av	1538 ± 6

run	wt, mg	ΔH, cal/g	
		c. ΔH_{fus}, Norbornanone	
1	2.02	7.45	
2	2.58	7.75	
3	4.45	7.93	av = 849 ± 22 cal/mol

[a] Uncertainties are given as twice the standard deviation from the mean ($2\bar{s}$).

Table II. Enthalpies of Hydrolysis of Dimethoxynorbornanes, Liquid Phase[a]

R	ΔH_{obs}	ΔH_{soln}	ΔH_{fus}	ΔH_r	$\Delta\Delta H_r$
H (**1a**)	6207 ± 13	1538 ± 5	849 ± 22	5491 ± 26	0
3-*endo*-Me (**4a**)	5652 ± 21	880 ± 27	-	4744 ± 34	-747
3-*exo*-Me (**3a**)	5493 ± 23	1251 ± 31	-	4213 ± 39	-1278
7-*syn*-Me (**6a**)	5064 ± 30	1261 ± 35	-	3775 ± 46	-1716
7,7-$(Me)_2$ (**7a**)	4233 ± 107	1892 ± 41	637 ± 54	2951 ± 127	-2540
1-Me (**2a**)	3956 ± 12	1321 ± 55	-	2608 ± 56	-2883
6,6-$(Me)_2$ (**8a**)	3025 ± 26	1297 ± 175	181 ± 19	1881 ± 178	-3610
1,7,7-$(Me)_3$ (**9a**)	2833 ± 13	2248 ± 83	1291 ± 14	1848 ± 85	-3643
3,3-$(Me)_2$ (**5a**)	2751 ± 11	1800 ± 44	359 ± 43	1282 ± 63	-4209
ΔH_{soln}, H_2O = -209.7 ± 9.0					
ΔH_{soln}, CH_3OH = -90.7 ± 3.6					

[a] Energies are given in calories/mole. The uncertainties are given as twice the standard deviation from the mean ($2\bar{s}$).

Table III. Enthalpies of Vaporization and Gas Phase Enthalpies of Hydrolysis (kcal/mol)[a]

		ΔH_v[a]			
R	ΔH_r(l)	ketone	ketal	ΔH_r(g)	$\Delta\Delta H_r$(g)
H (**1**)	5.49 ± 0.03	11.30	12.67*	11.49	0.00
3-*endo*-Me (**4**)	4.74 ± 0.03	11.87	13.35	10.63	-0.86
3-*exo*-Me (**3**)	4.21 ± 0.04	11.87*	13.36*	10.10	-1.39
7-*syn*-Me (**6**)	3.78 ± 0.05	11.99	13.30*	9.81	-1.68
7,7-$(Me)_2$ (**7**)	2.95 ± 0.13	12.58	13.99	8.91	-2.58
1-Me (**2**)	2.61 ± 0.06	11.79	13.06*	8.71	-2.78
6,6-$(Me)_2$ (**8**)	1.88 ± 0.18	12.58	13.94	7.89	-3.60
1,7,7-$(Me)_3$ (**9**)	1.85 ± 0.09	13.08	14.65	7.65	-3.84
3,3-$(Me)_2$ (**5**)	1.28 ± 0.06	12.36	13.94	7.06	-4.43
H_2O, ΔH_v = 10.51					
CH_3OH, ΔH_v = 8.94					

[a] Values marked by asterisks are experimental data (±0.02 kcal/mol), the rest were estimated based on a group equivalent scheme (est. uncertainty ±0.05 kcal/mol).

in most cases, but in the cases of camphenilone (**5**), 6,6-dimethylnorcamphor (**8**), and camphor (**9**), repeated treatments were needed, and in the case of **8**, complete conversion could not be effected. It was not possible to convert fenchone (**10**) to its ketal using methyl orthoformate or other commonly used reagents. With the exception of **8**, the ketals could be obtained in pure form by heating to reflux over and distilling from sodium.

The enthalpies of hydrolysis were measured using 65% dioxane containing 0.01 M perchloric acid as the reaction medium. Data for the hydrolysis of norbornyl ketal are shown in Table I. In order to be able to calculate the enthalpy of hydrolysis in the pure liquid state, the enthalpies of solution of the corresponding norbornanones also were determined. In addition, the enthalpies of fusion of the solid ketones were determined via differential scanning calorimetry. The results for the series of ketals is shown in Table II. It can be seen that they cover a wide range of values with the difference in enthalpies of reaction between the ketals of **1** and **5** being 4.2 kcal/mol.

Comparison with calculated quantities derived via molecular mechanics or molecular orbital theory requires that the enthalpies of reaction be known in the gas phase. The enthalpies of vaporization of several compounds were determined[8] and were related to a group equivalent estimation of these quantities. In this way, an estimate of all

---

(8) The enthalpies of vaporization were measured by M. A. Murcko, who also estimated the enthalpies of vaporization via a new group correlation scheme. The details of this work will be presented elsewhere.

Table IV. Results of Molecular Mechanics Calculations, ΔH_f (kcal/mol)[a]

compound	ketone	ketal A	ketal B	ketal C	ΔH(calc)	ΔH(obs)
norbornanone (**1**)	-38.54	**-89.59**	-86.16	-83.63	12.71	11.49
endo-3-methyl (**4**)	-45.28	**-95.27**	-92.02	-89.90	11.65	10.63
exo-3-methyl (**3**)	-45.47	-92.22	**-95.33**	-89.21	11.52	10.10
syn-7-methyl (**6**)	-44.34	**-94.06**	-93.72	-89.70	11.38	9.81
7,7-dimethyl (**7**)	-49.49	**-97.85**	-97.66	-93.18	10.02	8.91
1-methyl (**2**)	-48.24	**-96.41**	-92.76		9.83	8.71
6,6-dimethyl (**8**)	-52.50	-98.88	**-100.01**	-95.66	9.17	7.89
1,7,7-trimethyl (**9**)	-58.54	**-103.56**	-100.56	-100.77	6.68	7.65
3,3-dimethyl (**5**)	-51.77	-97.49	**-97.90**	-89.37	7.79	7.06

[a] The values in boldface were used to calculate the estimated change in ΔH.

Table V. Transketalization Data, 1,2-Dimethoxyethane Solution

R1	R2	K	ΔG_r	ΔG°[a]	$\Delta\Delta G^\circ$
3-*endo*-Me	H	19.3 ± 5.0	-1.75 ± 0.14	-4.55 ± 0.15	-1.75
3-*exo*-Me	H	6.65 ± 1.0	-1.12 ± 0.08	-3.92 ± 0.09	-1.12
7-*syn*-Me	3-*endo*-Me	1.47 ± 0.13	-0.23 ± 0.5	-4.78 ± 0.16	-1.98
7,7-$(Me)_2$	3-*endo*-Me	1.78	-0.34	-4.89 ± 0.18	-2.09
7,7-$(Me)_2$	3,3-$(Me)_2$	0.89	+0.07	-4.89 ± 0.21	
1-Me	3-*endo*-Me	1.6	-0.28	-4.83 ± 0.18	-2.03
1-Me	3,3-$(Me)_2$	0.75	+0.17	-4.79 ± 0.21	
6,6-$(Me)_2$	3-*endo*-Me	2.05	-0.42	-4.97 ± 0.18	-2.17
6,6-$(Me)_2$	3,3-$(Me)_2$	1.1	-0.06	5.02 ± 0.21	
1,7,7-$(Me)_3$	3,3-$(Me)_2$	1.18 ± 0.15	-0.10 ± 0.07	-5.06 ± 0.19	-2.26
3,3-$(Me)_2$	3-*endo*-Me	2.0 ± 0.4	-0.41 ± 0.10	-4.96 ± 0.18	-2.16

[a] Free energy change for the conversion of the ketal (Rl) to the corresponding ketone based on norbornanone ketal ΔG = 2.80 ± 0.05 kcal/mol.

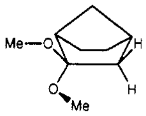
Table VI. Transketalization Data, Methanol Solution

R1	R2	K	ΔG_r	ΔG°[a]	$\Delta\Delta G^\circ$
3-*endo*-Me	H	7.4 ± 0.7	-1.18 ± 0.06	-3.98 ± 0.08	-1.18
3-*exo*-Me	H	16.0 ± 0.1	-1.64 ± 0.01	-4.44 ± 0.05	-1.64
7,7-$(Me)_2$	3-*endo*-Me	3.39 ± 0.4	-0.72 ± 0.07	-4.70 ± 0.11	-1.90
1-Me	3-*endo*-Me	6.7	-1.13	-5.11 ± 0.10	-2.31
1,7,7-$(Me)_3$	3,3-$(Me)_2$	1.8 ± 0.8	-0.35 ± 0.21	-5.60 ± 0.23	-2.80
3,3-$(Me)_2$	3-*endo*-Me	8.6 ± 0.75	-1.27 ± 0.05	-5.25 ± 0.09	-2.45

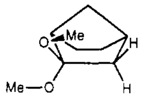
[a] Free energy change for conversion of the ketal (Rl) to the corresponding ketone based on norbornanone ketal ΔG = -2.80 ± 0.05 kcal/mol.

of the vaporization enthalpies was obtained, and the enthalpies of hydrolysis corrected to the gas phase are given in Table III.

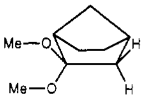
There are three basic conformations for the norbornyl ketals. Two (A and B) have the geometry required for anomeric stabilization and would be expected to have lower energies than conformation C. It was found that both the *exo*-3-methyl (**3a**) and *endo*-3-methyl (**4a**) ketals were destabilized with respect to norbornanone ketal (**1a**). The effect was relatively small since the ketal conformation (A or B) could be chosen which would minimize steric interactions. With the 3,3-dimethyl ketal (**5a**), however, such a choice is not possible since both the exo and endo positions are occupied. It is not surprizing that a very large effect would be found in this case.



A



B



C

The *syn*-7-methyl ketal (**6a**) and the 7,7-dimethyl ketal (**7a**) show the importance of the "buttressing effect" which was first observed in the activation energy for the racemization of sterically hindered biphenyls.[9] The second methyl group can have no direct interaction with the ketal center. However, its presence makes it more difficult for the *syn*-methyl group to bend away from the ketal, thereby increasing nonbonded interactions.

When there is a strong interaction between the methyl group and the ketal center, as with the 1-methyl ketal (**2a**) and the 7,7-dimethyl ketal (**7a**), the combination of the two types of substitution, as in camphor ketal (**9a**), leads to only a modest further change in enthalpy of reaction. The large effect of 6,6-dimethyl substitution (**8a**) also may be noted.

We wish to try to understand the experimental results in terms of the intramolecular interactions present in the molecules. Molecular mechanics provides a convenient framework for examining these interactions, and in this area Allinger's MM2 program[7,10] is probably the most widely used. The geometries of each of the ketals and ketones were optimized using MM2, giving the estimated enthalpies of formation listed in Table VI. All three ketal conformers (A, B, and C) were examined, and the one with the lowest calculated energy was used in calculating the enthalpy of reaction. The values thus obtained are compared with the experimental enthalpies of reaction in Figure 1. The line is drawn with a unit slope. It can be seen that the less substituted compounds fall reasonably near the line, but that the ketal of camphor gives a large deviation. It appears that most of the basic effects which contribute to the differences in heats of reaction are fairly

---

(9) Adams, R.; Yuan, H. C. *Chem. Rev.* **1933**, *12*, 261. Westheimer, F. H.; Mayer, J. E. *J. Chem. Phys.* **1949**, *14*, 733.

(10) The 1987 MM2 parameter set was used.

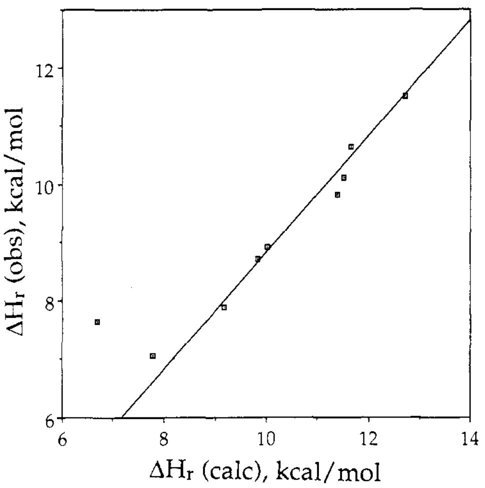


Figure 1. Relationship between the observed enthalpies of hydrolysis of norbornyl ketals and those calculated using MM2. The line is drawn with a unit slope.

well incorporated into the MM2 force field.

An examination of the individual values indicates that some of the group contribution terms may be in error. The calculated ΔH_f for norbornanone is −38.54 kcal/mol, which is reasonably close to the observed value, −40.1 ± 0.8 kcal/mol.[11] However, with camphor, the calculated ΔH_f is −58.54 kcal/mol whereas the observed value is −63.9 ± 0.7 kcal/mol.[12] Here, the deviation is over 5 kcal/mol.

The experimental data allow a calculation of ΔH_f for norbornanone ketal which is −90.4 ± 0.9 kcal/mol and may be compared with the MM2 value of −89.59 kcal/mol. They are in satisfactory agreement. In the case of camphor ketal, the observed ΔH_f is −109.9 kcal/mol whereas the MM2 enthalpy is −103.6 kcal/mol. As with camphor, the deviation is fairly large.

It must be remembered that molecular mechanics is dependent on having good experimental data in order to derive appropriate intramolecular potentials. Relatively few data have been available for compounds of the type studied in this investigation. It would be desirable to make use of the present data to derive improved parameters for MM2. However, there are difficulties in doing so. The enthalpies of reaction only give the difference in energy between the ketones and ketals, and neither type of molecule is easily modeled. The ketones are known to prefer a conformation with an alkyl group eclipsing the carbonyl in order to benefit from a dipole-induced dipole stabilization.[13] How will this interaction affect the *exo*- and *endo*-3-methylnorbornanones and 1-methylnorbornanone? Will there be an interaction between a *syn*-7-methyl group and the carbonyl? Similarly, with the ketals, how does the anomeric stabilization compete with steric interactions at the ketal group?

It is well established that the geometries and energies of a variety of alkanes may be well reproduced via molecular mechanics.[14] Alcohols represent a fairly simple perturbation on the structure and probably can be equally well modeled. We have recently developed a method for determining the enthalpies of reduction of ketones.[15] We plan to measure the heats of reduction of the norbornyl ketones to the more easily modeled alcohols. Additional information concerning steric interactions may be obtained by studying the equilibrium exo/endo ratios for the substituted norbornanols. A comparison of the measured heats of reduction, and the exo/endo energy differences with the predictions of molecular mechanics should allow a more careful examination of substituent effects on theses ketones. This, in turn, should facilitate a further study of the ketals.

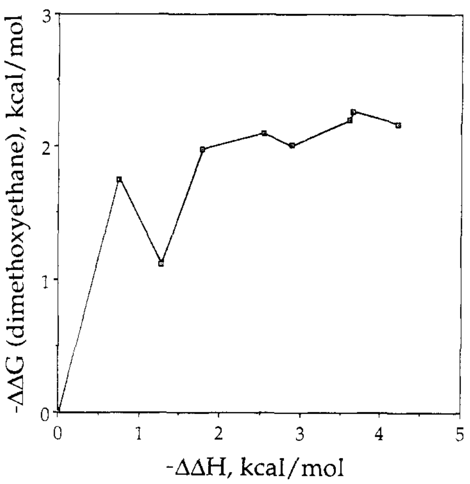
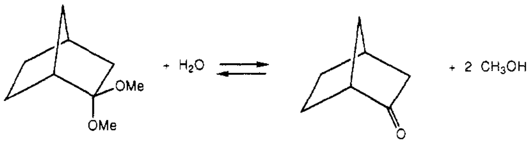
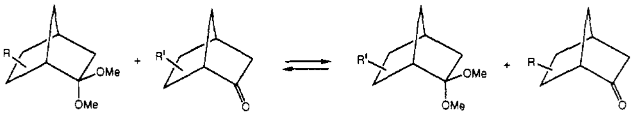


Figure 2. Relationship between the change in free energy of hydrolysis of norbornyl ketals in 1,2-dimethoxyethane and their enthalpies of hydrolysis.

It seemed important to know whether or not the enthalpy changes paralleled the free energy changes in this series of compounds. It was possible to measure the equilibrium constant for the reaction of norbornanone (1) with methanol:



The equilibrium constant was 113 ± 8 corresponding to ΔG° = −2.80 ± 0.05 kcal/mol. In no other case was it possible to observe this equilibrium. Therefore, the remaining compounds were studied via transketalization equilibria:



It was possible that there might be significant solvent effects on such equilibria. Therefore, they were studied in both an aprotic solvent, 1,2-dimethoxyethane-d_{10}, and in methanol-d_4. The former solvent might be expected to give nearly ideal solutions of ketones and ketals, whereas the latter would be typical of a strongly hydrogen-bonding solvent. It was possible to observe nmr signals for components of the mixtures at 500 MHz, and in most cases the equilibria were approached from both sides. The free energy charges are summarized in Table V, and the details of the equilibrium experiments are given in the Experimental Section.

A plot of ΔH_r vs ΔG_r (Figures 2 and 3) shows that in this case also, the two quantities are not well correlated. The values found in methanol show a reasonable trend, but the range of free energy changes was smaller than that for ΔH. In dimethoxyethane, any methyl substitution produces a significant change in ΔG, but the nature of the substitution has little effect. This may be a result of steric hindrance to solvation. The difference between the ΔH and ΔG

---

(11) Steele, W. V. *J. Chem. Thermodyn.* **1978**, *10*, 585.
(12) Steele, W. V. *J. Chem. Thermodyn.* **1977**, *9*, 311.
(13) Wiberg, K. B.; Martin, E. *J. Am. Chem. Soc.* **1985**, *107*, 5035.
(14) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127.
(15) Wiberg, K. B.; Crocker, L., to be published.

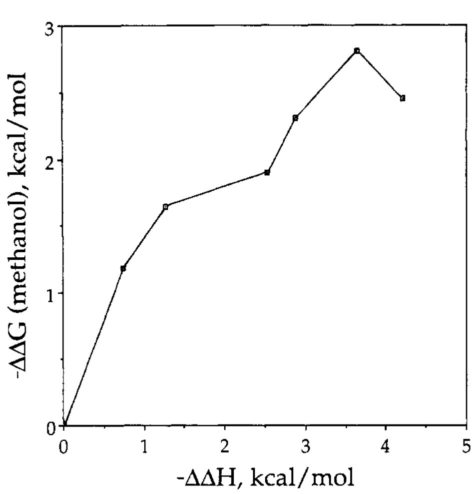


Figure 3. Relationship between the change in free energy of hydrolysis of norbornyl ketals in methanol and their enthalpies of hydrolysis.

values is of some importance since the equilibrium constant is usually of more practical importance than the enthalpy change.

Conclusions

The hydrolysis of methyl-substituted norbornane ketals has revealed a relatively large range of changes in steric interactions on going from ketal to ketone. These changes are fairly satisfactorily modeled via MM2. However, with camphor, the MM2 enthalpies of formation for the ketone and ketal, as well as the enthalpy of hydrolysis, are significantly in error. Further experimental data will be required in order to clarify the steric interactions in these compounds. A comparison of the free energies and enthalpies of reaction showed that the steric effect on the equilibrium had a significant entropy component.

Experimental Section

Materials. Norbornanone (1) and camphor (9) were commercial samples and were purified by sublimation. Analysis by GC showed no observable impurities. Tetrahydrofuran and dioxane were purified by distillation from benzophenone ketyl. Camphenilone (5) was prepared by the ozonization of camphene[16] and was purified by conversion to the ketal followed by careful distillation and hydrolysis back to the ketone. *endo*-3-Methylnorbornanone (4) was prepared by the hydrogenation of 3-methylenenorbornanone.[17] *exo*-3-Methylnorbornanone (3) was prepared by the alkylation of norbornanone[18] using LDA and methyl iodide at 25 °C (10 min) followed by preparative HPLC using 10% ethyl acetate in hexane. 1-Methylnorbornanone (2) was prepared from norbornanone via addition of methylmagnesium bromide, rearrangement, and oxidation.[19] 6,6-Dimethylnorbornanone (8) was prepared from 5,5-dimethylnorbornene[20] via epoxidation, reduction to the alcohol, and oxidation to the ketone. It gave 8 contaminated with ~5% of 5,5-dimethylnobornanone. They could be separated by preparative GC using a $^3/_8$ in. × 10 ft column having 20% DIDP on Chromosorb W.

***syn*-7-Methylnorbornanone (6).** To a stirred suspension of 76.0 g of *N*-bromosuccinimide in 200 mL of water at 0 °C was added 40.0 g of norbornene in portions over 15 min. It was allowed to warm to room temperature and was stirred overnight. The layers were separated, and the water layer was washed with ether. The organic solution was dried over magnesium sulfate, and the solvent was evaporated. The residue was distilled collecting material bp 70 °C at 0.3 mm, giving 21.0 g of *syn*-7-bromonorborneol, mp 25–28 °C.

To a round-bottomed flask equipped with a drying tube, reflux condenser, and nitrogen inlet was added 10.0 g of the bromo alcohol and 50 mL of ether. It was cooled to −78 °C, and 42 mL of 1.4 M methyllithium in ether was added. After the mixture was stirred for 0.5 h, 100 mL of ether was added, and the mixture was cooled to −78 °C. There was added 68 mL of 1.7 M *tert*-butyllithium in pentane. After being stirred for 15 min at −78 °C, the solution was allowed to warm to room temperature (30 min).

A dropping funnel was substituted for the drying tube, and dimethyl sulfate was added until refluxing stopped (~9 mL). The solution was stirred for 5 min and then quenched with water. Dilute aqueous ammonia was added, and the solution was vigorously stirred for 2 h. The layers were separated, and the aqueous layer was washed with ether. The organic layers were combined, dried over magnesium sulfate, and concentrated to give a solid. It was sublimed (2.0 mm at 60 °C) to give 7.9 g of a 1.4:1 mixture of *syn*-7-methylnorbornanol and norbornanol. The mixture was oxidized using chromic acid,[19] and the resultant ketone mixture was distilled through a 2 ft spinning band column at 100 mm. Norboranone distilled first and solidified in the condenser. Distillation was continued until liquid 8 began to appear. Distillation was halted and norbornanone was cleaned out of the apparatus. Continued distillation (110 °C) yielded 1.2 g of 8: ^{1}H NMR (250 MHz) δ 2.44 (s, 1 H), 2.37 (s, 1 H), 2.25 (br s 1 H), 3.15 (br m, 1 H), 2.93 (br d, 2 H), 2.30 (d, 1 H), 1.85 (d, 2 H), 1.06 (d, 3 H); ^{13}C NMR (250 MHz) δ 14.0, 54.1, 42.7, 39.4, 38.7, 27.8, 23.3, 11.8.

7,7-Dimethylnorbornanone. A mixture of 63 g of sodium, 700 mL of tetrahydrofuran, and 130 mL of *tert*-butyl alcohol was heated to reflux, and a solution of 20.6 g of 1-bromo-7,7-dimethylnorbornanone[21] in 100 mL of tetrahydrofuran was added dropwise over 1 h. The mixture was heated to reflux overnight. After cooling, the solution was decanted from the excess sodium, and an equal volume of water was added to the solution. The solution was extracted with petroleum ether, acidified, and extracted again. The organic layer was dried over magnesium sulfate and concentrated, giving 6.3 g of a 90:10 mixture of 7,7-dimethylnorbornanol and 7,7-dimethylnorbornanone. Oxidation of 12.8 g of the mixture with chromic acid[19] gave 11.8 g of a yellow oil. Sublimation under reduced pressure at room temperature gave 10.5 g of the ketone, mp 104–105 °C: ^{1}H NMR (500 MHz) δ 2.65 (br d, 1 H), 2.23 (m, 1 H), 1.7 (m, 2 H), 1.35 (s, 3 H), 1.33 (s, 3 H).

Formation of Ketals. To a flask with a reflux condenser was added under nitrogen 10.0 g of freshly sublimed camphor. Methanol (20 mL, distilled from $Mg(OMe)_2$) was added along with 15 mL of trimethyl orthoformate (1.5 equiv) and several crystals of *p*-toluenesulfonic acid. The mixture was heated to reflux overnight. It was cooled, and 10% potassium hydroxide solution was slowly added until two layers formed (~10 mL). The layers were extracted several times with 60:40 methylene chloride–pentane. The combined organic layers were dried over potassium carbonate. Removal of solvent gave 11.1 g (79%) of the ketal, which was purified by distillation (80 °C at 10 min). The distillate was checked by IR for the presence of a carbonyl band. The other ketals were prepared in the same manner.

If some ketone remained as an impurity, it could be removed in one of two ways. It could be heated to reflux over liquid sodium for 1 h, followed by distillation. As an alternative, it could be treated with 1 M diisobutylaluminum hydride in toluene, followed by distillation. With one exception, all of the ketones could be completely converted to their ketals. 6,6-Dimethylnorbornanone reacted partway, and its mixture with its ketone was used in the calorimetric study. The ratio of the ketal to ketone was determined by NMR. Fenchone could not be converted to its ketal and therefore was not included in this study. The spectral data for the ketals was as follows.

---

(16) Bailey, P. S. *Chem. Ber.* **1955**, *88*, 785.

(17) Alder, K.; Grell, A. *Chem. Ber.* **1956**, *89*, 2198.

(18) Corey, E. J.; Hartmann, R.; Vatekencherry, P. A. *J. Am. Chem. Soc.* **1962**, *84*, 2611.

(19) Berson, J. A.; Walia, J. S.; Remanick, A.; Suzuki, S.; Reynolds-Warnhoff, P.; Willner, D. *J. Am. Chem. Soc.* **1961**, *83*, 3986.

(20) Schleyer, P. v. R.; Donaldson, M. M.; Watts, W. E. *J. Am. Chem. Soc.* **1965**, *87*, 375.

(21) Fong, W. C.; Thomas, R.; Scherer, K. V., Jr. *Tetrahedron Lett.* **1971**, 3789.

Norbornyl ketal: ^{1}H NMR (500 MHz) δ 3.10 (s, 3 H), 3.07 (s, 3 H), 2.28 (m, 1 H), 2.16 (br s, 1 H), 1.67 (m, 1 H), 1.58 (d, 1 H), 1.45 (m, 2 H), 1.20 (m, 1 H), 1.14 (m, 1 H); ^{13}C NMR δ 100.36, 39.65, 37.20, 33.35, 31.40, 27.90, 26.37, 29.80, 12.12; d^{25} = 1.00 g/mL; bp 80–82 °C at 10 mm.

Camphor ketal: ^{1}H NMR (500 MHz) δ 3.12 (s, 3 H), 3.07 (s, 3 H), 2.05 (br d, 1 H), 0.93 (s, 3 H), 0.91 (s, 3 H), 0.82 (s, 3 H); ^{13}C NMR δ 108.70, 52.76, 49.73, 47.76, 44.17, 43.95, 40.65, 29.10, 27.09, 22.55, 20.25, 12.15; d^{25} = 0.967 g/mL; bp 40–41 °C at 0.03 mm.

1-Methylnorbornanone ketal: ^{1}H NMR (500 MHz) δ 3.13 (s, 3 H), 3.00 (s, 3 H), 2.15 (br s, 1 H), 1.97 (br dq, 1 H), 1.85 (m, 3 H), 1.72 (d, 1 H), 1.3–1.5 (m, 2 H), 1.37 (s, 3 H), 1.25 (dq, 1 H). ^{13}C NMR δ 108.14, 51.25, 50.85, 47.46, 46.97, 43.72, 35.81, 30.67, 17.49; d^{25} = 0.982 g/mL; bp 41–43 °C at 0.6 mm.

3,3-Dimethylnorbornanone ketal: ^{1}H NMR (500 MHz) δ 3.15 (s, 3 H), 3.08 (s, 3 H), 2.23 (dd, 2 H), 1.78 (d, 1 H), 1.63 (m, 2 H), 1.48 (m, 1 H), 1.33 (m, 1 H), 0.97 (s, 3 H), 0.88 (s, 3 H); ^{13}C NMR δ 109.47, 50.52, 50.89, 49.94, 45.37, 44.32, 33.55, 25.65, 23.63, 22.45, 21.34; d^{25} = 0.993; bp = 45–47 °C at 0.4 mm.

***endo*-3-Methylnorbornanone ketal**: ^{1}H NMR (500 MHz) δ 3.10 (s, 3 H), 3.05 (s, 3 H), 2.25 (br s, 2 H), 2.02 (br s, 1 H), 1.88 (br m, 1 H), 1.56 (d, 1 H), 1.45 (t, 2 H), 1.34 (t, 1 H), 0.82 (d, 3 H); ^{13}C NMR δ 107.3, 49.2, 46.4, 44.2, 42.0, 41.5, 36.0, 21.6, 20.9, 11.6; d^{25} = 1.00 g/mL; bp = 35–38 °C at 1 mm.

***exo*-3-Methylnorbornanone ketal**: ^{1}H NMR (60 MHz) δ 3.24 (s, 3 H), 3.12 (s, 3 H), 2.34 (br s, 1 H), 1.1–1.7 (br m, 7 H), 0.89 (d, 3 H); ^{13}C NMR δ 109.1, 49.3, 48.17, 45.73, 44.16, 41.50, 33.6, 29.5, 21.5, 9.7; d^{25} = 1.02 g/mL; bp = 42–45 °C at 1 mm.

***syn*-7-Methylnorbornanone ketal**: ^{1}H NMR (500 MHz) δ 3.08 (s, 3 H), 3.30 (s, 3 H), 2.20 (br s, 2 H), 2.06 (d, 1 H), 1.87 (q, 2 H), 1.30 (m, 2 H), 1.18 (m, 2 H), 0.94 (d, 3 H); d^{25} = 0.972 g/mL; bp = 30–32 °C at 1 mm.

7,7-Dimethylnorbornanone ketal: ^{1}H NMR (500 MHz) δ 3.06 (s, 3 H), 3.30 (s, 3 H), 2.10 (br d, 1 H), 1.57 (m, 5 H), 1.03 (s, 3 H), 0.97 (s, 3 H); the last two were superimposed on a 2 H multiplet; d^{25} = 1.09 g/mL; bp = 52–54 °C at 2 mm.

Calorimetric Measurements. The reaction enthalpies were determined using the automated calorimetric system previously described.[22] In each run, 100 mL of 65% dioxane containing 0.01 M perchloric acid was placed in the calorimetric cell, and the ketal was weighed into a glass ampoule. The temperature was measured to 0.0001° every 10 s, and when the system had come to equilibrium at 25.0 °C, the ampoule was broken. Data were continued to be collected at 10-s periods through the afterperiod. An electrical calibration was carried out for each calorimetric run.

The purity of the ketones was established by GC and was better than 99% in all cases. The purity of the ketals was determined by infrared spectroscopy. In all cases except 6,6-dimethylnorbornanone ketal, no carbonyl band was found. As little as 0.2% of ketone may be detected in this fashion. With the 6,6-dimethyl compound, the ratio of ketone to ketal was determined by NMR spectroscopy, and the observed enthalpies were corrected for the amount of ketone present.

In all cases, the hydrolysis reaction proceeded to completion (9 half-lives) within 10 min. The products of the hydrolyses were determined by NMR spectroscopy, and in each case the only product was the corresponding ketone.

Equilibrium Measurements. The equilibrium constant for the reaction of dimethoxynorbornanone with water to give norbornanone and methanol was determined by placing about 100 mg of the ketal or ketone in ~600 mg of anhydrous methanol-*d* to which was added 2–20 mg of water. A small crystal of *p*-toluenesulfonic acid was added, and the solution was transferred to an NMR tube. Spectra were taken at different times (15 min, 1 h, 2 h, 12 h, and 24 h), and after 2 h the spectrum no longer changed. The equilibrium constant was given by

$$K_{eq} = [\mathrm{ketone}][\mathrm{CH_3OH}]^2/[\mathrm{ketal}][\mathrm{H_2O}]$$

where the concentrations of methanol and of water are given as mol fractions, leading to a unitless equilibrium constant. The value was 113 ± 8.

The transketalization reactions were carried out in a similar manner. Accurately weighed quantities of a ketone and of a ketal of a different ketone (10–100 mg each) were dissolved in anhydrous 1,2-dimethoxyethane, and a small crystal of *p*-toluenesulfonic acid was added. The solution was equilibrated for 2 h, and a 500-MHz spectrum was taken. The receiver delay time was set to 2–3 s, and usually 80 scans were taken. Bands which were unique to each of the components were determined from their individual spectra, and the equilibrium constants were determined from the band areas. In many cases, the equilibrium was approached from both sides, and consistent results were obtained.

Several cross-checks were made by comparing groups of ketals and ketones, and again consistent results were obtained. The *endo*-3-methyl ketal and ketone were used in many of the studies since the equilibrium constants for the transketalization using the unsubstituted compounds were too large to allow accurate determinations.

Acknowledgment. This investigation was supported by the Office of Basic Energy Sciences, Department of Energy.

Registry No. 1, 497-38-1; **1a**, 10395-51-4; **2**, 10218-04-9; **2a**, 26327-56-0; **3**, 3915-75-1; **3a**, 124287-78-1; **4**, 4154-60-3; **4a**, 124287-79-2; **5**, 13211-15-9; **5a**, 124287-80-5; **6**, 23472-35-7; **6a**, 78365-95-4; **7**, 514-15-8; **7a**, 124287-82-7; **8**, 38476-45-8; **8a**, 124287-81-6; **9**, 76-22-2; **9a**, 10395-50-3; **10**, 1195-79-5; norbornene, 498-66-8; *syn*-7-bromonorborneol, 89892-92-2; 1-bromo-7,7-dimethylnorbornanone, 34252-16-9.

---

(22) Wiberg, K. B.; Squires, R. R. *J. Chem. Thermodyn.* **1979**, *11*, 773.