Polar Substituent Effects in 1,3-Disubstituted Bicyclo[1.1.1]pentanes

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The pK_a's of eight 3-substituted bicyclo[1.1.1]pentanecarboxylic acids have been measured and found to correlate well with σ_I constants. The value of ρ_I (2.23 ± 0.12) is large but not large enough to propose any special perturbation of normal field-inductive effects by the close proximity (about 1.88 Å) of the bridgehead carbons. Also determined were the products and rates of solvolyses of the *p*-nitrobenzoates of three 3-substituted 1-(2-hydroxy-2-propyl)bicyclo[1.1.1]pentanes. The products were primarily unrearranged, and the rates again showed no surprising substituent effects. A practical synthesis of 1,3-disubstituted bicyclo[1.1.1]pentanes has been developed and is described.

Bicyclo[1.1.1]pentane (1) has the very special property

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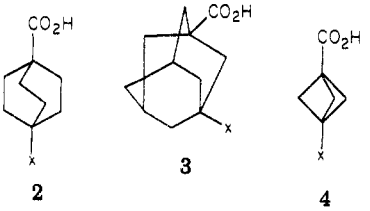
that the two bridgehead carbon atoms are closer together than any other two formally nonbonded carbons in organic chemistry. Measured values of this distance are 1.845 and 1.874 Å by electron diffraction on the hydrocarbon,[1,2] 1.850 Å by microwave spectroscopy on the 1-chloro derivative,[3] and 1.89 Å by X-ray diffraction on the (*p*-bromophenyl)urethane of 2-phenylbicyclo[1.1.1]pentan-2-ol.[4] The chemical consequences of such close proximity of nonbonded carbons are essentially unknown, but a striking physical effect is that the spin–spin coupling constant between the bridgehead protons is 18 Hz,[5] apparently a record for four-bond coupling. Theoretical discussions of the system have focussed on the possibility of significant overlap between the rear lobes of the bridgehead orbitals directed at the substituent protons.[6-8] The bicyclo[1.1.1]pentane system appeared to provide an unexcelled opportunity to look for chemical consequences of rear-lobe overlap, and the present work was undertaken to find out whether one bridgehead substituent in the system has any unusual effect, in kind or magnitude, on the chemical behavior of a functional group at the other bridgehead.

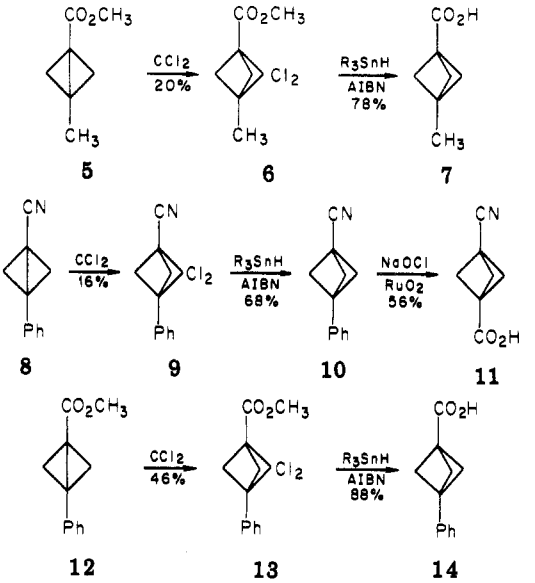
The literature already contains much information on polar substituent effects in rigid alicyclic systems suitable for qualitative comparison with the bicyclo[1.1.1]pentane system. The acidities of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids (2), in particular, have been thor-



2 3 4

oughly investigated by Roberts and Moreland,[9] Wilcox and McIntyre,[10] Ritchie and Lewis,[11] and Holtz and Stock.[12] These compounds were used to define the polar substituent constants, σ', like Hammett σ values but free of π-resonance effects.[9] The σ_I polar inductive constants were later defined so as to be comparable in magnitude to the σ' values[13] but to be measurable without the need to synthesize compounds of type 2. Another rigid system on which acidity measurements have been made is the 3-substituted adamantane-1-carboxylic acid (3) system,[14,15] which does not keep the substituent and carboxyl bond axes colinear as in 2 but does have the same separation in number of bonds between these groups as in 3-substituted bicyclo[1.1.1]pentane-1-carboxylic acids (4).

Scheme I[a]



5 6 7 8 9 10 11 12 13 14

[a] R = *n*-C_4H_9.

Synthetic Studies

At the outset of this study there were no attractive general synthetic routes to the bicyclo[1.1.1]pentane ring system, and the only 1,3-disubsitituted example was the

(1) Chiang, J. F.; Bauer, S. H. *J. Am. Chem. Soc.* **1970**, *92*, 1614.
(2) Almenningen, A.; Andersen, B.; Nyhus, B. A. *Acta Chem. Scand.* **1971**, *25*, 1217.
(3) Cox, K. W.; Harmony, M. D. *J. Mol. Spectrosc.* **1970**, *36*, 34.
(4) Padwa, A.; Shefter, E.; Alexander, E. *J. Am. Chem. Soc.* **1968**, *90*, 3717.
(5) Wiberg, K. B.; Connor, D. S. *J. Am. Chem. Soc.* **1966**, *88*, 4437.
(6) Newton, M. D.; Schulman, J. M. *J. Am. Chem. Soc.* **1972**, *94*, 773.
(7) Lehn, J. M.; Wipff, G. *Chem. Phys. Lett.* **1972**, *15*, 450.
(8) Whitman, D. R.; Chiang, J. F. *J. Am. Chem. Soc.* **1972**, *94*, 1126.
(9) Roberts, J. D.; Moreland, W. T., Jr. *J. Am. Chem. Soc.* **1953**, *75*, 2167.
(10) Wilcox, C. F.; McIntyre, J. S. *J. Org. Chem.* **1965**, *30*, 777.
(11) Ritchie, C. D.; Lewis, E. S. *J. Am. Chem. Soc.* **1962**, *84*, 591.
(12) Holtz, H. D.; Stock, L. M. *J. Am. Chem. Soc.* **1964**, *86*, 5188.
(13) Ritchie, C. D.; Sager, W. F. *Prog. Phys. Org. Chem.* **1964**, *2*, 323.
(14) Bagal, M. L.; Lantvoev, V. I. *J. Org. Chem. USSR (Engl. Transl.)* **1973**, *9*, 290.
(15) Stetter, H.; Mayer, J. *Chem. Ber.* **1962**, *95*, 667.

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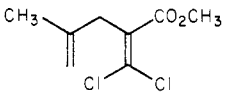
1,3-dichloro derivative, made in low yield by chlorination of the hydrocarbon.[16] The successful method reported here[17] is built upon the discovery that dichlorocarbene will add to certain 1,3-disubstituted bicyclo[1.1.0]butanes to give bicyclo[1.1.1]pentanes in usable quantities (Scheme I). One of these reactions, the conversion of **5** to **6**, had earlier been reported to occur in 3% yield.[18] By modifying the experimental conditions, we increased the yield of the product to 19%, only to discover that the structure was in fact **15** rather than **6**. The spectra were identical with



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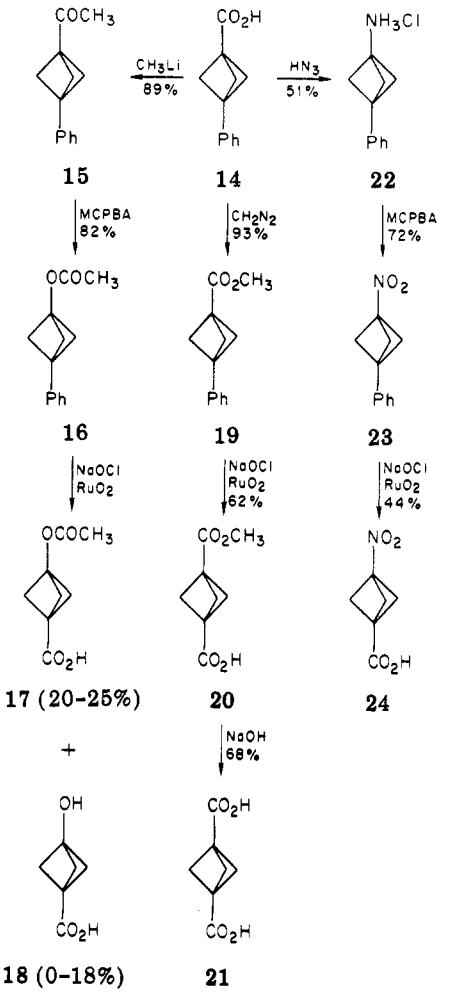
those reported, but upon taking a higher field NMR spectrum (100 instead of 60 MHz), we observed a two proton signal at δ 4.73, attributed to two of the ring hydrogens in **6**, to split into two distinct multiplets at δ 4.69 and 4.76, now assigned to the vinyl hydrogens in **15**. The compound also showed unsaturation in the Raman spectrum at 1620 and 1670 cm^{-1}, rapidly decolorized bromine in carbon tetrachloride, and had UV absorptions at 276 nm (log ϵ 3.65) and at 310.5 nm (log ϵ 1.64).

Further examination of the product mixture from **5** and dichlorocarbene revealed that **6** was present also and could be regularly isolated in 20% yield in crude form, with pure samples obtainable by gas chromatography. Compound **6** shows NMR singlets at δ 1.30 and 3.75 for the methyl groups and broad two-proton signals at δ 2.05 and 2.69 for the ring methylenes. The compound is unreactive with bromine and shows no olefinic peaks in the Raman spectrum.

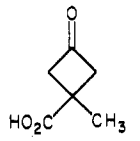
Bicyclobutanes **8** and **12** gave similar reactions with dichlorocarbene. All three of the dichlorobicyclo[1.1.1]pentanes (**6**, **9**, and **13**) were dechlorinated with tri-*n*-butyltin hydride and azobis(isobutyronitrile) (AIBN) to give the 1,3-disubstituted bicyclo[1.1.1]pentanes **7**, **10**, and **14**, respectively. All of these yielded NMR spectra with six-proton singlets for the ring methylenes (at δ 1.93, 2.45, and 2.32, respectively). The structure of **14** was further confirmed by a single-crystal X-ray diffraction study,[19] which also served to supply one more measurement of the interbridgehead distance (1.885 ± 0.009 Å).

A key reaction in the synthesis of our series of bicyclopentanes has been the oxidation of phenyl groups to carboxyl groups with sodium hyprochlorite and ruthenium dioxide.[20] In Scheme I this is seen in the conversion of **10** to 3-cyanobicyclo[1.1.1]pentane-1-carboxylic acid (**11**). The reaction is seen three more times in Scheme II, which outlines the conversion of **14** to the rest of the carboxylic acids needed for the pK_a determinations. The product characterizations are routine and therefore are discussed only in the Experimental Section. One interesting problem is that the acetoxy acid **17** is not easily hydrolyzed to the hydroxy acid **18** with aqueous base. A ring-opening side reaction consumes **18**. Under mildly basic conditions (potassium carbonate in aqueous ethanol) a 20% yield of

Scheme II



18 was obtained from **17**. The ring opening was not investigated in detail, but an oily, impure product with an NMR spectrum in agreement with a cyclobutanonecarboxylic acid **25** was obtained.



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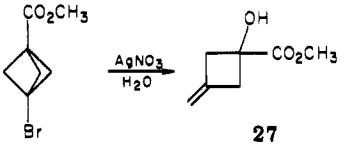
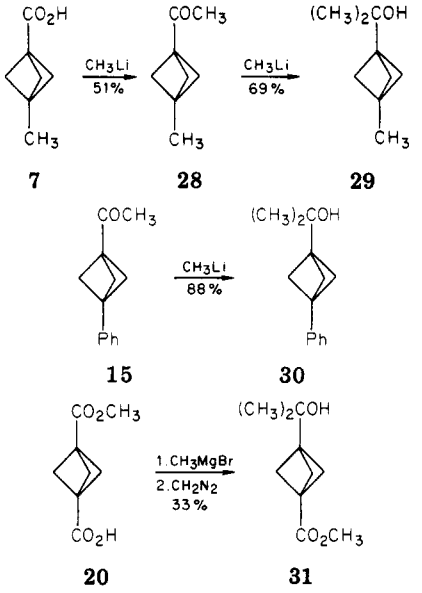
A different kind of instability of the bicyclopentane ring system was encountered in an attempt to prepare the 3-bromo carboxylic acid. Bromo ester **26** was prepared from **20** by the Cristol–Firth–Hunsdiecker reaction in 68% yield. Attempts to hydrolyze **26** with acid or base gave complex mixtures of unidentified materials. Compound **26** also reacted immediately with silver nitrate in 95% ethanol or water. In water the major product was hydroxy ester **27**, along with a minor product which was not fully



identified. The lability of the bromine in **26** is to be compared with the solvolysis of 1-chlorobicyclo[1.1.1]pentane, which is even more reactive than *tert*-butyl chloride and gives the same type of ring-opened product.[21]

(16) Wiberg, K. B.; Williams, V. Z., Jr. *J. Org. Chem.* **1970**, *35*, 369.
(17) A preliminary report of the synthetic method has been published: Applequist, D. E.; Wheeler, J. W. *Tetrahedron Lett.* **1977**, 3411.
(18) Hall, H. K., Jr.; Smith, C. D.; Blanchard, E. P.; Cherkofsky, S. C.; Sieja, J. B. *J. Am. Chem. Soc.* **1971**, *93*, 121.
(19) We thank Dr. E. N. Duesler, University of Illinois, for performing the X-ray structure determination. The thesis of T.L.R.[38] may be consulted for details.
(20) Lee, D. G.; van den Engh, M. In "Oxidation in Organic Chemistry, Part B"; Trahanovsky, W. S., Ed.; Academic Press: New York, 1973, pp 177–228.

Scheme III



In order to measure substituent effects through the bicyclo[1.1.1]pentane system on a reaction with a large electron demand in the transition state, three tertiary alcohols (**29–31**) were prepared as outlined in Scheme III. The alcohols were converted to their *p*-nitrobenzoates for solvolysis studies described below.

pK_a Measurements

The solvent chosen for pK_a measurements was 50% (by volume) ethanol–water, which had been used in most of the literature studies of rigid alicyclic acids and which was a good solvent for all of the bicyclopentane acids reported here. It seemed desirable to make comparisons with substituent effects in an open-chain model, namely, 4-substituted butanoic acids **32**, but data for these are apparently not available from 50% ethanol, and so five of them were measured here.

$XCH_2CH_2CH_2CO_2H$
32a, X = CH_3
b, X = C_6H_5
c, X = CO_2CH_3
d, X = $OCOCH_3$
e, X = CN

All measurements were made by potentiometric titrations at 25.0 °C with aqueous buffer solutions as pH standards. No corrections were made for liquid junction potentials, and all activity coefficients were assumed to have a value of 1. Each acid was titrated twice, and the calculated pK_a's were within 0.02 of a pK_a unit for the two titrations. The results of all determinations are collected in Table I. In addition, the pK values of three benzoic acids (unsubstituted, *m*-bromo, and *m*-nitro) were measured for comparison with literature values.[22] The new values were 5.66, 5.15, and 4.59, respectively, about 0.07 units below the literature values, but with good agreement in the differences.

It should first be noted that the bicyclopentane acids are more acidic than the butanoic acids and more acidic

Table I. Apparent Ionization Constants of 3-Substituted Bicyclo[1.1.1]pentane-1-carboxylic Acids and 4-Substituted Butanoic Acids in 50% (by Volume) Aqueous Ethanol at 25.0 ± 0.1 °C

substituent	bicyclopentane acid	pK_a	butanoic acid	pK_a
CH_3	7	5.67	**32a**	6.18
C_6H_5	14	5.38	**32b**	6.11
OH	18	5.14		
CO_2H	21	4.90[a]		
CO_2CH_3	20	4.85	**32c**	5.84
$OCOCH_3$	17	4.84	**32d**	5.79
CN	11	4.35	**32e**	5.51
NO_2	24	4.12		
CO_2^-	21	5.39[a]		

[a] The values of pK_a are corrected by the statistical factor of log 2 as required for comparison of dicarboxylic acid data with monocarboxylic acid data.

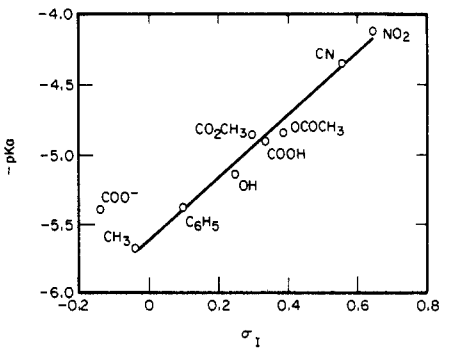


Figure 1. Relationship between apparent ionization constants of 3-substituted bicyclo[1.1.1]pentane-1-carboxylic acids and σ_I.

than the other bicyclic acids with which they will be compared below. Wiberg and Williams[16] had earlier reported a pK_a of 4.09 for bicyclo[1.1.1]pentane-1-carboxylic acid in water at 25 °C, to be compared with values of 4.75 and 5.05 for acetic and pivalic acids, respectively. They attributed the higher acidity of the bicyclopentane acid to the high s character (about 33%) of the bridgehead carbon orbital directed at the carboxyl carbon. That interpretation still seems reasonable.

The most revealing quantitative analysis of the data in Table I lies in correlations of the pK_a's with σ_I.[13,23] The correlation for the bicyclopentanes is shown in Figure 1. The regression line has a slope (ρ_I) of 2.23 ± 0.12 and was calculated without the point for the carboxylate ion (CO_2^-) substituent. Wepster[24] has shown that the substituent effects of charged groups vary widely and do not generally fit linear free energy relationships. The correlation coefficient r is 0.9915.

If the pK_a data for the 4-substituted butanoic acids are plotted against σ_I, a slightly poorer straight line (r = 0.9864) is obtained with ρ_I = 1.12 ± 0.11. Correlation of the acidity data of Roberts and Moreland[9] on bicyclo[2.2.2]octane acids **2** with σ_I gives a regression line with σ_I = 1.50 (r = 0.998). The data for adamantane acids **3** by Bagal and Lantvoev[14] give ρ_I = 1.49 (r = 0.988). It is clear that the substituent effects in the bicyclo[1.1.1]-pentane system are larger than previously observed effects through the same number of bonds but are normal in the sense that the relative electron-donating or -withdrawing

(21) (a) Wiberg, K. B.; Williams, V. Z. *J. Am. Chem. Soc.* **1967**, *89*, 3373. (b) Williams, V. Z., Jr. Ph.D. Thesis, Yale University, New Haven, CT, 1968.
(22) Roberts, J. D.; McElhill, E. A.; Armstrong, R. *J. Am. Chem. Soc.* **1949**, *71*, 2923.
(23) Ehrenson, S.; Brownlee, R. T. C.; Taft, R. W. *Prog. Phys. Org. Chem.* **1973**, *10*, 1.
(24) Hoefnagel, A. J.; Hoefnagel, M. A.; Wepster, B. M. *J. Org. Chem.* **1978**, *43*, 4720.

Table II. Calculated ΔpK_a Values for Substituted Bicyclo[2.2.2]octane- and Bicyclo[1.1.1]pentanecarboxylic Acids in 50% Ethanol by the Kirkwood-Westheimer Model

	bicyclooctane ΔpK_a[a]		bicyclopentane ΔpK_a	
substituent	calcd[b]	obsd[c]	calcd	obsd
H	0.0	0.01	0.0	
CH_3	(0.0)	(0.0)	(0.0)	(0.0)
OH	0.21	0.35	0.29	0.53
CN	0.67	0.86	0.87	1.32
NO_2	0.93	0.97	1.27	1.55

[a] $\Delta pK_a = \log (K_x/K_{CH_3})$. [b] $D_i = 2.0$[25] and $D = 53.8$.[30] [c] Values from ref 9 and 12, with corrections from 50% by weight ethanol-water to 50% by volume ethanol-water where needed.

abilities of the substituents are unchanged.

The remaining question to be answered is whether the size of the substituent effect ($\rho_I = 2.23$) is too large to be accounted for by the smaller distance between the substituent and carboxyl in the bicyclo[1.1.1]pentane acids. Existing theory is not good enough to provide a definitive answer to this question, but one can do calculations based upon the Kirkwood–Westheimer field model[25] to see if the experimental data can be accommodated without extraordinary assumptions in the input parameters. A number of variants of the original theory have evolved, and we have tried several of them, but perhaps no purpose would be served here to go beyond an illustration of the quality of the fit of theory to data.

The general form of the Kirkwood–Westheimer equation for the electrostatic influence of a dipole on the pK_a on an acid in solution is given by eq 1.[25] The parameters are

$$\Delta pK_a = \log (K_x/K_i) = eM\cos(\theta)/2.3kTR^2D_E \quad (1)$$

defined as follows: e is the charge on an electron, $M\cos(\theta)$ is the magnitude of the dipole moment of the substituent bond or group projected on a line connecting the removable proton and the point dipole, k is the Boltzman constant, T is the absolute temperature, R is the distance between the removable proton and the point dipole, and D_E is an average "effective" dielectric constant for the molecule and surrounding solvent. K_i is a hypothetical K_a for a molecule without a dipolar group at the substituent position. The value of D_E is the parameter most difficult to assign accurately, being dependent upon the dielectric constants within and outside of the molecular "cavity", upon the shape of the cavity, and upon the locations chosen for the dipole and proton.

In Table II are shown the results of calculations of $\log (K_x/K_{CH_3})$ for both the bicyclo[1.1.1]pentane acids and the bicyclo[2.2.2]octane acids (**2**) obtained by using the parametric assumption recommended by Tanford:[26] i.e., that the point dipole and removable proton are located at a depth, d, of 1.5 Å below the surface of a spherical cavity. The point dipoles were taken to lie midway between the projected positions of the two of more atoms which make up the polar group. It was assumed that no dipole exists between two bonded atoms of the same kind. The distance from the removable proton to the carboxyl carbon on the extension of the adjacent C–C bond was taken as 1.45 Å.[25] The distances between the bridgehead carbons were taken as 1.88 Å in the bicyclo[1.1.1]pentanes and as 2.59 Å in the bicyclo[2.2.2]octanes.[27] Standard bond distances and bond angles were assumed.[28] Dipole moments were taken from Smyth.[29]

Table III. Rate Constants for Solvolysis of *p*-Nitrobenzoates at 145.0 ± 0.0 °C in 80% Acetone

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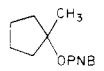
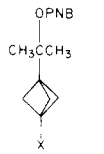
		124[a]
	X = CH_3	16.3 ± 0.1
	X = C_6H_5	5.88 ± 0.11
	X = CO_2CH_3	1.71 ± 0.01

[a] Extrapolated from the data of ref 31.

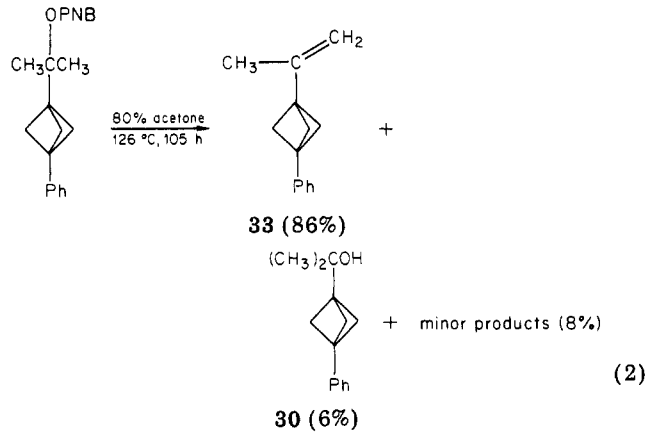
With the parameters chosen, the experimental observations on the bicyclooctane acids are fit more closely than are those on the bicyclopentane acids (Table II). However, the hybridization differences in the two systems might well make inappropriate the use of the same parameters for magnitudes and positions of the dipoles. The theory can be forced to fit the bicyclopentane data with relatively modest variations in the parameters M, R, and d. For example, if the value of R is reduced 0.24–0.32 Å while the same cavity size is maintained by increasing d, then the bicyclopentane data for substituents OH, CN, and NO_2 can be fit exactly. The adjustments do not appear to be unreasonable in light of the only approximate nature of the theory and the necessarily subjective parameter choices. It is concluded that the acidities of the 3-substituted bicyclo[1.1.1]pentane-1-carboxylic acids are not in conflict with the Kirkwood–Westheimer theory.

Solvolysis Studies

The first-order rate constants for solvolysis of the *p*-nitrobenzoates of tertiary alcohols **29–31** were measured at 145.0 °C in 80% (by volume) acetone. The values are shown in Table III. A literature value for 1-methyl-1-cyclopentyl *p*-nitrobenzoate is given for comparison which shows that all of the bicyclopentyl cases are slower than a typical tertiary *p*-nitrobenzoate, probably another consequence of the atypical hybridization of the bridgehead carbon atom.

Interpretation of the rates in terms of polar substituent effects on a simple carbocation requires that the mechanism of solvolysis be established as an alkyl–oxygen cleavage without neighboring-group participation. The reaction products support both parts of this requirement. Products were investigated for two of the three bicyclopentyl *p*-nitrobenzoates. The 3-phenyl derivative was solvolyzed in 80% acetone with 2 equiv of 2,6-lutidine as a buffer. The principal product, 86% by gas chromatographic analysis, was the alkene **33** (eq 2). There was a small amount of parent alcohol **30** and at least three minor products. The last were not identified but were apparently rearranged, since the NMR spectrum of a mixture of them did not contain the sharp singlet at ca. δ 2.0, characteristic of the ring methylenes in the bicyclopentanes. A control

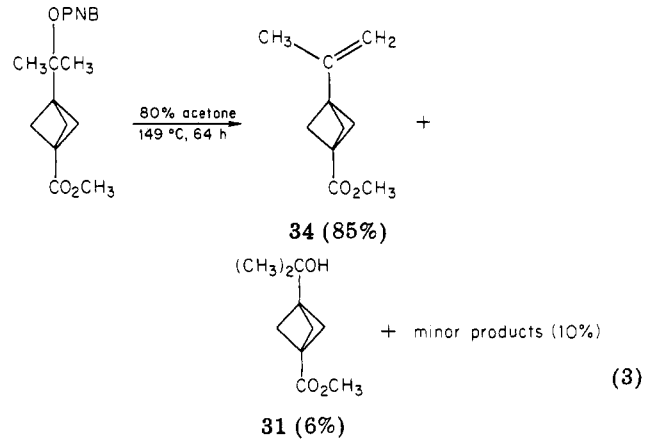
(25) Kirkwood, J. G.; Westheimer, F. H. *J. Chem. Phys.* **1938**, *6*, 506; **1938**, *6*, 513; **1939**, *7*, 437.
(26) Tanford, C. *J. Am. Chem. Soc.* **1957**, *79*, 5348.
(27) Yokozeki, A.; Kuchitsu, J.; Morino, Y. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 2017.
(28) "Tables of Interatomic Distances and Configuration in Molecules and Ions"; The Chemical Society: London, 1965; Suppl 1956–1959, Spec Publ No. 18.
(29) Smyth, C. P. "Dielectric Behavior and Structure"; McGraw-Hill: New York, 1955; pp 244, 253.
(30) LeHuérillot, C. R. *C. R. Hebd. Seances Acad. Sci.* **1964**, *258*, 2549.
(31) Brown, H. C.; Hammar, W. J. *J. Am. Chem. Soc.* **1967**, *89*, 6378.



(2)

showed that **33** was not formed by dehydration of **30** under the solvolysis conditions, ruling out a primary acyl–oxygen cleavage mechanism. The absence of significant skeletal rearrangement argues against, but does not rigorously exclude, neighboring-group participation in the transition state.

The products from the *p*-nitrobenzoate of the 3-carbomethoxy derivative **31** were investigated in the same medium, but at a higher temperature. The total yield of neutral products was only 82% in this case, but the composition of the neutral mixture was strikingly similar to that from the 3-phenyl derivative, with the unsaturated ester **34** being the major product (eq 3). Partial hydrolysis



(3)

of the ester function probably resulted in acidic products, which were lost. The hydrolysis of the ester also accounts for infinity titers higher than theoretical values in the kinetic runs on the 3-carbomethoxy *p*-nitrobenzoate.

Besides the solvolysis products, another kind of evidence for the alkyl–oxygen (S_N1) solvolysis mechanism is that all three of the bicyclic *p*-nitrobenzoates solvolyze faster than methyl *p*-nitrobenzoate. The latter was recovered in 91% yield after 48 h in 80% acetone at 145 °C, conditions corresponding to 95% reaction for the slowest of the bicyclic *p*-nitrobenzoates.

A plot of the three bicyclopentane rate constants in Table III against σ_I gives a straight line with a slope (ρ_I) of −2.87 ± 0.13 (r = 0.999). With only three points we cannot be as confident of the linearity of the relationship as in the case of the pK_a measurements, but it can at least be concluded that no nonlinearity is apparent with σ_I values in the range from −0.04 (methyl) to 0.30 (carbomethoxyl). There is also some uncertainty in the rate constant for the 3-carbomethoxyl derivative (Table III) because of hydrolysis of the methyl ester, producing a high infinity titer. It is estimated that the correct rate constant could be as high as 2.0×10^{-5}, which would change ρ_I to −2.68 (r = 0.997). The substituent effect reflected by these values of ρ_I is certainly not exceptionally large. For example, the solvolysis rate constants of m-CH_3, m-C_6H_5, and m-CO_2CH_3 derivatives of cumyl chloride in 90% acetone at 25 °C yield a ρ_I value of −5.81.[32] The larger ρ_I in this case must be partly due to the lower temperature and the poorer solvent which were needed to obtain convenient reaction rates in the more reactive cumyl system. The solvolysis data, in conclusion, simply reinforce the conclusion from the pK_a data, i.e., that the polar substituent effects through the bicyclo[1.1.1]pentane system are normal or near normal.

Experimental Section[33]

Melting points were determined with a Büchi melting point apparatus and are uncorrected. Proton magnetic resonance spectra were recorded on Varian Associates spectrometers (Models A 56/60, A60A, T-60, HA-100, HR-220, and EM-390). The ^{13}C nuclear magnetic resonance spectra (^{13}C NMR) were recorded on a JEOL FX-60 (15 MHz) spectrometer and were wide-band proton decoupled. All chemical shifts are given as δ values (parts per million relative to tetramethylsilane), and J values are given in hertz. Ultraviolet spectra were recorded on Cary Model 14 and Perkin-Elmer Model 202 spectrophotometers. Mass spectra were taken on a Varian-Mat CH-5 mass spectrometer. Elemental analyses were performed by J. Nemeth and associates at the University of Illinois.

Reaction of Methyl 3-Methylbicyclo[1.1.0]butane-1-carboxylate (5) with Sodium Trichloroacetate. Diglyme (12.5 mL), tetrachloroethylene (50 mL), sodium trichloroacetate (46.2 g, 0.25 mol), and methyl 3-methylbicyclo[1.1.0]butane-1-carboxylate[18] (7.4 g, 59 mmol) in a 1-L flask were stirred at reflux for 1 h. After the brown mixture cooled, pentane (600 mL) was added. The mixture was extracted with water (four 100-mL portions). The organic phase was dried over magnesium sulfate, filtered, and concentrated. Short-path distillation (100 °C, 5.0–0.3 mm) gave 17.0 g of liquid. GC (SE-30) showed that the liquid contained tetrachloroethylene (1.3 g), hexachlorocyclopropane (1.8 g), methyl 3-methyl-2,2-dichlorobicyclo[1.1.1]pentane-1-carboxylate (**6**; 3.22 g, 27%), 1,1-dichloro-2-carbomethoxy-4-methyl-1,4-pentadiene (**15**; 2.35 g, 19%), and methyl 2-[(1-methyl-2,2-dichlorocyclopropyl)methyl]-3,3-dichloropropenoate (9.0 g, 52%). GC collection gave pure compounds. Methyl 3-methyl-2,2-dichlorobicyclo[1.1.1]pentane-1-carboxylate (**6**): colorless solid; mp 47–48 °C; NMR (60 MHz, CCl_4) 1.30 (sharp s, 3 H), 2.05 (br s, 2 H), 2.60 (br s, 2 H), 3.75 (sharp s, 3 H); irradiation of δ 2.60 gave a sharp singlet for the δ 2.05 signal, and irradiation of δ 2.05 gave a sharp singlet for δ 2.60; Raman (CCl_4) 2970, 1760, 1460, 1400, 1340, 1060, 930, 870 cm^{-1}. Anal. Calcd for $C_8H_{10}Cl_2O_2$: C, 45.96; H, 4.82; Cl, 33.91. Found: C, 46.39, 45.58; H, 4.69, 4.60; Cl, 34.44. 1,1-Dichloro-2-carbomethoxy-4-methyl-1,4-pentadiene: colorless liquid; NMR and IR were identical with the spectra reported for methyl 2,2-dichloro-3-methylbicyclo[1.1.1]pentane-1-carboxylate;[18] Raman (neat) 2980, 1750, 1670, 1450, 980, 870, 840, 470, 450, 420, 380, 260; NMR (100 MHz) 1.47 (m, 3 H), 3.18 (symmetrical 9-line m, 2 H, J = 0.5), 3.72 (s, 3 H), 4.69 (m, 1 H), 4.77 (m, 1 H); irradiation of δ 3.18 gave a doublet of doublets (J = 1.5, 0.9) and irradiation of δ 4.74 gave a broad singlet for δ 1.74; irradiation of δ 4.73 gave a broad singlet for δ 3.18; irradiation of δ 1.74 gave δ 4.69 as a quartet (J = 1.5) and δ 4.76 as a less complex multiplet; irradiation of δ 3.18 gave δ 4.69 as a sextet (J = 0.8) and δ 4.76 as a quintet (J = 1.5); UV (EtOH) λ_{max} 276 nm (log ϵ 3.65), 310.5 (1.64). Methyl 2-[(1-methyl-2,2-dichlorocyclopropyl)methyl]-3,3-dichloropropenoate: colorless liquid; NMR (CCl_4) 1.37 (s, 3 H), 3.82 (s, 3 H), AB quartet at 1.28 (J = 7, $\Delta\delta$ = 6, 2 H), AB quartet at 2.87 (J = 15, $\Delta\delta$ = 10, 2 H); Raman (neat) 2960, 2940, 1740, 1620, 1450,

(32) Brown, H. C.; Okamoto, Y. *J. Am. Chem. Soc.* **1957**, *79*, 1913. Brown, H. C.; Okamoto, Y.; Inukai, T. *Ibid.* **1958**, *80*, 4964. Okamoto, Y.; Inukai, T.; Brown, H. C. *Ibid.* **1958**, *80*, 4969.

(33) Abstracted from the Ph.D. theses of J.W.W., University of Illinois, 1974, and T.L.R., University of Illinois, 1981.

(34) Kuivila, H. G.; Beumel, O. F., Jr. *J. Am. Chem. Soc.* **1961**, *83*, 1246.

1200, 920, 870, 720, 500, 470; UV (EtOH) end absorption 2000 Å (ε 3700), 2300 (2400), 2500 (400), 2900 (12.5).

Anal. Calcd for $C_9H_{10}O_2Cl_4$: C, 37.02; H, 3.45; Cl, 48.57. Found: C, 36.86; H, 3.42; Cl, 48.56.

Reaction of the starting bicyclobutane with sodium trichloroacetate at 100 °C, with thallium ethoxide and chloroform at 60 °C, with chloroform and potassium *tert*-butoxide at −20 °C, and with trichloromethyllithium at −65 °C gave increased ratios of diene to bicyclopentane as judged by the NMR of the crude reaction mixture.

Methyl 3-Methyl-2,2-dichlorobicyclo[1.1.1]pentanecarboxylate (6). To a stirred, heated (130 °C) solution of **5** (4.85 g, 38.5 mmol) in tetrachloroethylene (48 mL) and diglyme (14.5 mL) was added sodium trichloroacetate (28.5 g, 0.154 mol) over 20 min. The resulting mixture was stirred an additional 20 min. The cooled reaction mixture was filtered through Celite. The precipitate was washed with benzene. The filtrate was concentrated and distilled [60 °C (0.65 mm) to 110 °C (0.02 mm)] to give 11 g of liquid. An excess of bromine in carbon tetrachloride was added, and the solution was allowed to stand 4 h. The solution was washed with sodium bicarbonate solution, sodium thiosulfate solution, and saturated sodium chloride solution, dried over magnesium sulfate, filtered, and concentrated. Distillation through a 6-in. Vigreux column (65–100 °C, 0.4–0.2 mm) gave 2.46 g (20%) of oil which solidified in the ice-cooled collection flask. An NMR spectrum showed the product was only about 70% pure **6**, but this was found suitable for the reduction to **7**.

3-Methylbicyclo[1.1.1]pentane-1-carboxylic Acid (7). A solution of methyl 2,2-dichloro-3-methylbicyclo[1.1.1]pentane-1-carboxylate (24.5 g, 0.117 mol), tri-*n*-butyltin hydride[34] (216 g, 0.745 mol), and azobis(isobutyronitrile) (AIBN, 0.2 g) was heated under nitrogen at 130 °C. Every 24 h the NMR spectrum was recorded. If the doublet at δ 4.2 was still present, AIBN (0.2 g) was added to the reaction mixture, and heating under nitrogen was continued. After a total of 108 h the reaction mixture was added to a solution of 100 g of sodium hydroxide in 900 mL of water, and the resulting mixture was heated at reflux for 2 h. This mixture was washed with four 250-mL portions of hexane, and then the aqueous layer was acidified with concentrated hydrochloric acid and extracted with five 250-mL portions of ether. The ether layers were combined, dried over magnesium sulfate, and concentrated to afford 15.7 g of slightly yellow solid. Recrystallization from hexane followed by sublimation (2 mm, 90 °C) gave 9.07 g of white solid, mp 118.5–121 °C. A second (0.987 g; mp 117–121 °C) and a third crop (0.652 g; mp 113–120 °C) of crystals were obtained by concentration of the mother liquor followed by sublimation: 10.71 g (72%) total. A portion of the first crop of material was recrystallized three times from hexane and then sublimed to give analytically pure material: mp 122–122.5 °C; ^{13}C NMR ($CDCl_3$) 17.75, 36.65, 37.59, 53.26, 176.53; IR (KBr) 3400, 3000, 2600, 1695, 1520, 1440, 1425, 1380, 1335, 1290, 1215, 1060, 960, 750, 505 cm^{-1}; NMR ($CDCl_3$) 1.17 (s, 3 H), 1.93 (s, 6 H), 10.30 (s, 1 H).

Anal. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 8.00. Found: C, 66.82; H, 7.96.

3-Phenyl-2,2-dichlorobicyclo[1.1.1]pentane-1-carbonitrile (9). 3-Phenylbicyclo[1.1.0]butanecarbonitrile (**8**; 6.72 g, 43.3 mmol),[35] sodium trichloroacetate (34 g, 0.18 mol), diglyme (18 mL), and tetrachloroethane (60 mL) were stirred at 100 °C for 4 h. The reaction mixture was filtered through Celite, and the salts were washed with benzene. The filtrate was concentrated, and the diglyme was removed by distillation at reduced pressure to give 15 g of black oil. The oil was chromatographed on 800 g of silica gel with 400-mL fractions of 3:7 benzene/hexane. Fractions 11–18 were combined to give 1.9 g (16.3%) of yellow crystals: NMR ($CDCl_3$) 2.55 (d, J = 1, 2 H), 3.20 (d, J = 1, 2 H), 7.28 (s, 5 H). The material was sublimed (0.05 mm, 60 °C) to give an analytical sample (0.23 g): mp 122–123 °C; IR (KBr) 2227, 1450, 1370, 1235, 1150, 1090, 1010, 935, 855, 700 cm^{-1}.

Anal. Calcd for $C_{12}H_9NCl_2$: C, 60.53; H, 3.81; Cl, 29.78. Found: C, 60.25; H, 4.05; Cl, 29.97.

3-Phenylbicyclo[1.1.1]pentanecarbonitrile (10). A mixture of 0.97 g (4.07 mmol) of **9**, 6.55 g (22.5 mmol) of tri-*n*-butyltin hydride, and 0.083 g (0.56 mmol) of AIBN was heated at 130 °C for 35 h and then distilled (0.05 mm, oil bath at 150 °C) to give 2.53 g of colorless oil. This oil was chromatographed on 250 g of silica gel. The column was eluted with 1250 mL of hexane, with 2 L of 1:2 benzene/hexane, and then with benzene (750 mL) to give, after concentration, 0.472 g (68%) of solid: mp 35–42 °C; NMR ($CDCl_3$) 2.45 (s, 6), 7.2 (m, 5). The solid was recrystallized twice from pentane at 0 °C and then sublimed (0.03 mm, 30 °C): mp 51.5–52 °C; IR (KBr) 2240, 1500, 1450, 1360, 1230, 1160, 810, 750, 700 cm^{-1}.

Anal. Calcd for $C_{12}H_{11}N$: C, 85.17; H, 6.55; N, 8.28. Found: C, 84.90; H, 6.44; N, 8.02.

3-Cyanobicyclo[1.1.1]pentane-1-carboxylic Acid (11). To a stirred mixture of 500 mL of Clorox (0.755 M in sodium hypochlorite, 0.377 mol), 85 mL of carbon tetrachloride, and 0.61 g (15.3 mmol) of sodium hydroxide was added 54.4 mg of ruthenium dioxide dihydrate which immediately was oxidized to yellow ruthenium tetraoxide. 3-Phenylbicyclo[1.1.1]pentane-1-carbonitrile (**10**; 1.82 g, 10.8 mmol) was added, and the mixture was stirred until the solution turned black (93 h) from precipitated ruthenium dioxide. The layers were separated. The aqueous phase was washed with two 100-mL portions of carbon tetrachloride, acidified with concentrated hydrochloric acid, and extracted with five 100-mL portions of ether. The ether extracts were combined, dried over magnesium sulfate, and concentrated to give 1.321 g of white solid, mp 178–184 °C. The material was recrystallized from cyclohexane/ethyl acetate and then sublimed (0.2 mm, 100 °C) to give 0.8331 g (56.5%) of white solid: mp 189–189.5 °C; NMR ($CDCl_3$) 2.5 (s, 6), 9.50 (s, 1); IR (KBr) 3400, 3020, 2940, 2760, 2660, 2580, 2240, 1700, 1515, 1450, 1340, 1245, 1230, 940, 755, 480 cm^{-1}.

Anal. Calcd for $C_7H_7NO_2$: C, 61.31; H, 5.14; N, 10.21. Found: C, 61.21; H, 5.06; N, 10.18.

Methyl 3-Phenyl-2,2-dichlorobicyclo[1.1.1]pentanecarboxylate (13). Methyl 3-phenylbicyclo[1.1.0]butanecarboxylate (**12**;[18] 9.0 g, 48 mmol), diglyme (18 mL), and tetrachloroethylene (60 mL) were stirred in a 2-L three-necked flask in an oil bath (145 °C). After the temperature of this solution reached 122 °C, sodium trichloroacetate (34 g, 0.18 mol) was added over 30 min. The resulting mixture was stirred at 140 °C for an additional 30 min. The reaction mixture was filtered through Celite, and the salts were washed with benzene. The filtrate was concentrated, and diglyme was removed by distillation at reduced pressure to give 20 g of black oil. The oil was chromatographed on 800 g of silica gel with 400-mL fractions of 3:7 benzene/hexane. Fractions 13–20 were combined to give 4.57 g (27%) of methyl 2-[(1-phenyl-2,2-dichlorocyclopropyl)methyl]-3,3-dichloropropenoate as a yellow solid: mp 78–82 °C; NMR ($CDCl_3$) 1.85 (AB q, $\Delta\delta$ = 9, J = 8, the downfield two peaks were doublets, J = 1, 2 H), 3.53 (s, 3 H), 7.25 (s, 5 H). An analytical sample was obtained by recrystallization from pentane: mp 86.5–87.0 °C; 280–290 °C dec; IR (KBr) 1730, 1600, 1450, 1440, 1270, 1210, 1130, 1040, 930, 900, 780, 710, 540 cm^{-1}.

Anal. Calcd for $C_{14}H_{12}Cl_4O_2$: C, 47.49; H, 3.42; Cl, 40.05. Found: C, 47.71; H, 3.50; Cl, 40.32.

Fractions 15–20 were combined to give 5.94 g (46%) of methyl 3-phenyl-2,2-dichlorobicyclo[1.1.1]pentanecarboxylate (**13**) as a yellow solid: mp 61–65 °C; NMR ($CDCl_3$) 2.4 (s, 2 H), 3.1 (s, 2 H), 3.8 (s, 3 H), 7.4 (s, 5 H). An analytical sample was obtained by recrystallization from cyclohexane and sublimation (0.1 mm, 75 °C): mp 80–82 °C; 240–250 °C dec; IR (KBr) 1730, 1490, 1430, 1380, 1310, 1210, 1010, 860, 760, 700 cm^{-1}.

Anal. Calcd for $C_{13}H_{12}Cl_2O_2$: C, 57.58; H, 4.47; Cl, 26.15. Found: C, 57.82; H, 4.58; Cl, 26.29.

The above yields varied only a few percent in various runs. Addition of trinitrotoluene (mp 81 °C; 0.18 g, 0.8 mmol) to the tetrachloroethylene reduced the yield of **13** to 25%.

3-Phenylbicyclo[1.1.1]pentane-1-carboxylic Acid (14). Methyl 2,2-dichloro-3-phenylbicyclo[1.1.1]pentane-1-carboxylate (**13**; 46.8 g, 0.173 mol), tri-*n*-butyltin hydride (217.6 g, 0.748 mol), and azobis(isobutyronitrile) (AIBN, 0.5 g) were stirred under nitrogen at 130 °C for 13.5 h. The ^1H NMR spectrum of the reaction mixture indicated, from the absence of a signal at δ 3.1, that the starting material had all reacted. A doublet at δ 4.6 indicated that there was still monochloride present. The NMR integration showed that of the total bicyclic material present ca.

(35) Hall, H. K., Jr.; Blanchard, E. P., Jr.; Cherkofsky, S. C.; Sieja, J. B.; Sheppard, W. A. *J. Am. Chem. Soc.* **1971**, *93*, 110.

40% was the monochloride. The IR spectrum showed that much tri-*n*-butyltin hydride was still present (from the Sn–H stretch at 1800 cm^{-1}). AIBN (0.4 g) was added to the reaction mixture, and the solution was once again stirred under nitrogen at 130 °C. After 21.5 h the spectra showed that ca. 13% of the monochloride remained and that most of the tri-*n*-butyltin hydride had reacted. Tri-*n*-butyltin hydride (26.6 g, 0.0914 mol) and AIBN (0.4 g) were added to the reaction mixture, and stirring at 130 °C was resumed. After 21 h the spectra indicated that ca. 5% of the monochloride remained and that some hydride was still present. AIBN (0.3 g) was added, and stirring at 130 °C was resumed. After 20 h the mixture was poured onto a solution of 100 g of sodium hydroxide in 900 mL of water. The resulting mixture was heated at reflux for 2 h. The layers were separated, and the aqueous phase was washed with four 300-mL portions of hexane, acidified with concentrated hydrochloric acid, and extracted with five 300-mL portions of ether. The combined ether extracts were dried over magnesium sulfate and concentrated to give 32.4 g of slightly yellow solid. Recrystallization from water afforded 28.6 g (88.1%) of fluffy solid: mp 176–176.5 °C; ^1H NMR ($CDCl_3$) 2.32 (s, 6 H), 7.28 (s, 5 H), 11.2 (s, 1 H); IR (KBr) 3700–3300, 3000, 2600, 1695, 1430, 1310, 1220, 1130, 950, 750, 700 cm^{-1}. A portion of the material was sublimed (0.2 mm, 110 °C) to give white powder: mp 176–176.5 °C; ^{13}C NMR ($CDCl_3$) 36.91, 41.80, 53.31, 125.99, 126.97, 128.28, 139.36, 176.69 cm^{-1}.

Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.69; H, 6.29.

3-Acetyl-1-phenylbicyclo[1.1.1]pentane (15). A solution of 2.00 g (10.6 mmol) of 3-phenylbicyclo[1.1.1]pentane-1-carboxylic acid (**14**) in 70 mL of dry ether was placed under a nitrogen atmosphere. To this stirred solution of 0 °C was added 42 mL of a solution of methyllithium in ether (0.555 M, 23.3 mmol) over 1 h. Stirring was continued for an additional 3.15 h at room temperature. The turbid reaction mixture was then poured onto ice and acidified with hydrochloric acid. The layers were separated, and the organic layer was washed with 30 mL of a saturated sodium bicarbonate solution and then with 30 mL of water. The organic layer was dried over magnesium sulfate and then concentrated. Distillation (94 °C, 0.1 mm) afforded 1.765 g (89%) of clear, colorless liquid: NMR (CCl_4) 2.05 (s, 3 H), 2.25 (s, 6 H), 7.12 (s, 5 H); IR (neat) 2940 (s), 2875 (m), 2840 (m), 1700 (vs), 1360 (vs), 1190 (vs), 793 (s), 695 cm^{-1} (vs).

Anal. Calcd for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 83.49; H, 7.35.

3-Acetoxy-1-phenylbicyclo[1.1.1]pentane (16). A solution of 1.90 g (10.2 mmol) of 3-acetyl-1-phenylbicyclo[1.1.1]pentane (**15**) in 4.8 mL of chloroform was added to a stirred mixture of 3.13 g (15.4 mmol) of *m*-chloroperbenzoic acid in 18.3 mL of chloroform at room temperature. The solution was stirred in the dark for 24 h. A large quantity of *m*-chlorobenzoic acid appeared as a white precipitate in the course of the reaction. The mixture was filtered, and the filtrate was washed with 10% sodium bicarbonate and then water. The organic layer was dried over magnesium sulfate and then concentrated. Distillation (80–81 °C, 0.4 mm) afforded 1.69 g (82%) of clear, colorless liquid: NMR (CCl_4) 1.96 (s, 3 H), 2.38 (s, 6 H), 7.13 (s, 5 H); IR (neat) 2950 (m), 1750 (vs), 1600 (w), 1362 (m), 1220 (br, vs), 1142 (m), 1010 (m), 965 (m), 923 (m), 790 (m), 695 cm^{-1} (m).

Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 76.91; H, 6.90.

3-Acetoxybicyclo[1.1.1]pentane-1-carboxylic Acid (17) and 3-Hydroxybicyclo[1.1.1]pentane-1-carboxylic Acid (18). To a stirred mixture of 47 mL of Clorox (0.755 M in sodium hypochlorite, 35.5 mmol) and 10 mL of carbon tetrachloride was added 20 mg of ruthenium dioxide dihydrate. 3-Acetoxy-1-phenylbicyclo[1.1.1]pentane (**16**; 184 mg, 0.910 mmol) was added to the yellow mixture, and stirring was continued for 48 h. The layers were separated. The aqueous phase was washed with three 20-mL portions of carbon tetrachloride, acidified, and then extracted with four 10-mL portions of ether. The combined ether layers were dried and concentrated to give 139 mg of gummy solid, mp 69–80 °C. The material was recrystallized twice from hexane/ethyl acetate and then sublimed (0.7 mm, 80 °C) twice to afford 81 mg (52%) of a white solid, identified as 3-acetoxybicyclo[1.1.1]pentane-1-carboxylic acid (**17**): mp 106–107 °C; NMR ($CDCl_3$) 2.03 (s, 3 H), 2.50 (s, 6 H), 9.25 (br s, 1 H); IR (KBr) 3000 (br, m), 1740 (s), 1690 (s), 1420 (s), 1220 (vs), 1045 (s), 790 cm^{-1} (m).

Anal. Calcd for $C_8H_{10}O_4$: C, 56.47; H, 5.92. Found: C, 56.18; H, 5.84.

It was observed that considerable hydrolysis of the acetate **17** took place under the reaction conditions to form the alcohol **18** when a larger excess of Clorox was used. The following was a typical procedure used to separate these materials.

A mixture of 1.2 g (5.9 mmol) of 3-acetoxy-1-phenylbicyclo-[1.1.1]pentane, 390 mL of Clorox (294 mmol of sodium hypochlorite), 72 mL of carbon tetrachloride, and 300 mg of ruthenium dioxide dihydrate was stirred for 54 h. The aqueous layer was washed with carbon tetrachloride, and then a small amount of sodium bisulfite was added. After acidification with hydrochloric acid and the addition of solid sodium chloride (ca. 50 g), the aqueous mixture was extracted with eight 100-mL portions of ether. The ether extracts were combined, dried, and concentrated to give 0.755 g of semisolid material. Flash chromatography was performed by using 70 g of silica gel (Woelm, 32–63 μm) on a 34-mm-o.d. column with a pressure of 6 psi. Hexane/ethyl acetate (1:1) was used as the solvent, and ca. 20 mL fractions were taken and analyzed by thin-layer chromatography. Fractions 9–13 were combined and concentrated to give 200 mg of crude acetate **17**, mp 99–103 °C. Fractions 19–30 were combined to afford 138 mg of the crude alcohol **18**, mp 118–121 °C. the total yield of material was 38%.

The alcohol **18** was recrystallized from hexane/ethyl acetate and then sublimed (1 mm, 90 °C) to give white solid: mp 128.5–129.0 °C; NMR (Me_2SO-d_6) 1.97 (s, 6 H), 6.33 (br s, 1 H, removable with D_2O), 12.2 (br s, 1 H, removable with D_2O); IR (KBr) 3000 (br, s), 1685 (vs), 1510 (w), 1415 (m), 1263 (s), 1205 (s), 1050 cm^{-1} (m).

Anal. Calcd for $C_6H_8O_3$: C, 56.25; H, 6.29. Found: C, 55.99; H, 6.10.

The acetate **17** was recrystallized from hexane/ethyl acetate and then sublimed (0.2 mm, 90 °C) to afford white solid: mp 106.5–107.5 °C. The NMR spectrum was identical with that described above.

Methyl 3-Phenylbicyclo[1.1.1]pentane-1-carboxylate (19). A solution of diazomethane in ether was prepared by using Diazald (Aldrich, 14.1 g, ca. 47 mmol of diazomethane expected). To 8.00 g (42.6 mmol) of 3-phenylbicyclo[1.1.1]pentane-1-carboxylic acid in 62 mL of ether, chilled in an ice/salt bath, was added the diazomethane solution (ca. 180 mL) over 10 min. The color of the resultant solution was only slightly yellow. After an additional 0.5 h at this temperature, a small amount of concentrated hydrochloric acid was added to the reaction mixture with no color change. The ether solution was extracted with 50 mL of 5% sodium bicarbonate and then with 50 mL of water. The bicarbonate layer was acidified with hydrochloric acid and then extracted with 50 mL of ether. This ether solution was dried and concentrated to give 1.70 g of starting material; mp 172–174 °C. The original ether layer was dried over magnesium sulfate and concentrated to give a yellow liquid. Distillation (85–90 °C, 0.4 mm) afforded clear, colorless liquid: 6.278 g (93% based on unrecovered acid); NMR ($CDCl_3$) 2.26 (s, 6 H), 3.62 (s, 3 H), 7.15 (s, 5 H); IR (neat 2950 (s), 1725 (vs), 1600 (w), 1485 (m), 1430 (s), 1355 (s), 1295 (s), 1200 (vs), 1115 (vs), 985 (m), 788 (m), 750 (s), 697 cm^{-1} (s).

Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.42; H, 6.85.

3-Carbomethoxybicyclo[1.1.1]pentane-1-carboxylic Acid (20). To a stirred mixture of 1.50 mL of Clorox (0.755 M in sodium hypochlorite, 1.13 mol) and 275 mL of carbon tetrachloride was added 0.15 g of ruthenium dioxide dihydrate. Methyl 3-phenylbicyclo[1.1.1]pentane-1-carboxylate (**19**; 6.278 g, 31.1 mmol) was added and the mixture stirred for 47 h. The layers were separated. The aqueous phase was washed with two 100-mL portions of carbon tetrachloride, acidified, and extracted with 12 250-mL portions of dichloromethane. The organic extracts were combined, dried over magnesium sulfate, and concentrated to give 4.551 g (86%) of white solid, mp 124–128 °C. Recrystallization from hexane afforded 3.266 g (62%) of white plates: mp 139.5–140.2 °C; NMR ($CDCl_3$) 2.30 (s, 6 H), 3.65 (s, 3 H), 10.4 (br s, 1 H); IR (KBr) 3450 (br, m), 3200 (br, s), 1738 (vs), 1707 (vs), 1434 (s), 1342 (s), 1300 (s), 1226 (vs), 1207 (s), 1180 (s), 1043 (m), 946 cm^{-1} (m).

Anal. Calcd for $C_8H_{10}O_4$: C, 56.47; H, 5.92. Found: C, 56.22; H, 5.90.

Bicyclo[1.1.1]pentane-1,3-dicarboxylic Acid (21). A solution of 0.500 g (2.94 mmol) of 3-carbomethoxybicyclo[1.1.1]pentane-1-carboxylic acid (**20**) and 1.6 g (40 mmol) of sodium hydroxide in 15 mL of water was heated at reflux for 1.5 h. The yellowish solution was then washed with 15 mL of ether, acidified with hydrochloric acid, and extracted with six 15-mL portions of ether. The combined extracts were dried over magnesium sulfate and concentrated to give 435 mg of slightly yellow solid. The material was sublimed at high vacuum (5×10^{-4} mm, 150 °C), recrystallized from ethyl acetate, and then sublimed again to afford 310 mg (68%) of white solid: sublimed without melting at 260 °C; NMR (acetone-d_6) 2.28 (s, 6), 8.18 (s, 2); IR (KBr) 3400, 3020, 2930, 2860, 2600, 1705, 1425, 1300, 1230, 1210, 1150, 1040, 950, 740 cm^{-1}; Raman (solid) 3020, 2960, 2900, 1660, 1460, 1430, 1340, 1160, 1140, 1120, 1060, 740.

Anal. Calcd for $C_7H_8O_4$: C, 53.85; H, 5.16. Found: C, 53.85; H, 5.05.

1-Phenylbicyclo[1.1.1]pent-3-ylamine hydrochloride (22) was prepared by the Schmidt reaction of 3-phenylbicyclo-[1.1.1]pentane-1-carboxylic acid (**14**). Chloroform (40 mL) was added to a paste composed of sodium azide (6.5 g, 0.10 mol) and water (6.5 g). Concentrated sulfuric acid (5.1 g, 0.05 mol) was added to this vigorously stirred mixture at 0 °C over 30 min. The chloroform layer was then decanted and dried over anhydrous sodium sulfate. The strength of the hydrazoic acid solution was determined to be 1.58 M by shaking 2.0 mL of the solution with 35 mL of distilled water and titrating with 0.1 M sodium hydroxide. To a vigorously stirred solution of **14** (6.00 g, 31.9 mmol) in 30 mL of chloroform and 14 mL of concentrated sulfuric acid at 40 °C was added 32 mL of the hydrazoic acid solution (50.6 mmol) over 2 h. The mixture was stirred at 40 °C for 2 h and then made alkaline with 33% sodium hydroxide. Water was added, and the mixture was steam distilled into 100 mL of 3 N hydrochloric acid. The distillate was concentrated in vacuo to give a purple solid. This material was taken up in 1-butanol, precipitated with ether, filtered, and dried to give 3.187 g (51%) of slightly purple material: NMR (D_2O, 1,4-dioxane as internal standard, chemical shifts adjusted to tetramethylsilane) 2.35 (s, 6 H), 7.25 (s, 5 H), 3.70 (s, 1,4-dioxane), 4.60 (s, DOH); IR (KBr) 3450 (br, m), 2975 (br, s), 1605 (m), 1498 (m), 1450 (m), 1253 (s), 740 (m), 515 cm^{-1} (m). A portion of the material was taken up in 1-butanol and precipitated by adding ether. The small crystals were filtered, washed with ether, and dried to give white solid, mp 230 °C dec.

Anal. Calcd for $C_{11}H_{14}NCl$: C, 67.51; H, 7.21; N, 7.16; Cl, 18.12. Found: C, 67.46; H, 7.16; N, 7.54; Cl, 18.34.

3-Nitro-1-phenylbicyclo[1.1.1]pentane (23). 3-Phenylbicyclo[1.1.1]pent-1-ylamine hydrochloride (**22**; 0.250 g, 1.28 mmol) was added to 25 mL of a 10% sodium hydroxide solution, and the resulting mixture was extracted with two 12-mL portions of ether. The combined ether layers were dried over magnesium sulfate. The ether was evaporated under a stream of nitrogen to give the free amine. A mixture of *m*-chloroperbenzoic acid (85%, 1.037 g, 5.11 mmol) and 7 mL of 1,2-dichloroethane was heated to reflux, and a solution of the amine in 3.5 mL of 1,2-dichloroethane was added dropwise over 30 min. The resulting mixture was heated at reflux for 3 h and then cooled. Much white precipitate appeared and dichloromethane was added until it dissolved. The solution was washed with two 20-mL portions of 1 N sodium hydroxide and 10 mL of 10% potassium chloride. The organic layer was dried over magnesium sulfate and then concentrated in vacuo to give 216 mg of brown oil which partially solidified. The oil was chromatographed on 10 g of silica gel with 2:1 hexane/dichloromethane as the solvent, taking 6–7-mL fractions. Fractions 4–8 were combined to give 115 mg of slightly brown solid, mp 80.0–81.7 °C. Sublimation (4 mm, 75 °C) gave 102 mg (42%) of white solid: mp 81.5–82.0 °C; NMR ($CDCl_3$) 2.62 (s, 6 H), 7.25 (m, 5 H); IR (KBr) 2975 (m), 2900 (w), 1510 (vs), 1440 (m), 1375 (s), 1355 (s), 1200 (s), 805 (s), 745 (s), 696 cm^{-1} (s).

Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.66; H, 5.93; N, 7.65.

Increase of the reaction scale to 2.000 g (10.22 mmol) of the hydrochloride **22** and 8.30 g (40.9 mmol) of *m*-chloroperbenzoic acid afforded 1.399 g (72.3%) of sublimed material, mp 80.5–82.0 °C.

3-Nitrobicyclo[1.1.1]pentane-1-carboxylic Acid (24). To a stirred mixture of 52.5 mL of Clorox (0.755 M in sodium hypochlorite, 39.6 mmol) and 15 mL of carbon tetrachloride was added 30 mg of ruthenium dioxide dihydrate. 1-Nitro-3-phenylbicyclo[1.1.1]pentane (**23**; 0.250 g, 1.32 mmol) was added, and the mixture was stirred with a glass paddle. The mixture turned black due to precipitated ruthenium dioxide within 7 h. Clorox (4.0 mL) was added, and stirring was continued for an additional 48 h. The layers were separated. The aqueous phase was washed with two 20-mL portions of carbon tetrachloride, acidified with hydrochloric acid, and then extracted with four 40-mL portions of ether. The combined ether layers were dried over magnesium sulfate and concentrated to give yellow gummy material. Sublimation (0.5 mm, 90 °C) afforded a slightly yellow solid. This solid was recrystallized twice from benzene and then sublimed to give 92 mg (44%) of white powder: mp 165–165.5 °C; ^1H NMR ($CDCl_3$) 2.67 (s, 6 H), 10.05 (br s, 1 H); ^{13}C NMR ($CDCl_3$) 31.50, 55.03, 64.24, 173.72; IR (KBr) 2900 (br, m), 1700 (vs), 1530 (s), 1435 (m), 1330 (m), 1220 (s), 950 (w), 813 (w), 758 cm^{-1} (w).

Anal. Calcd for $C_6H_7NO_4$: C, 45.87; N, 4.49; N, 8.91. Found: C, 45.65; H, 4.45; N, 8.84.

Reaction of 3-Acetoxybicyclo[1.1.1]pentane-1-carboxylic Acid (17) in Refluxing Aqueous Potassium Hydroxide. A solution of 10 mg (0.049 mmol) of acetate **17** in 2 mL of 10% potassium hydroxide was heated at reflux for 30 min. The mixture was poured onto ice, acidified to ca. pH 3 with 1 N hydrochloric acid, and extracted with ether. The ether layer was dried over anhydrous sodium sulfate and concentrated to give an oil. The major signals in the NMR spectrum of this material correspond favorably with those expected for 3-carboxy-3-methylcyclobutanone (**25**): NMR ($CDCl_3$) 1.63 (s, 3 H), 2.92, 3.64 (two sets of doublets of multiplets, J = 20, total 4 H), 8.33 (br s, integrated to 2 H, but probably wet). No further purification of this material was attempted.

Methyl 3-bromobicyclo[1.1.1]pentane-1-carboxylate (26) was prepared by a similar method to that described by Baker, Holtz, and Stock[36] for the synthesis of 1-bromobicyclo[2.2.2]octane. To a stirred suspension of 1.000 g (5.88 mmol) of 3-carbomethoxybicyclo[1.1.1]pentane-1-carboxylic acid (**20**) and 0.909 g (4.20 mmol) of red mercuric oxide in 22 mL of 1,2-dibromoethane heated to 80 °C was added a solution of 1.442 g (9.02 mmol) of bromine in 10 mL of 1,2-dibromoethane over 5 min. Stirring at 80 °C was continued for 1 h. The reaction mixture was washed with two 20-mL portions of 5% sodium bicarbonate, 20 mL of 10% sodium thiosulfate, and 10 mL of water. The organic layer was dried over magnesium sulfate. Most of the 1,2-dibromoethane was removed by distillation (63 °C, 80 mm) as 5.4 g of solution remained. Preparative gas chromatography [5% silicone rubber, SE-30, on Chromosorb G (60/80)] afforded 0.826 g (68%) of white solid: mp 45–47.5 °C; NMR ($CDCl_3$) 2.50 (s, 6 H), 3.68 (s, 3 H). An analytical sample was obtained by recrystallizing a small portion of the material from hexane at −78 °C three times: mp 49.0–49.5 °C; IR (KBr) 3025 (w), 2960 (w), 1750 (s), 1520 (w), 1450 (m), 1330 (s), 1210 (s), 1155 (m), 996 (m), 875 cm^{-1} (m).

Anal. Calcd for $C_7H_9BrO_2$: C, 41.00; H, 4.42; Br, 38.97. Found: C, 41.05; H, 4.57; Br, 38.71.

Reaction of Methyl 3-Bromobicyclo[1.1.1]pentane-1-carboxylate (26) with Aqueous Silver Nitrate. A solution of the ester (64.2 mg, 0.313 mmol) and silver nitrate (1.1 g, 6.47 mmol) in 50 mL of water was stirred at room temperature for 3.5 h. A yellowish precipitate formed shortly after the reactants were mixed. The pH of the solution was determined to be 5–6 by using Hydrion A paper. The reaction mixture was extracted with two 15-mL portions of dichloromethane. The combined organic extracts were dried and concentrated. Analysis by gas chromatography showed three components in a ratio of 5:88:7. The major component was collected from the gas chromatograph and identified as 1-carbomethoxy-3-methylenecyclobutanol (**27**): 15 mg; mp 38.5–39.5 °C; NMR (CCl_4) 2.82, 3.08 (two sets of doublets of multiplets of equal area, J_1 = 16, J_2 = 2, total 4 H), 3.30 (s,

(36) Baker, F. W.; Holtz, H. D.; Stock, L. M. *J. Org. Chem.* **1963**, *28*, 514.

1 H), 3.75 (s, 3 H), 4.78 (quintet, J = 2, 2 H); IR (CCl_4) 3500 (m), 3050 (w), 2920 (m), 1750 (vs), 1680 (m), 1435 (s), 1400 (m), 1280 (s), 1200 (vs), 1120 (s), 1060 (m), 980 (m), 885 cm^{-1} (s); mass spectrum, m/e 142 (molecular ion).

The last component was also collected (1 mg) and tentatively identified as methyl 4-oxo-2-methylenepentanoate: NMR (CCl_4) 2.10 (s, 3 H), 3.25 (s, 2 H), 3.70 (s, 3 H), 5.35 (br s, 1 H), 6.17 (br s, 1 H); IR (CCl_4) 2980 (w), 2925 (w), 1725 (s), 1640 (w), 1435 (m), 1360 (m), 1330 (m), 1204 (m), 1148 (m), 952 cm^{-1} (m). The other component was not characterized. The aqueous reaction mixture was continuously extracted with ether for 5 days but yielded no additional material.

1-Acetyl-3-methylbicyclo[1.1.1]pentane (28). A solution of 2.00 g (15.9 mmol) of 3-methylbicyclo[1.1.1]pentane-1-carboxylic acid (**7**) in 100 mL of dry ether was cooled to 0 °C and placed under a nitrogen atmosphere. To this stirred solution was added 48.4 mL of a solution of methyllithium in ether (0.704 M, 34.1 mmol) over 1.5 h. Stirring was continued for an additional 4 h at room temperature. The turbid reaction mixture was then poured onto ice and acidified with concentrated hydrochloric acid. The layers were separated and the organic layer was extracted with 40 mL of a 10% sodium carbonate solution and then with 20 mL of water. The ether solution was dried over magnesium sulfate and concentrated. Distillation (60–61 °C, 50 mm) afforded 1.00 g (51%) of clear, colorless liquid: NMR ($CDCl_3$) 1.18 (s, 3 H), 1.88 (s, 6 H), 2.08 (s, 3 H); IR (neat) 2930 (s), 2880 (m), 2840 (m), 1700 (vs), 1375 (m), 1355 (m), 1330 (m), 1168 cm^{-1} (s).

An analytical sample was obtained by preparative gas chromatography on silicone rubber. Anal. Calcd for $C_8H_{12}O$: C, 77.38; H, 9.74. Found: C, 77.11; H, 9.73.

3-Methyl-1-(2-hydroxy-2-propyl)bicyclo[1.1.1]pentane (29). A solution of 2.4 g (19.3 mmol) of 1-acetyl-3-methylbicyclo[1.1.1]pentane (**28**) in 8 mL of dry ether was added dropwise over 1.5 h to an ice-cold stirred solution of methyllithium in ether (32.2 mL, 83.7 mmol) under a nitrogen atmosphere. Stirring at 0 °C was continued for 2 h and then at room temperature for 22 h. The mixture was cooled in an ice bath, and aqueous saturated ammonium chloride (10 mL) was added slowly. The layers were separated, and the aqueous phase was extracted with 10 mL of ether. The ether layers were combined, washed with 10 mL of water, dried over magnesium sulfate, and concentrated to give sticky white material. Recrystallization from cold pentane (−25 °C) gave 1.863 g (69%) of white solid: mp 47.5–50.0 °C; NMR ($CDCl_3$) 1.12, 1.15 (2 s, total 9 H), 1.30 (s, 1 H), 1.51 (s, 5 H). A portion of the material was sublimed (150 mm, 45 °C) twice to give an analytical sample: mp 50.0–50.5 °C; IR ($CHCl_3$) 3615 (m), 3465 (br, m), 2980 (vs), 1450 (s), 1380 (s), 1370 (s), 1280 (s), 1187 (s), 1170 (s), 1105 (m), 955 (s), 936 cm^{-1} (s).

Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 76.84; H, 11.33.

3-Phenyl-1-(2-hydroxy-2-propyl)bicyclo[1.1.1]pentane (30). A solution of 1.726 g (9.27 mmol) of 3-acetyl-1-phenylbicyclo[1.1.1]pentane (**15**) in 4 mL of dry ether was added dropwise over 1.5 h to an ice-cold stirred solution of methyllithium in ether (16.9 mL, 18.5 mmol) under nitrogen. A sticky white precipitate separated from solution midway through the addition. The mixture was stirred at room temperature for 12 h. A workup using a procedure analogous to that described for the 3-methyl derivative **29** afforded 2.1 g of white solid, mp 62–70 °C. This material was sublimed (30 mm, 90 °C) to give 1.642 g (88%) of product, mp 71–75 °C. A portion of this material was recrystallized twice from aqueous ethanol and then sublimed (0.2 mm, 50 °C) three times to afford an analytical sample: mp 75.5–76.0 °C; NMR ($CDCl_3$) 1.23 (s, 7 H), 1.93 (s, 6 H), 7.23 (s, 5 H); IR ($CHCl_3$) 3685 (w), 3608 (m), 3470 (br, w), 3020 (s), 2980 (vs), 2910 (s), 2875 (s), 1600 (m), 1445 (m), 1366 (m), 1198 (s), 1180 (s), 938 cm^{-1} (s).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.19; H, 9.02.

3-Carbomethoxy-1-(2-hydroxy-2-propyl)bicyclo[1.1.1]pentane (31). A solution of 1.00 g (5.88 mmol) of 3-carbomethoxybicyclo[1.1.1]pentane-1-carboxylic acid (**20**) in 15 mL of dry tetrahydrofuran (distilled from sodium benzophenone ketyl) was placed under an atmosphere of nitrogen. To this stirred mixture was added a solution composed of 7.3 mL of methylmagnesium bromide (3.2 M, 23.5 mmol) in ether and 10 mL of dry tetrahydrofuran over 3.5 h at room temperature. The mixture was stirred for an additional 6 h, poured onto ice, acidified with 1 N hydrochloric acid, and extracted with four 50-mL portions of ether. The combined organic extracts were dried over magnesium sulfate and concentrated to give white solid. This material was taken up in anhydrous ether (100 mL). The resulting solution was cooled in an ice/salt bath, and excess diazomethane in ether (prepared from Diazald, Aldrich) was added. After 2 h at this temperature, a small amount of concentrated hydrochloric acid was added to destroy excess diazomethane. The ether solution was extracted with 75 mL of aqueous saturated sodium bicarbonate, dried, and concentrated to give a yellow oil. Chromatography on silica gel (30 g) with dichloromethane as the solvent afforded a gummy material, which was sublimed (70 mm, 90 °C) to give 359 mg (33%) of white solid, mp 45–48 °C. A portion of the material was recrystallized by slow evaporation of a heptane/ether solution to give white rods: mp 51.5–53.0 °C; NMR ($CDCl_3$) 1.17 (s, 6 H), 1.30 (br s, 1 H), 1.95 (s, 6 H), 3.67 (s, 3 H); IR ($CHCl_3$) 3680 (w), 3610 (m), 3490 (w), 2990 (s), 1728 (vs), 1267 (s), 1180 (s), 1040 (m), 940 cm^{-1} (m).

Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.08; H, 8.95.

***p*-Nitrobenzoates of alcohols 29–31** were prepared by a method like that of Paulsen.[37] A mixture of 0.802 g (5.72 mmol) of 1-methyl-3-(2-hydroxy-2-propyl)bicyclo[1.1.1]pentane (**29**), 5.40 g (29.1 mmol) of *p*-nitrobenzoyl chloride, 0.141 g (1.15 mmol) of 4-(dimethylamino)pyridine, and 23 mL of dry pyridine was stirred at 43 °C for 46 h under an atmosphere of nitrogen. The brown reaction mixture was then poured on ice. Water and acetone were added (approximately 75 mL of each) to dissolve the precipitate. Solid sodium bicarbonate was then added until the mixture became saturated. The resulting mixture was stirred for 1.5 h and then concentrated in vacuo. Water and chloroform (100 mL of each) were added to the solid, and the mixture was shaken vigorously in a separatory funnel. The layers were separated. The organic phase was washed successively with 100 mL of water, 100 mL of 1 N hydrochloric acid, 100 mL of water, 100 mL of 5% sodium bicarbonate, and 100 mL of water. The chloroform solution was dried over anhydrous potassium carbonate and concentrated to give 1.48 g of slightly yellow solid, mp 155–158 °C. This material was taken up in dichloromethane and eluted through 5 g of silica gel to remove colored impurities. Recrystallization of the concentrated material from hexane followed by sublimation (0.3 mm, 120 °C) afforded 1.14 g (69%) of only slightly yellow solid: mp 159–160 °C; NMR ($CDCl_3$) 1.20 (s, 3 H), 1.55 (s, 6 H), 1.66 (s, 6 H), 8.07 (d, J = 9 Hz, 2 H), 8.24 (d, J = 9 Hz, 2 H); IR ($CHCl_3$) 2973 (s), 2915 (w), 2875 (m), 1725 (s), 1608 (m), 1535 (m), 1350 (s), 1295 (vs), 1130 (s), 842 cm^{-1} (w).

Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.41; H, 6.74; N, 4.66.

By the same method was prepared the *p*-nitrobenzoate of **30** in 74% yield: mp 163.0–163.5 °C; NMR ($CDCl_3$) 1.63 (s, 6 H), 2.08 (s, 6 H), 7.24 (s, 5 H), 8.10 (d, J = 9, 2 H), 8.25 (d, J = 9, 2 H); IR ($CHCl_3$) 3035 (w), 3015 (w), 2900 (m), 2910 (w), 2875 (m), 1722 (s), 1607 (m), 1532 (m), 1352 (m), 1290 (vs), 1157 (m), 1120 (s), 1102 (m), 1013 (m), 873 (m), 843 cm^{-1} (m).

Anal. Calcd for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02; N, 3.99. Found: C, 72.01; H, 6.20; N, 4.16.

Similarly, the *p*-nitrobenzoate of **31** was prepared in 64% yield: mp 149–150 °C; NMR ($CDCl_3$) 1.60 (s, 6 H), 2.10 (s, 6 H), 3.70 (s, 3 H), 8.10 (d, J = 9, 2 H), 8.28 (d, J = 9, 2 H); IR ($CHCl_3$) 3040 (w), 2998 (m), 2928 (w), 2890 (w), 1730 (vs), 1610 (m), 1535 (s), 1353 (s), 1290 (vs), 1170 (s), 1130 (s), 1105 (s), 1040 (m), 1016 (m), 874 (m), 845 cm^{-1} (m).

Anal. Calcd for $C_{17}H_{19}NO_6$: C, 61.25; H, 5.75; N, 4.20. Found: C, 61.26; H, 5.64; N, 4.15.

4-Substituted Butyric Acids 32a–e. Valeric acid (**32a**), 4-phenylbutyric acid (**32b**), and methyl glutarate (**32c**) were obtained from commercial sources and purified by distillation (**32a** and **32c**) or crystallization and sublimation (**32b**).

4-Cyanobutyric acid (**32e**) was made by the method of Reppe;[38] mp 38–39 °C (lit.[39] mp 37.5–38.0 °C).

(37) Redlich, H.; Neumann, H. J.; Paulsen, H. *Chem. Ber.* **1977**, *110*, 2911. See also: Holfe, G.; Steglich, W.; Vorbruggen, H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 569.

(38) Reppe, W.; et. al. *Justus Liebigs Ann. Chem.* **1955**, *596*, 198.

4-Acetoxybutyric acid (**32d**) was prepared by the procedure of Kricheldorf and Kaschig:[40] bp 85–86 °C (0.2 mm) [lit.[40] bp 98–99 °C (0.02 mm)]; NMR ($CDCl_3$) 1.8–2.1 (m, sharp s at 2.03, total 5 H), 2.46 (t, J = 7, 2 H), 4.12 (t, J = 6, 2 H), 11.8 (br s, 1 H); IR (neat) 3000 (br, s), 1730 (vs), 1705 (vs), 1400 (br, s), 1240 (br, s), 1040 cm^{-1} (s).

Anal. Calcd for $C_6H_{10}O_4$: C, 49.31; H, 6.90. Found: C, 49.17; H, 6.77.

Determination of Apparent pK_a in 50% Ethanol. All organic acids of noncommercial origin were of analytical purity.

The titrations were performed under nitrogen in a water bath thermostated to 25.0 ± 0.1 °C. For each titration, an approximately 0.01 M solution of the carboxylic acid was prepared by dissolving ca. 0.15 mmol of the acid in 15.0 mL of 50% ethanol–water and using a 15-mL volumetric pipet. The titrant was 0.1 M potassium hydroxide, obtained by dilution of the commercial Acculute solution (Anachemia) with 50% (by volume) ethanol–water. "Absolute" grade ethanol was distilled, the fraction boiling at 77.5–78.0 °C being collected. Distilled water was degassed by boiling under nitrogen for 15 min. The ethanol and water had been equilibrated for several days at 25 °C prior to the mixing of equal volumes.

The titrant was delivered from either a 5- or 10-mL syringe through polyethylene tubing. The tubing was immersed directly into the solution being titrated. The syring was driven by a continuous-drive mechanism such that the titrant was added over 12–15 min at a constant rate. Attached to the drive mechanism was a potentiometer, the voltage output of which was controlled by movement of the drive mechanism. Efficient mixing of the solution during the titration was accomplished by using a Teflon-coated stir bar and an air-driven magnetic stirrer.

A solid-state digital readout (to 0.01 pH unit) pH meter and a Sargent-Welch silver–silver chloride and glass combination electrode (catalog No. S-300070-10) were used for pH measurements. Voltage outputs from both the potentiometer and the pH meter were input into a Hewlett-Packard Model 7015-A X-Y recorder such that a normal titration curve (i.e., a plot of volume added vs. pH) was recorded for that portion of the curve up to slightly past the equivalence point.

Primary standard aqueous buffer solutions (Curtin Matheson Scientific Co.) at pH 4.01 ± 0.01 and 7.00 ± 0.01 were used to calibrate the chart paper (graduated in millimeters) before each titration. The electrode was allowed to equilibrate in the appropriate solution a minimum of 10 min prior to the recording of each buffer calibration and the actual titration. Each buffer was replaced with fresh solution after it had been used for two or three calibrations.

The pK_a values were calculated for several points along each titration curve. The interpolated pH values were taken as the negative logarithms of the hydrogen ion concentrations. No corrections were made for liquid-junction potentials, and unit activity coefficients were assumed for all species. Benzoic acids were titrated periodically to ensure the consistency of the method.

The recorder was adjusted such that the pen movement corresponding to the volume of potassium hydroxide solution added was approximately 150 mm from the beginning of the titration to the equivalence point. The distance between the pH 4.01 and 7.00 buffer calibration lines was approximately 90 mm, which corresponds to a change of about 0.033 pH unit/mm. All distances were estimated to 0.05 or 0.1 mm and are probably accurate to ca. 0.2 mm. The equivalence point for each titration was estimated adequately by visual inspection of the curve. The results of the pK_a determinations are given in Table I.

Prior to performing titrations, a study was undertaken to show that the recorded pen movement corresponding to added volume was indeed linearly related to the quantity of liquid discharged from the syringe. Various quantities of 50% ethanol were collected and weighed, and the pen movement was recorded. A least-squares analysis of a plot of pen movement vs. weight of discharged liquid gave an excellent correlation (eight points, r = 0.999 99). The results of this study indicated that the error in calculated pK_a values from either a nonlinear relationship between pen movement and added base or pen movement prior to addition of any base is less than 0.003 pK unit. Also, no detectable increase in the pH of the solution was observed upon halting the addition of base during a titration.

Preparation of 80% Aqueous Acetone. Aqueous acetone (80% by volume at 25 °C) was prepared by mixing 1 volume of distilled water and 4 volumes of acetone, which had been refluxed over and fractionally distilled from anhydrous calcium chloride. The acetone and water had been equilibrated for several days at 25 °C prior to mixing.

Solvolysis of the *p*-Nitrobenzoate of 3-Phenyl-1-(2-hydroxy-2-propyl)bicyclo[1.1.1]pentane in 80% Acetone at 126 °C (Buffered). A thick-walled ampule containing 0.141 g (0.400 mmol) of the *p*-nitrobenzoate of **30**, 20.0 mL of 80% acetone, and 0.093 mL (ca. 0.80 mmol) purified 2,6-lutidine[41] was immersed in a dry ice/2-propanol bath and purged with a stream of nitrogen for a few minutes. The ampule was sealed and placed in an oil bath at 126 °C for 105 h. It was then cooled and opened, and the contents poured into a solution of 10% aqueous sodium bicarbonate (80 mL). The aqueous mixture was extracted with 40 mL of dichloromethane. The organic extract was washed with 20 mL of water, dried over anhydrous sodium and magnesium sulfates, and concentrated in vacuo until approximately 2 mL of yellow solution remained. This mixture was analyzed by gas chromatography (GC) with 15% Carbowax 20M on Chromosorb G with a helium flow rate of 75 mL/min. The column temperature was programmed from 150 to 225 °C with an increase of approximately 6.8 deg/min. The trace showed four peaks: retention times 5.57, 7.7, 8.6, and 11.0 min with relative areas of 86, 6, 2, and 6, respectively. Samples from several injections were collected.

The material corresponding to the first peak was identified as 3-phenyl-1-(2-propenyl)bicyclo[1.1.1]pentane (**33**). Clear, colorless liquid was collected: 41.5 mg (0.225 mmol); NMR (CCl_4) 1.72 (sharp m, J = 1, 3 H), 2.03 (s, 6 H), 4.70 (m, 2 H), 7.12 (s, 5 H); IR (neat) 3020 (m), 2920 (s), 1640 (m), 1600 (w), 1490 (m), 1440 (s), 1375 (m), 1310 (m), 1200 (s), 1130 (w), 1030 (w), 890 (s), 825 (w), 745 (s), 695 cm^{-1} (s).

Anal. Calcd for $C_{14}H_{16}$: C, 91.25; H, 8.75. Found: C, 91.56; H, 8.81.

The second peak corresponded to two small overlapping peaks which were unresolvable on the column. A small amount of the olefin from peak A contaminated the collected sample. The material gave a complex NMR spectrum (CCl_4) with large singlets at δ 1.13 and 1.22 (relative integration 1:2, respectively) and small multiplets at δ 1.86, 2.70, 3.50, 4.63, 4.70, 4.87, 5.95, 6.20, 6.33, and 6.50. A large, broad multiplet appeared in the aromatic region at δ 7.2. The absence of a major singlet at ca. δ 2.0 and the presence of the numerous olefinic signals suggests that the major portion of this material does not contain the bicyclo[1.1.1]pentane ring system. No further purification or characterization of this sample was attempted.

The material collected from the third peak gave an NMR spectrum (CCl_4) almost exactly like that described for the second peak, which suggests contamination of the sample. The major differences are the absence of the multiplet at δ 3.50 and the presence of two singlets at δ 4.65 and 4.87 in place of the multiplets. No further purification or characterization of this material was performed.

The fourth peak was identified as corresponding to 3-phenyl-1-(2-hydroxy-2-propyl)bicyclo[1.1.1]pentane (**30**). Slightly yellow solid was obtained: 5.1 mg (0.025 mmol); mp 72–74 °C. The NMR spectrum ($CDCl_3$) was identical with that described above.

Stability of 3-Phenyl-1-(2-hydroxy-2-propyl)bicyclo-[1.1.1]pentane (30) under Solvolytic Conditions. An ampule containing 16.2 mg (0.080 mmol) of the alcohol **30**, 4.0 mL of 80% acetone, 0.019 mL (ca. 0.16 mmol) of 2,6-lutidine, and 13.4 mg (0.08 mmol) of *p*-nitrobenzoic acid was placed in a dry ice/2-propanol bath and purged with nitrogen. The ampule was then sealed, placed in an oil bath at 126 °C for 38 h, cooled, and opened, and the contents were poured into a solution of 10% aqueous

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sodium bicarbonate (16 mL). The aqueous mixture was extracted with 5 mL of dichloromethane. The organic extract was washed with water, dried, and concentrated until approximately 0.5 mL remained. Analysis by gas chromatography indicated the presence of only starting alcohol and 2,6-lutidine.

Solvolysis of the *p*-Nitrobenzoate of 3-Carbomethoxy-1-(2-hydroxy-2-propyl)bicyclo[1.1.1]pentane in 80% Acetone at 149 °C (Buffered). A thick-walled ampule containing 0.133 g (0.400 mmol) of the *p*-nitrobenzoate of **31**, 20.0 mL of 80% acetone, and 0.093 mL (ca. 0.80 mmol) of 2,6-lutidine was placed in a dry ice/2-propanol bath and purged with a stream of nitrogen for a few minutes. The ampule was sealed and placed in an oil bath at 149 °C for 64 h. It was then cooled and opened, and the contents were poured into a solution of 10% aqueous sodium bicarbonate (80 mL). The aqueous mixture was extracted with two 30-mL portions of dichloromethane. The combined organic extracts were washed with 20 mL of water and then dried over anhydrous sodium and magnesium sulfates. To a portion of the solution (15.3%) was added 11.5 mg of 1-octanol as an internal standard. Both mixtures were then concentrated and analyzed by gas chromatography (Carbowax 20M) with a helium flow rate of 50 mL/min. The column temperature was programmed from 120 to 225 °C with an increase of approximately 4.8 °C/min. The trace for the product mixture showed four peaks: retention times 8.2, 10.2, 16.0, and 19.3 min with relative areas of 85, 7, 3, and 6, respectively. Samples from several injections were collected.

The material corresponding to the first peak was identified as 3-carbomethoxy-1-(2-propenyl)bicyclo[1.1.1]pentane (**34**). Clear, colorless liquid was collected: 29.8 mg (0.179 mmol); NMR (CCl_4) 1.67 (sharp m, J = 1, 3 H), 2.03 (s, 6 H), 3.62 (s, 3 H), 4.70 (br m, 2 H); IR (CCl_4) 3050 (w), 2950 (m), 1730 (s), 1430 (m), 1350 (m), 1297 (s), 1205 (s), 1160 (s), 1040 (m), 897 cm^{-1} (m).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.44; H, 8.63.

The NMR spectrum (CCl_4) of the material collected from the second peak contained all of the signals corresponding to the olefin of the first peak which indicated that the sample was contaminated. The other signals consisted of singlets at δ 1.90 and 3.70 (approximately of equal area) and multiplets at δ 3.22, 4.92, 4.97, 5.16, 5.43, and 6.12. Further purification or characterization of this material was not attempted.

The third peak corresponded to two small overlapping peaks which were unresolvable on the column. Only a very small amount of material was collected, and an NMR spectrum could not be obtained.

The fourth peak was identified as corresponding to 3-carbomethoxy-1-(2-hydroxy-2-propyl)bicyclo[1.1.1]pentane (**31**). A colorless oil was obtained (2.5 mg, 0.014 mmol). The NMR spectrum ($CDCl_3$) was identical with that previously described.

By measuring the relative GC trace areas for a known mixture of 1-octanol and the olefin **34**, the relative molar area ratios for these materials were determined to be the same within experimental error. From the relative trace areas of 1-octanol and the combined solvolysis products (43.4:24.7) and the known amount of 1-octanol in the mixture, the yield of the combined materials (peaks 1–4) was calculated to be 0.328 mmol (82%).

Reaction of Methyl *p*-Nitrobenzoate in 80% Acetone at 145 °C. A heavy-walled ampule containing 72.5 mg (0.4 mmol) of methyl *p*-nitrobenzoate (mp 94–95 °C) and 20 mL of 80% acetone was immersed in a dry ice/2-propanol bath and purged with nitrogen. The ampule was sealed, placed in an oil bath at 145 °C for 48 h, and cooled, and the contents were poured into a solution of 10% aqueous sodium bicarbonate (80 mL). The aqueous mixture was extracted with 40 mL of dichloromethane. The organic layer was washed with 20 mL of water, dried, and concentrated to give 66.0 mg (91.0%) of recovered ester, mp 93.5–94.5 °C. A similar experiment with added 2,6-lutidine as buffer gave nearly the same result.

Kinetic Procedures for Solvolysis of *p*-Nitrobenzoate Esters in 80% Acetone at 145.0 °C. Standard solutions of the *p*-nitrobenzoate of **29** (0.00489 M) and the *p*-nitrobenzoate of **31** (0.00998 M) in 80% acetone were prepared and distributed into several ampules, each containing ca. 3.2 mL of solution. The 3-methyl derivative would not readily go into solution at a higher concentration. Due to the insolubility of **30** *p*-nitrobenzoate in 80% acetone at room temperature, a standard solution of this ester could not be prepared. Instead, the ester (6–14 mg) was placed in several ampules, and the weight of material was accurately determined to 0.01 mg. Solvent (ca. 3.2 mL) was then added to each ampule. The exact amount of solvent present was determined by weighing the ampule prior to the addition of solvent and again after sealing. The volumes of solvent were then calculated from the experimentally determined density (0.8536 g/mL).

Since aqueous acetone solutions are known to develop an acid titer when heated in the presence of oxygen at high temperatures,[42] the ampules were cooled in a dry ice/2-propanol bath and purged with nitrogen prior to sealing. The sealed tubes were placed in a constant-temperature bath at 145.0 ± 0.1 °C. Ampules were removed at various times and immediately cooled in a water bath. Exact aliquots (2.986 mL) were taken by using a calibrated volumetric pipet and titrated with 0.0099 M aqueous sodium hydroxide which had been standardized against potassium hydrogen phthalate. Bromthymol blue was used as the indicator. A 10-mL microburet calibrated in 0.02-mL units was used for the titrations. The volumes of base added were estimated to 0.001 mL and were probably accurate to ca. 0.004 mL. Infinity titers were taken after 8–10 half-lives.

The rate constants were determined by linear least-squares regression analyses of the rate data corresponding to the integrated first-order rate expression: $\ln (A/(A - X)) = kt$, where X was the volume of base needed to neutralize the acid present at time t and A was the volume of base needed at the "infinity" point. Each rate constant k was taken as the slope of the regression line for a plot of $\ln (A/(A - X))$ vs. time. A computer program was used to carry out all calculations.

The data for **29** and **30** gave linear first-order plots through 3.5 and 4.5 half-lives, respectively. The data for **31** were linear for only 1.8 half-lives, with a theoretical infinity titer, which was done because the observed titer was greater than the theoretical value, probably due to hydrolysis of the methyl ester. The observed infinity titer (less than theoretical) was used for **29**, and a "floating" titer (to optimize linearity) was used for **30**, because of a large uncertainty in the experimental values in this case. Only the linear portions of the plots were used in the calculation of the rate constants.

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