Solvolytic Studies of Tricyclo[4.2.0.0^{2,4}]octan-5-yl Derivatives. Effect of Cyclopropane and Cyclobutane Orbital Alignments on Reactivity and Proclivity for Rearrangement

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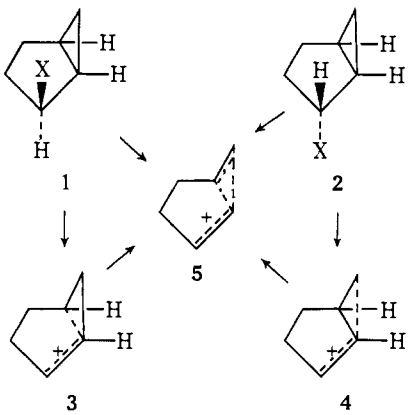
Abstract: The kinetics of hydrolysis of the four possible stereoisomeric tricyclo[4.2.0.0^{2,4}]octan-5-yl 3,5-dinitrobenzoates and *p*-nitrobenzoates in 80% aqueous alcohol have been studied at several temperatures. A striking feature of the present results is the convergence of both pairs of isomers to two related but noninterconverting cations (**51** and **52**), only the latter of which is capable of cyclobutane ring opening or ring expansion for stereoelectronic reasons. Both 1α,2β,4β,6α-dinitrobenzoates gave identical product mixtures (after 10 half-lives) consisting of *exo-cis*-bicyclo[4.2.0]oct-2-en-5-ol (**21a**) and its internally returned ester **21b**. Ionization in the 1α,2α,4α,6α series led to formation of the epimeric *cis*-bicyclo[3.3.0]oct-2-en-6-ols (**26** and **27**, 52–58%), *endo-cis*-bicyclo[4.2.0]oct-2-en-5-ol (**28**, 33–41%), and the alcohols of retained tricyclic structure (**17** and **20**, 7–9%). The formation of the [4.2.0] bicyclic alcohols with hydroxyl orientation inextricably linked to a specific precursor geometry implicates a rigid cation geometry and highly directed discharge by solvent. Studies of the products obtained from hydrolysis of deuterium labeled ester **42** showed the absence of deuterium scrambling and excluded the operation of cyclopropylcarbinyl–cyclopropylcarbinyl rearrangement. Carbocationic leakage of the homoallylic → allylic type was also not in evidence. A connection is drawn between various [3.1.0] bicyclic systems and the reactivity features of these molecules are discussed. Further consideration is given the general questions of bisected bishomoallylic cation intervention and of cyclobutane neighboring group involvement.

Study of the solvolytic reactions of cyclopropylcarbinyl derivatives has over the years provided strong evidence for very large conjugative interaction between a three-membered ring and an adjacent sp^2-hybridized carbon.[2] In systems which are conformationally flexible, adoption of the bisected rather than perpendicular geometry usually obtains.[3] In more rigid molecules such as the *endo*-1- and *exo*-2-substituted bicyclo[3.1.0]hexanes (**2**),[4] the situation is less clear. Accelerated solvolytic behavior in accord with anchimeric assistance is seen in the two isomers, but the rates and products of reaction in both instances are essentially identical. This behavior was not entirely anticipated since initial conversion of **1** to **3** and of **2** to **4** was expected by analogy. Although the initial intervention of these different delocalized cations is not presently discounted,[4f] the data require that the **1** → **3** and **2** → **4** reactions have near comparable activation energies and that rapid equilibration of both to **5** occur prior to solvent attack. Alternatively, **1** and **2** could experience



direct ionization to the identical bisected bishomoallyl cation (**5**), a conclusion supported by the effects of alkyl substitution at C_1 and C_5.[4b,g] This striking convergence to a single conformationally unique [3.1.0] bicyclic carbonium ion points to the existence of intriguing geometric effects in cyclopropylcarbinyl cation stabilization.[5] Similar behavior has been encountered with *exo*- and *endo*-bicyclo[4.1.0]hept-2-yl systems,[6] but as the size of the larger ring is increased to include 5–7 carbon atoms, the attendant enhancement of conformational flexibility (in the cis fused series) permits ionization to structurally distinct cationic intermediates.[7]

By comparison, cyclobutylcarbinyl cations have been much less extensively investigated and our knowledge

(1) (a) Lubrizol Fellow, 1967–1968; (b) National Science Foundation Trainee, 1970–1972.

(2) Recent reviews on cyclopropylcarbinyl systems include: (a) P. R. Story and B. C. Clark, Jr., in "Carbonium Ions," Vol. 3, G. Olah and P. v. R. Schleyer, Ed., Interscience, New York, N. Y., 1972, p 1007 ff; (b) H. G. Richey, Jr., *ibid.*, p 1201 ff; (c) K. B. Wiberg, B. A. Hess, Jr., and A. J. Ashe, III, *ibid.*, p 1295 ff; (d) M. Hanack and H. J. Schneider, *Angew. Chem., Int. Ed. Engl.*, **6**, 666 (1967); *Fortschr. Chem. Forsch.*, **8**, 554 (1967).

(3) (a) B. R. Ree and J. C. Martin, *J. Amer. Chem. Soc.*, **92**, 1660 (1970); (b) V. Buss, R. Gleiter, and P. v. R. Schleyer, *ibid.*, **93**, 3927 (1971); (c) G. A. Olah, C. L. Jewell, D. P. Kelly, and R. D. Porter, *ibid.*, **94**, 146 (1972), and earlier references cited in these papers; (d) V. Buss, P. v. R. Schleyer, and L. C. Allen, *Top. Stereochem.*, **7**, 253 (1973).

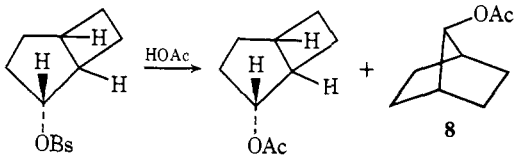
(4) (a) P. R. Brook, R. M. Ellam, and A. S. Bloss, *Chem. Commun.*, 425 (1968); (b) G. H. Schmid and A. Brown, *Tetrahedron Lett.*, 4695 (1968); (c) E. C. Friedrich and M. A. Saleh, *ibid.*, 1373 (1971); (d) R. N. McDonald and G. E. Davis, *J. Amer. Chem. Soc.*, **94**, 5078 (1972); (e) E. C. Friedrich, M. A. Saleh, and S. Winstein, *J. Org. Chem.*, **38**, 860 (1973); (f) E. C. Friedrich and M. A. Saleh, *J. Amer. Chem. Soc.*, **95**, 2617 (1973); (g) P. G. Gassman, R. N. Steppel, and E. A. Armour, *Tetrahedron Lett.*, 3287 (1973); (h) A. S. Bloss, P. R. Brook, and R. M. Ellam, *J. Chem. Soc., Perkin Trans. 2*, 2165 (1973).

(5) For other considerations, see (a) R. D. Bach, J. H. Siefert, M. T. Tribble, R. A. Greengard, and N. A. LeBel, *J. Amer. Chem. Soc.*, **95**, 8182 (1973); (b) C. F. Wilcox, L. M. Loew, and R. Hoffmann, *ibid.*, **95**, 8192 (1973).

(6) (a) H. L. Goering and K. E. Rubenstein, Abstracts, 151st National Meeting of the American Chemical Society, Mar 1966, Pittsburgh, Pa., p K-11; (b) R. E. Friedrich and G. B. Schuster, *Tetrahedron Lett.*, 3171 (1971).

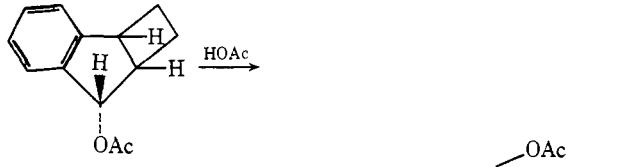
(7) (a) A. C. Cope, S. Moon, and C. H. Park, *J. Amer. Chem. Soc.*, **84**, 4850 (1962); (b) C. D. Poulter, E. C. Friedrich, and S. Winstein, *ibid.*, **92**, 4274 (1970); (c) C. D. Poulter and S. Winstein, *ibid.*, **92**, 4282 (1970); (d) L. E. Friedrich and F. R. Wight, *ibid.*, **92**, 1807 (1970).

of the effects of varied cyclobutane orbital alignments on reactivity is minimal. Of the few instances where anchimeric assistance is claimed, brosylate **6** under conditions of acetolysis leads stereospecifically to acetates **7** and **8**.[8] Benzo fusion to the bicyclo[3.2.0]heptane



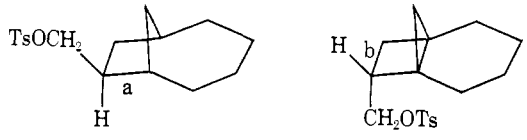
6 7 8

framework as in **9** causes a marked changeover in product distribution, indenyl acetate **10** predominating over **11** by a factor of 98:2.[9] Solvolysis of tosylates **12**



9 10 11

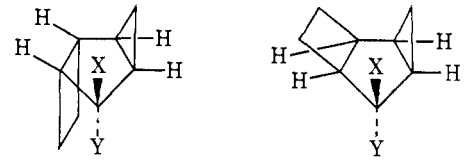
and **13** in 90% aqueous acetone proceeds by stereo-



12 13

specific ring expansion (bond a in **12**; bond b in **13**) to widely differing alcohol mixtures.[10]

With such considerations in mind, we have assessed the solvolytic chemistry of the four possible isomeric tricyclo[4.2.0.0^{2,4}]octan-5-yl 3,5-dinitrobenzoates (**14a,b** and **15a,b**) where stereoelectronic interaction of the



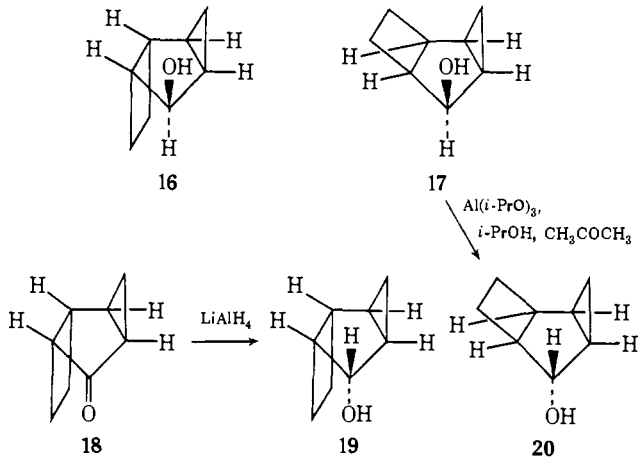
14a, X = ODNB; Y = H
b, X = H; Y = ODNB

15a, X = ODNB; Y = H
b, X = H; Y = ODNB

developing cationic center with adjacent suitably aligned cyclopropyl and cyclobutyl C–C bonds is varied considerably. At issue was whether cyclopropylcarbinyl stabilization would dominate in each instance, whether identical cations would again arise if such were operative, and whether the individually unique orbital constructs of the various isomers would lead to differing products of carbon framework rearrangement. We now show that only two structurally distinct ions are formed as intermediates, with that derived from **15a** and **15b** alone exhibiting a propensity for "double-barreled" expansion of both small rings to the *cis*-bicyclo[3.3.0]oct-6-en-2-yl systems.[11]

Results

The synthesis of alcohols **16** and **17** has been previously described.[12] Lithium aluminum hydride reduction of known[12] ketone **18** afforded a 6:1 mixture of **19** and **16**, the two components of which could be conveniently separated by column chromatographic techniques. Alcohol **20** was obtained from the reaction of



16 17 18 19 20

17 with aluminum isopropoxide in isopropyl alcohol using acetone as the coreactant.[13] This equilibration afforded an 87:13 mixture of **20** and **17** from which the major component could be isolated by preparative scale vpc. The cis relationship of the hydroxyl and cyclopropyl groups in **16** and **17** has been assigned based upon the well-recognized stereospecificity consistently observed in the addition of iodomethylzinc iodide to 2-cyclopentenols and closely related allylic alcohols.[12,14] Consequently, **19** and **20**, respectively, are of opposite stereochemistry at C_5. These assignments are in full agreement with the pmr data. As revealed in Figures 1 and 2, the >C*H*OH protons in **19** (δ 4.23, d, J = 6.5 Hz) and **20** (δ 3.85, s) which enjoy a cis relationship to the cyclopropyl group appear at significantly higher chemical shift than the same protons in **16** (δ 4.50, d, J = 6.5 Hz) and **17** (δ 4.65, dd, J = 5.0 and 8.5 Hz). This shielding capability of cyclopropane rings is widely recognized and has been observed in related systems.[15]

Additional information about the gross structure of these alcohols was gained from the multiplicity of the C_5 proton signal. From the dihedral angle[16] this proton makes with the adjacent protons at C_4 and C_6 (assuming a planar cyclobutane ring), the prediction can be made

(8) S. Winstein, F. Gadient, E. T. Stafford, and P. E. Klinedinst, Jr., *J. Amer. Chem. Soc.*, 80, 5895 (1958); see also B. Funke and S. Winstein, *Tetrahedron Lett.*, 1477 (1971).

(9) H. Tanida, Y. Hata, and H. Ishitobi, *Tetrahedron Lett.*, 361 (1967).

(10) P. G. Gassman and E. A. Armour, *J. Amer. Chem. Soc.*, **95**, 6129 (1973).

(11) A preliminary account of this work has appeared: L. A. Paquette, O. Cox, M. Oku, R. P. Henzel, and J. A. Schwartz, *Tetrahedron Lett.*, 3295 (1973).

(12) L. A. Paquette and O. Cox, *J. Amer. Chem. Soc.*, 89, 5633 (1967).

(13) (a) A. L. Wilds, *Org. React.*, 2, 178 (1944); (b) F. F. Nelson, Ph.D. Dissertation, University of Wisconsin, 1960. (c) Equilibrium was, however, not approached from both directions.

(14) S. Winstein and J. Sonnenberg, *J. Amer. Chem. Soc.*, **83**, 3235 (1961); W. G. Dauben and G. H. Berezin, *ibid.*, **85**, 968 (1963); W. G. Dauben and A. C. Ashcraft, *ibid.*, **85**, 3673 (1963); R. Wiechert, O. Engelfried, U. Kerb, H. Laurent, H. Miller, and G. Schultz, *Chem. Ber.*, **99**, 1118 (1966).

(15) See, for example (a) L. Birladeanu, T. Hanafusa, and S. Winstein, *J. Amer. Chem. Soc.*, **88**, 2315 (1966); (b) R. S. Boikess and S. Winstein, *ibid.*, **85**, 343 (1963); (c) P. K. Freeman, F. A. Raymond, and M. F. Grostic, *J. Org. Chem.*, **32**, 24 (1967).

(16) M. Karplus, *J. Chem. Phys.*, 30, 11 (1959).

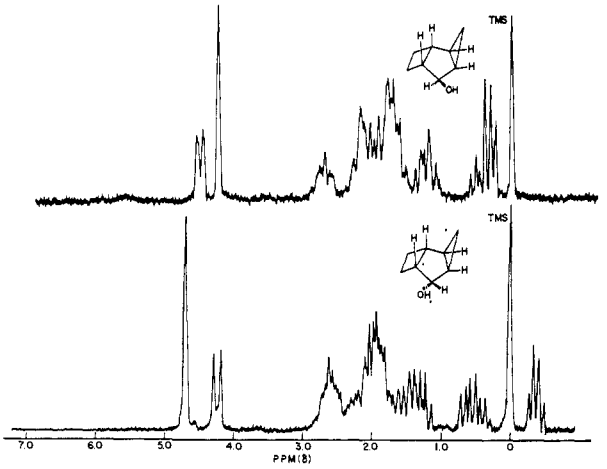


Figure 1. The 60-MHz pmr spectra of **16** (top) and **19** (bottom) (CCl_4 solution).

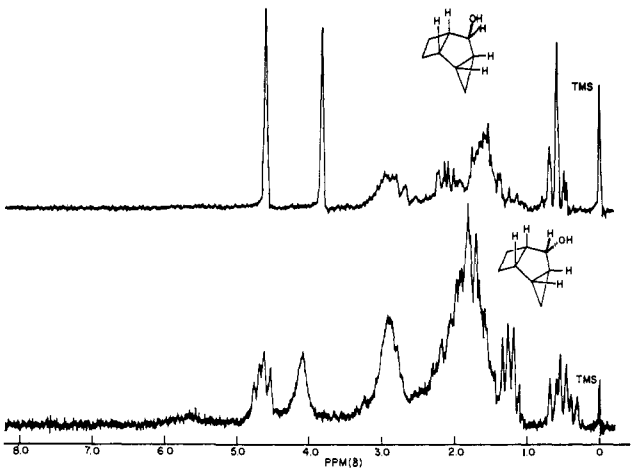


Figure 2. The 60-MHz pmr spectra of **20** (top) and **17** (bottom) (CCl_4 solution).

that this absorption should appear as a doublet in **16** ($\theta_{4,5}$ = 25°; $\theta_{5,6}$ = 107°), **19** ($\theta_{4,5}$ = 94°; $\theta_{5,6}$ = 10°), and **20** ($\theta_{4,5}$ = 90°; $\theta_{5,6}$ = 130°) whereas in **17** ($\theta_{4,5}$ = 38°; $\theta_{5,6}$ = 0°) it should appear as a doublet of doublets. The predicted multiplicity is observed in all cases except **20** which displays a rather sharp singlet ($W_{1/2}$ = 2.5 ppm). This discrepancy can be rationalized if one considers the cyclobutane ring to be slightly puckered.[17]

Attempts to prepare the tosylate and brosylate esters of **16** met with failure.[18] The *p*-nitrobenzoates and 3,5-dinitrobenzoates of the four alcohols were, however, readily available when the pyridine method[1] was utilized. That no isomerization occurred during these conversions was ascertained by saponification of a portion of each ester, which afforded the unchanged parent alcohols. In addition, the pmr and infrared spectra of the derivatives gave evidence that no gross structural changes had resulted.

The solvolysis rates of the 3,5-dinitrobenzoates were determined in acetone–water (80:20) by titration of the acid liberated. The rate constants, derived thermodynamic parameters, and values extrapolated to 25° are listed in Table I. In every case, less than the theoretical amount of acid was liberated. The rate constants were determined using the "infinity titer" observed after 10 half-lives at the reaction temperature, and represent an average of two independent runs. The reactions were followed for at least 2 half-lives and good first-order plots were uniformly obtained.

Table I. Rates of Hydrolysis in 80% Aqueous Acetone

3,5-Dinitrobenzoates	Temp, °C[a]	10^5k_1, sec^{-1}	115°, k_{rel}	$\Delta H^{\pm}$, kcal/mol	$\Delta S^{\pm}$, eu
14a	114.8	(107.2 ± 0.2)	70	27.3	−2.5
	100.4	(26.6 ± 0.5)			
	85.4	(5.49 ± 0.09)			
	25	1.96×10^{-3} [b]			
14b	130.0	(128.9 ± 0.6)	20	27.1	−5.3
	114.8	(33.3 ± 0.0)			
	100.4	(8.23 ± 0.07)			
	25	8.12×10^{-4} [b]			
15a	130.0	(7.03 ± 0.31)	1	30	−3.4
	114.8	(1.55 ± 0.02)			
	25	7.98×10^{-6} [b]			
15b	130.0	(7.77 ± 0.18)	1	31	−0.37
	114.8	(1.62 ± 0.05)			
	25	6.16×10^{-6} [b]			

[a] All temperatures were maintained at ±0.1°. [b] Extrapolated values using the activation parameters.

In order to ensure that alkyl-oxygen rather than acyl-oxygen cleavage was occurring, the dinitrobenzoates were also solvolyzed in tetrahydrofuran–methanol (25:75). These rates were likewise determined by titration of liberated acid and good first-order plots were again realized. The rate data are summarized in Table II. Furthermore, as will be subsequently discussed, only methyl ethers were produced in these experiments. These data are consequently in agreement with a carbonium ion mechanism.

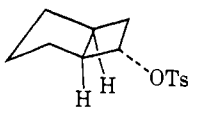
Table II. Rates of Methanolysis in (75:25) Methanol–Tetrahydrofuran

3,5-Dinitrobenzoate	Temp, °C[a]	10^5k_1, sec^{-1}	$\Delta H^{\pm}$, kcal/mol	$\Delta S^{\pm}$, eu
14a	114.8	(39.1 ± 0.5)	27.4	−4.1
	100.4	(9.58 ± 0.19)		
14b	114.8	(17.1 ± 0.9)		
15a	130.0	(6.00 ± 0.30)		
15b	130.0	(7.23 ± 0.14)		

[a] All temperatures were maintained at ±0.1°.

To remove the possibility that starting esters **15a** and **15b** were rapidly interconverting (note similarity in

(17) It has been pointed out by Wiberg [K. B. Wiberg and A. J. Ashe III, *J. Amer. Chem. Soc.*, **90**, 63 (1968)] that the cyclobutyl ring in i is



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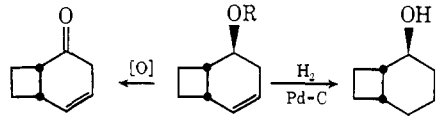
puckered. Consequently, an extrapolation of this conclusion to the present tricyclic alcohols is not unreasonable.

(18) The failure to obtain these derivatives is attributed to rearrangement and/or destruction during their attempted formation and isolation. Using a factor of 500 for converting solvolysis rates of 3,5-dinitrobenzoates in 60% aqueous acetone at 100° to solvolysis rates of tosylates in acetic acid at 25° [J. E. Baldwin and W. D. Foglesong, *J. Amer. Chem. Soc.*, **89**, 6372 (1967); **90**, 4303, 4311 (1968)], a rate constant of 1.3×10^{-1} sec^{-1} is estimated for the rate of acetolysis of **16**-OTs at 25°.

(19) H. L. Goering, W. D. Closson, and A. C. Olson, *J. Amer. Chem. Soc.*, **83**, 3507 (1961).

rates), the solvolysis of **15b** was interrupted at several points (*e.g.*, 21%, 40%, etc. conversion). Pmr analysis revealed the total absence ($\leq 3\%$) of detectable **15a** (H_5 in **15a** appears at δ 5.63; H_5 of **15b** is seen at 5.18).

The products formed upon hydrolysis of **14a** and **14b** were identical. When the reactions were conducted in unbuffered 80% acetone for 10 half-lives, the only alcohol to result was **21a**. Structural assignment to **21a** follows from its oxidation with Jones reagent[20] to ketone **22** which exhibits a carbonyl stretching frequency at 1705 cm^{-1} characteristic of a nonconjugated cyclohexanone, and catalytic hydrogenation over palladium to give a dihydro derivative identical in all respects with authentic **23**.[21]

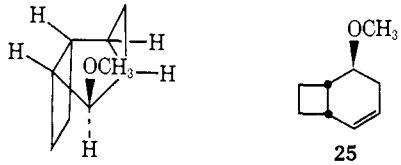


22 **21a**, R = H; **b**, R = DNB **23**

Recourse to buffered[22] aqueous acetone solutions (80:20) led after 10 half-lives at 100° to a 3:1 mixture of **21a** and **16**. Curtailment of the solvolysis after 1 half-life altered the ratio to 3:2. Under the conditions in which **14a** would have reacted to the extent of 10 half-lives, a sample of **16** underwent isomerization to **21a**, whereas **19** was stable. When this experiment was repeated in the presence of urea[22a] for the extent of 1 half-life, **16** was found to undergo 28% conversion to **21a**. Lastly, a carbon tetrachloride solution of **14a** after being heated at 115° for 3 hr (10 half-lives), returned unchanged dinitrobenzoate in quantitative yield.

The other product in these solvolyses at short reaction times was internally returned ester **21b**. Identification was based upon its hydride reduction to **21a**.

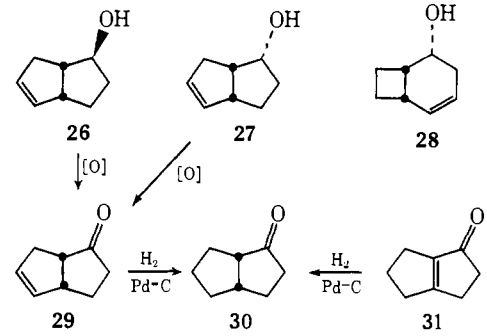
The products obtained upon methanolysis of **14a** and **14b** (2,6-lutidine as buffer) were ethers **24** (60%) and **25**



24 **25**

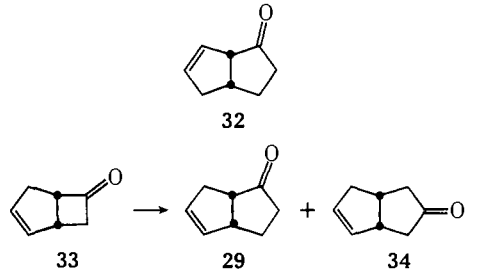
(40%). The structure of **24** was established by spectral comparison with an authentic sample prepared by reaction of **16** with sodium hydride and methyl iodide in benzene solution. The strong resemblance of the pmr spectra of **25** and **21a** attested to the identity of the carbon framework in these molecules.

Comparable buffered hydrolysis of **15a** gave, in contrast, a quite different spectrum of products consisting of **26** (23%), **27** (29%), **28** (41%), **17** (2%), and **20** (5%). Similar reactivity was observed for **15b**: 24, 34, 33, 5, and 4%, respectively. The epimeric nature of alcohols **26** and **27** was readily established by their quantitative oxidation to a single ketone (**29**, 2,4-DNP, mp 165–166°; semicarbazone, mp 185–186°). This substance displays an infrared carbonyl stretching band at 1735 cm^{-1} and a pmr signal at δ 5.58–5.80 of area 2 suggestive of a nonconjugated five-membered ring ketone. Hydrogenation of **29** at atmospheric pressure gave **30** whose infrared spectrum was identical with that reported by Roberts.[23] Unequivocal proof of structure followed its exclusive isolation from the catalytic reduction of **31**.[24]



26 **27** **28** **29** **30** **31**

Despite the rigor of these experiments and the obvious nonidentity of **29** and **32**,[25] there remained some degree of confusion. In 1952, Roberts first described the synthesis of **29** by Tiffeneau–Demjavov ring expansion of **33** and reported a semicarbazone mp of 164–166°.[23] Later, LeBel prepared **29** by a similar procedure and cited mp 175–175.5° for the semicarbazone.[25] In 1971, the mp of the 2,4-DNP derivative of **29** was reported as 112–114° by Julia.[26] None of the above papers described the spectral properties of **29**. Most recently, Baldwin performed the ring expansion of **33** with diazomethane.[27] His pmr spectral description of ketone **34** matched with that of our oxidation product. These confusing data forced us to prepare **29** independently. In our hands, ring expansion of **33** with diazomethane gave a 60:40 mixture of two ketones. The major component proved to be identical (ir, pmr, mass spectra) with **29**; furthermore, upon hydrogenation high yield conversion to **30** was again realized. Consequently, Baldwin's assignments are incorrect and the earlier samples of **29** were invar-



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33 **29** **34**

(20) H. C. Brown and C. P. Garg, *J. Amer. Chem. Soc.*, **83**, 2952 (1961).

(21) We thank Professor P. K. Freeman for his generous gift of a sample of **23**.

(22) Urea and 2,6-lutidine were employed as acid sequestering agents. For references to previous utilization of these procedures, see, for example (a) W. S. Trahanovsky, M. P. Doyle, and P. D. Bartlett, *J. Org. Chem.*, **32**, 150 (1967); (b) W. G. Dauben, J. L. Chitwood, and K. V. Scherer, Jr., *J. Amer. Chem. Soc.*, **90**, 1094 (1968); (c) W. D. Closson and G. T. Kwiatkowski, *Tetrahedron*, **21**, 2779 (1965).

(23) J. D. Roberts and W. F. Gorham, *J. Amer. Chem. Soc.*, **74**, 2278 (1952).

(24) S. B. Kulkarni and S. Dev, *Tetrahedron*, **24**, 553 (1967); we thank Dr. Eugene Armour for a generous sample of **31**.

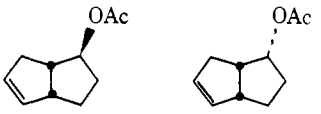
(25) N. A. LeBel and L. A. Spurlock, *Tetrahedron*, **20**, 215 (1964). We thank Professor LeBel for a generous sample of ketone **32**.

(26) M. Julia and E. Colomer, *An. Quim.*, 199 (1971).

(27) J. E. Baldwin and M. S. Kaplan, *J. Amer. Chem. Soc.*, **93**, 3969 (1971).

iably contaminated with lesser (and varied) quantities of **34**.[28]

Ketone **29** was reduced with lithium aluminum hydride under conditions conducive to steric approach control[30] and the resulting alcohols were directly acetylated to give acetates **35** (7%) and **36** (93%). When



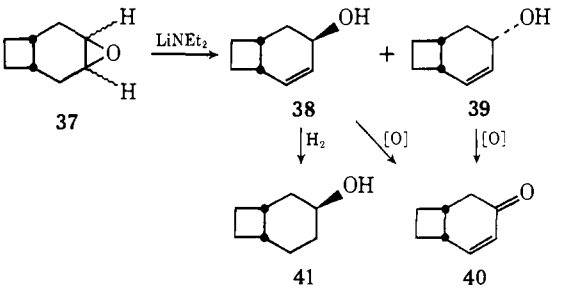
35 **36**

the mixtures of **26** and **27** isolated from the hydrolysis runs were acetylated, **36** proved to be the major component (57–59%).

Alcohol **28** was readily available from sodium borohydride reduction of **22** (92% stereoselectivity), and together with **26** and **27** was shown to be stable to the reaction conditions.

To confirm the stereochemistry of the minor products (**17** and **20**), the mixture was acetylated, separated by vpc methods, and shown to be identical (ir and vpc retention time) with authentic samples of **17**-OAc and **20**-OAc. Examination of the stability of **17** revealed this alcohol to undergo partial conversion to **26** (7%), **27** (15%), and **28** (10%) when heated for 6 days at 125° in the buffered solvolysis medium. Alcohol **20** was also labile, giving rise to **26** (6%), **27** (13%), and **28** (9%) under comparable conditions.

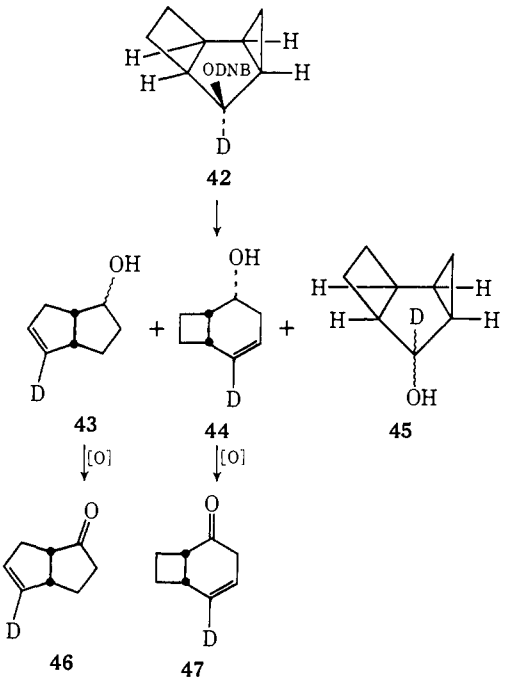
Because some carbocationic leakage of the homoallylic → allylic type has been reported in closely related systems,[4] preparation of the isomeric pair of allylic alcohols **38** and **39** was undertaken. Treatment of epoxides **37**[31] with lithium diethylamide[32] gave a mixture of alcohols, Jones' oxidation of which afforded conjugated ketone **40**. The pmr spectrum of **40** was identical with that provided by Farrissey.[33] The major alcohol isomer (**38**) was hydrogenated to give **41** whose infrared spectrum was identical with that of an authentic sample.[34] Hydride reduction of **40** at 0° re-



37 **38** **39** **41** **40**

turned **38** and **39** in a 43:57 ratio. Neither alcohol was detected in the solvolysis mixtures (vpc analysis).

Hydrolysis of deuterated dinitrobenzoate **42** proceeded to furnish the isotopically labeled products **43–45** in a ratio of 55:39:6. Alcohols **43** and **44** both



42 **43** **44** **45** **46** **47**

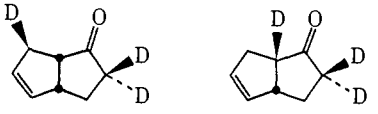
showed a lone olefinic absorption in their pmr spectra. Further positional assignment to the deuterium was made possible by spin decoupling of the corresponding ketones **46** and **47** (see Experimental Section). These findings indicate that **15a** solvolyzes in a manner which maintains deuterium bonded exclusively to that incipient trigonal carbon positioned adjacent to the ring fusion in the products. In particular, degenerate cyclopropylcarbinyl–cyclopropylcarbinyl cation rearrangements do not operate.[35]

Lastly, to permit direct comparison to be made with the kinetic behavior of a variety of related compounds, the four *p*-nitrobenzoates were likewise solvolyzed in 80% aqueous acetone. The rate data for this series are compiled in Table III.

Discussion

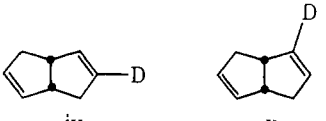
Initial consideration of the reactivity levels of the tricyclooctyl derivatives is instructive. Comparison of the hydrolysis rate constants of **16**-OPNB and **17**-OPNB (extrapolated to 25°) with those of several re-

(28) Baldwin and Kaplan[27] have also attempted a deuterium exchange of **34** (incorrectly assigned as **29** by them) and observed incorporation of three deuterium atoms. These data were interpreted in terms of structure ii, later revised to iii,[29] but should presently be more properly



ii iii

viewed as incomplete exchange in **34**. In this light, it becomes important to indicate a second misassignment of structure; the diene prepared by these workers and labeled iv should be v.



iv v

(29) J. E. Baldwin and M. S. Kaplan, *J. Amer. Chem. Soc.*, **94**, 1794 (1972).

(30) H. C. Brown and J. Muzzio, *J. Amer. Chem. Soc.*, **88**, 2811 (1966).

(31) E. Casadevall, C. Largeau, and P. Moreau, *Bull. Soc. Chim. Fr.*, 1515 (1968).

(32) J. A. Marshall and R. Ruden, *J. Org. Chem.*, **37**, 659 (1972).

(33) W. J. Farrissey, Jr., R. H. Perry, Jr., F. C. Stehling, and N. F. Chamberlain, *Tetrahedron Lett.*, 3635 (1964). We are indebted to Dr. Farrissey for a copy of the relevant pmr spectrum.

(34) A. C. Cope and R. W. Gleason, *J. Amer. Chem. Soc.*, **84**, 1928 (1962). We thank Professor Gleason for the infrared spectrum of **41**.

(35) For leading references to this subject, see (a) K. B. Wiberg and G. Szeimies, *J. Amer. Chem. Soc.*, **92**, 571 (1970); (b) G. A. Olah, D. P. Kelly, C. L. Jeuell, and R. D. Porter, *ibid.*, **92**, 2544 (1970); (c) Z. Majerski and P. v. R. Schleyer, *ibid.*, **93**, 665 (1971); (d) T. M. Brennan and R. K. Hill, *ibid.*, **90**, 5614 (1968); (e) H. E. Zimmerman, *et al.*, *ibid.*, **90**, 5612 (1968); **91**, 434 (1969).

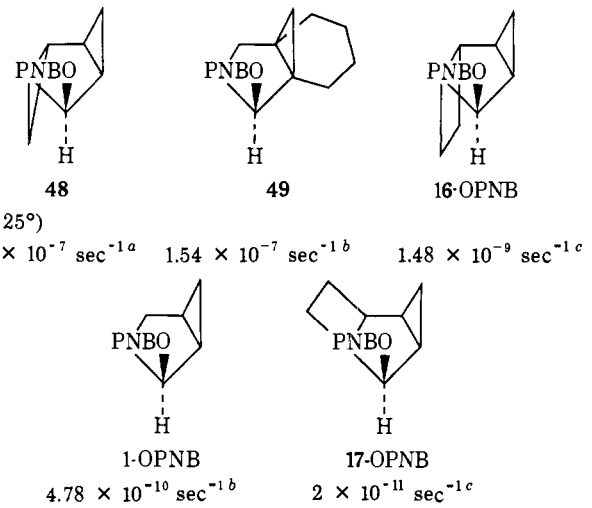
Table III. Rates of Hydrolysis of *p*-Nitrobenzoates in 80% Aqueous Acetone

p-Nitrobenzoate	Temp, °C[a]	$10^5 k_1$, sec^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
16-OPNB	125.3	(31.7 ± 1.4)	28.2	−4.3
	100.4	(2.76 ± 0.16)		
	25	1.48×10^{-4} [b]		
19-OPNB	100.4	(0.666 ± 0.066)		
20-OPNB	114.8	$(1.28 \pm 0.01) \times 10^{-1}$		
17-OPNB	100.4	$(3.2 \pm 0.04) \times 10^{-2}$		

[a] All temperatures were maintained at ±0.1°. [b] Extrapolated value using the activation parameters.

lated *p*-nitrobenzoates, summarized in Scheme I, reveals the dicyclopropylcarbinyl system **48**[36] to be the most reactive of the series,[37,38] followed rather closely by the 1,5-tetramethylene bridged derivative **49**.[4g] When allowance is made for solvent differences, the ionization rates of **1-OPNB** and **17-OPNB**[39] appear rather comparable and comprise the slowest of the set. The rate constant for **16-OPNB**, on the conservative side because of ion pair return, is of an intermediate order of magnitude. The sequence of observed reactivity in the C_5 epimeric series (as the 3,5-dinitrobenzoates at 100°) is **14a** > **15a** ≥ **2-ODNB**.[4f] The large difference in the level of ionization for *both* series compared to the parent cyclopentane derivative[40] is fully in agreement with the concept that the proximally positioned cyclopropyl rings participate quite effectively during formation of the carbonium ions.

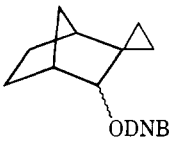
Scheme I



[a] 90% aqueous acetone. [b] 70% aqueous ethanol. [c] 80% aqueous acetone.

Obviously, **48** is rather more reactive than its cyclobutane congener **16-OPNB**. Both structures are conformationally rigid and angular environments around the ionizing center are not greatly dissimilar; yet their rates differ by a factor of 10^2. On this evidence, a cyclopropane ring anti to the leaving group is seen to be capable of a higher level of stabilizing backside participation in the development of carbonium ion character than a proximate cyclobutane ring. This expected finding is in accord with the ordering of efficiencies with which three- and four-membered rings provide long range anchimeric assistance to ionization of 7-norbornyl tosylates[41] and to cheletropic expulsion of nitrogen from bicyclic azo compounds.[42]

Thus, in agreement with theory,[43] cyclopropyl participation swamps out *initial* involvement by the cyclobutyl group. This situation is reminiscent of a related observation made by Wilcox and Jesaitis[44] who interpreted the low exo/endo rate ratio for 3,5-dinitrobenzoates **50** in terms of the ineffectiveness of the norbornane neighboring group to compete with the cyclopropane ring for effective stabilization of the secondary cationic center.

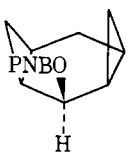


50

The relative ionization rates of anti epimers **14a** and **14b** are seen to differ by a factor of 3–4 at 115°, again indicating little kinetic dependence on leaving group geometry. That the solvolysis rates of syn epimers **15a** and **15b** are essentially identical may be a result of the greater ground-state strain in alcohol **17**, *RT* ln 6.7, which is suggested from actual experiment.[13c] That

(36) J. J. Gajewski and C. N. Shih, *Tetrahedron Lett.*, 2967 (1970).

(37) Notwithstanding its preeminent position in this series, **48** remains 125-fold less reactive than *cis-syn*-tricyclo[5.1.0.0^{3,5}]octan-2-yl *p*-nitrobenzoate (vi) [L. Birladeanu, T. Hanafusa, B. Johnson, and S. Winstein, *J. Amer. Chem. Soc.*, **88**, 2315 (1966)].



vi

(38) Note should be taken of the different solvent systems employed for the various *p*-nitrobenzoates. Indication of the changes in solvent polarity is given by their *Y* values: 90% acetone, $Y = -1.856$; 80% ethanol, $Y = 0.000$; 70% ethanol, $Y = 0.595$ [A. H. Fainberg and S. Winstein, *J. Amer. Chem. Soc.*, **78**, 2770 (1956)].

(39) Due to very limited quantities, a rate constant for **17-OPNB** at 25° was not actually determined nor is a value obtainable from our data (Table III) by extrapolation from the thermodynamic parameters. The value given consists of an approximation reliably based upon the assumption of a 70-fold rate decrease relative to **16-OPNB** as judged by their relative solvolytic behavior at 100° (Table III) and by the rate spread of the structurally related 3,5-dinitrobenzoates at 25° (Table I).

(40) For the acetolysis of cyclopentyl tosylate, consult A. P. Krapcho and D. E. Horn, *Tetrahedron Lett.*, 6107 (1966).

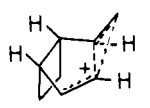
(41) (a) H. Tanida, T. Tsuji, and T. Irie, *J. Amer. Chem. Soc.*, **89**, 1953 (1967); (b) M. A. Battiste, C. L. Deyrup, R. E. Pincock, and J. Haywood-Farmer, *ibid.*, **89**, 1954 (1967); (c) J. Haywood-Farmer and R. E. Pincock, *ibid.*, **91**, 3020 (1969); (d) M. A. Battiste, J. Haywood-Farmer, H. Malkus, P. Siedl, and S. Winstein, *ibid.*, **92**, 2144 (1970); (e) M. Sakai, A. Diaz, and S. Winstein, *ibid.*, 92, 4452 (1970); (f) M. A. Battiste and J. W. Nebzydowski, *ibid.*, **92**, 4450 (1970); (g) R. M. Coates and K. Yano, *Tetrahedron Lett.*, 2289 (1972); (h) R. M. Coates and K. Yano, *J. Amer. Chem. Soc.*, **95**, 2203 (1973); (i) R. M. Coates and J. L. Kirkpatrick, *ibid.*, 90, 4162 (1968); **92**, 4883 (1970).

(42) (a) E. L. Allred and J. C. Hinshaw, *Chem. Commun.*, 1021 (1969); (b) *Tetrahedron Lett.*, 387 (1972); (c) L. A. Paquette, *J. Amer. Chem. Soc.*, **92**, 5766 (1970); (d) R. Askani, *Tetrahedron Lett.*, 3349 (1970); (e) L. A. Paquette and L. M. Leichter, *J. Amer. Chem. Soc.*, **92**, 1765 (1970); **93**, 4922, 5128 (1971); (f) L. A. Paquette, R. E. Wingard, Jr., and R. K. Russell, *ibid.*, 94, 4739 (1972); (g) E. L. Allred and K. J. Voorhees, *ibid.*, **95**, 620 (1973); (h) L. A. Paquette and M. J. Epstein, *ibid.*, **93**, 5936 (1971); **95**, 6717 (1973).

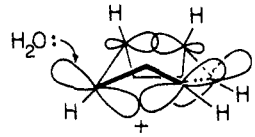
(43) (a) R. Hoffmann, *J. Chem. Phys.*, 40, 2480 (1964); (b) R. Hoffmann, *Tetrahedron Lett.*, 3819 (1965); (c) K. B. Wiberg, *Tetrahedron*, 24, 1083 (1968); (d) L. Radom, J. A. Pople, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **94**, 5935 (1972); (e) W. J. Hehre and P. C. Hiberty, *ibid.*, **94**, 5917 (1972); (f) C. F. Wilcox, L. M. Loew, and R. Hoffmann, *ibid.*, **95**, 8192 (1973).

(44) C. F. Wilcox, Jr., and R. G. Jesaitis, *Tetrahedron Lett.*, 2567 (1967).

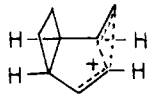
essentially identical mixtures of products are formed within a given stereochemical subset demands also that each pair of dinitrobenzoates react *via* an identical activation complex, *i.e.*, *anti* → **51** and *syn* → **52**.[45]



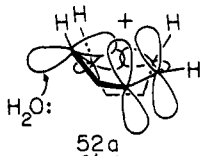
51



51a



52

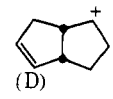


52a

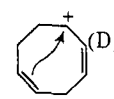
Within the limits of our experiments, these cations are noninterconverting[46] and represent separate potential energy minima. That the hydrolyses give only *cis*-bicyclo[4.2.0]oct-4-en-2-ols with hydroxyl orientation inextricably linked to a specific tricyclic precursor geometry strongly implicates highly directed attack of solvent nucleophile. This stereospecificity in homoallylic alcohol formation is sterically the same for both **51** and **52** *as far as the cyclopropylcarbinyl system is concerned*, the fused cyclobutane ring acting as a stereochemical marker (*cf.* the somewhat simplified formulas **51a** and **52a**).

Another feature of the rigid three-dimensional orbital constructs in these cations is the stereochemistry of hydration at C_2 to return tricyclic alcohol. Under conditions of kinetic control, dinitrobenzoates **14a** and **14b** returned significant quantities of alcohol **16** but no **19**. This stereospecificity did not extend to **15a** and **15b** which provided similar amounts of the epimeric alcohols **17** and **20**. We see that discharge of **51** at C_2 by the aqueous medium is forced for reasons of steric accessibility to occur only at the exo (syn to cyclopropyl) lobe. The situation prevailing in **52** is strikingly different insofar as both lobes appear almost equally available for bonding to water.[47]

Once **51** is formed, there is no pathway available for its conversion to products of cyclobutane ring opening because of the poor stereoelectronic alignment of the four-membered ring bonds with the bisected bishomoallyl cation center. Bond cleavage is well recognized to occur most readily when maximum bonding can be achieved at all times. This effect is dramatically demonstrated in cation **52** where the homoallylic p orbital at C_5 is now canted so as to permit direct interaction with the internal cyclobutane bond. In **51**, this p orbital is oriented well out of plane. Our data do not distinguish between a 1,2 carbon shift in **52** to give **53** directly or a more circuitous pathway involving ring opening to the 2,5-cyclooctadienyl cation **54** and subsequent transannular cyclization to **53**.



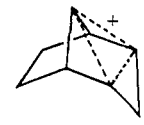
53



54

C_2 deuterium labeling does not resolve this issue. However, as previously noted, it effectively rules out the operation of cyclopropylcarbinyl–cyclopropylcarbinyl rearrangement. Intermediate **52** presumably does not undergo such degenerate isomerization because the favored two-step mechanism[35a] would require intervention of a prohibitively strained bicyclobutonium species.

Lastly, it is of some interest that passage to nonclassical ion **55** by interaction of the cyclobutyl bond with the developing positive charge at C_5 in **15a** and **15b** is not seen to operate.



55

Experimental Section

Melting points are corrected and boiling points are uncorrected. Proton magnetic resonance spectra were obtained on Varian A60-A, Varian HA-100, and Joelco MH-100 spectrometers; apparent splittings are given in all cases. Infrared spectra were determined on Perkin-Elmer Model 137 and 467 instruments. Mass spectra were recorded on a CEC-MS9 spectrometer at an ionization potential of 70 eV. Elemental analyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark. Preparative vpc work was done on a Varian Aerograph A90-P3 instrument equipped with a thermal conductivity detector.

Hydride Reduction of 1α,2β,4β,6α-Tricyclo[4.2.0.0^{2,4}]octan-7-one (18).[48] To a stirred slurry of 2.35 g (61.0 mmol) of lithium aluminum hydride in 200 ml of anhydrous ether cooled to 10° under a nitrogen atmosphere was added dropwise a solution of 6.0 g of **18**[12] in 100 ml of the same solvent at a rate such as not to exceed 10°. Upon completion of the addition, the mixture was allowed to stir for 2 hr at room temperature. With ice cooling, there was added 20 ml of water followed by 20 ml of 33% sodium hydroxide solution and 30 g of anhydrous magnesium sulfate. The inorganic salts were removed by filtration and the filter cake was washed well with ether. Evaporation and distillation of the combined ether layers gave 5.8 g (96.5%) of colorless liquid, bp 57–59° (0.8 mm). Vpc analysis of this distillate on column A[49] at 149° showed it to consist of **19** and **16** in a ratio of 85:15.

A 4.0-g portion of this mixture was subjected to column chromatography through 400 g of silica gel with petroleum ether (30–60°)–ether mixtures as eluent. By this procedure, there was isolated 2.50 g (63%) of pure **19**, bp 44–45° (0.4 mm), $n_D^{23.5}$ 1.5049; $\delta_{TMS}^{CCl_4}$ see Figure 1.

The 3,5-dinitrobenzoate (**14b**) was obtained as white crystals, mp 90.5–91°, from hexane.

Anal. Calcd for $C_{15}H_{14}N_2O_6$: C, 56.60; H, 4.43; N, 8.80. Found: C, 56.85; H, 4.54; N, 8.60.

The *p*-nitrobenzoate proved to be a white crystalline solid, mp 62–63° (from pentane).

Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.83; H, 5.51; N, 5.10.

The *p*-nitrobenzoate (338 mg, 1.22 mmol) was saponified by dissolving the material in 10 ml of methanol containing 129 mg (2.33 mmol) of potassium hydroxide, heating this solution at reflux for 4 hr, pouring into 25 ml of water, and extracting with pentane.

(45) For a discussion of these cations in a different context, see ref 41c.

(46) For the pioneering work in noninterconverting homoallylic cations, consult (a) S. Winstein and E. M. Kosower, *J. Amer. Chem. Soc.*, 81, 4399 (1959); (b) G. H. Whitham and J. A. F. Wickramasinghe, *J. Chem. Soc.*, 1655 (1964); (c) W. G. Dauben and L. E. Friedrich, *Tetrahedron Lett.*, 1735 (1967).

(47) Electronic factors could, of course, introduce an imbalance in the preference for reaction at one or the other face (see in particular ref 5a).

(48) For an explanation of the nomenclature usage, consult ref 12, footnote 24.

(49) The following vpc columns were utilized in this work: A, 10 ft × 0.25 in. 15% QF-1 on Chromosorb W; B, 10 ft × 0.25 in. 15% FFAP on Chromosorb W; C, 6 ft × 0.25 in. 5% SE-30 on Chromosorb G; D, 7 ft × 0.25 in. 6% QF-1 on Chromosorb G; E, 5.5 ft × 0.25 in. 10% FFAP on Chromosorb G; F, 6 ft × 0.25 in. 5% Carbowax 20 M-1% KOH on Chromosorb G.

The pale yellow oil so produced was shown to be pure **19** by vpc analysis on column B (145°).[49]

1α,2α,4α,6α-Tricyclo[4.2.0.0^{2,4}]octan-5α-ol (20). An aluminum isopropoxide solution was prepared from 4.0 g (0.15 g-atom) of purified aluminum in 70 ml of dry isopropyl alcohol and 0.1 g (0.4 mmol) of mercuric chloride according to the procedure described by Nelson.[13b] To 10 ml of this solution were added 0.2 ml of acetone and 1.00 g (8.05 mmol) of **17** and the resulting mixture was refluxed for 36 hr. After cooling, 50 ml of water and 50 ml of 35% sodium hydroxide solution were added and the product was extracted with ether (5 × 50 ml). The combined extracts were concentrated to *ca.* 5 ml, taken up in 50 ml of ether, washed with water (2 × 25 ml), dried, and evaporated. The light yellow oil so obtained (0.80 g, 80%) consisted of **20** and **17** in a 8:1 ratio (column B,[49] 145°). Preparative scale vpc isolation gave pure **20**; $\delta_{TMS}^{CCl_4}$ see Figure 2.

The *p*-nitrobenzoate was obtained as white flakes, mp 105–106°, from pentane.

Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 66.03; H, 5.58; N, 5.19.

The 3,5-dinitrobenzoate (**15b**) was obtained as white crystals, mp 121–122°, from hexane.

Anal. Calcd for $C_{15}H_{14}N_2O_6$: C, 56.60; H, 4.43; N, 8.80. Found: C, 56.68; H, 4.63; N, 8.67.

1α,2β,4β,6α-Tricyclo[4.2.0.0^{2,4}]octan-5α-ol 3,5-dinitrobenzoate (14a) was available from our earlier study, mp 82.5–83°.[12]

The *p*-nitrobenzoate was obtained as white crystals, mp 84.8–85.2°, from pentane.

Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 66.16; H, 5.83; N, 5.22.

1α,2α,4α,6α-Tricyclo[4.2.0.0^{2,4}]octan-5β-ol 3,5-dinitrobenzoate (15a) was prepared in standard fashion from **17**,[12] mp 115.5–116.5° (from hexane).

Anal. Calcd for $C_{15}H_{14}N_2O_6$: C, 56.60; H, 4.43; N, 8.80. Found: C, 56.58; H, 4.53; N, 8.90.

The *p*-nitrobenzoate was isolated as white crystals, mp 99–100°, from pentane.

Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.89; H, 5.65; N, 5.16.

Preparative Scale Hydrolysis of 14a. A. Unbuffered 80% Aqueous Acetone. A solution of 1.43 g (4.50 mmol) of **14a** in 100 ml of 80:20 acetone–water mixture was sealed in a thick wall glass tube and heated at 100° for 12 hr (*ca.* 10 half-lives). The resulting solution was made alkaline to phenolphthalein with 0.2 *N* sodium bicarbonate solution and continuously extracted with pentane for 24 hr. The pentane layer was dried and evaporated to leave 658 mg of a yellow oil which showed hydroxyl and carbonyl infrared bands and which gave evidence of only one volatile component (column A,[49] 100°).

Chromatography on silica gel (elution with petroleum ether–ether mixtures) led first to isolation of a noncrystalline 3,5-dinitrobenzoate (**21b**, 125 mg, 19%). Lithium aluminum hydride reduction of this material afforded an alcohol which displayed an infrared spectrum and vpc retention time identical with that of the second component (**21a**).

Alcohol **21a** was eluted next (320 mg, 50%): $\delta_{TMS}^{CCl_4}$ 2.02 (7 H), 2.87 (1 H), 3.80 (2 H), and 4.62 (2 H).

Anal. Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.08; H, 9.76.

B. Unbuffered without Isolation of Internal Return Product. Into a sealed glass tube was placed 9.65 g (0.03 mol) of **14a** and 400 ml of 80:20 (v/v) acetone–water. After being heated overnight at 100°, the solvolysis mixture was processed as above to give 4.28 g of light brown oil. This material was dissolved in 75 ml of methanol and 10 ml of water containing 1.7 g of potassium hydroxide and the solution was stirred at room temperature overnight. Dilution with water and repeated extraction with ether–pentane (1:1) afforded 3.18 g of brown oil which exhibited no ir carbonyl absorption. Distillation furnished 2.89 g of alcohol **21a**, bp 97–103° (18 mm), vpc analysis of which (column C,[49] 140°) indicated it to be of >95% purity.

C. Buffering with Urea. A solution of 500 mg (1.57 mmol) of **14a** and 100 mg (1.67 mmol) of reagent grade urea in 50 ml of 80:20 acetone–water was heated as above at 100° for 12 hr. The usual work-up gave 190 mg of an oil which when subjected to vpc analysis (column A,[49] 100°) was seen to consist of a 3:1 mixture of **21a** and **16**. The pmr spectrum of this material was consistent with the presence of these two components.

This experiment was repeated using 250 mg (0.785 mmol) of **14a** and 50 mg (0.83 mmol) of urea in 25 ml of 80:20 acetone–water. The mixture was heated at 100° for 45 min (*ca.* 1 half-life). Work-up afforded 80 mg (36%) of unreacted **14a**, mp 83–84°, and 50 mg of an oil consisting of **21a** and **16** in an 11:9 ratio.

Preparative Scale Hydrolysis of 14b. A. Buffered 80% Aqueous Acetone. A solution of 500 mg (1.57 mmol) of **14b** in 30 ml of acetone–water (80:20) contained in a sealed glass vessel was heated at 100° for 12 hr (*ca.* 3.5 half-lives). Work-up as before gave 154 mg of a volatile yellow oil which was isolated by preparative scale vpc and shown to be pure **21a**.

B. Buffering with 2,6-Lutidine. A solution of 500 mg (1.57 mmol) of **14b** in 50 ml of 80:20 acetone–water which was 0.08 *M* in 2,6-lutidine was heated at 100° for 12 hr. Work-up in the predescribed manner afforded 190 mg of an oil which consisted (vpc analysis on column A,[49] 100°) of **21a** and **16** in a 3:1 ratio. These assignments were corroborated by ir and pmr spectral comparisons.

In an independent experiment using the above conditions, the reaction was stopped after 1 half-life and processed in the customary manner. The residue which remained after removal of unreacted 3,5-dinitrobenzoate was identified by vpc, ir, and pmr methods as a mixture of **21a** (11 parts) and **16** (9 parts).

***cis*-Bicyclo[4.2.0]oct-2-en-5-one (22).** To a cold (0°) solution of **21a** (1.75 g, 0.014 mol) in 50 ml of acetone was added dropwise 6.0 ml of 2.67 *M* Jones reagent during 45 min. The mixture was diluted with water and extracted with pentane (5 × 50 ml). The combined pentane layers were washed with saturated sodium bicarbonate and sodium chloride solutions, and dried. Evaporation and distillation furnished 1.13 g (65%) of **22**, bp 66–68° (5 mm).

An analytical sample was prepared by preparative vpc isolation from column D[49] at 135°.

Anal. Calcd for $C_8H_{10}O$: C, 78.65; H, 8.25. Found: C, 78.30; H, 8.28.

***cis-exo*-Bicyclo[4.2.0]octan-2-ol (23).** A solution of 150 mg (1.21 mmol) of **21a** in 15 ml of anhydrous ether was hydrogenated at atmospheric pressure over 50 mg of prereduced 10% palladium on charcoal. After 1 equiv of hydrogen had been consumed, the catalyst was separated by filtration, the filtrate was evaporated, and the residual oil was subjected to molecular distillation. There was obtained 131 mg (87%) of **23** as a colorless oil whose infrared spectrum and vpc retention time were identical with those of an authentic sample.[21]

Control Experiments Concerned with the Stability of 16. A solution of 166 mg (1.32 mmol) of **16** and 280 mg (1.32 mmol) of 3,5-dinitrobenzoic acid in 25 ml of acetone–water (80:20) was heated as before at 100° for 12 hr. There was isolated 125 mg (76%) of a brown oil consisting of one component by vpc analysis (column A,[49] 100°). This material was subjected to molecular distillation to give 100 mg (60.5%) of pure **21a**.

The above experiment was repeated using 125 mg (1.05 mmol) of **16**, 106 mg (0.50 mmol) of 3,5-dinitrobenzoic acid, and 60 mg (1.05 mmol) of urea in 25 ml of 80:20 acetone–water. This mixture was heated at 100° for 45 min and processed in the usual fashion. The oil so obtained (69 mg, 55%) was found to consist of **16** and **21a** in a 1:2.6 ratio.

Methanolysis of 14a. A solution of 1.25 g (3.92 mmol) of **14a** in 100 ml of methanol–tetrahydrofuran (75:25) which was 0.08 *M* in 2,6-lutidine contained in a sealed glass vessel was heated at 100° for 12 hr. After cooling, the contents were made alkaline to phenolphthalein using 0.2 *N* sodium bicarbonate solution and extracted with ether (5 × 50 ml). The combined ether extracts were successively washed with cold 3% hydrochloric acid (2 × 50 ml) and brine (2 × 50 ml), dried, and evaporated. The residual yellowish oil (512 mg) was found to consist of two volatile components in a 3:2 ratio (vpc analysis). These were separated by molecular distillation to give 376 mg (70%) of a mixture of ethers. The residue amounted to 130 mg and displayed the characteristic infrared spectrum of a 3,5-dinitrobenzoate. The pair of ethers was separated by preparative scale vpc (column E,[49] 100°).

The more rapidly eluted product was identified as **24** by spectral comparison with an authentic sample (see below). The less volatile ether was assigned structure **25** on the basis of its pmr spectrum: $\delta_{TMS}^{CDCl_3}$ 2.08 (7 H), 2.88 (1 H), 3.34 (1 H), and 5.64 (2 H).

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 77.95; H, 10.34.

Methanolysis of 14b. When 1.00 g (3.15 mmol) of **14b** was treated as above, there was obtained 500 mg of yellowish oil the ir spectrum of which was identical with that recorded in the case of **14a**. Furthermore, vpc analysis (column E[49]) showed the material to consist of two volatile components in a ratio of 3:2. Bulb-to-bulb distillation afforded 350 mg of the ether mixture, the

components of which were separated by preparative vpc (column E,[49] 100°) and identified as **24** (major product) and **25**.

Methyl 1α,2β,4β,6α-Tricyclo[4.2.0.0^{2,4}]octan-5α-yl Ether (24). To a solution of 1.00 g (8.10 mmol) of **16** in 20 ml of dry benzene was added 350 mg (8.10 mmol) of sodium hydride and 2 drops of anhydrous methanol. The mixture was stirred under nitrogen until hydrogen evolution ceased and 1.42 g (10 mmol) of methyl iodide was added dropwise. After 24 hr at room temperature, the precipitated sodium iodide was removed by filtration and the organic layer was washed with brine (2 × 10 ml). The benzene solution was dried and evaporated and the residual oil was distilled to afford 700 mg (62%) of **24** as a colorless oil, bp 67–68° (2.75 mm). An analytical sample was collected by preparative vpc: n^{24}D 1.4798; $\delta_{TMS}^{CDCl_3}$ 0.30 (m, 1 H), 0.54 (m, 1 H), 1.32 (m, 1 H), 1.96 (m, 6 H), 2.67 (m, 2 H), 3.23 (s, 3 H), and 4.07 (d, J = 6 Hz, 1 H).

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.40; H, 10.15.

Preparative Scale Hydrolysis of 15a. A solution of 5.00 g (15.7 mmol) of **15a** in 400 ml of acetone–water (80:20) which was 0.08 M in 2,6-lutidine was heated in a sealed glass vessel for 6.6 days at 125°. Work-up in the predescribed manner afforded 1.87 g (95%) of yellow oil, vpc analysis of which on column A[49] showed it to consist of a mixture of **26** and **27** (52%), **28** (41%), and a mixture of **17** and **20** (7%). On column B[49] the components were resolved into five partially overlapping peaks. The epimeric ratios of **26**/**27** (23:29) and **17**/**20** (2:5) were determined by prior conversion to the corresponding acetates with acetic anhydride in pyridine.

The solvolysis was repeated with 2.00 g (6.3 mmol) of **15a** and 160 ml of the buffered solution (6 days, 115°). There was isolated 582 mg (29%) of unreacted **15a**, mp 114–116°, and 274 mg (35%) of an alcohol mixture consisting of **26** (23%), **27** (30%), **28** (41%), **17** (2%), and **20** (5%).

Anal. for **26**/**27**. Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.19; H, 9.72.

Preparative Scale Hydrolysis of 15b. A solution of 2.50 g (7.85 mmol) of **15b** in 200 ml of acetone–water (80:20) which was 0.08 M in 2,6-lutidine was heated at 125° for 6.6 days. Work-up led to isolation of 1.33 g of a yellowish oil from which 400 mg of **15b** was recovered upon precipitation by addition of pentane. Vpc analysis of the filtrate on column B[49] at 115° showed the residual oil (928 mg) to be composed of **26** (24%), **27** (34%), **28** (33%), **17** (5%), and **20** (4%).

Alcohol **28** was isolated pure by preparative vpc from both solvolyses (**15a** and **15b**) and shown to be identical with an independently prepared sample (see below).

***cis*-Bicyclo[3.3.0]oct-2-en-6-one (29).** A 30-mg (0.24 mmol) sample of the **26**/**27** mixture (from solvolysis of **15a**) dissolved in 1 ml of acetone was cooled to 0° and 0.3 ml of Jones' reagent (prepared from 7.0 g of chromium trioxide, 11.2 g of concentrated sulfuric acid, and 30 ml of water) was slowly added at this temperature. Stirring was continued at room temperature for 20 min, the excess oxidant was decomposed with saturated sodium sulfite solution, the acetone was evaporated under reduced pressure, and the aqueous mixture was extracted with chloroform (3 × 10 ml). The combined organic layers were washed successively with water (10 ml), saturated sodium bicarbonate solution (15 ml), and brine (10 ml), dried, and evaporated. The residual oil (24 mg, 80%) was homogeneous on vpc (column A[49]) and identical (ir, pmr) with authentic **29** (see below). The 2,4-dinitrophenylhydrazone derivative melted at 165–166° (from ethanol) and the semicarbazone melted at 185–186° (from ethanol).

***cis*-Bicyclo[3.3.0]octan-2-one (30). A. Hydrogenation of 29.** A solution of 30 mg (0.24 mmol) of **29** in 10 ml of ethyl acetate containing 2 mg of 10% palladium on charcoal was hydrogenated at atmospheric pressure and room temperature for 1 hr. Removal of the catalyst and evaporation left 28 mg (94%) of colorless oil, the ir spectrum of which was superimposable upon that illustrated in the literature;[23] $\delta_{TMS}^{CCl_4}$ 1.17–3.18 (m).

B. Hydrogenation of 31. A 150-mg (1.23 mmol) sample of **31**[24] was reduced as described above and gave 152 mg (99%) of **30**; ν_{max}^{neat} 2950 (s), 2870 (s), 1735 (s) cm^{-1}. The product was spectroscopically identical with the authentic material.

Ring Expansion of *cis*-Bicyclo[3.2.0]hept-2-en-6-one (33). To ethereal diazomethane (prepared from 1.26 g of *N*-nitroso-*N*-methylurea and 5 ml of 40% potassium hydroxide solution in 20 ml of ether) was added dropwise a solution of 1.08 g (10 mmol) of **33**[23] in 10 ml of anhydrous methanol. The reaction mixture was stirred at room temperature for 4 hr and a few drops of acetic acid were added to decompose the excess diazomethane. Water (50 ml) was added, the organic solvents were evaporated under reduced pressure, and the aqueous mixture was extracted with ether (5 × 30 ml). The combined dried ether extracts were evaporated to give 986 mg of colorless oil, the three components in which (55% of **29**, 37% of **34**, and 5% of unreacted **33**) were separated by preparative scale vpc on column A.[49]

For **29** (shorter retention time): ν_{max}^{neat} 1736 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 1.95–2.28 (m, 4 H), 2.48–2.74 (m, 3 H), 3.35–3.75 (m, 1 H), and 5.58–5.80 (m, 2 H).

Catalytic hydrogenation of this sample afforded only **30**.

For **34** (longer retention time): ν_{max}^{neat} 1740 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 1.65–3.12 (m, 7 H), 3.15–3.60 (br m, 1 H), and 5.5–5.85 (m, 2 H). Calcd for $C_8H_{10}O$ *m/e* 122.0732; found 122.0733.

Hydride Reduction 29. A 20-mg/sample of **29** (0.16 mmol) was treated as previously described with 20 mg (0.53 mmol) of lithium aluminum hydride in 8 ml of anhydrous ether. After standing at room temperature for 10 min, the mixture was processed in the customary manner. The mixture of alcohols so produced (17 mg, 84%) was directly dissolved in 2 ml of pyridine to which was added dropwise 0.5 ml of acetic anhydride. This solution was heated at 60° for 3 min, cooled, carefully evaporated, and treated with water (10 ml). The combined chloroform extracts were washed successively with cold 3% hydrochloric acid, brine, saturated sodium bicarbonate solution, and brine. The acetates isolated in 91% yield were separated on column A.[49] Exo acetate **35** (7%) exhibited strong ir bands at 1738 and 1242 cm^{-1} and proved identical in all respects with the acetylation product of the minor [3.3.0] bicyclic alcohol formed upon hydrolysis of **15a** and **15b**. Calcd for $C_{10}H_{14}O_2$: *m/e* 166.0994; found 166.0993.

Endo acetate **36** (93%) exhibited intense ir bands at 2945, 2868, 1736, 1374, 1360, 1243, 1054, and 708 cm^{-1} and proved identical in all respects with the acetylation product of the major [3.3.0] bicyclic alcohol formed upon hydrolysis of **15a** and **15b**. Calcd for $C_{10}H_{14}O_2$: *m/e* 166.0994; found 166.0994.

***endo-cis*-Bicyclo[4.2.0]oct-2-en-5-ol (28).** To a cold (−30°) solution of **22** (200 mg, 7.6 mmol) in 10 ml of absolute methanol was added 250 mg (6.5 mmol) of sodium borohydride portionwise during 5 min. The mixture was kept at ice-bath temperature for 6 hr, diluted with water (50 ml), and extracted with ether–pentane (1:1, 4 × 50 ml). The combined organic phases were washed with brine, dried, and evaporated to give 200 mg of crude product. Vpc analysis of this material on column F[49] at 140° indicated two major products (92:8) and a small (1%) impurity. These were separated on this column and the minor component proved identical by ir and pmr with **21a**.

The major component was characterized as **28** and was identical with the third alcohol produced during hydrolysis of **15a** and **15b**; $\delta_{TMS}^{CDCl_3}$ 1.0–2.95 (br m, 13 H) and 3.30–3.85 (br, 1 H). Calcd for $C_8H_{12}O$: *m/e* 124.0888; found 124.0889.

Anal. Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.07; H, 9.62.

1α,2α,4α,6α-Tricyclo[4.2.0.0^{2,4}]octan-5β-ol Acetate (17-OAc). Pure alcohol **17** was acetylated as above in 89% yield; ν_{max}^{neat} 2980, 2942, 1730, 1373, 1248, 1046, 1022, and 992 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 0.4–0.9 (m, 1 H), 1.08–1.37 (m, 1 H), 1.40–2.50 (m, 6 H), 2.05 (s, 3 H), 2.70–3.50 (m, 2 H), and 5.10–5.45 (m, 1 H).

1α,2α,4α,6α-Tricyclo[4.2.0.0^{2,4}]octan-5α-ol Acetate (20-OAc). Pure alcohol **20** was acetylated in 90% yield: ν_{max}^{neat} 2940, 1730, 1363, 1241, 1018, and 977 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 0.5–0.95 (m, 1.5 H), 1.32–2.50 (m, 6.5 H), 1.93 (s, 3 H), 2.65–3.35 (m, 2 H), and 4.75 (br s, 1 H).

Control Experiments Concerned with the Stability of Alcohols 17, 20, and 26–28. A solution of 20 mg (0.16 mmol) of **26**/**27** (7:93) and 32 mg (0.16 mmol) of 3,5-dinitrobenzoic acid in 1.6 ml of acetone–water (80:20) which was 0.08 M in 2,6-lutidine was heated at 125° for 6 days in a sealed tube. The usual work-up returned 16 mg (80%) of the above alcohol mixture.

The identical treatment of **28** (20 mg, 0.16 mmol) afforded 17 mg (85%) of unreacted starting alcohol.

When 200 mg of **17** was subjected to the same conditions, there was isolated 178 mg (89%) of yellowish oil. For convenience in analysis, this mixture was acetylated and shown to consist of **35** (7%), **36** (15%), **28**-OAc (10%), and **17**-OAc (68%).

Comparable treatment of **20** (100 mg, 0.80 mmol) returned 91 mg (91%) of an alcohol mixture which after acetylation was found to be composed of **35** (6%), **36** (13%), **28**-OAc (9%), and **20**-OAc (72%).

***exo-cis*- and *endo-cis*-Bicyclo[4.2.0]oct-2-en-4-ol (38 and 39).** To 48 ml of 2.25 M *n*-butyllithium in hexane (0.108 mol) cooled to −20° and maintained under nitrogen was added dropwise a solution of 16 ml (*ca.* 0.3 mol) of diethylamine in 50 ml of dry ether.

After 30 min at −20°, this mixture was allowed to warm to room temperature and was treated dropwise with a solution of 3:0 g (24 mmol) of **37** (purportedly an 85:15 exo/endo epoxide mixture[31]) in 20 ml of dry ether. The contents was stirred for 20 hr and carefully poured into ice-cold saturated ammonium chloride solution. The organic phase was separated, washed with water, dried, and evaporated to give 2.53 g (84%) of oil, vpc analysis of which (column A[49]) showed it to be a two-component mixture (86:14). Preparative scale vpc separation led to isolation of pure **38**: $\nu_{max}^{CCl_4}$ 3340, 2930, 2860, 1053, and 1000 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 1.1–3.10 (m, 8 H), 2.0 (br s, 1 H), 4.37 (m, 1 H), and 5.87 (m, 2 H).

Anal. Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.08; H, 9.82.

***cis*-Bicyclo[4.2.0]oct-2-en-4-one (40).** To a cold (0°) solution of the **38**/**39** mixture (86:14, 100 mg, 0.80 mmol) in 3 ml of acetone was added dropwise during 10 min 0.8 ml of the above Jones' reagent. Work-up commenced after 20 min at room temperature and there was isolated 78 mg (80%) of **40** as a colorless oil with a pmr spectrum identical with that supplied by Farrissey.[33]

Hydride Reduction of 40. Reduction of 1.0 g (8.2 mmol) of **40** with 350 mg (9.20 mmol) of lithium aluminum hydride in anhydrous ether (15 ml) as previously described (not above 0°) furnished 950 mg (83%) of **38** and **39** in a ratio of 43:57 (column A[49]). Isolation by preparative vpc led to characterization of the less dominant isomer as **38** by spectral comparison. Endo alcohol **39** was now obtained pure: $\nu_{max}^{CCl_4}$ 3330, 2933, 2863, 1054, and 1033 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 1.25–3.10 (m, 8 H), 1.87 (br s, 1 H), 4.00–4.60 (m, 1 H), and 5.76 (m, 2 H).

Anal. Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.13; H, 9.96.

***exo-cis*-Bicyclo[4.2.0]octan-3-ol (41).** Catalytic reduction of 100 mg (0.80 mmol) of **38** over 15 mg of 10% palladium on charcoal in ethyl acetate solution (20 ml) gave 98 mg (97%) of **41**, the infrared spectrum of which was superimposable upon that of an authentic sample;[34] $\delta_{TMS}^{CDCl_3}$ 1.0–2.95 (m, 12 H), 1.76 (br s, 1 H), and 3.65–4.20 (m, 1 H).

Deuterium-Labeled 3,5-Dinitrobenzoate 42. To a stirred slurry of 189 mg (4.5 mmol) of lithium aluminum deuteride in 5 ml of dry ether cooled to 0° was added dropwise a solution of 1.80 g (14.7 mmol) of 1α,2α,4α,6α-tricyclo[4.2.0.0^{2,4}]octan-7-one[12] in 5 ml of the same solvent. Work-up as before gave 1.65 g (90%) of labeled endo and exo alcohols (86:14; vpc analysis performed on derived acetates).

A 1.30-g (10.4 mmol) portion of this mixture was converted to the 3,5-dinitrobenzoate. Fractional recrystallization from chloroform–hexane furnished pure **42** as lightly yellowish crystals, mp 116–116.5°.

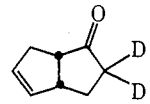
Preparative Scale Solvolysis of 42. A solution of 1.20 g (3.79 mmol) of **42** in 120 ml of 80:20 acetone–water which was 0.08 *M* in 2,6-lutidine was heated at 130° for 4 days. The usual work-up afforded 420 mg (89%) of an oil, vpc analysis of which on column A[49] showed it to consist of **43** (55%), **44** (39%), and **45** (6%). These were separated by preparative methods.

For **43**: ν_{max}^{neat} 3350, 2940, 2900, 2865, 1087, 1064, 1000, and 636 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 1.20–3.50 (m, 8 H), 3.00 (br s, 1 H), 3.70–4.40 (m, 1 H), and 5.40–5.78 (m, 1 H).

For **44**: ν_{max}^{neat} 3340, 2925, 2860, 1080, 1051, 1037, and 618 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 1.20–3.10 (m, 8 H), 3.33 (s, 1 H), 3.40–4.10 (m, 1 H), and 5.42–5.75 (br q, 1 H).

For **45**: $\delta_{TMS}^{CCl_4}$ 0.58 (m, 2 H), 1.0–2.3 (m, 6 H), 2.08 (s, 1 H), and 2.85 (m, 2 H).

Oxidation of 43. Jones' oxidation of **43** (25 mg, 0.20 mmol) afforded 21 mg (85%) of **46**; ν_{max}^{neat} 2935, 2908, 1735, and 1127 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 2.05 (m, area 4, H_{7exo}, H_{7endo}, and the pair of H_8's), 2.56 (m, area 3, H_{4exo}, H_1, and H_{4endo}), 3.50 (m, area 1, H_5), and 5.65 (m, area 1, H_3). A deuterium exchange experiment on **29** provided **29**-d_2 whose pmr spectrum supported these assignments;



29-d_2

the multiplet at δ 2.56 showed diminished relative intensity to 2 H (absence of H_{7endo}), the multiplet at 2.05 was decreased in area to 3H (absence of H_{7exo}), and the olefinic signal at 5.65 doubled in area (H_2 now present).

That the deuterium in **46** was positioned at C_2 was established by double resonance studies on **29** and **46**. For example, in **46** double irradiation of the residual vinyl proton collapsed H_{4exo} to a doublet (J = 4 Hz) while spin decoupling of H_5 also had a similar effect—collapse to a doublet of J = 1.5 Hz. Triple irradiation of H_3 and H_5 left H_{4exo} as a sharp singlet, a result consistent only with nonadjacent positioning of the isotopic label to this methylene group.[50]

A similar analysis on ketone **47** established the presence of the =CHCH$_2$CO– moiety rather than the –CH=C(D)CH$_2$CO group.

Kinetic Method. A. Reagents. Anhydrous acetone and absolute methanol were obtained by treating the reagent grade materials as described by Fieser and Fieser.[51] Dry tetrahydrofuran was prepared by distillation from lithium aluminum hydride. Aqueous acetone (80% v/v) was obtained by mixing 250 ml of distilled water and 1000 ml of purified acetone. A stock solution of methanol–tetrahydrofuran (75:25) was prepared by mixing 750 ml of absolute methanol and 250 ml of dry tetrahydrofuran. The solvents were allowed to equilibrate thermally at 25° prior to mixing. 2,6-Lutidine was dried over potassium hydroxide pellets and distilled before use.

B. Kinetics Procedure. A solution (*ca.* 0.045 *M*, accurately weighed) of the 3,5-dinitrobenzoate or *p*-nitrobenzoate was prepared in a 10 ml volumetric flask. Aliquots of this solution (*ca.* 1.1 ml) were removed and sealed in glass ampoules which had been previously flushed with nitrogen. The ampoules were placed in a constant-temperature bath and an accurate timer was started. The ampoules were removed at approximately timed intervals and immediately quenched in ice–water. The ampoules were allowed to warm to room temperature, whereupon 0.923 ml of solution was removed from the aliquot by means of a calibrated automatic pipet and immediately titrated against standardized sodium hydroxide solution using phenolphthalein as indicator.

All rates were determined utilizing an infinity titer except in the **15a** and **15b** cases which solvolyzed very slowly. Infinity titers were considered to be reached after 10 half-lives. In most cases the infinity titer did not correspond to 100% reaction due to internal return to a less reactive ester. Rate constants and activation parameters were evaluated by the method of least squares.[52]

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(50) For a recent informative pmr study of *cis*-bicyclo[3.3.0]oct-7-en-2-yl derivatives, see K. Fujita, K. Hata, R. Oda, and I. Tahishi, *J. Org. Chem.*, **38**, 2640 (1973).

(51) L. Fieser and M. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1957.

(52) All relevant numerical data may be found in the Ph.D. Thesis of O. Cox, The Ohio State University, 1968.