Steric Factors in the Cationic Rearrangement of Substituted Cyclobutanes

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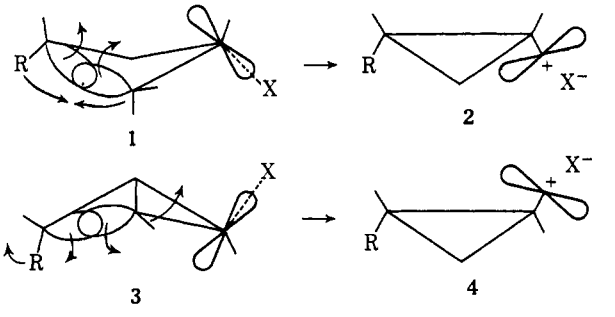
Abstract: The solvolysis and deamination of the cis and trans isomers of 3-methyl- and 3-isopropylcyclobutyl derivatives are discussed and compared. The data support a mechanism which has as its rate-determining step the concerted and stereospecific rearrangement of the cyclobutyl precursor to an intermediate (2-alkylcyclopropyl)-carbinyl ion pair. Differences in solvolytic rates are related to the steric effect of the substituent on the orbital opening and overlap modes involved in this process. The kinetic effect of α-deuterium substitution is normal for both *cis*- and *trans*-3-isopropylcyclobutyl solvolysis, and larger for cis. These facts are consistent with a small charge on the 1-carbon of the cyclobutane encountered in a concerted rearrangement, and hindrance to anchimeric assistance in the cis isomer. Differences in isomeric product distribution are ascribed to differences in the behavior of the primary isomeric (2-alkylcyclopropyl)carbinyl intermediates **2** and **3**; rationales are suggested. The specificity of the deuterium label position observed in solvolysis and deamination of 1-labeled cyclobutane derivatives supports this sequential genesis of products from the cyclobutanes; further confirmation is provided by solvolysis of the appropriately substituted cyclopropyl compounds. Major product differences are observed in solvolysis *vs.* deamination of the *cis*-, but not the *trans*-cyclobutyl compounds. A secondary cyclopropylalkylcarbinyl intermediate (**6**), which results from an apparently favored transformation of the *cis*-(2-alkylcyclopropyl)-carbinyl precursor **2**, is implicated as the source of such differences. These product variances appear due to the inability of this secondary cation to escape solvent capture and function as an intermediate in deamination of both isomers, and in trans solvolysis.

New insight into the mechanism of the cationic cyclobutyl–cyclopropylcarbinyl rearrangement has accrued in the course of study of deamination[2-4] and solvolysis[5-7] of isomeric 3-substituted cyclobutane derivatives, and solvolysis of fused cyclobutane derivatives.[8-11] As a consequence, it has become evident that opening of the cyclobutane ring is concerted with rearrangement, and is a stereospecific process quite sensitive to conformational factors. A similar pattern of steric influence on orbital rotation prerequisite to overlap accompanying ring opening has been previously observed in electrocyclic reactions of cyclopropanes,[12] *inter alia*. In both the cyclopropyl and cyclobutyl cases,[13] disrotatory orbital opening inward facilitates maximum overlap of the opening orbitals with the vacating rear lobe of the p orbital bonding the leaving group. Thus, for a *cis*-3-alkylcyclobutyl isomer, opening of the C_2–C_3 bond generates R–H bond oppositions in the transition state leading to overlap with the developing vacant orbital at C_1 (**1** → **2**). On the other hand, the analogous process entails no such steric constraints in the trans isomer (**3** → **4**).[2,3,5,13] With the assumption that these steps are rate determining[14] in the solvolysis of the 3-isopropylcyclobutyl brosylates,[5] the trans rate preference observed is thus ascribable to relative absence of steric retardation.



R = CH_3, *i*-C_3H_7
X = $ArSO_3$, N_2^+

In similar fashion, isomeric product differences observed in both solvolysis and deamination implicate further differential behavior of intermediates **2** and **4**. It has been suggested that analogous steric influences on orbital opening modes in these intermediates could account for the respective product distribution in the deamination of the isomeric 3-methylcyclobutylamines, as well as the differences in these product ratios from those for the 3-isopropyl case.[3] The observation that the deuterium label in 3-isopropylcyclobutylamine-*1-d* was found specifically at the 1-carbon in the cyclopropylcarbinyl products of deamination lends support to these inferences.[15]

To examine further the validity of this rationale, it was deemed of interest to investigate the α-deuterium isotope effect in solvolysis as an important corrolary to

(1) To whom correspondence should be addressed at Miami-Dade Junior College (South), Miami, Florida 33156.
(2) I. Lillien and R. A. Doughty, *J. Org. Chem.*, **33**, 3841 (1968).
(3) I. Lillien and L. Handloser, *ibid.*, **34**, 3058 (1969).
(4) I. Lillien, *Chem. Commnu.*, 1009 (1968).
(5) I. Lillien, G. F. Reynolds, and L. Handloser, *Tetrahedron Lett.*, 3475 (1968).
(6) C. F. Wilcox, Jr., and R. J. Engen, *ibid.*, 2759 (1966).
(7) L. J. Dolby and C. Wilkins, *ibid.*, 2379 (1964).
(8) K. B. Wiberg, J. E. Hiatt, and K. Hseih, *J. Amer. Chem. Soc.*, **92**, 544 (1970).
(9) K. B. Wiberg, V. Z. Williams, and L. E. Friedrich, *ibid.*, **92**, 564 (1970).
(10) K. B. Wiberg and J. G. Pfeiffer, *ibid.*, **92**, 553 (1970).
(11) K. B. Wiberg, R. A. Fenoglio, V. Z. Williams, Jr., and R. W. Ubersax, *ibid.*, **92**, 568 (1970); *cf.* also preceding papers in this series.
(12) C. H. De Puy, *Accounts Chem. Res.*, **1**, 33 (1968).
(13) K. B. Wiberg and G. Szeimies, *J. Amer. Chem. Soc.*, **92**, 571 (1970).
(14) It has been concluded that the ion initially formed on solvolysis of various cyclopropylcarbinyl derivatives must have the cyclopropylcarbinyl cation structure; *cf.* K. B. Wiberg and A. J. Ashe, III, *ibid.*, **90**, 63 (1968).
(15) I. Lillien and L. Handloser, *Tetrahedron Lett.*, 1035 (1969).

the deamination results. Further, it appeared desirable to carry out a solvolytic study with the 3-methylcyclobutyl brosylates to obtain a more quantitative assay of the substituent steric effect. The present paper is thus concerned with the presentation and comparison of these new data with previous results. The sequential kinetic rationale has been tested by the solvolysis of several cyclopropylcarbinyl arenesulfonates which could lead to suspected intermediates.

Synthesis

A mixture of isomers of 3-isopropylcyclobutylamine-*1-d* was synthesized from the carboxylic-*1-d* acid by the Schmidt reaction.[2] This was prepared in turn by decarboxylation of the dideuterated 1,1-dicarboxy acid obtained by neutralization of the dipotassium salt from prior synthesis with DCl in D_2O. Nmr analysis revealed that the dicarboxy acid contained better than 95% of the expected deuterium, and that the carboxylic-*1-d* acid contained at least 99 ± 1% of the expected deuterium.

Almost isomerically pure (96 ± 1%) *cis*-3-isopropylcyclobutanol-*1-d* was obtained by the lithium aluminum deuteride reduction of 3-isopropylcyclobutanone, prepared in good yield from the alcohol[2] by an Oppenauer oxidation. The brosylate was prepared by conventional treatment with brosyl chloride in pyridine, and after recrystallization, showed no discernible trans content[5] by nmr analysis.[16] *trans*-Alcohol was obtained in low yield by inversion of the *cis*-brosylate with tetramethylammonium acetate in dry acetone followed by saponification, and was converted to the brosylate in the usual fashion. After recrystallization, the *trans*-brosylate contained no cis isomer by nmr criteria. The ring protons are seen as a single sharp singlet at 2.17 ppm. Both *cis*- and *trans*-brosylates were shown by nmr to contain no 1-H.

The 3-methylcyclobutanols were prepared, separated, and assigned configuration as has been described.[2,17] Brosylates were prepared conventionally, and their purity was confirmed by nmr analysis.

(2-Methylcyclopropyl)carbinol was prepared as described.[17] (2-Isopropylcyclopropyl)carbinol was prepared by lithium aluminum hydride reduction of the product of the reaction of ethyl diazoacetate and 3-methyl-1-butene.[18] In both cases, the isomeric carbinols were completely separated by preparative vpc. The basis of isomeric assignment for these compounds has been described.[2,3,18] All efforts to convert them to brosylates by treatment with sulfonyl chloride in pyridine failed. It was found, however, that the desired products could be prepared by substitution of triethylamine for pyridine. The product brosylates are oils which were purified by passage of their pentane solutions over neutral alumina. They were used without further delay. The brosylate of cyclopropylmethylcarbinol was prepared by reaction of the sodium salt of the carbinol, prepared in dry ether with powdered sodium, with brosyl chloride. It was purified by passage of its solution over alumina and used immediately. The various cyclopropylcarbinyl brosylates gave satisfactory nmr spectra after passage over alumina. The 3,5-dinitrobenzoates of the cyclopropylcarbinols were prepared as has been described.[18]

3-Penten-1-ol and 5-methyl-3-hexen-1-ol were prepared as isomeric mixtures as described.[19] Isomers were readily separated by preparative vpc. Isomeric assignment was based on infrared analysis; the trans isomers show a band at *ca.* 980 cm^{-1} which is diagnostic for a trans double bond.[19,20] The brosylates were prepared conventionally, and are oils which gave satisfactory nmr spectra without further treatment.

Cyclobutanol was prepared as reported[21] and converted to its brosylate without difficulty.

The Problem of Interpretation. Some years ago, Roberts and coworkers proposed that the common intermediate in cyclobutyl–cyclopropylcarbinyl–homoallyl cationic transformations was a tricyclobutonium ion[22] or a system of interconverting bicyclobutonium ions.[23] Since that time, conflicting views on the interpretation of these reactions have arisen, giving rise to considerable controversy concerning the structure of the intermediate or intermediates. It has been argued on the basis of further consideration by several authors, *inter alia*, that the available data on cyclobutyl–cyclopropylcarbinyl interconversions may be adequately explained without interpolation of common bicyclobutonium *intermediates*.[14,24–26] We have previously summarized our evidence supporting this viewpoint.[2,3]

Most recently, the structure of the intermediate cyclopropylcarbinyl cation has been subjected to more detailed scrutiny.[27–31] It is now generally accepted that there is compelling evidence for some sort of charge delocalization into the cyclopropane ring, and it is now known that definite geometric constraints on participation exist.[32,33] A convincing description of the nature of this interaction, however, has so far remained elusive. While several possible delocalized structures of varying symmetry have been proposed,[29,31] it is at present difficult to estimate with any degree of certainty the relative contributions which these structures may make to the real intermediate, or to estimate the relative contributions of partial bonds to the structures themselves. Moreover, the simple alternative rationale of rapidly equilibrating cyclopropylcarbinyl cations can successfully cope with the known data. It should be recalled that experimental conditions in recent direct observations of cyclopropylcarbinyl cations in

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(19) L. Crombie, J. Gold, S. H. Harper, and B. J. Stokes, *J. Chem. Soc.*, 136 (1956).
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(21) M. C. Caserio, W. H. Graham, and J. D. Roberts, *Tetrahedron*, **11**, 171 (1960).
(22) J. D. Roberts and R. J. Mazur, *J. Amer. Chem. Soc.*, **73**, 3542 (1951).
(23) R. H. Mazur, W. N. White, D. A. Semenov, C. C. Lee, M. S. Silver, and J. D. Roberts, *ibid*, **81**, 4390 (1959).
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(30) C. V. Pittman, Jr., and G. A. Olah, *ibid.*, **87**, 2998, 5123 (1965).
(31) G. A. Olah, D. P. Kelley, C. L. Juell, and R. D. Porter, *ibid.*, **92** 2544 (1970).
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(33) B. R. Ree and J. C. Martin, *ibid.*, **92**, 1660 (1970).

Table I. Solvolysis of Brosylates, 70% Aqueous Acetone[a,b]

Brosylate	$k \times 10^4$, sec^{-1} 41.1°	k_{rel} 41.1°	$k \times 10^4$, sec^{-1} 50.6°	$\Delta H^{\pm}$, kcal/mol	$\Delta S^{\pm}$, eu
Cyclobutyl	5.850 ± 0.014	1.00	15.19 ± 0.07	19.7	−11
trans-3-Methylcyclobutyl	3.358 ± 0.035	0.57	8.17 ± 0.07	18.3	−16
trans-3-Isopropylcyclobutyl	2.140 ± 0.02	0.37	5.75 ± 0.09	20.4	−11
cis-3-Methylcyclobutyl	0.552 ± 0.004	0.09	1.361 ± 0.069	18.6	−19
cis-3-Isopropylcyclobutyl	0.335 ± 0.01	0.06	0.902 ± 0.005	20.4	−14
trans-3-Isopropylcyclobutyl-*1-d*	1.93 ± 0.02	0.32			
cis-3-Isopropylcyclobutyl-*1-d*	0.258 ± 0.02	0.04			
2-Methyl-5-hexen-3-yl	0.151 ± 0.03	0.03			
5-Methyl-3-hexen-1-yl	0.040 ± 0.005	0.007			

[a] Linearity followed to at least five half-lives. [b] Average deviations are shown.

super acid[30,31] which have led to quite explicit structural conclusions do not parallel experimental conditions (*e.g.*, deamination, solvolysis) in which real intermediates are encountered.[34]

Thus, portrayal of the cyclopropylcarbinyl cation intermediate in a localized sense, while it may be oversimplification, does not preclude contribution from delocalized bonds, but rather seeks to avoid the high degree of speculativeness otherwise necessary. It is evident that the circumscribed stereochemistry which has been observed in the cyclopropylcarbinyl–cyclopropylcarbinyl interconversion,[13] which can explain the isotope-scrambling results observed in this system[23] in a direct manner, is a consequence which is difficult to reconcile with equilibrating bicyclobutonium ions.

On the other hand, there is at present no experimental evidence which requires that the cation containing the intact cyclobutane ring have a unique structure. Indeed, the cation formed from cyclobutane under normal circumstances appears to be the cyclopropylcarbinyl cation resulting from rearrangement concerted with ionization.[2-11] It has been shown that when this rearrangement is thwarted by electronic[4,35] or steric[36] factors, the cyclobutane derivatives exhibit drastically curtailed proclivity for rearrangement or rate enhancement.

It appears desirable, therefore, that the interpretation of the present experimental results consider the two distinct aspects of the overall problem: one, factors governing the cyclobutyl–cyclopropylcarbinyl rearrangement; and two, factors governing the fate of the cyclopropylcarbinyl intermediate.

Kinetic Results. The rate data for solvolysis are presented in Table I. The presumption that the choice of solvent (70% aqueous acetone) is one which should minimize[18,25] internal return[37] due to its relatively high water content is strengthened by several observations. These are (1) the failure of olefinic or cyclopropylcarbinyl compounds to produce any discernible traces of 3-substituted cyclobutanols; (2) the failure of the homoallylic brosylates to reproduce the product distribution of their ostensible solvolytic precursors, the cyclopropylcarbinyl brosylates; and (3) the unimportance of isomeric crossover (*i.e.*, no two isomeric brosylates yield nearly identical product mixtures); see Table II. The usual assumption is made that in kinetically controlled steps, product ratios mirror relative abundance of cationic antecedents. Attempts were made to ascertain the presence of rearranged brosylates in the representative case of *cis*-3-isopropylcyclobutyl brosylate by quenching buffered solvolysis mixtures at one-half, one, and two half-lives. Examination by nmr revealed no rearrangement of the recovered brosylates. Thus it is fairly safe to assume that the observed rate constants are not complicated by internal return pathways.

Solvolysis of cyclopropylcarbinyl compounds is expected to be faster than solvolysis of their cyclobutyl analogs. Cyclopropylcarbinyl mesylate solvolyzes over 90 times faster than cyclobutyl mesylate in 60% aqueous diglyme at 40°,[38a] while the α-naphthalenesulfonates differ by a factor of 390 in 90% aqueous dioxane at 25°.[38b] The rate-determining step for cyclopropylcarbinyl solvolysis is not necessarily analogous to that for cyclobutyl solvolysis. It is rather likely that while the latter is fully concerted, the former involves considerable ion-pair separation prior to rearrangement. Evidence in this regard is the uniform rate-accelerating effect of *trans*-2-alkyl substitution in solvolysis of the cyclopropylcarbinyl 3,5-dinitrobenzoates[18,28] and the only small cis–trans rate differences found in that series (*e.g.*, trans/cis 2-methyl = 1.3) as compared to the cyclobutyl ratios. It is probable, therefore, that molecular reorganization has not proceeded to as great an extent in the cyclopropylcarbinyl ionization step as in the cyclobutyl ionization step. The clean SN1 rate behavior of the cyclopropylcarbinyl compounds[28] requires that their ionization be the slowest step in conversion to products. Since their rate constants reflect ionization rates which are more rapid than the rates for **1** → **2** and **3** → **4** for the cyclobutanes, it is obvious that the rate of irreversible collapse of **2** and **4** to products will be even more rapid.

It is thus reasonable to regard the cyclobutyl brosylates as parents of a *series of sequential rearrangements* whose slowest steps are **1** → **2** for the cis and **3** → **4** for the trans isomers. This premise forms the basis of the kinetic rationale offered below.

The differences in cis and trans rates for the 3-alkylcyclobutyl compounds reflect both the differences in ground state energies for the brosylates and the differences in the energies of the corresponding transition

(34) In fact, it has been suggested that the actual parallelism of super acid solution chemistry is with gaseous molecule–ion reactions; *cf.* G. A. Olah, J. Shen, and R. H. Schlosberg, *J. Amer. Chem. Soc.*, **92**, 3831 (1970).

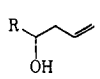
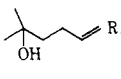
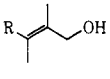
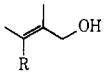
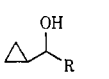
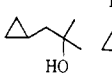
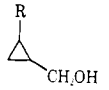
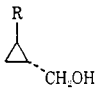
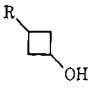
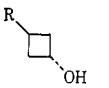
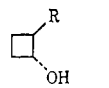
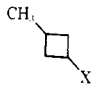
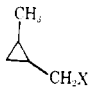
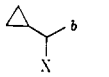
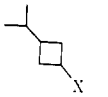
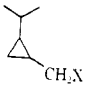
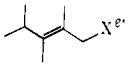
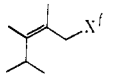
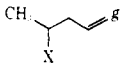
(35) I. Lillien and L. Handloser, *Tetrahedron Lett.*, 1213 (1970).

(36) Deamination of *cis*-3-*tert*-butylcyclobutylamine yields almost 50% unrearranged *cis*-3-*tert*-butylcyclobutanol, which is a unique result for the 3-alkylcyclobutyl series (I. Lillien and L. Handloser, unpublished results), and a consequence of severe steric opposition to route **1** → **2**.

(37) K. L. Servis and J. D. Roberts, *Tetrahedron Lett.*, 1369 (1967).

(38) (a) Z. Majerski, S. Borčić, and D. E. Sunko, *Tetrahedron*, **25**, 301 (1969); (b) R. A. Sneen, K. M. Lewandowski, I. A. Taha, and B. R. Smith, *J. Amer. Chem. Soc.*, **83**, 4843 (1961).

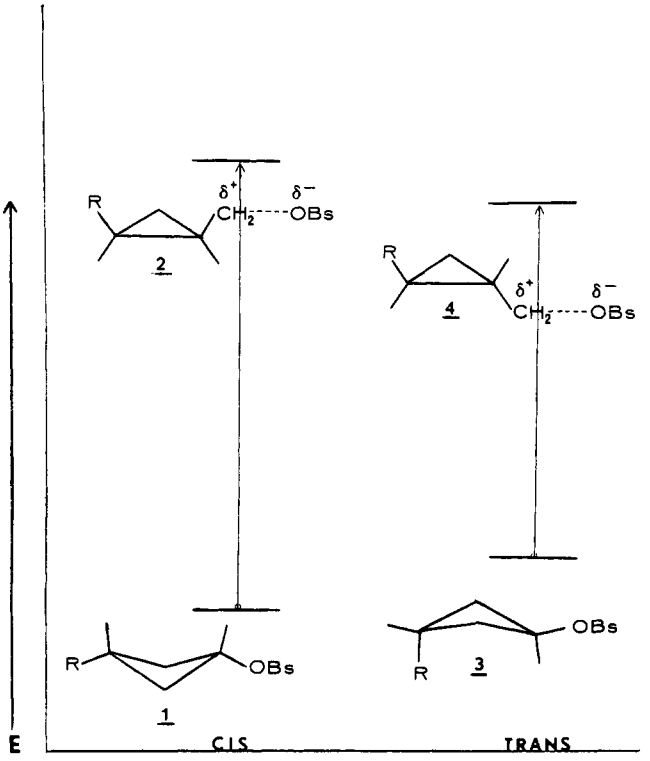
Table II

X = BsO, NH_2	Solvolysis/deamination, % products										
	 7	 8	 9	 10	 11	 12	 13 (*cis*)	 14	 15 (*cis*)	 16	 17 (*trans*)
	Cis[a] 37.3/18.3		16.8/0	2.4/0	23.2/59.4		3.3/17.7	4.7/1.8	Trace/2.0	Trace/0.8	5.2/0
	Trans 44.1/58.8		0/0	0/0	28.8/19.2		0/0	27.1/21.1	0/0.7	0/0.2	0/0
	Cis 38.1		28.2	5.0	9.1		6.6	7.0	0	0	6.0
	Trans 45.0		1.5	0	11.7		0	41.8	0	0	0
	4.7		38.0	5.0	28.2		Trace	1.4	0	0	14.0
	Cis 2.0[c]	4.2	5.4	13.6	31.3	2.7	22.1	5.1	13.6	Trace	Trace
	7.2/9.8[d]	4.6/0	45.0/0	6.1/0	2.8/68.1	10.0/0	8.7/11.1	4.9/2.2	5.7/7.6	Trace/1.2	5.0/0
	Trans 1.3/6.0	1.1/0	0/0	0/0	15.8/28.6	1.3/0	0/0	80.5/55.0	0/7.3	0/3.1	0/0
	Cis 4.0	2.9	50.4	8.7	10.6	2.8	10.2	4.0	0	0	6.4
	Trans 3.7	2.7	0	0	34.6	2.5	0	56.5	0	0	0
	Trace	Trace	33.3	11.5	55.2						
	Trace	Trace	Trace	32.6	67.4						
	79.2		0	0	3.6						

[a] Product contained 7.1% 1-penten-3-ol. [b] Product contained 1.9% unknown, and 6.8% 1-penten-3-ol. [c] Solvolysis quenched after 3 hr reflux. [d] Solvolysis carried out to completion. [e] Product contained trace amounts of other materials. [f] Product contained trace amounts of other materials. [g] Product contained 4.1% unknown, and 13.1% 1-penten-3-ol.

states, as depicted in Scheme I. The puckered conformer of the *cis*-cyclobutane isomer is more stable than the trans isomer by several kilocalories. However, the trans transition state (leading to **4**) must be more stable than the cis by several kilocalories, due to the greater stability of the resultant *trans*-cyclopropyl system. Thus $\Delta E_{cis}^{\ddagger}$ would be expected to be larger than $\Delta E_{trans}^{\ddagger}$ at the outset, resulting in anticipation of a smaller cis rate. This rate difference is *augmented* by the conformational barrier encountered in the cis transformation **1** → **2**, which is substituent dependent.

Scheme I



Thus the *cis*-3-alkyl substituent causes a rate retardation,[39] with the ratio at 41.1° being in the order 17.5:1.6:1.0 for $H:CH_3:i\text{-}C_3H_7$, respectively. The trans/cis rate ratios for the methyl- and isopropylcyclobutyl brosylates are respectively *ca.* 6.1 and 6.4 at 41.1° and 6.0 and 6.4 at 50.6°. The similarity of these ratios is not unexpected, since the conformational free energies of methyl and isopropyl are only slightly different.[40] To the extent that the transition state involving isopropyl requires a slightly larger energy of activation,[3] the methyl retardation is somewhat less in magnitude. The difference in $\Delta G^{\ddagger}$ for the two *cis*-3-alkyl rates (at 41.1°) is about 0.3 kcal, which is identical with the difference in conformational free energies for methyl and isopropyl as measured in cyclohexane.[40]

(39) An analogous but much larger effect is observed in *cis*-3-*tert*-butylcyclobutyl tosylate solvolysis; *cf.* P. v. R. Schleyer, P. LePerchec, and D. J. Raber, *Tetrahedron Lett.*, 4389 (1969). The approximate rate constants, extrapolated to present conditions, are cis, 0.04; trans, 1.9×10^{-4}.

(40) N. L. Allinger and L. A. Freiberg, *J. Org. Chem.*, **31**, 894 (1966).

The magnitude of this cis increment is thus in accord with the expected rate-retarding contribution of conformational repulsion in process **1** → **2**.

It is more difficult to reconcile the difference in rates between the trans isomers of the 3-substituted cyclobutanes with that of the parent cyclobutane, which solvolyses more rapidly (1.7 times faster than the *trans*-3-methyl compound at 41.1°).[41] It is unlikely that the transition state for formation of the *trans*-(2-alkylcyclopropyl)carbinyl cation would possess intrinsically greater energy than that for the formation of the cyclopropylcarbinyl cation itself. This rate-lowering effect does not appear to be of a simple inductive nature, nor are developing conformational repulsions inherent in process **3** → **4**. Inductively, *trans*-alkyl substitution generally might be expected to accelerate the rate of a cationic solvolysis; further, isopropyl is more effective in sterically unencumbered electron release than methyl.[42] However, the isopropyl compound has the slowest rate of the three. Three possible factors may be responsible in whole or in part. Most likely, the conformational energy of an axial alkyl group causes a corresponding increase in transition state energy.[43] Additionally, it is possible that the increasing bulk of the substituent shifts the equilibrium in cyclobutane to the conformer with equatorial alkyl and axial brosylate, which is less suited for solvolysis. It is also possible that a ponderal effect[44] of the 3-substituent is in effect here, resulting from its need to be moved through space as part of the disrotatory orbital opening process of the C_2–C_3 bond.

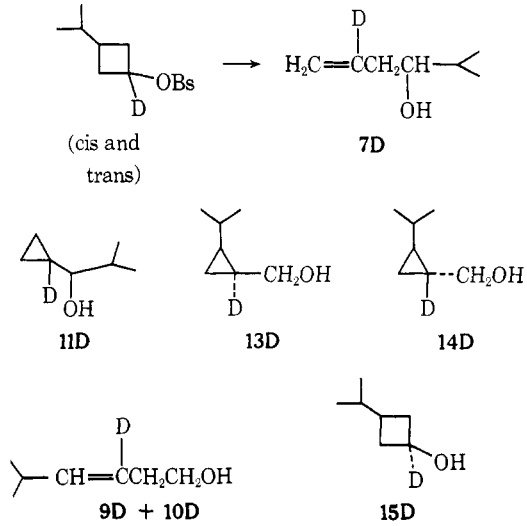
The secondary deuterium kinetic isotope effect observed for *trans*-3-isopropylcyclobutyl-*1-d* brosylate is small (k_H/k_D = 1.11 ± 0.01), and approximately that observed for simple alkyl tosylates such as isopropyl.[45] The cis isotope effect, however, is larger (k_H/k_D = 1.29 ± 0.02). The ratio of these isotope effects for the set of isomers parallels that observed in the solvolysis of the α-deuterated *exo*- and *endo*-2-norbornyl brosylates (respectively 1.10 and 1.20[46]). The reduced exo value may be taken as an indication of anchimeric assistance to ionization. It is evident that charge dispersal in the SN1 transition state should effect a reduction in k_H/k_D as compared to charge localization for α-deuterium substitution, since the isotopic carbonium ion will be of less significance.[47] The same reasoning appears applicable to the present instance. In the transition state for trans rearrangement **3** → **4**, C_3 orbital overlap is unimpeded, and reduction of cationic character at C_1 can occur early on the energy slope. On the other hand, the conformational hindrance to similar cis overlap allows a greater charge to accumulate at C_1 at an analogous point on the reaction coordinate. Thus, the larger cis isotope effect reflects a greater degree of charge localization in the transition state.[48] The product analysis (Scheme II) indicates that deuterium scrambling[46] has not taken place.

The table of kinetic data includes the rates of several olefinic brosylates measured under the same conditions. Their relative slowness, as well as the product analysis discussed below, eliminates them as potential intermediates.[49]

Product Analysis. Product analyses are detailed in Table II. Several key observations may serve to summarize much of this data. For solvolysis, the faster reacting *trans*-cyclobutyl isomers produce a much simpler product array than their cis counterparts. Both sets of (2-alkylcyclopropyl)carbinyl brosylates produce product mixtures whose compositions are strikingly similar to those of their cyclobutyl analogs,[50] with the exception that the former yield no 3-alkylcyclobutanols. Isomeric crossover in all cases is absent or minimal.

The major difference between the two sets of *trans*-alkyl compounds is that the methyl substituent produces a majority of terminal olefin **7**, while the isopropyl group results in a preponderance of *trans*-(2-isopropylcyclopropyl)carbinol **14**. Little significant difference appears in the trans cases between solvolysis and deamination. Comparison of product distribution in the trans series with that for the cis series indicates that solvent capture of the first open carbonium ion formed from **4** must take place at a rate comparable to that of its further rearrangement. Thus, product **14** is of high yield in the trans series irrespective of other considerations. Results of the isotopic solvolysis

Scheme II. Products of Solvolysis of 3-Isopropylcyclobutyl-*1-d* Brosylate[a,b]



[a] Other products were not isolated for purposes of this study. The ratios of all deuterated products did not differ by more than 2–3% from those in undeuterated solvolysis. [b] Deuterium distribution by nmr.

(41) The solvolytic rate constant for the *trans*-3-*tert*-butyl group under present conditions would be slightly less than that of *trans*-3-isopropyl, as predicted.[39]

(42) P. v. R. Schleyer and C. Woodworth, *J. Amer. Chem. Soc.*, **90**, 6528 (1968).

(43) The equatorial leaving group is energetically favored in cyclobutane; *cf.* ref 27.

(44) C. K. Ingold, *Quart. Rev., Chem. Soc.*, **11**, 1 (1957).

(45) E. R. Thornton, "Solvolysis Mechanisms," Ronald Press, New York, N. Y., 1964, p 202.

(46) (a) C. C. Lee and E. W. C. Wong, *J. Amer. Chem. Soc.*, **86**, 2752 (1964); (b) B. L. Murr and J. A. Conkling, *ibid.*, **92**, 3462 (1970).

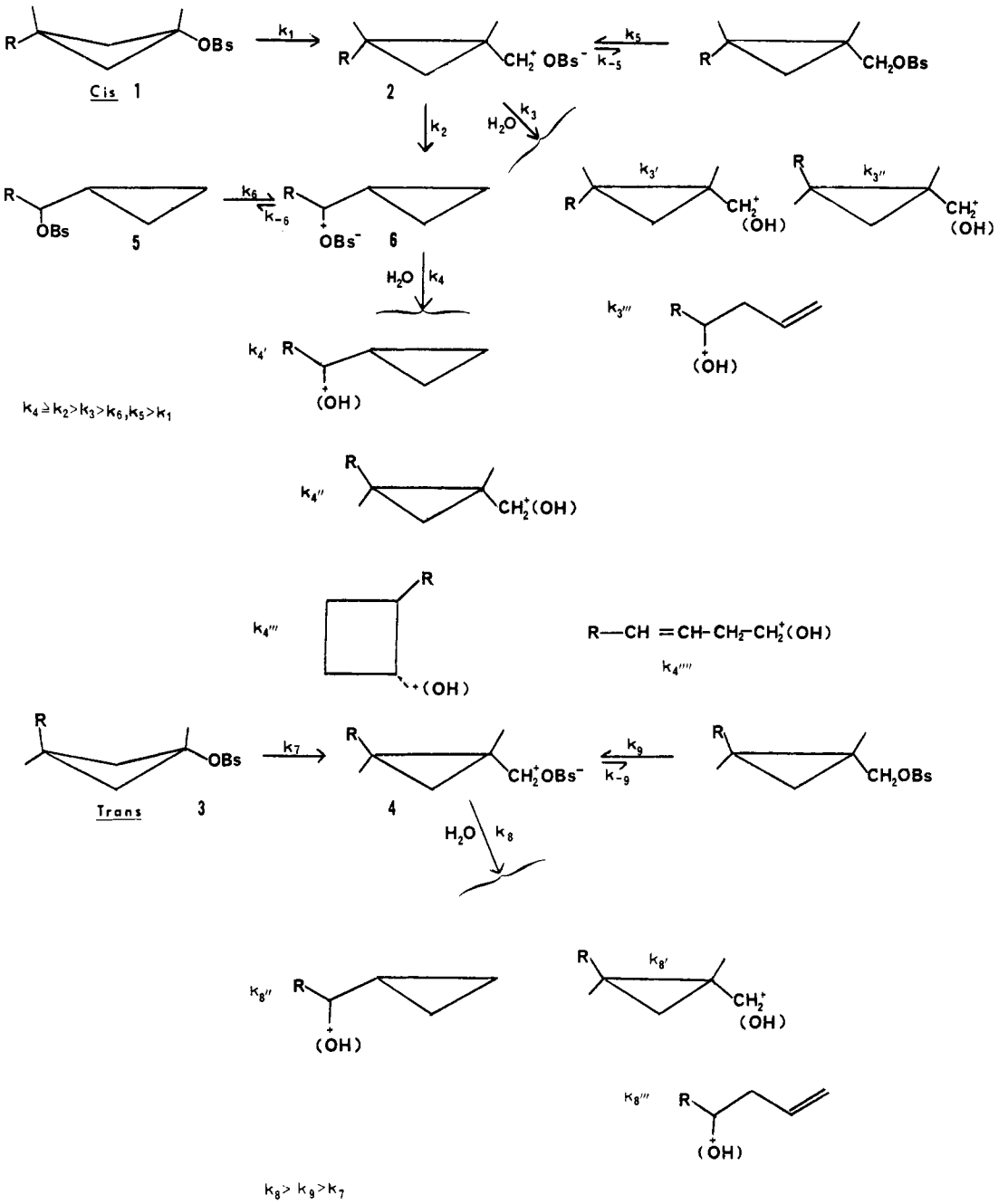
(47) S. Hartman and R. E. Robertson, *Can. J. Chem.*, **38**, 2033 (1960).

(48) The view that the magnitude of the α-deuterium isotope effect in solvolysis depends on the limiting (SN1) or nucleophilic (SN2) character of analogous reactions has been recently confirmed; *cf.* V. J. Shiner, M. W. Rapp, and H. R. Pinnick, Jr., *J. Amer. Chem. Soc.*, **92**, 232 (1970).

(49) Solvolytic data for allylic and homoallylic systems have been discussed; *cf.* ref 37; and M. Hanack and H.-J. Schneider, *Angew. Chem., Int. Ed. Engl.*, **6**, 666 (1967).

(50) The validity of the (2-alkylcyclopropyl)carbinyl and the cyclopropylmethylcarbinyl solvolytic results was confirmed by solvolysis of the corresponding 3,5-dinitrobenzoates. Product ratios did not deviate more than 2–5%, well within the bounds to be expected from change in leaving group and solvolysis conditions (see Experimental Section).

Scheme III[a]



[a] The constants k_3, k_4, and k_8 represent summed rates for competitive solvent capture routes of open carbonium ions: $k_3 = k_3' + k_3'' + k_3'''$; $k_4 = k_4' + k_4'' + k_4''' + k_4''''$; $k_8 = k_8' + k'' + k_8'''$.

(Scheme II) show that this product does not result from a further rearrangement sequence of **4**. It must ensue from direct solvent capture relatively synchronous with the formation of the solvent-separated carbonium ion.

In the cis series, significant differences appear between solvolysis and deamination, and for isopropyl *vs.* methyl substitution. For either substituent the major product of deamination is the cyclopropylalkylcarbinol **11**, while in cyclobutyl solvolysis the major products are **7**, **9**, and **11** for methyl, and only **9** for isopropyl. The early interruption of *cis*-2-isopropylcyclobutyl solvolysis (at *ca.* 1.5 half-lives) permits **11** to be found as the major product, in contrast to **9** at completion.

Solvolysis of cyclopropylmethylcarbinyl esters provides a product composition entirely similar to that obtained from the *cis*-methyl series, with several key distinctions: (1) the virtual absence of (2-alkylcyclopropyl)carbinols; (2) the higher yield of **9**, which is further seen to be progressive in the order 3-methylcyclobutyl < (2-methylcyclopropyl)carbinyl < cyclopropylmethylcarbinyl; and (3) the greatly reduced (by 33%) yield of **7**.

Discussion and Conclusions

Both the rate and product data clearly support the view that the cyclobutyl compounds are indeed the initial point for a sequential rearrangement whose slowest steps are **1** → **2** for the cis and **3** → **4** for the trans isomers. We propose a kinetic outline for this rearrangement in Scheme III. It is concluded that the major solvolytic difference between cis and trans isomers is the presence of a secondary rearrangement step k_2 in

the cis sequence which is absent in the trans sequence. It is also absent in deamination for both isomers. Evidence supporting this conclusion may be gained from comparison of product data.

In the solvolysis of cyclopropylmethylcarbinyl brosylate (**5**) itself, aside from a small amount of other olefinic material, the major rearrangement products are parent carbinol **11**, olefin **9**, and *trans*-2-methylcyclobutanol **17**. These are indeed the products whose presence distinguishes solvolysis in the cis series from trans solvolysis and deamination, and from cis deamination. The relative yields of **9**, **10**, and **17** are greatest in the case of the immediate cyclopropylcarbinyl precursor (**5**), while the relative yield of **7** dwindles sharply. In addition, **13**, whose presence reveals solvent capture of the (2-alkylcyclopropyl)carbinyl intermediate **2**, is almost absent in the latter case. A similar relationship among the products **9**, **10**, and **17** is seen in the comparison of the *cis*-isopropyl solvolyses.

It is thus evident that **7** is a product of (2-alkylcyclopropyl)carbinyl rearrangement, while **9**, **10**, and **17** are products of rearrangement of the secondary intermediate **6**, which does not undergo significant return to **2**. A perfectly analogous relationship can be deduced from the relative yields of **11** for the two sets of *cis*-brosylate precursors. The fact that early interruption of solvolysis of **1** for R = isopropyl gives a much higher ratio of **11** to **9**, **10**, and **17** further supports the identification of the cyclopropylalkylcarbinyl cation **6** as the secondary intermediate.

Implicit in the fact that the relative abundance of products **9**, **10**, and **17** bears a relationship to the immediacy of their ultimate solvolytic precursor is the suggestion that the "age" or openness of the secondary cyclopropylalkylcarbinyl cation **6** will determine the extent of contribution of its own rearrangement routes. When the precursor is the *cis*-cyclobutyl brosylate (two steps removed) the secondary ion pair will be of greatest "age" with respect to initial counterion separation. It will be subject to a greater accumulation of charge density, as the leaving group has had a greater opportunity to withdraw than when the precursor is **2** (one step removed), and therefore more subject to solvent capture. This singular observation logically appears to be significant in explaining the cis differences in solvolysis and deamination.

For k_2 to be important solely in solvolysis, it is likely that the rate process k_1 leads to a relatively intimate ion pair or counterion-shielded carbonium ion version of **2** which can undergo rearrangement k_2 at a rate at least competitive with solvent capture. Alternative solvent-capture routes are summarized as k_3, which is intended to represent collapse of carbonium ion more "open" than **2**.

As in the deamination of deuterated 3-isopropylcyclobutylamine,[15] solvolysis of 3-isopropylcyclobutyl-*1-d* brosylate yields products in which the deuterium is found unscrambled at specific locations (Scheme II). These results substantiate the genesis of products presented in Scheme III. The important cis series cyclopropylisopropylcarbinyl intermediate **6** can arise in only one way by specific rearrangement of its precursor *cis*-(2-isopropylcyclopropyl)carbinyl cation, as indicated by location of deuterium in the respective carbinols. This sequential rearrangement route would appear to specifically exclude such processes as hydride-shift rearrangement[2] or partitioning of bicyclobutonium ions[17] as important sources of product **11D**. Were the latter mechanism in effect, at least 50% of the deuterium would be expected to be found at other ring positions. In addition, the formation of olefinic carbinols **9** and **10** solely *via* a route from cyclopropylalkylcarbinyl cation is confirmed.

Thus, in cis solvolysis, the lifetime of the cyclopropylalkylcarbinyl intermediate **6** is somehow protracted, in contrast to trans solvolysis, or to deamination, to the extent that its own combined rates leading to solvent capture (k_4) compete with k_3. In trans solvolysis, k_7 must lead to an intermediate **4** whose intrinsic proclivity to rearrange *prior* to solvent capture is more limited than that of **2**. None of the rearrangement products of the cyclopropylalkylcarbonium ion are observed in the trans series, then, because the achievement of a steady-state concentration adequate for further transformation at a rate competitive with k_8 is inhibited. The combined rate process k_8 represents solvent capture of relatively open carbonium ions in a manner analogous to k_3.

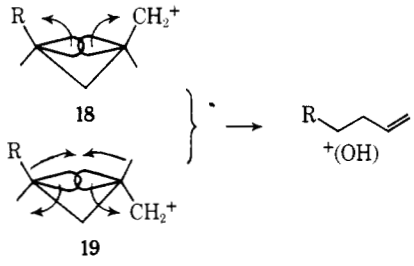
There are several possible reasons apparent for this basic disparity in behavior of the intermediates **2** and **4** in solvolysis, although they cannot be weighted with certainty on the basis of the present data. It is not unexpected that k_2 is a favorable route, since the secondary cyclopropylalkylcarbinyl cation is expected to be a more stable one than the primary (2-alkylcyclopropyl)carbinyl cation of either geometry. It is conceivable, however, that k_2 may be stereochemically more facile for **2** than a similar trans route for **4**, perhaps through the effect of the substituent on orbital rotation accompanying rearrangement.[3] It is also possible that the cis isomer **2** is slightly more energetic due to substituent–hydrogen interactions.[6] Another factor is that intermediate **2** is of higher kinetic energy than **4** because k_1 is smaller than k_7, requiring a larger energy of activation for the cis process, and this additional energy may be transmitted to drive k_2 prior to solvent capture. Finally, counterion separation may be less efficient for **2** than for **4**, due to less effective anchimeric displacement in k_1, resulting in protracted viability in the medium with accompanying rearrangement before continued counterion departure leads to solvolysis.

A clue that the first reason may be significant can be gleaned from observation of the ratio of products **7** to **9** and **10** in the solvolytic series. Bearing in mind that **7** is a product of the (2-alkylcyclopropyl)carbinyl intermediate **2** (**4**), and that **9** and **10** are products of the secondary cyclopropylalkylcarbinyl intermediate **6**, it would appear that the secondary route is more competitive when R = i-C_3H_7 than when R = CH_3. It follows that formation of **7** (k_3''' or k_8''') from either **2** or **4** is facile when R = CH_3 (*i.e.*, $k_3''' \geq k_2$, and $k_8''' > k_8'$) whereas when R = i-C_3H_7, $k_2 > k_3'''$ and $k_8' \gg k_8'''$. The difference in trans reactivity for methyl *vs.* isopropyl *cannot be due entirely to a simple difference in the relative energies of* **4**. If anything, isopropyl-substituted **4** ought to have a higher energy than methyl-substituted **4**, since the former solvolyzes more slowly, although the rate difference reflects too small an energy of activation difference to account for the disparity in formation of **7** in either event. How-

ever, it is the *trans*-methyl homolog which is more easily opened to **7**.

Similar reasoning leads to the conviction that a difference in relative energies alone cannot suffice to explain the differing product ratios of the cis intermediate **2** for the two substituents. It is tempting to ascribe part of the greater solvolytic rearrangement reactivity of **2** as compared to **4** to greater cisoid conformational strain[6] in **2**, aside from the intrinsically greater energy available from route k_1. However, this reasoning begs the question as to why, then, methyl-substituted **2** also rearranges to **7** to a greater extent than isopropyl-substituted **2** prior to occurrence of k_2.[51]

It thus appears that while the hypothesis of a difference in intrinsic energy may initially provide a rationale for the difference in reactivity of **2** and **4** for each substituent, it is inadequate to explain the difference in reactivity between the homologs of **2** and **4**. We suggest that a major difference, *i.e.*, the yield of **7**, may be attributable to a combination of several factors: (1) the carbonium ion precursor of methyl-substituted **7** is stabilized electrically to a greater extent than that of isopropyl-substituted **7**;[52] (2) ring strain energy would normally provide a driving force for formation of olefin **7** from **2** or **4** by routes k_3''' or k_8''' unless the intermediates were otherwise diverted; (3) there is a conformational distinction between the two substituents for the most likely disrotatory ring opening mode,[3] detailed as **18** and **19** for **2** and **4**, respectively. This mode is that which provides maximum conservation of orbital overlap during rearrangement. It should be unopposed for the cis isomer (**18**), but more opposed by R–H repulsive interactions developed for R = i-C_3H_7 than for R = CH_3 in **19** (trans). This suggestion must

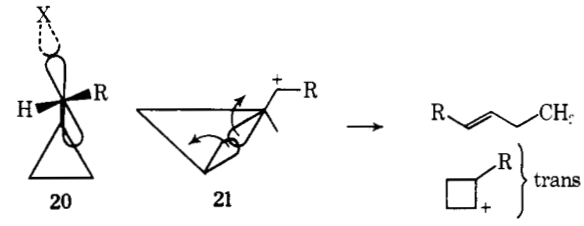


remain speculative at present, however, inasmuch as the cyclopropylcarbinyl–cyclopropylcarbinyl rearrangement has been shown to have a stereochemistry incompatible with a similar disrotatory mode of orbital opening, at least in the case in which the cation is formed from a reaction of bicyclobutane.[13]

(51) This factor, however, may be of unusual significance in the solvolysis of the *tert*-butylcyclobutyl tosylates reported in ref 39, in which a preponderance of terminal olefinic alcohols corresponding to **7** and **8** was obtained in an apparent reversal of the order of alkyl steric effectiveness in forming **7** reported in the present paper. Conformational strain in the *cis*-2-*tert*-butylcyclopropylcarbinyl intermediate may weaken the C_1–C_2 bond to an unusual degree, permitting ring-opening collapse of this intermediate to take priority over alternative route sequence k_2–k_4. This explanation seems to be borne out by the absence of several products of collapse of the cyclopropylalkylcarbinyl intermediate **6** in the *tert*-butyl solvolysis (*viz.* those corresponding to **17** and **9**, while that corresponding to **10** was quite low in yield), implying that its effective concentration must be less than in the other cases reported here. The potent conformational effect of the *tert*-butyl group in this system is also notable in the deamination of 3-*tert*-butylcyclobutylamine reported in ref 36.

(52) This suggestion is formally analogous to the suggestion of Roberts and coworkers (*cf.* ref 17) that bicyclobutonium ion intermediates are subject to preferential electrical stabilization.

A second significant product difference is the relative ratio of **9** and **10** to **11** for R = CH_3 *vs.* R = i-C_3H_7 in solvolysis. It appears at first glance that conversion of the secondary cyclopropylalkylcarbinyl intermediate **6** to **9** and **10** (k_4'''') is more favored for the isopropyl than for the methyl case. This is in part deceptive, and can be partially attributed instead to a higher rate of competitive diversion of **2** to **7** *via* k_3''' when R = CH_3, as described above. However, a steric rationale may also be suggested. A predilection for the most stable conformation for the secondary intermediate **20** (top view), in which bulky leaving group X still shields the carbinyl carbon (which places R at a maximum distance from ring protons), is more likely for the isopropyl case. This conformer corresponds to the most favorable orientation for linear overlap accompanying disrotatory orbital opening mode **21**, which would give products of indicated stereochemistry only.[53]



A scrutiny of the major distinctions between deamination and solvolysis discloses that, at least in the cis series, the kinetic course of deamination appears to be shorter in sequence (Scheme III). The products of route k_4 are absent for the cis homologs, while a heightened degree of solvent trapping of the ostensible precursor is reflected in greatly increased yields of **11** in deamination. No such sharp differences can be discerned in the trans series, where product ratios in the two reactions are much more similar. The key distinction between deamination and solvolysis again appears to be the relative significance of route k_2, which is thus concluded to be absent in cis deamination.

We suggest that this distinction may be caused by the different structural environment encountered by the secondary cyclopropylalkylcarbinyl cation in the two types of reactions. Solvation of the carbonium ion is expected to be more important at an earlier kinetic juncture in deamination, where the separation of the solvated gegenion is increased by the "hole" left by the departing nitrogen molecule.[54,55] The significance of this ion-pair phenomenon in water (in which the present deamination results have been obtained) has been recently demonstrated.[54] The participation of ion pairs in the deamination process in nonaqueous solvents has previously been known to play an important role in product determination.[56–58]

(53) An examination of models discloses that stereospecificity of products (including **17**) derived from **21** results from attack by solvent (*i.e.*, water) in an equatorial plane backside to the breaking bond of the cyclopropylcarbinyl carbon atom which is to become the carbinol carbon. An alternate mode of disrotatory ring opening to yield these products would give *cis*-2-alkylcyclobutanol (*cis*- **17**), which was not found. Although cis olefinic carbinol **10** was found, it may thus result from inversion of some trans ionic intermediate.

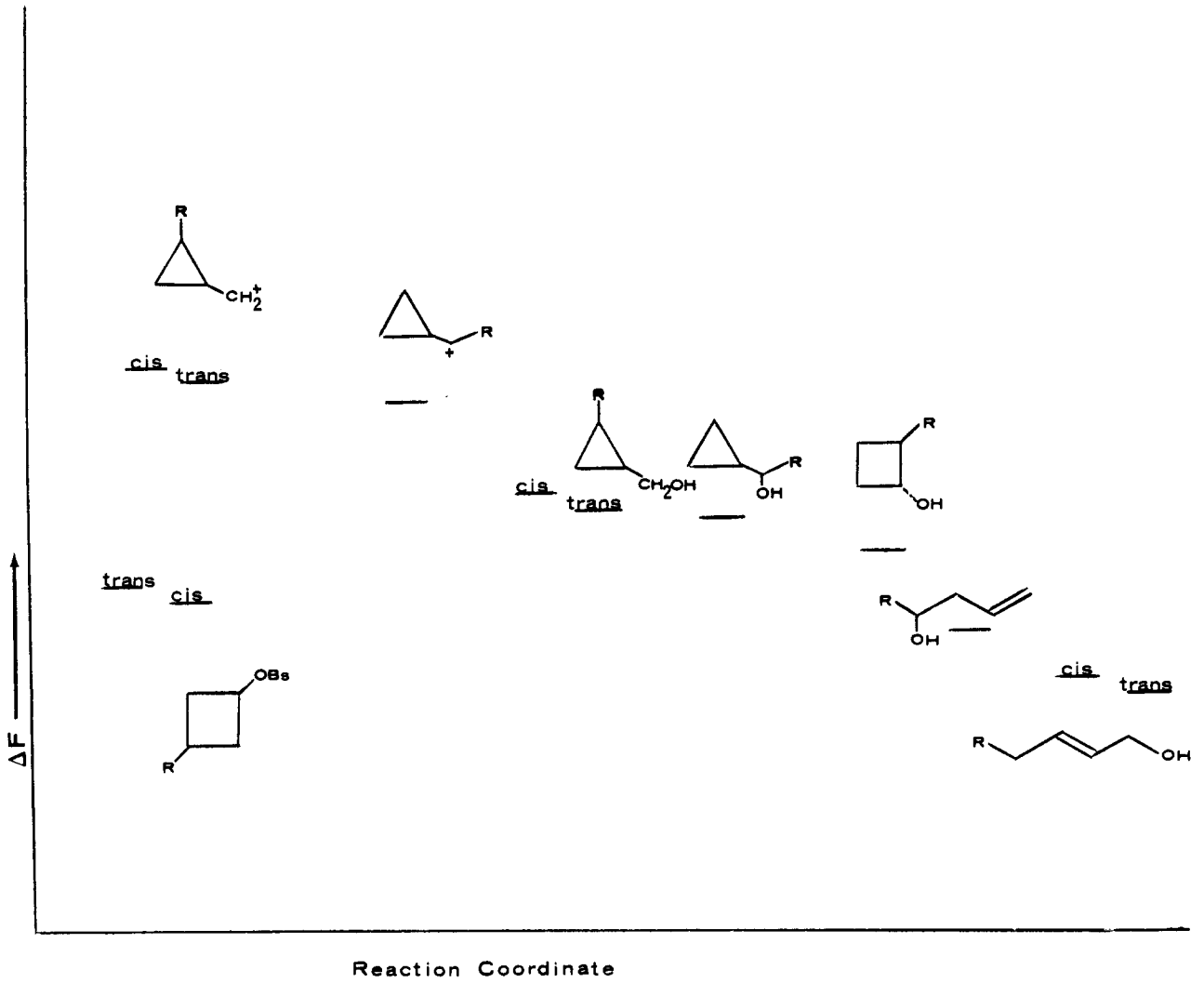
(54) R. A. Moss, D. W. Reger, and E. M. Emery, *J. Amer. Chem. Soc.*, **92**, 1366 (1970).

(55) E. H. White and C. A. Elliger, *ibid.*, **89**, 165 (1967).

(56) T. Cohen and A. R. Daniewski, *ibid.*, **91**, 533 (1969).

(57) J. H. Bayless, A. T. Jurewicz, and L. Friedman, *ibid.*, **90**, 4466 (1968).

Scheme IV



Were counterion separation advanced to a further degree in deamination, the enhanced consequence of abortive solvent capture of the secondary intermediate would be an expected outcome. The deamination of cyclopropylmethylcarbinylamine has been reported to proceed with no rearrangement.[59] Since this result differs so markedly from the present solvolytic results, it is apparent that in deamination, rapid solvent capture has superseded anchimerically assisted rearrangement to a very high degree. We find this supportive of the inference that the lifetime of the secondary cyclopropylalkylcarbinyl cationic intermediate is curtailed in deamination, and protracted in cis solvolysis. The present conclusion that carbonium ion–solvation shell interaction at a critical kinetic stage may preclude further rearrangement is not qualitatively different from the consequences of the Streitwieser hypothesis,[60] which proposes that carbonium ions from deamination require a lower energy of activation for possible reaction pathways than those produced as a result of solvolysis.

The direction of sequential product transformation in cyclobutyl solvolysis is such as to provide thermodynamic relief of ring strain *via* a stepwise decrease in the energies of the intermediate carbonium ions by irreversible solvent capture, which becomes more significant as the carbonium ion becomes more open. This is particularly evident from the comparison of deamination *vs.* solvolysis. The energy relationships among the various products are illustrated in Scheme IV.[49] The homoallylic alcohols possess the lowest energy of the possible products due to relief of ring bond-angle strain and optimum thermodynamic stabilization. Thus both cyclobutyl and cyclopropylcarbinyl precursors, irrespective of special stabilizing influences, would tend to form olefinic alcohols in the absence of other factors. The major such factor is the facility with which orbital overlap assistance to ionization or charge dispersal in any precursor leads to rearrangement product with more open carbonium ion character, which can then be more rapidly trapped by solvent.

The present results augment the data which indicate that the steric effect of the substituent on these processes is a potent factor in product and rate determination.

Experimental Section

Kinetic Measurements. The reaction solvent, 70% aqueous acetone (v/v), was prepared by admixing a stock solution of 70 parts of acetone (chromatographic grade, distilled from permanganate) to 30 parts of "conductivity" water, by volume. The solvent had an observed conductance of *ca.* 2×10^5 ohm^{-1} at 41.1°. Rates were

(58) E. H. White, H. Maskill, D. J. Woodcock, and M. A. Shroeder, *Tetrahedron Lett.*, 1713 (1969).
(59) M. Vogel and J. D. Roberts, *J. Amer. Chem. Soc.*, **88**, 2262 (1966).
(60) A. Streitwieser, *J. Org. Chem.*, **22**, 861 (1957).

obtained conductometrically, employing 25–35-mg samples in 20 ml of solvent per run. A General Radio Model 1650-A impedance bridge operating at 1000 cps was used to measure resistance of the solvolysis solutions. Deflection was optimized by the use of a variable capacitor in the circuit. The cell employed was a simple glass conductivity cell having platinum black electrodes, with a cell constant of 1.0. The cell was immersed as far as possible in a circulating constant temperature bath, the temperature of which was controlled to ±0.05° by means of a Roto-Stat thermal actuator. A predetermined volume (20 ml) of solvent was run into the clean cell and allowed to reach thermal equilibrium, and the compound added all at once. After it was dissolved by rapid swirling,the clock was started, and readings were taken at equal time intervals. First-order rate constants were obtained from the slopes of the straight lines resulting when alternate values of conductances obtained at equal time intervals were plotted against each other[61] by application of the relationship $k = 2.303/\Delta t$ log slope. The slopes were obtained by computer least-squares analysis of the plot points. In all cases, rate constants are the averages of at least two or three runs at each temperature. For each of the compounds examined, solvolysis was carried out to maximum completion (*i.e.*, that point at which changes in conductance with time became negligible) to ensure linearity of the plots; all runs were plotted graphically. Runs used to obtain rate constants were completed to the extent of five half-lives. Solvolysis of each deuterated brosylate to the same extent revealed no deviation from linearity which could be attributed to isomeric contamination. Conductance measurements carried out with toluenesulfonic acid in the ranges of interest showed a linear variation with concentration. Tests with several solutions showed no important resistance changes upon standing for a period of several days.

Solvolyses. Analytical and preparative solvolyses of the brosylates were carried out at reflux (56°) in a solvent composed of 70 parts of acetone to 30 parts of aqueous buffer (Mallinckrodt BuffAR, pH 7.0). Reaction time was determined by the half-life for solvolysis ($t_{1/2} = 0.6933/k$), and was in all cases carried out to completion (*i.e.*, at least ten half-lives), with the exception of the 3-hr solvolysis for *cis*-3-isopropylcyclobutyl brosylate reported in Table II. Solvent was concentrated at reduced pressure, diluted with water, saturated with salt, and extracted with ether. Ether extracts were dried and concentrated for vpc analysis. For analytical purposes, it was found convenient to employ *ca.* 100 mg of brosylate in 10 ml of solvent. As a check on possible concentration effects, one run each for both the *cis*- and *trans*-3-isopropylcyclobutyl brosylates at the kinetic concentration of 130 mg/100 ml showed no important variations. For preparative purposes, up to several grams of brosylate in correspondingly larger volumes of solvent were used; again product ratios remained essentially constant. The stability of key products **7**, **8**, **9**, **10**, **11**, **13**, **14**, **16**, and **17** toward rearrangement in the solvolysis medium was demonstrated by nmr examination of samples subjected to reflux in the buffered solvent. Aliquots withdrawn for periods of up to 10 hr reflux time showed no perceptible changes. Because of their much slower solvolysis rates,[18] the cyclopropylcarbinyl 3,5-dinitrobenzoates were handled in different fashion: 0.1 *M* solutions were placed in glass tubes which were sealed and placed in an oven maintained at 100° for 10 days. Two runs for each ester were carried out, with results cited in ref 50.

Analyses. Vpc analyses and isolations were carried out with the F & M Model 700 vapor phase chromatograph. Columns employed were 30 ft × 0.25 in., and were packed with either 5% Igepal CO990 (Applied Science Laboratories) or 10% Ucon Polar on Chromosorb W. Helium flowrates averaged 50 ml/min, and column oven temperatures varied from 85 to 140°. Data for the separation of products for the 3-isopropylcyclobutyl solvolysis on the CO990 column is given as a typical example of retention time differences (minutes, $T = 85°$): 2-methyl-5-hexen-2-ol (**8**), 26.3; 2-methyl-5-hexen-3-ol (**7**), 27.4; cyclopropylmethyldimethylcarbinol (**12**), 27.6; cyclopropylisopropylcarbinol (**11**), 37.9; *trans*-2-isopropylcyclopropylcarbinol (**14**), 52.4; *trans*-2-isopropylcyclobutanol (**17**), 56.1; *trans*-5-methyl-3-hexen-1-ol (**9**), 61.2; *cis*-2-isopropylcyclopropylcarbinol (**13**), 64.4; *cis*-5-methyl-3-hexen-1-ol (**10**), 69.0; *cis*-3-isopropylcyclobutanol (**15**), 71.4; *trans*-3-isopropylcyclobutanol (**16**), 74.5. It was found possible to separate the majority of products encountered in this study by simple repetitive injections of 50–100 μl to a degree of purity sufficient for further analysis and identification. Instances of peak contamination for the more difficultly separable compounds were readily resolved by reinjection.

Identification of peaks isolated from vpc was accomplished by nmr analysis and elemental analysis in some cases. Compounds **7**, **11**, **15**, and **16** have been fully described elsewhere,[2,3] as have been compounds **9** and **10**.[19] Compound **8** was obtained commercially. Compounds **13** and **14** have been described for both the isopropyl[2] and methyl[3,17] substituents; an improved synthesis for R = *i*-C_3H_7 is given below. Compound **12**, obtained only in the isopropyl case, was not separately synthesized, but its identification from elemental analysis and nmr is unambiguous: nmr (CCl_4) 0.29–0.58 (multiplet, 5 H), 1.14 (sharp singlet, 6 H), 1.24–1.40 (doublet, 2 H), 2.80 (singlet, OH). *Anal.* Calcd for $C_7H_{14}O$: C, 73.63; H, 12.36. Found: C, 73.61; H, 12.52. Compound **17** has been prepared previously as an isomeric mixture for R = CH_3.[17] Configuration is assigned on the basis of the chemical shift for the proton geminal to OH; it is 3.5 ppm for the trans isomer. This proton is axial, and is at higher field than the equatorial proton geminal to OH in the cis isomer. The difference in chemical shift is analogous to that encountered in the isomeric 3-alkylcyclobutanols, where the axial proton geminal to OH in the cis isomer is at higher field than the corresponding equatorial proton in the trans isomer:[16] nmr (CCl_4) 0.88–1.20 (doublet, CH_3 and tertiary H), 1.37–2.35 (multiplet, 4 H), 3.50 (center of quintet, 1 H), 4.10 (singlet, OH). For R = *i*-C_3H_7, **17** was not synthesized, but readily identified by analogy with the methyl compound: nmr (CCl_4) 0.70–1.02 (doublet, 6 H, and multiplet, 2 H), 1.35–2.35 (multiplet, 4 H), 3.45 (center of quintet, 1 H), 4.0 (singlet, OH). *Anal.* Calcd for $C_7H_{14}O$: C, 73.63; H, 12.36. Found: C, 73.76; H, 12.20.

While compounds **15** and **16** have been reported for R = CH_3,[3] nmr spectra are here given for the first time: cis (**15**) (pyridine) 0.80–1.05 (doublet, 3 H), 1.20–1.85 (overlapped multiplets, 3 H), 1.85–2.58 (multiplet, 2 H), 3.83–4.47 (multiplet, 1 H), 4.74 (singlet, OH); trans 0.80–1.01 (doublet, 3 H), 1.40–2.50 (multiplet, 5 H), 4.25–4.83 (multiplet, 1 H), 5.00 (singlet, OH).

Analysis of deuterium-containing compounds was made by repeated integration of relatively large samples whose purity was evident from vpc analysis of isolated peaks. It is estimated that this procedure had an error of not more than ±2% in reproducibility. In product **7D**, the appearance and integration of the vinyl region clearly showed that only an internal vinyl proton had been replaced by d. In each of the cyclopropylcarbinols, the integrated value for the cyclopropane protons, carefully compared with undeuterated reference spectra, showed replacement of solely a single cyclopropyl proton. This was verified by the simplification of the splitting pattern for the proton geminal to OH for each case. For the 2-isopropyl isomers, this signal was simplified to a simple singlet; for **11**, the signal was simplified from an ABX quartet (J = 5.5, 7) to a simple doublet (J = 7).[15] For products **9D** and **10D**, deuterium location was very readily discerned from comparison of the vinyl proton pattern and integral value with reference spectra. For each isomer, the simplification of the splitting pattern for methylene protons on C_2 verified this deduction. For product **15**, the singular location of deuterium geminal to OH was seen from the disappearance of the signal for that proton, which is isolated from others in the spectrum, without otherwise affecting other integral values, but with considerable simplification of ring proton resonances.

Preparation of Brosylates. With the exception of the cyclopropylcarbinyl brosylates, the conventional pyridine method was employed. An illustration will suffice. *cis*-3-Methylcyclobutanol (0.749 g, 8.7 mmol) was dissolved in 20 ml of dry pyridine and the solution chilled in an ice bath. *p*-Bromobenzenesulfonyl chloride (4.6 g, 18.0 mmol) was added at once with swirling. After solution was achieved, the container was stored in the refrigerator for 2 days, the product poured into ice–water, and this extracted several times with ether. The ether was washed with cold dilute HCl, then saturated $NaHCO_3$ solution, and finally dried with magnesium sulfate. The ether solution was concentrated by gentle heating on a steam bath in a stream of nitrogen. The residue was further chilled to effect solidification, and was then recrystallized several times from dry pentane.

In the case of brosylates which would not crystallize despite prolonged efforts, purification was achieved by rapid passage of pentane solution over a short column of neutral alumina. This method was employed with the cyclopropylcarbinyl as well as the olefinic brosylates.

In the case of the cyclopropylcarbinols, repeated efforts to prepare brosylates by the above method failed. However, when triethylamine was substituted for pyridine, a poor yield of product resulted.

(61) E. A. Guggenheim, *Phil. Mag.*, **2**, 538 (1926).

Table III. Analytical Data for Solvolysis Materials

Compd	% yield	Mp, °C	Nmr	Calcd, % C	Calcd, % H	Found, % C	Found, % H
Cyclobutyl brosylate	73	52–53.5	1.05–2.47 (multiplet, 6 H), 4.50–5.05 (quintet, 1 H, centered at 4.78), 7.78 (singlet, 4 H)	41.26[a]	3.80	41.46	3.93
cis-3-Isopropylcyclobutyl brosylate	83	51.5–52.5	0.63–0.85 (doublet, 6 H), 1.20–2.50 (multiplet, 6 H), 4.32–4.81 (quintet, 1 H), 7.59 (singlet, 5 H)	46.86[b]	5.14	46.88	5.01
trans-3-Isopropylcyclobutyl brosylate	81	59–60	0.63–0.87 (doublet, 6 H), 1.15–1.55 (multiplet, 2 H), 1.95–2.17 (multiplet, 4 H), 4.55–4.95 (multiplet, 1 H), 7.55 (singlet, 4 H)			47.01	4.93
cis-3-Methylcyclobutyl brosylate	78	41.5–42.5	0.91–1.16 (doublet, 3 H), 1.53–2.52 (multiplet, 5 H), 4.30–4.80 (quintet, 1 H), 7.71 (singlet, 4 H)	43.30[c]	4.29	43.55	4.52
trans-3-Methylcyclobutyl brosylate	72	51–52	1.02–1.18 (doublet, 3 H), 1.67–2.51 (multiplet, 5 H), 4.68–5.13 (multiplet, 1 H), 7.72 (singlet, 4 H)			43.46	4.10
cis-3-Isopropylcyclobutyl-*1-d* brosylate	88	50.5–51.5	0.68–0.92 (doublet, 6 H), 1.15–2.53 (multiplet, 6 H), 7.72 (singlet, 4 H)	46.72[d]	5.43	46.85	5.85
trans-3-Isopropylcyclobutyl-*1-d* brosylate	59	58.5–60	0.69–0.96 (doublet, 6 H), 1.16–1.83 (multiplet, 2 H), 2.17 (singlet, 4 H), 7.72 (singlet, 4 H)			46.90	5.37
cis-(2-Isopropylcyclopropyl)-carbinyl brosylate		Oil	0.42–0.90 (multiplet, 2 H), 0.95–1.15 (doublet, 9 H), 4.10–4.51 (multiplet, 2 H), 7.75 (singlet, 4 H)				
trans-(2-Isopropylcyclopropyl)-carbinyl brosylate		Oil	0.40–0.68 (multiplet, 3 H), 0.80–1.28 (multiplet, 2 H), overlapped by strong singlet at 1.10, 6 H), 3.90–4.15 (triplet, 2 H), 7.80 (singlet, 4 H)				
cis-(2-Methylcyclopropyl)-carbinyl brosylate		Oil	0.50–1.45 (multiplet, overlapped by strong singlet at 1.35, 7 H), 4.08–4.46 (multiplet, 2 H), 7.78 (singlet, 4 H)				
trans-(2-Methylcyclopropyl)-carbinyl brosylate		Oil	0.30–1.05 (multiplet, 3 H), 1.10–1.25 (doublet, 4 H), 3.92–4.15 (multiplet, 2 H), 7.78 (singlet, 4 H)				
Cyclopropylmethylcarbinyl brosylate		Oil	0.10–0.51 (multiplet, 4 H), 0.52–1.10 (multiplet, 1 H), 1.12–1.28 (doublet, 3 H), 3.80–4.13 (multiplet, 1 H), 7.73 (singlet, 4 H)				
cis-(2-Isopropylcyclopropyl)-carbinyl 3,5-dinitrobenzoate	92	53.5–54.5	0.34–0.83 (multiplet, 2 H), 0.94–1.12 (doublet, 9 H), 4.32–4.56 (multiplet, 2 H), 9.18 (singlet, 3 H)	54.54[e]	5.23	54.73	4.98
trans-(2-Isopropylcyclopropyl)-carbinyl 3,5-dinitrobenzoate	89	65–66.5	0.44–0.75 (multiplet, 3 H), 0.80–1.31 (multiplet, 2 H, overlapped by strong singlet at 1.00, 6 H), 4.32–4.56 (multiplet, 2 H), 9.18 (singlet, 3 H)			54.50	5.06

[a] Calcd for $C_{10}H_{11}BrSO_3$. [b] Calcd for $C_{13}H_{17}BrSO_3$. [c] Calcd for $C_{11}H_{13}BrSO_3$. [d] Calcd for $C_{13}H_{16}DBrSO_3$. [e] Calcd for $C_{14}H_{16}O_6N_2$.

The initial procedure was the same, with the exception that the reaction mixtures were kept for several hours at room temperature prior to storage in the refrigerator. After 2 days of storage, the triethylamine solutions were poured into ice-cold solutions of dilute aqueous HCl which were vigorously stirred until all base was dissolved, and the resultant solution, slightly acid to pH paper, was extracted with ether which was then treated in the usual fashion.

(2-Isopropylcyclopropyl)carbinol. The procedure followed was that of Van Dine.[18] 3-Methylbutene (70 g, 1 mol) was added to 250 ml of dry hexane containing 4 g of anhydrous copper sulfate. The mixture was refluxed gently, using a water condenser and Dry Ice condenser in series, and ethyl diazoacetate (57 g, 0.5 mol) was added dropwise with stirring. After the commencement of reaction, as seen from the color change, external heating was discontinued, and addition continued. The mixture was refluxed overnight after addition was completed, filtered, and concentrated at aspirator pressure. Distillation of the residual liquid afforded 19.0 g (24.4%) of ethyl 2-isopropylcyclopropanecarboxylate, bp 79–84° (18 mm). Vpc analysis showed two peaks in the ratio of about 1:3. Isolation of the peaks revealed that these were, respectively, the trans and cis isomers:[18] nmr ($CDCl_3$) cis 0.55–1.50 (multiplet, overlapping peaks, 14 H, including strong multiplet at 0.88–1.06), 3.86–4.25 (methylene quartet, 2 H); trans 0.78–1.80 (multiplet, overlapping peaks, 14 H, including strong singlet at 0.98), 3.9–4.25 (methylene quartet, 2 H).

The ester (8.5 g, 0.054 mol) was reduced with 2.3 g (0.06 mol) of lithium aluminum hydride in conventional fashion. (2-Isopropylcyclopropyl)carbinol (5.1 g, 89.5%) was distilled at 74–75° (18 mm). Vpc showed two peaks in the same ratio as the precursor ester. The nmr spectra of the two isolated isomers[2] differed primarily in the high field cyclopropyl region and in the splitting pattern of the protons geminal to OH. The latter were at higher field for the trans isomer, and appeared as an A_2X doublet, while they were evident as an ABX multiplet for the cis isomer. *cis*-Cyclopropyl protons were also at lower field, and merged with the overlapping isopropyl singlet and methinyl proton resonances. The prominent cyclopropyl resonance centered at about 0.3 ppm for the trans isomer was more diffuse and at lower field for the cis.

The cis and trans isomers of (2-methylcyclopropyl)carbinol differed in an analogous fashion; their nmr spectra are given here: (pyridine) cis 0.42–1.27 (multiplet, 7 H, including strong singlet at 1.10), 3.62–3.94 (quartet, 2 H), 4.53 (singlet, OH); trans 0.16–0.91 (multiplet, 3 H), 0.92–1.10 (doublet, 4 H, J = 3.5 Hz), 3.53–3.78 (triplet, centered at 3.64, 2 H), 4.46 (singlet, OH).

3-Isopropylcyclobutanone. 3-Isopropylcyclobutanol (11.7 g, 0.102 mol) was placed in 600 ml of dry benzene along with 45 g of benzoquinone and 17 g of aluminum isopropoxide.[62] The mixture was refluxed 1 hr and allowed to stand overnight. It was then

(62) A. C. Cope, M. R. Kintner, and R. J. Keller, *J. Amer. Chem. Soc.*, **76**, 2757 (1954).

refluxed another hour, cooled, and washed thoroughly with 1 l. of 5% HCl. The benzene layer was then washed successively with three 700-ml solutions of 5% NaOH followed by water, and dried over sodium sulfate. The benzene was distilled, and the residue distilled at a range of 75–94° (18 mm). Vpc analysis revealed the presence of alcohol contaminant, and a pentane solution of the product was passed once through a column of acid-washed alumina for purification. After evaporation of the pentane, the resultant ketone (8.6 g, 75.4%) was pure by vpc and nmr standards: nmr (CCl_4) 0.86–1.04 (doublet, 6 H), 1.32–3.23 (multiplet, 6 H). *Anal.* Calcd for $C_7H_{12}O$: C, 75.95; H, 10.78. Found: C, 76.20; H, 10.57.

***cis*-3-Isopropylcyclobutanol-*1*-*d*.** 3-Isopropylcyclobutanone (3.59 g, 0.032 mol) was reduced with 0.7 g (0.167 mol) of lithium aluminum deuteride, to yield 3.35 g (92.4%) of deuterated alcohol after distillation (bp 64–67° (17 mm)). Vpc analysis revealed it to be better than 96% cis isomer. The brosylate (see Table III) was prepared directly from this product and after several recrystallizations gave excellent analytical data.

***trans*-3-Isopropylcyclobutanol-*1*-*d*.** *cis*-Brosylate (4.0 g, 0.012 mol) was refluxed in dry acetone with 6 g (excess) of freshly prepared, dry tetramethylammonium acetate for 20 hr. The precipitated tetramethylammonium brosylate was filtered, and the solution concentrated by distillation. The residual liquid was poured into water and extracted with ether. The ether was dried and evaporated, and the remaining acetate was hydrolyzed by reflux with aqueous KOH for several hours. The resultant alcohol was isolated by ether extraction. After evaporation of solvent, it weighed 0.92 g (67.2%), and was shown to be substantially pure trans isomer by vpc and nmr. This product was used for direct conversion to brosylate, which gave good analytical data (Table III) after several recrystallizations. Both brosylates exhibited sharp melting points which were depressed on admixture, and showed isomeric purity by nmr.

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Lithium Salt Catalyzed Epoxide–Carbonyl Rearrangement. I. Alkyl-Substituted Epoxides[1]

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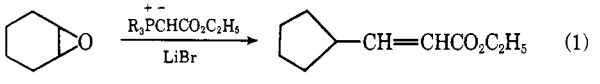
Abstract: Lithium bromide is solubilized in benzene by the addition of an equivalent amount of hexamethylphosphoramide (HMPA) or other phosphine oxide. The resultant complex is an efficient catalyst for the rearrangement of epoxides to aldehydes and/or ketones. The addition of a second equivalent of HMPA quenches this catalytic activity. Evidence is presented which supports a mechanism involving the lithium salt of the bromohydrin as an intermediate in the LiBr-catalyzed rearrangement. Lithium perchlorate is partially solubilized in benzene by epoxides and effects the rapid rearrangement of those systems involving a tertiary center in the oxirane ring. Combined kinetic and product analyses for cyclohexene, 1-methylcyclohexene, and 1,2-dimethylcyclohexene oxides show that the $LiClO_4$-catalyzed reaction occurs by a different mechanism, presumably involving a carbonium ion. This mechanistic dichotomy allows flexibility in choosing the product of rearrangement and enhances the synthetic utility of the reaction. Kinetic data and product analyses are presented for a number of simple cyclic and acyclic epoxides, illustrating the scope and limitations of the reaction.

In an attempt to prepare substituted carbethoxycyclopropanes by the reaction of stabilized ylides with epoxides,[4] we observed instead the formation of acrylic esters,[5] as exemplified by eq 1. This result was most



(1)

easily rationalized in terms of rearrangement of the epoxide to a carbonyl compound (*e.g.*, cyclopentanecarboxaldehyde in eq 1) with subsequent Wittig reaction with the ylide to give the observed product. Initial attempts to demonstrate the intermediacy of the carbonyl compound were unsuccessful,[5] however, and led instead to a number of unexplained experimental observations: (a) the reaction occurred readily with tri-*n*-butylcarbethoxymethylidenephosphorane, this reagent being prepared from the corresponding bromide salt by reaction with butyllithium; (b) no reaction was observed under the same conditions using the analogous triphenyl ylide, which was free of salt contaminants; (c) added lithium chloride had no effect on the reaction; (d) cyclopentene oxide gave cyclopropane product rather than acrylic ester.

Results and Discussion

Tri-*n*-butylcarbethoxymethylidenephosphorane is relatively unstable to water, and consequently the usual aqueous procedure for forming the analogous triphenyl ylide is unsuitable for generation of the aliphatic phosphorane. However, by using the procedure of Payne,[6] we were able to obtain a benzene solution of this ylide which gave a negative halide test; although this mate-

(1) A part of this work has been described in a preliminary communication: B. Rickborn and R. M. Gerkin, *J. Amer. Chem. Soc.*, **90**, 4193 (1968).
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