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NONPLANAR CYCLOBUTANE. SOLVOLYSIS OF CIS- AND TRANS-3-ISOPROPYLCYCLOBUTYL BROSYLATE.

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The interconvertibility and high rates of solvolysis of cyclopropylcarbinyl and cyclobutyl derivatives have led to consideration of common bicyclobutonium intermediates (1,2). More recently, evidence has been obtained which supports an essentially unrearranged cyclopropylcarbinyl cation in some cases deriving from cyclopropylcarbinyl derivatives (3-6). In work related to the general problem of mechanistic pathway in this system, we have observed that the deamination of the isomeric 3-isopropylcyclobutylamines results in a difference in product array which is consistent with conformational control of concerted processes involving localized-charge intermediates (7). We have further studied the solvolysis of the corresponding brosylates in aqueous acetone, and wish to report a small rate factor of 6.4 in favor of the trans isomer, with product distribution differing in a manner reminiscent of the deamination.

Cis and trans alcohols isolated from a synthetic mixture of 3-isopropylcyclobutanol by preparative vpc had an isomeric purity of better than 95%, and were converted to brosylates by conventional treatment with brosyl chloride in pyridine. After recrystallization to constant mp, purity of the esters was established by nmr, which also eliminated the possibility of rearrangement during preparation. The proton geminal to the ester group is centered at 4.55 ppm for the cis and 4.77 for the trans isomer, and shows different line patterns (60 MHz), enabling ready differentiation. Other cis-trans spectral differences are similar to those of the parent alcohols (8).

Table I presents pertinent kinetic data, while Table II shows the product distribution; the differences are evident. Whereas the trans brosylate reacts in

TABLE I

Rate Constants for Solvolysis, Aqueous Acetone[a]

Ester	MP[b] °C	Temp, °C	%Acetone	k x 10^4, sec^{-1}	$\Delta H^{\ddagger}$, kcal/mole	$\Delta S^{\ddagger}$, eu
Cyclohexyl Tosylate	46-46.5	41.1	70	0.0372		
Exo-Norbornyl Tosylate	57.5[c] 58.5	41.1	70	12.50	21.3	-8.9
		31.7	70	4.24		
Trans-3-Isopropyl-cyclobutyl Brosylate	59-60	41.1	70	2.14	23.5	-0.7
		31.7	70	0.650		
		31.7	90	0.345		
Cis-3-Isopropyl-cyclobutyl Brosylate	51.5-52.5	41.1	70	0.335	25.4	+0.8
		50.6	70	0.902		

[a]Rates were determined conductimetrically, and rate constants obtained from the slopes of least-squares treatment of the plot of alternate conductances against each other. Values are the means of two runs.

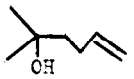
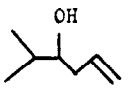
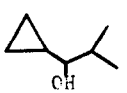
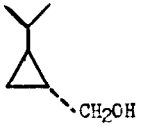
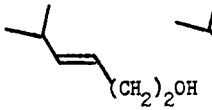
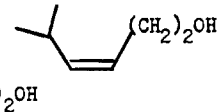
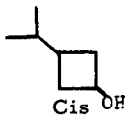
[b]Mps were determined on an electrically-heated block with a heating rate of 1 degree/minute, and are uncorrected.

[c]Reported mp: 53.7-54.6°; P. von R. Schleyer, M. M. Donaldson and W. E. Watts, J. Am. Chem. Soc., 87, 375 (1965).

a relatively straightforward fashion to produce stereoselectively as major product trans-(2-isopropyl)cyclopropylcarbinol (the major product of the trans deamination), the cis brosylate reacts in a highly complex way. If this solvolysis is interrupted in its early stages (e.g., 10-20% completion), the major product is the same as in the deamination: isopropylcyclopropylcarbinol (kinetically-favored). However, this product is negligible as the reaction goes to completion, being supplanted by a preponderance of trans-5-methyl-3-hexen-1-ol. That this was not a rearrangement product of isopropylcyclopropylcarbinol was shown when the latter survived reflux in the solvent medium. It is considered likely that internal return intermediate 2-isopropylcyclobutyl brosylate is involved; the presence of the corresponding isomeric alcohols as a contaminant of the vpc fraction of 5 is strongly supported by nmr study of numerous isolations. The possibility of 2 brosylate as an intermediate was tested; however solvolysis of this compound in

TABLE II

Products of Preparative Solvolysis, % Distribution[a]

Brosylate	Reflux In	 1	 2	 3	 Trans 4	 Trans 5	 Cis 6	d 7	 Cis 8
Cis	70% Acetone,3hr * b	4.2	4.7	31.3	5.0	5.4	13.6	22.1	13.6
	70% Acetone,15 hr *	4.6	17.2	2.8	4.9	40-50[c]	6.1	8.7	5.7
Trans	70% Acetone,3hr	1.5	6.0	26.5	66.0				
	70% Acetone,3hr *	1.1	2.6	15.8	80.5				
	90% Acetone,3hr *	1.7	9.7	10.6	78.0				

*Buffered; solvent prepared from Mallinckrodt "BuffAR" of pH 7.00.

[a]Product analysis tallied with that from kinetic runs.

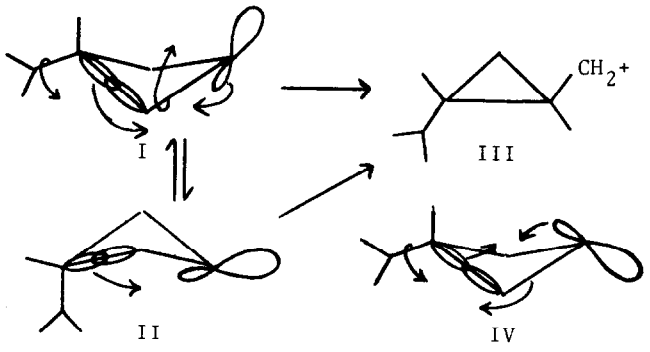
[b]Product distribution was about the same for the same length of time in unbuffered 70% acetone.

[c]Believed to contain approximately 10% 2-isopropylcyclobutanol.

[d]This compound is definitively identified as an alkyl-substituted cyclopropylcarbinol; however the nmr spectrum is such that unambiguous assignment of alkyl substitution is not directly possible; it contains, aside from OH resonance, a quartet at 4.6,and a multiplet at from 0.5-1.4 ppm which is overlapped by a strong singlet at 1.05. An inadequate amount for further analysis was available, and further work on this is progressing.

the same solvent produced only 1, 2 and 3.

For either conformation I or II of the trans isomer, concerted orbital movement shown leading to major product III is favorable, since such movement results



in a transoid transition state with reduction in nonbonded interactions. We prefer I since recent data contravene the likelihood of axial isopropyl in this system (9). For the cis isomer, analogous orbital movement (IV) leads to a sterically-unfavorable cisoid transition state. Thus a simple maximum-overlap pathway available to trans isomer is precluded for cis, which must hence react by more energetically costly routes possibly involving hydride migration during internal return to reactive isomer(s). We suggest that the small rate difference is reflective of this difference in transition state energies, with the slightly higher trans ground state energy possibly contributing some accelerative impetus. While the trans rate is depressed in 90% acetone, the proportion of major product remains about the same, further suggestive of the above concertion, which is not of necessity preceded by efficient ion-pair separation. Both the present results and the analogous deamination data provide no evidence for the presence of bicyclobutonium ion intermediates, although participation in I or II may be readily represented in "nonclassical" fashion. However, the small magnitude of the trans rate increment over the cis, where such a path is absent, is not compatible with preferential acceleration by a nonclassical intermediate. When corrected for the difference in leaving groups (10), the cis/cyclohexyl rate ratio of only ca. 4 is smaller than for the case of unsubstituted cyclobutyl (10), confirming the importance of conformational effects on rate in this system, and calling attention to

accelerative factors other than delocalization. While bond-angle strain considerations predict a slower solvolysis rate for cyclobutyl than cyclohexyl in the absence of participation (11), both the relief of non-bonded interaction in the formation of, and the unusual stabilization of rearrangement product cyclopropylcarbinyl carbonium ion, may suffice to invert the rates. Recent EHT calculations have shown that the classical cyclobutyl carbonium ion is of lower energy than that involving "nonclassical" 1,3 bridging, irrespective of dihedral angle (12).

Wiberg and coworkers have previously observed pseudoequatorial rate preference in solvolysis of several fused-ring cyclobutyl derivatives (13). However, both strain energies and conformations for these compounds are quite different than for the parent cyclobutanes. In the sole solvolyses of isomeric unfused cyclobutyl esters heretofore reported, trans-3-methyl- and trans-3-hydroxy-2,2,4,4--tetramethylcyclobutyl tosylates (and trans diester derivatives of the hydroxy compound) demonstrated faster rates than their cis isomers (14). Wiberg has suggested (15) that a cross-ring electronegative effect of the hydroxy group is responsible for decreased reactivity in the cis hydroxy compound. However, in the present work, in which the trans isomer also exhibits higher rate activity, no such effect is possible, as well as in the above case of trans-3-methyl--2,2,4,4-tetramethylcyclobutyl tosylate. It is thus reasonable to suspect that trans rate acceleration may be a normal occurrence in the unfused cyclobutanes, due to conformational facilitation of simple concertion providing a major, rate-determining rearrangement route in competition with others.

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REFERENCES

1. K. L. Servis and J. D. Roberts, J. Am. Chem. Soc., 87, 1331 (1965) and preceding papers in this series; cf. in particular R. H. Mazur, W. N. White,

D. A. Semenov, C. C. Lee, M. S. Silver and J. D. Roberts, ibid., 81, 4390 (1959), and J. D. Roberts and R. H. Mazur, ibid., 73, 2509, 3542 (1951).

2. S. Winstein and E. Kosower, ibid., 81, 4399 (1959).
3. H. G. Richey, Jr. and J. M. Richey, ibid., 88, 4971 (1966).
4. H. L. Goering and K. E. Rubinstein, Abstracts, 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., March 1966, p. 11K.
5. M. Vogel and J. D. Roberts, J. Am. Chem. Soc., 88, 2262 (1966).
6. P. von R. Schleyer and G. W. Van Dine, ibid., 88, 2321 (1966).
7. I. Lillien and R. A. Doughty, Tetrahedron Letters, 3953 (1967).
8. I. Lillien and R. A. Doughty, J. Am. Chem. Soc., 89, 155 (1967).
9. I. Lillien, J. Org. Chem., 32, 4132 (1967).
10. H. C. Brown and G. Ham, J. Am. Chem. Soc., 78, 2735 (1956).
11. P. von R. Schleyer, ibid., 86, 1854 (1964).
12. R. E. Davis and A. Ohno, Tetrahedron, 24, 2063 (1968).
13. K. B. Wiberg and A. J. Ashe III, J. Am. Chem. Soc., 90, 63 (1968), and preceding papers.
14. C. F. Wilcox, Jr. and R. J. Engen, Tetrahedron Letters, 2759 (1966); L. J. Dolby and C. Wilkins, ibid., 2379 (1964); C. F. Wilcox, Jr. and D. L. Nealy, J. Org. Chem., 28, 3450 (1963).
15. K. B. Wiberg, Tetrahedron, 24, 1083 (1968).