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NONPLANAR CYCLOBUTANE. STERIC CONTROL IN DEAMINATION OF *CIS*- AND *TRANS*-3-ISOPROPYLCYCLOBUTYLAMINE

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With contemporary awareness of nonplanarity prevalent in many cyclobutanes (1, 2, 3) the question of the possible relationship of conformation and mechanism for reactions in this system has become significant. We have interpreted the nuclear magnetic resonance spectra of *cis*- and *trans*-3-isopropylcyclobutylamine, in which the isopropyl group was intended to serve as a conformational anchor, in terms of a puckered ring having equatorial and axial amino groups, respectively (4). We wish to report that deamination of these isomeric amines results in a large difference in product ratios which is thus apparently conformation-dependent. To our knowledge, this is the first instance of such disparate *cis*-*trans* behavior in a reaction of this type observed in the unfused cyclobutane system (5).

Cis- and *trans*-3-isopropylcyclobutylamine were deaminated in aqueous acid to give a mixture of five products (6): 2-methyl-5-hexen-3-ol (1); isopropylcyclopropylcarbinol (2); *trans*-(2-isopropylcyclopropyl)carbinol (3); *cis*- (4) and *trans*-3-isopropylcyclobutanol (5). The relative percentages (averages of several runs) are given in Table 1.

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*Based in part on the dissertation submitted by R. A. D. to the Graduate School of the University of Miami in partial fulfillment of the requirements for the Ph. D. degree in chemistry.

TABLE 1

Amine	Product				
	1	2	3	4	5
Cis	9.8	68.1	2.2	11.1	8.8
Trans	6.0	28.6	55.0	7.3	3.1

The most striking features of these results are: (a) the large inversion of product ratios for 2 and 3; and (b) the stereospecific formation of trans-3 (and the absence of cis- [7]). A satisfying rationale for the course of this reaction should account adequately for both of these observations.

If we consider the invocation of completely delocalized bicyclobutonium ions I and II for the cis- and trans- routes, respectively* (8), we find that they cannot rationalize the almost equivalent formation of solely allylic alcohol 1. Ion I is expected to yield 5-methyl-3-hexen-1-ol to a measurable ex-

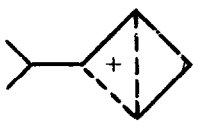
I II III

tent rather than exclusively 1**. It is unlikely that: (a) the isomeric homoallylic alcohol is completely converted to 1 after its formation (9); (b) alternate ion III, which should lead to 2-isopropyl-3-buten-1-ol, is involved; or (c) I cannot yield allylic alcohol (9) and must leak to II to produce any.

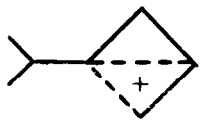
*Formulation of I as a homoallylic structure such as  would not alter the above argument.

**The method of vpc employed was accurate to a fraction of a percent, and could cleanly separate the isomeric homoallylic alcohols.

If II alone is the source of 1, since it leads to the formation of 3 to the extent of 55% for the trans- amine, it should do likewise were it to intervene in the cis- case. There seems no a priori reason to suspect that II would give different amounts of 3 for one isomer vs. the other. It is expected that this ion would exist in its most stable conformation, i.e., the bisected crown with equatorial isopropyl, regardless of its isomeric origin. Even in the event that a higher-energy (i.e., less stable conformer) species were formed from the trans- isomer, since it yields a substantial amount of 3, whatever its ultimate fate, a more stable conformer should do no less. Therefore it may be surmised that the intermediate ions are less delocalized, and 1 forms via a separate pathway. The 2 : 3 ratio may thus at first seem more compatible with the more rapid formation of IV and V from the cis- and trans- isomers, respectively, with V leaking to IV to account for 2. Intermediate formation can be



IV



V

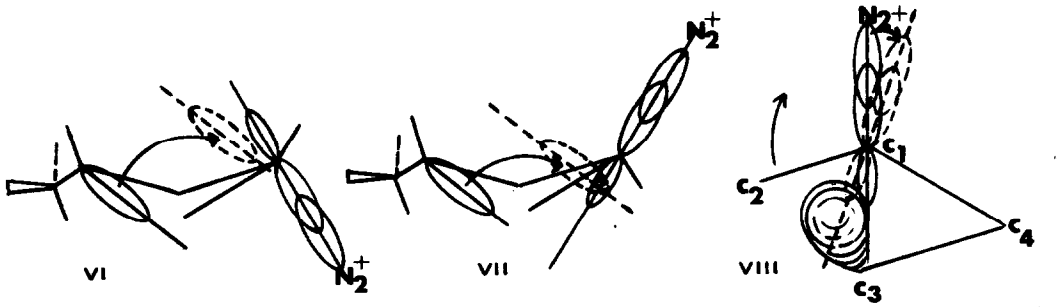
kinetically controlled by conformational factors*; and V may leak only slowly to IV compared to its rate of reaction with solvent in the trans- case. However, with this rationale, it is not at all evident how, or why, the cis- isomer would proceed directly to IV in lieu of formation of its expected pre-

*It has been proposed that "bicyclobutonium ion participation has a strong preference for a pseudoequatorial..group" on the basis that endo-bicyclo[2.1.1]-hexanyl-5 tosylate solvolyzes faster than its exo- epimer (ref 5b, c). However, conformational factors in fused and unfused systems, with possibly wide variances in ring dihedral angles in ground and transition states, may be quite altered, and thus mechanistic pathways not necessarily parallel.

cursor V.

Insight into possible conformational factors may be gained by considering the case of cyclohexane. In all rearrangements in this system, rearranging bonds must be in an anti- configuration. This severe steric limitation evidently involves a fine requirement for overlap of the rear lobe of the developing vacant 2p orbital at the migration terminus with the approaching orbital of the migrating group in a concerted process analogous to SN2 substitution. In the case of cyclohexane ring contraction, the migrating bond is exactly parallel to the axis of the leaving group, permitting favorable overlap. We suggest that the critical factor responsible for the reluctance of cis- amine to form 3 is the nonparallel alignment of bonds C_2-C_3 and C_1-N_2^+ in the intermediate cyclobutyldiazonium ion. This results from a ring dihedral angle of ca. 30-35°, which is much smaller than that of cyclohexane (ca. 54°). For a dihedral angle of 30°, a deviation of about 20° from parallel alignment of these bond axes results. Making the reasonable assumption that C_2-C_3 bond migration and C_1-N_2^+ heterolysis are concerted in leading to V or directly to 3, it is evident that optimal overlap of migrating bond orbital (C_2-C_3) with the developing vacant orbital at C_1 is hindered (VI). The vacant C_1 orbital assumes a more perpendicular orientation than would be the case for an equatorial leaving group in cyclohexane, preventing linear overlap. In contrast, the situation for the trans- isomer, with possibly a smaller dihedral angle than the cis-, is quite different. Here the migrating bond is favorably disposed toward a good degree of angular overlap with the C_1 orbital (VII)(10, 11, 12).

Intermediate V does not explain the stereospecificity in formation of trans-3. However, if formation of 3 is viewed as a direct consequence of the concertion suggested above, an inspection of models will show that steric selectivity is not unexpected. As bond C_2-C_3 becomes relocalized, C_1 can undergo a clockwise torsional twist (viewed from the front) to maximize orbital



overlap. In effect, the C_2-C_3 bond is now making an inverting displacement on the "backside" of C_1 and forcing substituent CH_2 to the same side as the leaving group, resulting in exclusively trans-3* (VIII).

We ascribe the formation of products 4 and 5 to direct solvolytic displacement of the N_2^+ group, as was suggested in the case of 3-methylcyclobutylamine (2). This occurs to a larger extent for the (equatorial) cis- isomer, as expected by reference to cyclohexane.

Since other products may thus be formed by routes not necessarily involving delocalized intermediates, 2 may likewise result from a classical sequence directly from the cyclobutyldiazonium precursor; viz., a successive or concurrent $C_2 \longrightarrow C_1$ hydride shift and $C_3 \longrightarrow C_4$ bond migration. This pathway, being more complex, would not compete successfully with the sterically favored route to 3 except where the latter were disallowed, as for the cis- isomer.

We therefore submit that the product ratios and stereochemistry in the present work are most commensurate with the rationale of competing classical pathways, with at least one strongly dependent on steric facilitation of concertion. Conformational control appears to be at least as important in this system as it has proven to be in the cyclohexanes.

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*In possible further explanation of the small amount of 3 formed from the cis-amine, a referee has interestingly pointed out that in order for overlap between the C_2-C_3 and C_1 orbitals to occur in that case, C_1 would have to undergo a counterclockwise twist leading to a sterically unfavorable cisoid transition state.

Acknowledgement

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3. Cf for example (a) W. G. Rothschild, J. Chem. Phys. 45, 1214 (1966); (b) J. B. Lambert and J. D. Roberts, J. Am. Chem. Soc. 87, 3884, 3891 (1965); (c) N. L. Allinger and L. A. Tushaus, J. Org. Chem. 30, 1945 (1965); (d) K. B. Wiberg and G. M. Lampman, J. Am. Chem. Soc. 88, 4429 (1966).

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5. Differences in solvolytic behavior of exo- and endo- isomers of fused cyclobutane derivatives have been observed; cf (a) K. B. Wiberg and B. A. Hess, Jr., J. Am. Chem. Soc. 88, 4433 (1966); (b) K. B. Wiberg and A. J. Ashe III, Tetrahedron Letters 1533 (1965); (c) K. B. Wiberg and R. Fenoglio, ibid. 1273 (1963); (d) K. B. Wiberg, B. R. Lowry, and T. H. Colby, J. Am. Chem. Soc. 83, 3998 (1961).

6. All products were unequivocally characterized by quantitative and spectral analysis. Complete details will be presented in the full paper.

7. Experimentally verified by synthesis of both isomers.

8. Cf K. L. Servis and J. D. Roberts, J. Am. Chem. Soc. 87, 1331 (1965), and preceding papers in this series.

9. In the aqueous deamination of allylcarbinylamine, this species of ion has been cited as a source of crotyl alcohol, found along with α-methylallyl and allylcarbinyl alcohols; J. D. Roberts and R. H. Mazur, J. Am. Chem. Soc. 73, 2509 (1951).

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12. Because the quite low $\Delta F^{\ddagger}$ for deamination is in the range of conformational energy barriers, such concerted processes critically conformation-dependent may often be a normal pathway for deamination; cf A. Streitwieser, Jr., J. Org. Chem. 22, 861 (1957).