Tetrahedron Letters No. 49, pp 4365 - 4368, 1975. Pergamon Press. Printed in Great Britain.

ON THE CONFORMATIONS AND RELATIVE STABILITIES OF 1,3-DISUBSTITUTED CYCLOBUTANES

Saul Wolfe* and Myung-Hwan Whangbo
Department of Chemistry, Queen's University, Kingston, Ontario, Canada K7L 3N6

(Received in USA 4 September 1975; received in UK for publication 28 October 1975)

Ugi and his coworkers have stated recently (1) that retention of configuration is observed in the displacement of brosylate and bromide from cis-1-OBs or Br-3-ethoxycyclobutanes under SN2 experimental conditions (LiI, NaBr, refluxing acetone, five days), and they have proposed that these reactions proceed via pentacoordinated intermediates. These are extraordinary conclusions, because of the extensive evidence that nucleophilic displacement reactions on cyclobutyl and cognate systems proceed with inversion of configuration (2). The work of Tang and Mislow (2b) is particularly relevant because, although sulfur is, in principle, a much more favorable nucleus than carbon for the detection of a pentacoordinated intermediate (3), the cis- and trans- isomers of 1-ethoxy-3-methylthietanium hexachloroantimonate undergo base-catalyzed hydrolysis with essentially complete inversion of configuration (2b,4). In the experiments of Wiberg and Lampman (2a), the same equilibrium mixtures of 1,3-dichloro-, 1,3-dibromo- and 1,3-diiodocyclobutanes, containing an excess of the cis- isomer in each case, were obtained from both directions upon exposure of 1,3-dihalocyclobutanes to the appropriate lithium halide in acetone at 124.4°C. These latter results are incompatible with retentive displacement mechanisms.

It seemed probable, therefore, that inversion mechanisms are also operative in Ugi's work, but that the extended reaction times employed lead in each case to equilibrium mixtures of 1-halo-3-ethoxycyclobutanes in which the trans isomer was not detected by the particular analytical procedure employed. For example, if the cis- isomer predominates at equilibrium in this system, and epimerization is extremely rapid, then the unfortunate choice of cis-1,3-disubstituted cyclobutanes for the initiation of all reactions would necessarily lead to results suggestive of retention of configuration.

Although Wiberg and Lampman's equilibrium mixtures range from cis/trans = 59/41 for the 1,3-dichlorocyclobutanes to 68.5/31.5 for the 1,3-diiodocyclobutanes, it is known (5) that oxygen and, especially, fluorine can engage in non-bonded attraction with other atoms bearing unshared electron pairs. If the conformations of these cyclobutanes facilitate such effects, it was possible that very high cis/trans equilibrium ratios might result. We have, therefore, been prompted to examine theoretically the conformational behaviour and relative stabilities of the cis- and trans- isomers of 1,3-difluoro (**1**) and 1,3-dimethylcyclobutane (**2**). The former is the most favorable system for the detection of a cis (a,a) conformation; and an experimental estimate of the gas phase cis/trans enthalpy difference of **2** is available (6) to provide a test of the reliability of the computational procedure employed (7).

The computations were performed using the STO-3G basis set (8) of the Gaussian 70 program system (9), modified for the Burroughs B6700 computer of Queen's University. It was known from previous experimental (10) and theoretical (11) studies that cyclobutane and 1,3-disubstituted cyclobutanes (2a, 12) are non-planar. We did not attempt to optimize the geometrical parameters (13), except for the ring puckering angle θ between the two C-C-C planes. The work of Wright and Salem (11b) had demonstrated the importance of methylene rocking in the puckered conformation of cyclobutane. In the present work it was assumed that the degree of rocking of the CH_2 or CHX group is proportional to the ring puckering (methylene rocking of 2.4° for ring puckering of 15° (11b)).

The results are summarized in Table 1 and Figure 1. The cis (a,a) conformations are not stable in either system, so that non-bonded attraction is unimportant in the case of cis (a,a)-1,3-difluorocyclobutane. The optimized dihedral angles θ for the cis (e,e) conformations of **1** and **2** are 19.9° and 23.7°, respectively. Both of these are somewhat larger than the value (θ = 15°) computed for cyclobutane (11b). The trans isomers of **1** and **2** are less puckered than the cis (e,e) conformations. Thus trans-**1** is virtually planar (θ=0.62°) and trans-**2** has θ= 12.7°.

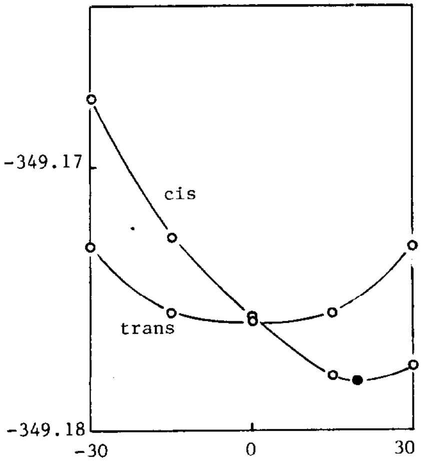

Figure 1a. The total energy of 1,3-difluorocyclobutane as a function of θ. The symbols o and • refer to calculated and interpolated values.

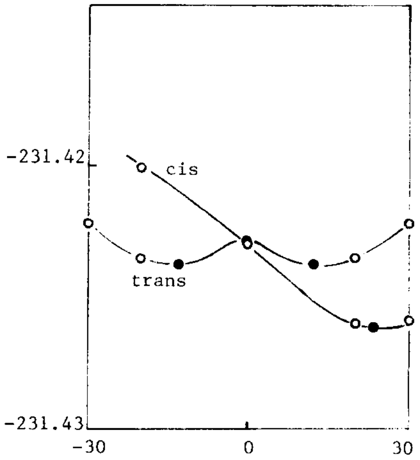

Figure 1b. The total energy of 1,3-dimethylcyclobutane as a function of θ. The symbols o and • refer to calculated and interpolated values.

Table 1. The computed total energies of 1,3-disubstituted cyclobutanes as a function of the ring puckering dihedral angle θ[a].

1,3-Difluorocyclobutane			1,3-Dimethylcyclobutane		
θ	cis[b]	trans	θ	cis[b]	trans
-30	-349.16753	-349.17300	-30		-231.42220
-15	-349.17263	-349.17554	-20	-231.42032	-231.42344
0	-349.17568	-349.17585	0	-231.42294	-231.42289
0.62[c]		-349.17585[c]	12.7[c]		-231.42371[c]
15	-349.17792	-349.17554	20	-231.42599	-231.42344
19.9[c]	-349.17807[c]		23.7[c]	-231.42606[c]	
30	-349.17746	-349.17300	30	-231.42584	-231.42220

[a] Energies are in atomic units (1 a.u. = 627.71 kcal/mole).

[b] A negative θ corresponds to a cis (a,a) conformation.

[c] These values were obtained by fitting the three calculated points to a quadratic equation in θ.

Our results agree with the experimental deductions that the trans isomers of 1,3-disubstituted cyclobutanes are less puckered (12a) and more flexible (14) than the cis (e,e) isomers, and that the cis (a,a) conformation is not stable (12b). It thus appears that the STO-3G basis set and the geometrical constraints described above are able to reproduce adequately the interactions in this system. The cis isomers of these 1,3-disubstituted cyclobutanes are probably anancomeric (15) (e,e) rather than a mixture of (e,e) and (a,a) conformations (16).

The calculated energy differences between the cis and trans isomers of **1** and **2** are 1.39 and 1.48 kcal/mole, respectively. The value for **2** is in the range estimated experimentally for this system (6); this lends additional support to the reliability of the computational procedure that we have employed. Neglecting entropy effects, the calculated energy differences correspond to equilibrium ratios of 89.4/10.6 and 90.6/9.4 for **1** and **2** at 56°C (the temperature of refluxing acetone). Since the entropy of the trans isomer will be higher because of its greater flexibility, the proportion of the trans isomer in an equilibrium mixture will be slightly higher than these values, and this isomer should be detectable (17).

Acknowledgements. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Research Council of Canada for financial support of this research.

REFERENCES AND NOTES

1. T. ElGomati, D. Lenoir and I. Ugi. Angew. Chem. 87, 66 (1975).
2. (a) K.B. Wiberg and G.M. Lampman. J. Amer. Chem. Soc. 88, 4429 (1966); (b) R. Tang and K. Mislow. J. Amer. Chem. Soc. 91, 5644 (1969); (c) S. Wolfe, W.S. Lee, G. Kannengiesser and J.B. Ducep. Can. J. Chem. 50, 2894 (1972).
3. B.W. Christensen. Chem. Commun. 597 (1971).
4. C.R. Johnson and D. McCants, Jr. J. Amer. Chem. Soc. 87, 5404 (1965).
5. (a) S. Wolfe. Accounts Chem. Res. 5, 102 (1972); (b) N.D. Epiotis. J. Amer. Chem. Soc. 95, 3087 (1973)
6. A.R. Venkitaraman. PhD Dissertation. University of Rochester, 1970 (Diss. Abstr. Int. B. 31, 1888 (1970)). This work reports a gas phase kinetic study of the thermal decomposition and isomerization of cis- and trans-1,3-dimethylcyclobutane. On the basis of rate measurements at five temperatures between 415 and 455°C, the enthalpy of the cis isomer was estimated to be lower than that of the trans by 0.5-1.5 kcal/mole.
7. Since the computations refer to the isolated molecules in the gas phase, solvation effects are not taken into account. Calculations on the known 1,3-dichlorocyclobutane system were not performed because of the much larger amounts of computer time required in this case, and because the difluoro system is known (5) to be a more favorable case for the occurrence of non-bonded attraction.
8. W.J. Hehre, R.F. Stewart and J.A. Pople. J. Chem. Phys. 51, 2657 (1969).
9. W.J. Hehre, W.A. Lathan, R. Ditchfield, M.D. Newton and J.A. Pople. Quantum Chemistry Program Exchange. Indiana University, Bloomington, Indiana. No. 236.
10. (a) J.B. Lambert and J.D. Roberts. J. Amer. Chem. Soc. 87, 3884, 3891 (1965); (b) D.A. Dows and N. Rich. J. Chem. Phys. 47, 333 (1967); (c) T. Ueda and T. Shimanouchi. J. Chem. Phys. 49, 470 (1968); (d) J.M.R. Stone and I.M. Mills. Mol. Phys. 18, 631 (1970); (e) S. Meiboom and L.C. Snyder. J. Chem. Phys. 52, 3857 (1970).
11. (a) J.S. Wright and L. Salem. Chem. Commun. 1370 (1969); (b) J.S. Wright and L. Salem. J. Amer. Chem. Soc. 94, 322 (1972).
12. (a) V.T. Aleksanyen, G.M. Kuz'yants and M. Yu. Lukina. J. Struct. Chem. 8, 569 (1967); (b) A. Almenningen, O. Bastiansen and L. Walløe. Selected Topics in Structure Chemistry. Edited by P. Andersen, O. Bastiansen and S. Furberg. Universitetsforlaget, Oslo, 1967, p91.
13. The CC and CH bond lengths and the HCH valence angles were taken from Ref 11b, which describes the results of ab initio calculations using a minimal basis set of Slater type orbitals. The HCX (X = F, CH_3) valence angle was assumed to be the same as the HCH valence angle. The CF bond length was that of octafluorocyclobutane (H.P. Lemaire and R.L. Livingston. J. Amer. Chem. Soc. 74, 5732 (1952), and the CH_3-C bond length was that of ethane (H.C. Allen, Jr. and E.K. Plyler. J. Chem. Phys. 31, 1062 (1959)).
14. G.M. Lampman, G.D. Hager and G.L. Couchman. J. Org. Chem. 35, 2398 (1970).
15. (a) M. Anteunis, D. Tavernier and F. Borremans. Bull. Soc. Chim. Belg. 75, 396 (1966).
16. (a) N.L. Allinger and L.A. Tushaus. J. Org. Chem. 30, 1945 (1965); (b) N.L. Allinger, J.A. Hirsch, M.A. Miller, I.J. Tyminski and F.A. Van Catledge. J. Amer. Chem. Soc. 90, 1199(1968).
17. After the completion of this manuscript, we were informed by Professor Kurt Mislow that the cis and trans-3-ethoxycyclobutyl brosylates in fact undergo displacement with complete inversion of configuration under the conditions reported by Ugi (1).