Tetrahedron Letters No.26, pp. 2171-2174, 1965. Pergamon Press Ltd.
Printed in Great Britain.

THE ENERGY OF THE BOAT FORM OF A SIMPLE CYCLOHEXANONE*

Norman L. Allinger and Frederick M. Karkowski

Department of Chemistry
Wayne State University
Detroit, Michigan 48202

(Received 5 April 1965; in revised form 8 May 1965)

During the last few years the existence of a number of cyclohexane and cyclohexanone systems in boat forms has been well documented.[1] Consideration of the torsional barrier in ethane led to the prediction[2] that the boat form of cyclohexane would be less stable than the chair form by approximately 5.6 kcal./mole, and values of this order have been found experimentally in various systems.[3-5] Similar torsional considerations in cyclohexanone led to the prediction[6] that the conformational energy of the boat form would be only about half that found for cyclohexane. A more accurate estimation of this energy for cyclohexanone required a knowledge of the torsional barrier about the carbon-carbon bond of a ketone. The magnitude of the barrier was known for acetone from a microwave study[7], but it has not been determined which configuration corresponds to the minimum of energy, and which to the maximum. The available evidence on this point is conflicting and indecisive.[8]

The best estimate of the conformational energy of the boat form of cyclohexanone previously available was 2.8 ± 1.0 kcal./mole.[6] Because of the rather wide occurance of boat forms in cyclohexanone systems, and because of the importance of this conformation in determining such properties as NMR spectra and optical rotatory dispersion curves, it was deemed desirable to establish experimentally the value for the energy difference between the boat and chair forms of a simple cyclohexanone. One such

---

* This investigation was supported by Public Health Service Research Grant A-5836 from the National Institute of Arthritis and Metabolic Diseases.

experimental determination reported earlier[9] was in the 2,4-di-t-butylcyclohexanone system, but the equatorial 2-t-butyl substituent was so located in the chair form of that compound as to exhibit a substantial van der Waals interaction with the oxygen, and hence the measured free energy difference is a minimum value for cyclohexanones in general.

The principles and methods which were employed in the present work are quite similar to those used to establish the corresponding conformational energy in the cyclohexane case.[4] The cis isomer of 3,5-di-t-butylcyclohexanone exists substantially all in the chair form at room temperature, while the trans isomer can a priori, exist as a chair form with an axial t-butyl group, or it can exist in a boat form in which it is possible for both of the t-butyl groups to simultaneously assume equatorial positions. From the earlier work it might be supposed that the energy of the axial t-butyl group would be so high that the trans isomer would exist primarily in the boat form. That this is in fact the case is shown by the present work.

The synthesis of the required cis isomer was carried out starting with 3,5-di-t-butyltoluene, which was converted to 3,5-di-t-butylphenol via the acid, amide and amine.* Hydrogenation of the latter to the cyclohexanol followed by oxidation of the product gave the pure cis ketone. This ketone was converted to the equilibrium mixture of cis and trans isomers in the liquid phase at different selected temperatures[4], and the mixtures were analyzed by gas phase chromatography on a column composed of a six-foot length packed with 10% XE -60 on diatoport S, followed by another six-foot length packed with 10% TCEP on chromsorb P. This column cleanly separated both of the isomeric ketones, two of the possible diesteromeric alcohols (prepared separately) and the phenol. One of the possible alcohols was not detected,which is the one in which the t-butyl groups are trans. It should have been formed in quite small amounts, and apparently was not separated from one of the other alcohols.

---

* Adequate analytical data were obtained for all new compounds.

That the peak assigned to the trans ketone actually corresponds to that compound was shown by the fact that a mixture of cis and trans ketones underwent a Wolf-Kishner reduction to give the known cis and trans hydrocarbons (identified by VPC) in the same ratio as the starting ketones.

Samples were equilibrated for varying lengths of time, until the proportions of alcohols and ketones became constant. The equilibrium with respect to phenol was established more slowly but the ketone epimerization data were shown to correspond to an equilibrium and not a steady state.* In a few runs two peaks were observed in the gas chromatography which correspond to 1, 3-di-t-butylbenzene and the corresponding cyclohexane in a 1 to 3 ratio. These compounds apparently were formed by dehydration of the alcohol and disproportionation of the resulting olefin. The system was not at equilibrium with respect to these components, but their presence did not influence the other equilibria. The data are summarized in the table.

Equilibration Data for the 3, 5-di-t-butylcyclohexanones

$T^{o}K$	483	497	513	537	567
% trans	9.30	10.24	11.48	13.36	15.74

From these data the thermodynamic quantities for the isomerization (trans→cis) were calculated.[4] It was found that $\Delta G^{o}_{525} = -2.05 \pm .04$ kcal./mole, $\Delta H^{o} = -3.91 \pm .10$ kcal./mole, and $\Delta S^{o} = -3.56 \pm .10$ eu. The entropy change is too great to be accounted for in terms of chair forms (bearing out the supposition that the trans isomer would exist largly as a boat), and is similar to those observed in other chair to boat reactions.[4, 9, 10]

From the data it may be calculated that $\Delta G^{o}_{298} = -2.8$ kcal./mole, and this value will be of most general use in discussions of boat forms of cyclohexanones. It is noted that this value is in good agreement with that estimated earlier[6, 8], and is substantially lower than that found in the corresponding cyclohexane ring.[4] It thus provides direct experimental

---

* We wish to emphasize that mistaking a steady-state for an equilibrium in such studies can lead to invalid conclusions.

evidence for the existence of substantial amounts of boat forms in most cyclohexanone derivatives under most conditions, (which fact has previously been inferred from various calculations and measurements[1, 8, 11]), and it now permits justifiable interpretations of a number of apparently anomolous results.[12] Further discussion will be differed to the full paper.

REFERENCES

1. A recent review is: E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. B. Morrison, Conformational Analysis, Interscience Division of John Wiley, Inc., N. Y., 1965. p. 469.
2. K. S. Pitzer, Science, 101, 672 (1945).
3. W. S. Johnson, V. J. Bauer, J. L. Margrave, M. A. Frisch, L. H. Dreger, and W. N. Hubbard, J. Am. Chem. Soc., 83, 606 (1961); J. L. Margrave, M. A. Frisch, R. G. Bautista, R. L. Clarke, and W. S. Johnson, ibid., 85, 546 (1963).
4. N. L. Allinger and L. A. Freiberg, J. Am. Chem. Soc., 82, 2393 (1960).
5. C. W. Beckett, K. S. Pitzer and R. Spitzer, J. Am. Chem. Soc., 69, 2488 (1947).
6. N. L. Allinger, J. Am. Chem. Soc., 81, 5727 (1959).
7. J. D. Swalen and C. C. Costain, J. Chem. Phys., 31, 1562 (1959).
8. N. L. Allinger, J. Allinger, and M. A. DaRooge, J. Am. Chem. Soc., 86, 4061 (1964).
9. N. L. Allinger and H. M. Blatter, J. Am. Chem. Soc., 83, 994 (1961).
10. R. D. Stolow and C. B. Boyce, J. Am. Chem. Soc., 83, 3722 (1961).
11. C. Djerassi, Proc. Chem. Soc., 314 (1964).
12. For example: C. Beard, C. Djerassi, J. Sicher, F. Sipos and M. Tichy, Tetrahedron, 19, 919 (1963); C. Djerassi, J. Burakevich, J. W. Chamberlin, D. Elad, T. Toda and G. Stork, J. Am. Chem. Soc., 86, 465 (1964); E. W. Garbisch, Jr., ibid., 86, 1780 (1964); H. R. Nace and R. B. Turner, J. Org. Chem., 25, 1403 (1960).