[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FLORIDA STATE UNIVERSITY]

Cyclopropanes. III. Rate of Racemization of 2,2-Diphenylcyclopropyl Cyanide

BY H. M. WALBORSKY AND F. M. HORNYAK[1]

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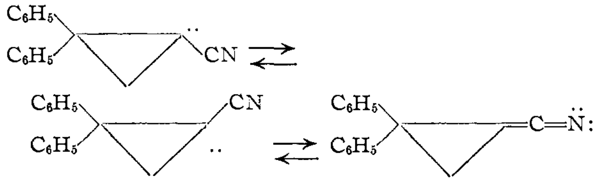
The rates and activation parameters of the sodium methoxide catalyzed racemization of 2,2-diphenylcyclopropyl cyanide and methylethylacetonitrile are reported and discussed in the light of Brown's I-strain theory.

Introduction

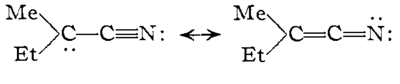
Although cyclopropane ring hydrogen atoms generally do not exhibit as much prototropic activation as is normally shown by hydrogen atoms alpha to an electron-accepting group, the ring hydrogen atoms in certain cyclopropane derivatives can be removed to form a stable cyclopropyl anion.[2,3] The activation of the hydrogen is believed to be lessened because of the additional strain of the exocyclic double-bonded resonance form in the resultant anion.[4]

It has been shown[5] that optically active 2,2-diphenylcyclopropyl cyanide is readily racemized when treated with lithium diisopropyl amide. This work showed that although according to Brown's I-strain theory[6] the planar carbanion (I) is of high energy, the barrier to planarity is not sufficient to cause the carbanion to retain its optical activity. In this respect the cyclopropyl carbanion is similar to carbanions of the unstrained type.



I

The present research was carried out to determine the rates and activation parameters of the base-catalyzed racemization of 2,2-diphenylcyclopropyl cyanide and methylethylacetonitrile and to compare quantitatively the ease of proton removal or formation of a planar anionic intermediate. The carbanion derived from methylethylacetonitrile (II) is expected to be of much lower energy since the open chain structure imposes no important restriction on bond angles or hybridization of the α-carbon atom. Therefore, if I-strain is the predominant deciding factor, a higher activation energy is predicted for the cyclopropane derivative



$$\overset{\mathrm{Me}}{\underset{\mathrm{Et}}{>}}\ddot{C}-C\equiv N: \longleftrightarrow \overset{\mathrm{Me}}{\underset{\mathrm{Et}}{>}}C=C=\ddot{N}:$$

Experimental

Materials.—The 2,2-diphenylcyclopropyl cyanide was prepared as described elsewhere[5] and was optically pure.

Methylethylacetonitrile was prepared from optically active methylethylacetic acid as described by Heintzeler[7] by forming the amide and dehydrating. The acid was partially resolved by the method of Schutz and Marckwald[8] by forming the brucine salt and recrystallizing it four times from water. It then had a specific rotation $[\alpha]^{24}\text{D}$ -52.5 (in water) and subsequently gave the acid with $[\alpha]^{24}\text{D}$ -4.72 (neat); the amide, m.p. 109.2–111°, $[\alpha]^{26}\text{D}$ -5.93 (in acetone); the nitrile, b.p. 122–124°, $[\alpha]^{26}\text{D}$ -8.92 (in methanol).

Sodium methoxide solution was prepared from sodium and absolute methanol under nitrogen and was standardized by titration at 25°.

Apparatus and Method.—The Kern Polarimeter (Kern and Co., Ltd., Arrau, Switzerland) was the instrument used and could be read to 0.025°. The light source was either a sodium vapor lamp or a white bulb with sodium D-line filter. A one-decimeter tube was used for all experiments.

Nitrile solutions of known base concentration were made up in a volumetric flask under nitrogen at 25° using the standard sodium methoxide and anhydrous methanol. Expansion experiments with the solution in a sealed graduated tube showed that the literature data[9] on the thermal expansion of methanol could be extrapolated and used to calculate base strengths (within 1%) at elevated temperatures. About 1.5 ml. of methylethylacetonitrile and about 0.10 g. of 2,2-diphenylcyclopropanecarbonitrile, respectively, were present in 10 ml. of final solution. Portions of the solution were sealed in nitrogen-flushed Pyrex glass ampules and placed in constant temperature baths. For a reading a tube was withdrawn at a known time, immediately cooled in ice and broken open. (A slight precipitate usually had to be centrifuged out of solution.) The liquid was placed in the polarimeter tube at 25 ± 2° and 20–25 angle measurements recorded. Racemization during observation was negligible.

Product Analysis for the Racemization of Methylethylacetonitrile.—A 4.00-ml. quantity of racemic nitrile having $n^{24}\text{D}$ 1.3894 (reported[10] $n^{25}\text{D}$ 1.3885) and d^{26} 0.7755 g./cm.^{3} was sealed in a glass tube with 27.0 ml. of 1.9 *M* sodium methoxide–methanol solution. After heating 72 hours at 100° and allowing to stand at room temperature for three weeks the tube was broken open. The solution was poured into 25 ml. of saturated sodium chloride solution and extracted five times with 20-ml. portions of *n*-pentane. The pentane extracts were washed once with 10 ml. of concentrated calcium chloride solution. After drying over drierite the pentane solution was fractionally distilled giving 3.20 ml. (80%) of methylethylacetonitrile boiling at 122–124° and having $n^{24}\text{D}$ 1.3890, d^{23} 0.7739.

Product Analysis for the Racemization of 2,2-Diphenylcyclopropyl Cyanide.—A 0.100-g. quantity of racemic nitrile was placed in a glass tube containing 10 ml. of 1.0 *M* sodium methoxide in methanol. The tube was sealed and placed in a steam chamber for eight days. The tube was opened and the methanol evaporated to about 4 ml. Addition of water precipitated 0.090 g. of pure white 2,2-diphenylcyclopropanecarbonitrile. After washing with water and drying the precipitate melted at 104–106° and a mixed melting point with starting material was 105.5–107°.

Results

The derived rate equation[11] for the pseudo first-

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[1] This paper is based on a portion of the thesis submitted by F. M. Hornyak in 1955 to the Florida State University in partial fulfillment of the requirements for the Ph.D. degree in chemistry.

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[3] F. J. Piehl and W. G. Brown, THIS JOURNAL, **75**, 5023 (1953).

[4] H. M. Walborsky, *ibid.*, **74**, 4962 (1952).

[5] H. M. Walborsky and F. M. Hornyak, *ibid.*, **77**, 6026 (1955).

[6] H. C. Brown, R. S. Fletcher and R. B. Johannesen, *ibid.*, **73**, 212 (1951); H. C. Brown and M. Borkowski, *ibid.*, **74**, 1894 (1952).

[7] M. Heintzeler, *Ann.*, **569**, 7 (1950).

[8] O. Schutz and W. Marckwald, *Ber.*, **29**, 52 (1896).

[9] C. D. Hodgeman, "Handbook of Chemistry and Physics," 13th Ed., Chemical Rubber Publishing Co., Cleveland, Ohio.

[10] C. L. Stevens and T. H. Coffield, THIS JOURNAL, **73**, 103 (1951).

[11] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 110.

order racemization involving a planar intermediate is, in terms of the polarimeter angle, a, and the time, t

$$\ln a = -k_1 t + \ln a_0$$

where a_0 is the angle at zero time.

The pseudo first-order rate constants, k_1, are listed in Table I and were calculated by least squares.

TABLE I

Run	Temp., °C.	Base concn. (molarity)	$k_1 \times 10^6$, sec.$^{-1}$	Duplicate k_1
		2,2-Diphenylcyclopropyl cyanide		
1	75.71 ± 0.02	0.992	0.363 ± 0.007	0.368 ± 0.005
2	92.59 ± .03	0.971	3.25 ± .05	3.81 ± .07
3	75.69 ± .02	2.10	1.73 ± .04	
		Methylethylacetonitrile		
4	75.70 ± 0.02	0.992	18.6 ± 0.4	18.2 ± 0.5
5	92.22 ± .03	0.992	132.0 ± 3.0	134.0 ± 2.0
6	75.69 ± .01	1.78	57.9 ± 1.3	59.8 ± 1.2
7	50.19 ± .02	1.86	2.34 ± 0.07	2.22 ± 0.07

The activation parameters were calculated from the transition state theory equation[12] and are

$$k = (kT/h) \exp(-\Delta H^{\ddagger}/RT - \Delta S^{\ddagger}/R)$$

shown in Table II.

TABLE II

Run	Activation parameters $\Delta H^{\ddagger}$, kcal.	$\Delta S^{\ddagger}$, e.u.
2,2-Diphenylcyclopropyl cyanide, runs 1 and 2	33.3 ± 0.8	8.3 ± 4
Methylethylacetonitrile, runs 4 and 5	29.6 ± .2	4.4 ± 2
Methylethylacetonitrile, runs 6 and 7	27.9 ± .2	1.4 ± 2

The activation enthalpies and errors were calculated by the method of least squares by considering each of the four rate constants as separate points on a log k_1/T *vs.* $1/T$ plot. Entropies were calculated from average rate constants and the errors were computed from deviations from the average.

Discussion

For both compounds, as seen in Table I, doubling the base concentration produced approximately a fourfold increase in racemization rate. This indicates that the reaction is either second order with respect to sodium methoxide or that it is first order with a large salt (ionic strength) effect. At higher base concentrations the methoxide ion is less solvated and would behave as a stronger base which would also tend to increase the rate more than would be expected on the basis of first-order base dependence. Although the order of the reaction is not certain, the transition state must be planar and the theory of I-strain can be applied. At a base concentration of 0.992 *M*, methylethylacetonitrile racemized faster than the cyclopropane derivative by a factor of 51 at 75° and by a factor of 38 at 92°. Such decreases in rate for reactions taking place at a cyclopropane ring are commonly observed and interpreted in terms of I-strain. However, the differences would be expected to be of a larger magnitude than observed.

In the present pseudo first-order racemization the entropies of activation are dependent on the over-all order of the reaction whereas the enthalpies are not. The entropies were calculated for first- and second-order base dependence and were found to be constant in the present cases. The rate-determining step very likely involves a proton transfer between the nitrile and the methoxide ion and the planar transition state will include an incipient carbanion. Since the free energy goes through a maximum in the transition state the methoxide charge, since methoxide is the weaker base, should be more nearly neutralized by the proton. The anion has its charge spread out and over-all desolvation on going to the activated state is expected on the basis of the decreased electrostatic field. This may be responsible for the positive entropies which are observed.[13] This point of view is supported by the fact that the entropy of activation for the racemization of methylethylacetonitrile decreases on increasing the base concentration. At higher base concentration the methoxide ion is less solvated and neutralizing its charge would not produce as much desolvation.

The cyclopropane derivative has a significantly higher activation enthalpy which is in accord with the concept of a strained planar carbanion intermediate. The activation enthalpy difference of about 3 kcal. is not as much as might have been expected on the basis of the I-strain theory.

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TALLAHASSEE, FLORIDA

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