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Carbon-14 Isotope Effect on sp^2-sp^3 Hybridization in the Prototropic Equilibrium of *N*-Benzylidenebenzylamine

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Isotope effects on equilibria can be calculated exactly on the basis of mechanical properties of two stable states involved, which can be observed directly. Accurate determination and theoretical consideration of these effects serve to elucidate the more complex problem of inferring from observed kinetic isotope effects something about transition state structure. *N*-Benzylidenebenzylamine system is known to show a prototropic equilibrium (Eq. (1)) in the presence of a strong base.[1]

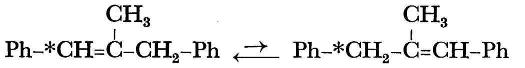
$$\text{Ar-CH=N-CH}_2\text{-Ar}' \rightleftarrows \text{Ar-CH}_2\text{-N=CH-Ar}' \qquad (1)$$

Substitution of an aliphatic carbon with a carbon-14 isotope should cause a carbon isotope effect on equilibrium (I⇄II).

$$\underset{\text{(I)}}{\text{Ph-*CH=N-CH}_2\text{-Ph}} \rightleftarrows \underset{\text{(II)}}{\text{Ph-*CH}_2\text{-N=CH-Ph}}$$

It is the effect accompanying the change in sp^2-sp^3 hybridization of a carbon atom.

Gamboa and coworkers reported the isotope fractionation of 60—70% in the equilibrium of the 1,3-diphenyl-1-propene system (Eq. (2)), but it seems



$$\text{Ph-*CH=}\overset{\text{CH}_3}{\overset{|}{\text{C}}}\text{-CH}_2\text{-Ph} \rightleftarrows \text{Ph-*CH}_2\text{-}\overset{\text{CH}_3}{\overset{|}{\text{C}}}\text{=CH-Ph} \qquad (2)$$

abnormally large.[2] On the other hand, Kresge and coworkers[3] observed a small reverse isotope effect in the ionization of triphenylmethyl chloride-1-^{13}C. In these respects, the carbon-14 isotope effect on the equilibrium (I⇄II) was measured and compared with a theoretically calculated value.

Results and Discussion

N-Benzylidenebenzylamine(methine-^{14}C) (I) was prepared by condensation of benzaldehyde(carbonyl-^{14}C) with benzylamine. The equilibrium was effected by the action of 30 parts of 1.45N alcoholic sodium ethoxide at 40.0 and 82.0°C. Definite portions of the reaction mixture were added into 2N hydrochloric acid solution of saturated 2,4-dinitrophenylhydrazine at appropriate time intervals. Precipitates of benzaldehyde 2,4-dinitrophenylhydrazone (III) were collected and purified by recrystallisation. Samples of III were oxidized with the Van Slyke-Folch mixture and the radioactivity of the carbon dioxide generated was measured by the ionization chamber counting method.

TABLE 1. SPECIFIC RADIOACTIVITY DATA FOR THE METHYLENEAZOMETHINE EQUILIBRIUM AT 40.0±0.1 AND 82.0±0.1°C

No.	Compound	Temp (°C)	Time (hr)	Specific activity (mCi/mol)
1	I			1.0492±0.0011
2	III	40.0	0	1.0419±0.0009
3			1	0.9663
4			2	0.8237
5			4	0.6721
6			8	0.5798
7			24	0.5323±0.0007
8			36	0.5302±0.0005
9			50	0.5284±0.0003
10		82.0	0	1.0457±0.0001
11			0.5	0.5276±0.0008
12			1.0	0.5286±0.0005

The results are summarized in Table 1.

The small difference between the radioactivity of the starting material (I) and that of the 2,4-dinitrophenylhydrazone (III) at initial stage in each of thest two experiments can be attributed to the partial isomerization of I to II during the course of the preparation under mild basic conditions. It is apparent that the equilibrium was reached within 36 hr at 40°C and 30 min at 82°C. The equilibrium constant *K*, whose value corresponds to that of the isotope effect in this case, is calculated by Eq. (3);

$$K = [\text{II}]/[\text{I}] = (\text{A}-\text{B})/\text{B} \qquad (3)$$

where A is the specific activity of the starting material (I) and B is that of the 2,4-dinitrophenylhydrazone (III) at equilibrium. The results thus obtained show small isotope effects on the equilibrium: $K=0.983\pm 0.002$ at 40.0°C and $K=0.986\pm0.002$ at 82.0°C. The equilibrium constants smaller than unity indicate that the equilibrium is in favor of the carbon-14 atom at the sp^2-position.

Theoretical values of isotope effects on equilibrium can be calculated by the Bigeleisen equation (Eq. (4)),[4]

$$K = 1 + \sum_i \left(\frac{1}{2} - \frac{1}{u_i} + \frac{1}{e^{u_i}-1}\right)\Delta u_i \qquad (4)$$

where $u_i = hc\omega_i/kT$, Δu_i is the difference in u_i between isotopes, and ω_i is the wave number of the *i*th normal mode. For calculation of Eq. (4), only stretching vibrations were used, which are usually considered as the most effective factors of isotope effects. An observed infrared spectrum was analyzed and vibrational fre-

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[1] C. K. Ingold, "Structure and Mechanism in Organic Chemistry", 2nd ed., Cornell University Press, Ithaca, N. Y. (1969), p. 808.

[2] J. M. Gamboa, R. P. Ossorio, and R. Rapún, *Anales Real Soc. Españ. Fis. Quim.*, **57B**, 607 (1961).

[3] A. J. Kresge, N. N. Lichtin, K. N. Rao, and R. E. Weston, Jr., *J. Amer. Chem. Soc.*, **87**, 437 (1965).

[4] J. Bigeleisen and M. G. Mayer, *J. Chem. Phys.*, **15**, 261 (1947).

quencies were determined as follows:[5] C=N, 1640; C–N, 1200; C–H (in =CH–), 3030; C–H (in $-CH_2-$), 2865 and 2835 cm^{-1}. Stretching frequencies for carbon-carbon single bonds in =CH–Ph and $-CH_2-Ph$ were arbitrarily taken as 1050 and 1000 cm^{-1}, respectively. Frequencies for a carbon-14 isotope were calculated by the following relationship: $\omega_1/\omega_2=(\mu_2/\mu_1)^{1/2}$, where μ means a reduced mass. The equilibrium constants K calculated as above are 0.986 at 40°C and 0.987 at 82°C. Although inclusion of bending vibrations may give a better result, these calculated values are in fair agreement with the observed values, considering the errors in measurement of radioactivity and the simple approximation used for theoretical calculation.

Experimental

Material. Benzaldehyde(carbonyl-^{14}C) was prepared according to the procedure of Ott.[6]

N-*Benzylidenebenzylamine(methine-^{14}C) (I).* Benzaldehyde(carbonyl-^{14}C) was treated with 5.0 m*l* of benzylamine for 30 min at 80—90°C. After being cooled, the reaction mixture was diluted with 20 m*l* of ether. The ether solution was washed with 10 m*l* of 2% acetic acid, 10 m*l* of saturated sodium bicarbonate solution, and 20 m*l* of distilled water, successively, and finally dried over anhydrous potassium carbonate. The solvent was removed and the colorless oil remained was distilled under reduced pressure; bp 158.5°C/4.8 mmHg, yield 5.85 g (78.5%).

Methyleneazomethine Rearrangement. *N*-Benzylidenebenzylamine(methine-^{14}C) (I, 1.847 g) was added all at once into 60.204 g of 1.45N alcoholic sodium ethoxide in a reaction vessel preheated in a constant temperature bath at 40.0± 0.1°C. Six m*l* aliquot of the reaction mixture was pipetted into 50 m*l* of 2N hydrochloric acid solution containing saturated 2,4-dinitrophenylhydrazine at appropriate time intervals. The solutions were kept to stand for 24 hr at 50°C for complete precipitation of 2,4-dinitrophenylhydrazone (III). After being cooled to room temperature, 10 m*l* of distilled water was added. Crystals of III were filtered, washed thoroughly with 2N hydrochloric acid and distilled water, successively, and then dried for 12 hr at 80—90°C. Samples of III purified by recrystallization three or four times from acetone were assayed for radioactivity.

In the same manner, 0.991 g of I was rearranged in 29.243 g of 1.45N alcoholic sodium ethoxide solution at 82.0±0.1°C.

Measurement of Radioactivity. About 10 mg of accurately weighed III was oxidized with the Van Slyke-Folch mixture[7] in a Nuclear-Chicago Model GW1 carbon glassware system, and the carbon dioxide generated was swept into a Model DC 250 ion chamber with tank carbon dioxide. The ion current was measured with a Nuclear-Chicago Model 6010 Dynacon electrometer system.

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[5] Infrared spectra were recorded on a JASCO Model DS-402G IR Spectrophotometer in carbon tetrachloride (4000—1300 cm^{-1}) and in carbon disulfide (1300—660 cm^{-1}).

[6] *cf.* A. Murray, III and D. L. Williams, "Organic Syntheses with Isotopes", Part I, Interscience Publishers, New York, N. Y. (1958), p. 626.

[7] D. D. Van Slyke, J. Plazin, and J. R. Weisiger, *J. Biol. Chem.*, **191**, 299 (1951).