Table V. Solvent Decomposition in Methanol-O-d-Dimethyl Sulfoxide-d_6 (75:25)[a] Solutions Which Contain Potassium Methoxide at 135°

Time, hr	Wt %[b] dimethyl-d_6 sulfoxide	Potassium methoxide concn, M
0.0	31.9 ± 0.2	0.0475
24.0	31.8 ± 0.1	0.0095
52.5	31.6 ± 0.1	0.0000
89.3	31.6 ± 0.1	0.0000
91.7	30.9 ± 0.1	0.0000

[a] Per cent by volume at room temperature before mixing. [b] Mean value of triplicate analyses with the indicated standard deviation.

Control on Isotopic Fractionation during Crystallization. A mixture of 31.2 mg of triphenylmethane and 172.1 mg of triphenyldeuteriomethane (82.4% of one atom of deuterium) was dissolved in carbon tetrachloride, divided into two equal aliquots, and evaporated to dryness. Residual solvent was removed *in vacuo*. One aliquot was recrystallized from methanol. The recrystallized and untreated samples were weighed and dissolved in 0.200 ml of carbon tetrachloride. The infrared absorbance at 2020 cm^{-1} was measured. Recrystallized and untreated triphenylmethane samples gave values of 4.96 and 4.89, respectively, for (absorbance × 10^3/mg of sample). Estimated maximum errors of ±0.2 mg in sample weights at ±0.5% in absorbances indicate that these values are identical with experimental error. Hence, isotopic fractionation did not occur to any measurable extent.

Electrophilic Substitution at Saturated Carbon. XXXVII. A Kinetic–Thermodynamic Acidity Correlation of Carbon Acids[1]

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Abstract: Rate constants and activation parameters for potassium methoxide catalyzed exchange of fluorene, 9-phenylxanthene, 4-biphenylyldiphenylmethane, triphenylmethane, and diphenylmethane with methanol-O-d-dimethyl-d_6 sulfoxide (75:25 by volume) were measured and extrapolated to 75°. These kinetic acidities varied by a rate factor of *ca.* 10^7 and were correlated by the Brønsted relationship with reported thermodynamic acid dissociation constants that varied by a factor of about 10^{10}. Substrate kinetic isotope effects for racemization of 2-(N,N-dimethylcarboxamido)-9-methylfluorene (k_H/k_D = 6.75 at 25°) and 4-biphenylylmethoxyphenylmethane (k_H/k_D = 2.5 at 126°) in the same medium were also measured. The curvature in the Brønsted plot coupled with the variation of the kinetic isotope effect and changes in activation parameters with pK_a of the carbon acids are interpreted in terms of changes in mechanism that occur for the isotopic exchange reaction as the ΔpK_a's (pK_a of carbon acid − pK_a of methanol) change.

Thermodynamic and kinetic acidity characteristics of carbon acids have been reviewed to 1965.[2] Since that time Streitwieser,[3] working in cyclohexylamine, and Steiner,[4] Bowden and Stewart,[5] and Ritchie,[6] working in dimethyl sulfoxide, have developed a large body of thermodynamic acidity data for carbon acids in the 11–32 pK_a range. The extensive work of Shatenshtein and coworkers on both kinetic and thermodynamic acidity in liquid ammonia–potassium amide has been reviewed in English.[7] Much of the work of Streitwieser and coworkers on both thermodynamic and kinetic acidity has been reviewed,[8] as has the kinetic work of Cram and coworkers.[2]

A number of authors have correlated thermodynamic and kinetic acidities of carbon acids with Brønsted relationships. The classic attempt at correlation was published by Pearson and Dillon who treated carbon acids in the pK_a range of 5–20.[9] Bell and coworkers have studied Brønsted relationships in depth.[10] Shatenshtein correlated isotopic exchange rates of carbon acids in liquid ammonia with their pK_a's in ether.[7] This is the only study to date which involved correlation of thermodynamic and kinetic acidities of carbon acids in the pK_a range of 20–30. More recently Shatenshtein observed good Hammett σ–ρ plots for isotopic exchanges at the *ortho* and *meta* positions of monosubstituted benzenes.[11] Dessy and coworkers[12] correlated the rates of exchange of carbon acids in dimethylformamide–deuterium oxide with pK_a values in other solvents. Streitwieser and coworkers reported a Brønsted relationship for the exchange of a series of substituted tritiated fluorenes in methanol.[3a] Streitwieser and coworkers also obtained good Hammett σ–ρ plots for

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[1] This research was sponsored by the U. S. Army Research Office, Durham, N. C. The authors extend their thanks.

[2] D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, Chapter 1.

[3] (a) A. Streitwieser, Jr., J. I. Brauman, J. H. Hammons, and A. H. Pudjaatmaka, *J. Am. Chem. Soc.*, **87**, 384 (1965); (b) A. Streitwieser, Jr., J. H. Hammons, E. Ciuffarin, and J. I. Brauman, *ibid.*, **89**, 59 (1967); (c) A. Streiwieser, Jr., E. Ciuffarin, and J. H. Hammons, *ibid.*, **89**, 63 (1967).

[4] (a) E. C. Steiner and J. M. Gilbert, *ibid.*, **87**, 383 (1965); (b) E. C. Steiner and J. D. Starkey, *ibid.*, **89**, 2751 (1967).

[5] K. Bowden and R. Stewart, *Tetrahedron*, **21**, 261 (1965).

[6] C. D. Ritchie and R. E. Uschold, *J. Am. Chem. Soc.*, **89**, 1721, 2752 (1967).

[7] A. I. Shatenshtein, *Advan. Phys. Org. Chem.*, **1**, 155 (1963).

[8] A. Streitwieser, Jr., and J. H. Hammons, *Progr. Phys. Org. Chem.*, **3**, 41 (1965).

[9] R. G. Pearson and R. L. Dillon, *J. Am. Chem. Soc.*, **75**, 2439 (1953).

[10] (a) R. P. Bell, "Acid-Base Catalysis," Oxford University Press, Oxford, 1941, and references cited; (b) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, and references cited; (c) R. P. Bell and J. E. Crooks, *Proc. Roy. Soc.* (London), **A286**, 285 (1965), and references cited; (d) R. P. Bell, *Discussions Faraday Soc.*, **39**, 16 (1965), and references cited; (e) R. P. Bell and D. M. Goodall, *Proc. Roy. Soc.* (London), **A294**, 273 (1966), and references cited.

[11] A. I. Shatenshtein, *Tetrahedron*, **18**, 95 (1962).

[12] R. E. Dessy, Y. Okuzumi, and A. Chen, *J. Am. Chem. Soc.*, **84**, 2899 (1962).

isotopic exchanges of 9-tritiated 2-substituted fluorenes in methanol[8] and α-tritiated *meta*- and *para*-substituted toluenes in cyclohexylamine solutions.[8] The same group also found that isotopic exchanges of 9-substituted fluorenes correlated with the pK_a's of the corresponding acetic acid derived from the same substituents.[13]

The present work was undertaken to examine in the methanol-O-*d*-dimethyl-d_6 sulfoxide–potassium methoxide system: (a) the relationship between the two types of acidities of the carbon acids in the pK_a range of 20–30; (b) the changes in activation parameters for isotopic exchange rates with change in relative pK_a of methanol and the carbon acids; (c) the change in kinetic isotope effect with the change in pK_a of carbon acid. This particular medium was selected for a number of reasons. The pK_a's of most of the carbon acids used have been determined in dimethyl sulfoxide, and it had been demonstrated that methanolic dimethyl sulfoxide also produced the same pK_a scale.[4] This medium allowed the kinetic acidity to be measured for carbon acids of a wide range of thermodynamic acidity. This medium provided a large isotopic reservoir in which to drown the exchanged proton of the carbon acid. The carbon acids chosen for the correlation were fluorene, 9-phenylxanthene, 4-biphenylyldiphenylmethane, triphenylmethane, and diphenylmethane. The anions of these acids all owe their stability to charge delocalization effects, and involve little geometric change upon going to anion. The kinetics of isotopic exchange of diphenylmethene and triphenylmethane were reported in connection with another study.[14] The carbon acids used in the isotope effect study were optically active 2-(N,N-dimethylcarboxamido)-9-methylfluorene and 4-biphenylylmethoxyphenylmethane. Data for the latter compound were already available.[14] The pK_a's of the last two carbon acids have not been determined, but can be easily estimated.

Methods and Results

Starting Materials, Media, and Rate Constants. Formic acid reduction of 9-phenylxanthydrol[15] and 4-biphenylyldiphenylmethanol[16] gave 9-phenylxanthene and 4-biphenylyldiphenylmethane, respectively. Preparation of optically active 2-(N,N-dimethylcarboxamido)-9-methylfluorene and its 9-deuterio derivative has been described elsewhere.[17] Deuterated solvents, kinetic solutions, and base titers were prepared or determined as reported previously.[14] Pseudo-first-order rate constants were calculated as before.[14]

Isotopic Analyses. Hydrogen–deuterium analyses for isotopically exchangeable positions of 9-phenylxanthene and 4-biphenylyldiphenylmethane utilized infrared bands present with one isotope but absent with the other. Deuterated analogs of known isotopic purity were required to prepare calibration curves. Treatment of 9-phenylxanthene with *n*-butyllithium followed by a deuterium oxide quench gave the 9-deuterated analog. Potassium methoxide catalyzed isotopic exchange of 4-biphenylyldiphenylmethane in the kinetic medium provided the corresponding deuterated analog. Partially exchanged samples of 4-biphenylyldiphenylmethane and 9-phenylxanthene were recrystallized during isolation of material from each kinetic point. An appropriate control experiment with the latter compound demonstrated that no isotopic fractionation occurred during this procedure. Deuterated fluorene (9 position) was prepared by exchange of fluorene with deuterium oxide–sodium methoxide–dimethoxyethane. The deuterium-labeled standards were analyzed by the combustion and falling-drop method.

Isotopic analyses of the benzylic position in fluorene were based on nmr spectral integrations and comparisons between aromatic and benzylic protons. Known mixtures of fluorene and analyzed 9,9-dideuteriofluorene were prepared and analyzed, and Tables I and II show the accuracy and precision.

Table I. Accuracy of Isotopic Analyses for Fluorene

% H actual	% obsd	% H actual	% obsd
6.7	1.7	62.1	61.5
32.8	31.8	77.7	77.0[a]
44.9	46.1[a]	90.2	90.9[a]

[a] Average value for three determinations.

Table II. Precision of Isotopic Analyses for Fluorene

% H obsd[a]	Average[b]
45.2, 47.0, 46.0	46.1 ± 0.9
76.5, 77.5, 77.0	77.0 ± 0.5
90.9, 90.6, 91.1	90.9 ± 0.3

[a] Triplicate analyses of the samples. [b] Standard deviation.

Exchange and Racemization Data. Tables III, IV, and V list the first- and second-order rate constants for fluorene, 9-phenylxanthene, and 4-biphenylyldiphenylmethane, respectively, in methanol-O-*d*-dimethyl-d_6 sulfoxide (75:25, by volume). In each case the ampoule method was employed, and the rate constants were calculated from 7 to 8 points covering one to two half-

Table III. Hydrogen–Deuterium Exchange Rates for Fluorene in Methanol-O-*d*–Dimethyl Sulfoxide-d_6 (75:25)[a] Catalyzed by Potassium Methoxide

Run	Temp,[b] °C	Substrate concn, *M*	Base concn, *M*	$k_1 \times 10^5$, sec^{-1}[c] ± %	$k_2 \times 10^3$, l./mol sec[d] ± %
1	0	0.0604	0.0174	1.97 ± 3.5	1.13 ± 4.5
2	0	0.0603	0.0111	1.16 ± 6.0	1.04 ± 7.0
3	0	0.0603	0.0177	1.88 ± 2.7	1.06 ± 3.7
4	0	0.0604	0.0308	2.80 ± 5.0	0.908 ± 6.0
5	0	0.0604	0.0080	0.879 ± 2.0	1.10 ± 3.0
6[e]	15	0.0805	0.0132	7.07 ± 1.7	5.36 ± 2.7
7	0	0.1009	0.0295	2.83 ± 1.8	0.959 ± 2.8
8[e]	0	0.0362	0.0245	2.51 ± 1.6	1.03 ± 2.6
9	0	0.0809	0.0347	3.32 ± 1.2	0.957 ± 2.2
10[f]	25	0.100	0.0094	16.1	17.1
11[f]	50	0.100	0.0094	183	195
12[f]	25	0.100	0.0094	16.6	17.7
13[f]	50	0.100	0.0094	190	202

[a] Per cent by volume at room temperature before mixing. [b] 0 = 0.00°; 15 = 14.92 ± 0.02°; 25 = 25.00 ± 0.05°; 50 = 50.00 ± 0.05°. [c] Standard deviation indicated. [d] $k_2 = k_1$/base concentration, 1.0% added to standard deviation to account for error in base concentration. [e] These runs were used to calculate activation parameters. [f] One-point rate constants.

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(13) A. Streitwieser, Jr., A. P. Marchand, and A. H. Pudjaatmaka, *J. Am. Chem. Soc.*, **89**, 693 (1967).

(14) W. D. Kollmeyer and D. J. Cram, *ibid.*, **90**, 1784 (1968).

(15) M. Gomberg and L. H. Cone, *Ann.*, **370**, 142 (1909).

(16) N. N. Lichtin and H. Glazer, *J. Am. Chem. Soc.*, **73**, 5537 (1951).

(17) D. J. Cram and L. Gosser, *ibid.*, **86**, 5445 (1964).

Table IV. Hydrogen–Deuterium Exchange Rates for 9-Phenylxanthene in Methanol-O-*d*-Dimethyl Sulfoxide-d_6 (75:25)[a] Catalyzed by Potassium Methoxide

Run	Temp,[b] °C	Substrate concn, *M*	Base concn, *M*	$k_1 \times 10^6$, $\sec^{-1\,c}$ ± %	$k_2 \times 10^4$, l./mol $\sec^{d,e}$ ± %
14	61	0.0388	0.0272	6.66 ± 2.8	2.45 ± 3.8
15	61	0.0390	0.0273	7.17 ± 2.1	2.63 ± 3.1
16	75	0.0369	0.0266	36.9 ± 3.0	13.9 ± 4.0
17	75	0.0368	0.0271	36.4 ± 4.4	13.4 ± 5.4

[a] Per cent by volume at room temperature before mixing. [b] 61 = 60.90 ± 0.05°; 75 = 75.05 ± 0.05°. [c] Standard deviation indicated. [d] $k_2 = k_1$/base concentration, 1.0% added to standard deviation to account for error in base concentration. [e] The average of the duplicate determinations was used to calculate activation parameters.

Table V. Hydrogen–Deuterium Exchange Rates for 4-Biphenylyldiphenylmethane in Methanol-O-*d*-Dimethyl Sulfoxide-d_6 (75:25)[a] Catalyzed by Potassium Methoxide

Run	Temp,[b] °C	Substrate concn, *M*	Base concn, *M*	$k_1 \times 10^6$, $\sec^{-1\,c}$ ± %	$k_2 \times 10^4$, l./mol $\sec^{d,e}$ ± %
18	85	0.0469	0.0273	3.49 ± 2.4	1.28 ± 3.4
19	85	0.0469	0.0273	3.54 ± 3.8	1.30 ± 4.8
20	100	0.0469	0.0273	16.9 ± 4.1	6.20 ± 5.1
21	100	0.0469	0.0273	17.5 ± 2.7	6.40 ± 3.7

[a] Per cent by volume at room temperature before mixing. [b] 85 = 85.50 ± 0.05°; 100 = 100.10 ± 0.05°. [c] Standard deviation indicated. [d] $k_2 = k_1$/base concentration, 1.0% added to standard deviation to account for error in base concentration. [e] The average of the duplicate determinations was used to calculate activation parameters.

lives. Table VI lists the first-order rate constants for racemization and isotopic exchange of 2-(N,N-dimethylcarboxamido)-9-methylfluorene in the same medium. The rate constants here were calculated from 8 to 12 points covering about two half-lives. At the low concentrations of potassium methoxide employed, the second-order rate constants remained invariant with respect to base concentration. Thus, in runs 5 and 9 of Table III, a base concentration change from 0.0080 to 0.0347 *M* gave second-order rate constants (× 10^3) of 1.10 ± 3% and 0.957 ± 2.2% l./mol sec. Second-order rate constants were not sensitive to substrate concentration. Thus, in runs 7 and 8 of Table III, a change in substrate from 0.1009 to 0.0362 *M* produced a change in second-order rate constant (× 10^3) of 0.959 ± 2.8% to 1.03 ± 2.6% l./mol sec.

Table VI. Hydrogen–Deuterium Exchange Rates and Racemization Rates for 2-(N,N-Dimethylcarboxamido)-9-methylfluorene in Methanol-O-*d*-Dimethyl Sulfoxide-d_6 (75:25)[a] Catalyzed by Potassium Methoxide at 24.80 ± 0.05°

Run	Substrate concn, *M*	Base concn, *M*	$k_1 \times 10^4$, $\sec^{-1\,b}$ ± %
22[c]	0.0942	0.0026	1.40 ± 1.7
23[d]	0.0942	0.0026	1.56 ± 0.8
24[d]	0.0234	0.0068	5.33 ± 0.2
25[d,e]	0.0214	0.0068	0.790 ± 0.5

[a] Per cent by volume at room temperature before mixing. [b] Standard deviation indicated. [c] Exchange run. [d] Racemization run. [e] Substrate was the 9-deuterio analog.

Activation Parameters. Both second-order rate constants and activation parameters for isotopic exchange at 75° were calculated and are given in Table VII. Calculations for fluorene involved a considerable temperature extrapolation from the 0–15° region. In order to check for possible aberrations in behavior of the enthalpy of activation with changes in temperature, duplicate one-point rate constants for exchange were measured at 25 and 50° by means of a special technique described in the Experimental Section. A plot of the logarithm of the second-order rate constant *vs.* the reciprocal of the absolute temperature for 0, 15, 25, and 50° was linear (runs 6, 8, 10–13 of Table III). Corrections of other rate constants for temperature changes involved much smaller temperature extrapolations.

Calculations for fluorene, 9-phenylxanthene, and 4-biphenylyldiphenylmethane refer to rates measured in the 0.01–0.03 *M* potassium methoxide range. Calculations for triphenylmethane and diphenylmethane were made with rate data taken from ref 18. The computations were carried out for both infinitely dilute and 0.200 *M* base concentrations. Data for the latter were determined by interpolation of logarithmic plots of pseudo-first-order rate constants *vs.* base concentration. Rate constants for infinitely dilute base were obtained by extrapolation of observed second-order rate constants *vs.* base concentration plots as described in ref 14. The extrapolated values are subject to the validity of this procedure. Although the medium effect observed by increasing the base concentration is appreciable at 0.200 *M*,[14] Table VII reveals that either computational method gives similar activation parameters and rate constants which differ by only a factor of about 3 for triphenylmethane. On the other hand, markedly dissimilar activation parameters and rate constants which differed by a factor of 10 were obtained for diphenylmethane. For both substrates the results computed by either method can serve as reasonable limits for the true values in the 0.01–0.03 *M* potassium methoxide range.

Brønsted Plot. The correlation of kinetic and thermodynamic acidities is shown in Figure 1. The pK_a values refer to Steiner's work,[4] while the kinetic acidities are those given in Table VII with the exception of diphenylmethane and triphenylmethane.[14] For these two carbon acids the average computed from the kinetic acidity at infinitely dilute and 0.200 *M* base is shown. The indicated range spans the limiting values. The correlation is good considering that a span of 10 pK_a units is covered. If one wishes to describe the correlation by a straight line then the slope is 0.7. However, the correlation can be somewhat better described as a curve which exhibits increasing slope at higher pK_a values.

Isotope Effects. Racemization can be used to determine an exchange isotope effect when both processes occur at the same rate. Optically active 2-(N,N-dimethylcarboxamido)-9-methylfluorene (pK_a = *ca.* 20) had a racemization isotope effect of 6.75 at 25° (see Table VI). Optically active 4-biphenylylmethoxyphenylmethane (pK_a = *ca.* 30) had a racemization isotope effect of 2.5 at 126° which is equivalent to about 3.4 at 25°.[18] Both values approximate exchange isotope

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(18) K. B. Wiberg, *Chem. Rev.*, **55**, 713 (1955).

Table VII. Activation Parameters and Second-Order Rate Constants for Hydrogen–Deuterium Exchange in Methanol-O-*d*-Dimethyl Sulfoxide-d_6 (75:25)[a] Catalyzed by Potassium Methoxide at 75.0°

Compound	pK_a[d]	$\Delta F^{\ddagger}$, kcal/mol	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, cal/deg mol	k_2, l./mol sec[e] ± %
Fluorene	20.5	20.5 ± 0.1	16.7 ± 0.6	−10.8 ± 2.1	$5.00 \pm 20.6 \times 10^{-1}$
9-Phenylxanthene	25.8	25.1 ± 0.03	26.9 ± 1.3	5.2 ± 3.8	$1.36 \pm 4.7 \times 10^{-3}$
4-Biphenylyldiphenylmethane	27.3	27.5 ± 0.04	28.2 ± 1.2	1.8 ± 3.5	$3.80 \pm 9.1 \times 10^{-5}$
Triphenylmethane[b]	28.8	28.2 ± 0.1	29.6 ± 1.8	3.9 ± 5.6	$1.39 \pm 17.6 \times 10^{-5}$
Triphenylmethane[c]	28.8	28.9 ± 0.1	30.5 ± 1.3	4.6 ± 4.0	$5.42 \pm 17.9 \times 10^{-6}$
Diphenylmethane[b]	30.2	29.8 ± 0.2	33.5 ± 1.1	10.7 ± 3.5	$7.39 \pm 23.3 \times 10^{-7}$
Diphenylmethane[c]	30.2	31.4 ± 0.2	37.5 ± 2.0	17.5 ± 6.3	$7.30 \pm 29.5 \times 10^{-8}$

[a] Per cent by volume at room temperature before mixing. [b] Calculated from data in ref 14 for 0.200 *M* potassium methoxide. [c] Calculated from data in ref 14 for infinitely dilute potassium methoxide. [d] Reference 4. [e] Rate constants corrected, where necessary, for statistical factors.

effects because in either instance the two processes did not differ in rate by more than 10%. The first estimated pK_a is based upon a kinetic acidity which is *ca.* sixfold greater than that of fluorene (pK_a = 20.5) after application of a statistical factor; *e.g.*, see runs 10 and 12 in Table III and run 22 in Table VI. The second estimated pK_a is based upon a kinetic acidity which is *ca.* 0.7 times that of diphenylmethane (pK_a = 30.2) after application of a statistical factor; *e.g.*, in ref 14 see run 10 in Table I and run 25 in Table II.

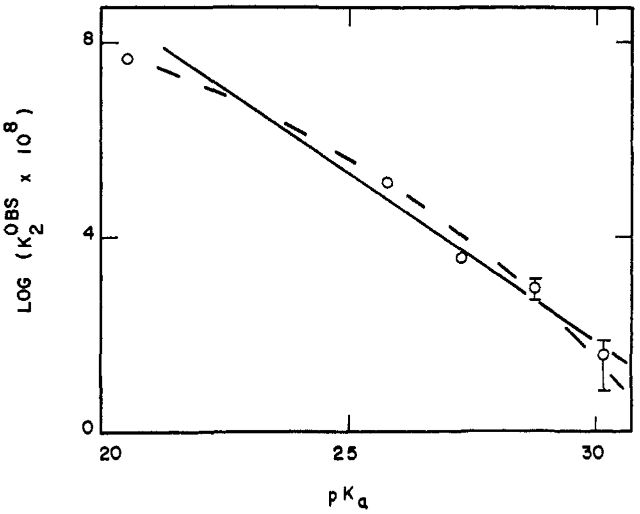
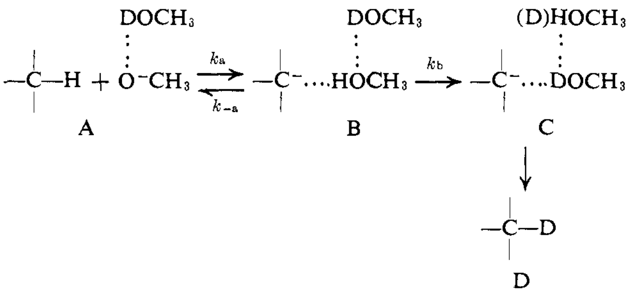


Figure 1. A correlation of kinetic and thermodynamic acidities o some di- and triarylmethanes; slope = 0.7.

Discussion

In the exchange reactions studied, the pK_a's of the carbon acids varied from about 20 to 30. The pK_a of methanol which is produced by proton abstraction is about 16. Hence, the ΔpK_a between carbon acid and the conjugate acid of the basic catalyst varied from about 4 to 14 as the carbon acids became weaker. Three trends are visible in the results. (1) As ΔpK_a increases, the slope of the Brønsted plot increases. (2) The entropy of activation becomes dramatically more positive as ΔpK_a increases. (3) The kinetic isotope effect for racemization (and hence exchange) decreases as ΔpK_a increases.

Chart I



In Chart I is outlined a general mechanistic scheme for isotopic exchange with CH_3O^- as base. Dissociation of carbon acid A is undoubtedly the slow step (k_a), and application of the steady-state approximation produces eq 1 which relates k_{obsd} (pseudo-first-order rate constant for isotopic exchange) to k_a, k_{-a}, and k_b. In A → B, a covalent bond is broken and a hydrogen bond is made, whereas in B → C one hydrogen bond is exchanged for a second. If B goes to C faster than it returns to A, then eq 2 applies. If B returns to A faster than it goes to C, then eq 3 relates the rate constants. Thus, eq 2 and 3 describe two discrete

$$k_{\text{obsd}} = \frac{k_a k_b}{k_{-a} + k_b} \tag{1}$$

$$k_{\text{obsd}} = k_a \text{ if } k_b \gg k_{-a} \tag{2}$$

$$k_{\text{obsd}} = \frac{k_a}{k_{-a}} k_b = K k_b \text{ if } k_{-a} \gg k_b \text{ and } K = k_a/k_{-a} \tag{3}$$

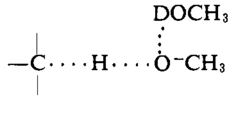
mechanisms for isotopic exchange and racemization. In cases where isotopic exchange and racemization have been studied in nonpolar solvents, examples of $k_{-a} > k_b$ have been observed. These examples always involved ion-pair intermediates rather than free anions,[19] and either exchange with retention or isoinversion (inversion without exchange) were the observed stereochemical courses. Even in a methanolic potassium methoxide medium, evidence has accumulated that $k_{-a} \sim k_b$ in systems where ΔpK_a was considerably less than 10.[20] In the first example, 1,5-intramolecular proton transfer competed with intermolecular proton transfer,[20a] and in the second, isoinversion competed with inversion with exchange.[20b]

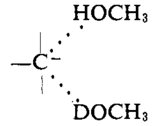
It is reasonable to assume that as ΔpK_a increases, the value of k_{-a} would grow relative to k_b. At one extreme

[19] (a) D. J. Cram, C. A. Kingsbury, and B. Rickborn, *J. Am. Chem. Soc.*, **83**, 3688 (1961); (b) D. J. Cram, D. A. Scott, and W. D. Nielsen, *ibid.*, **83**, 3696 (1961); (c) ref 17; (d) D. J. Cram and L. Gosser, *ibid.*, **86**, 5457 (1964).

[20] (a) D. J. Cram, F. Wiley, H. P. Fischer, H. M. Relles, and D. A. Scott, *ibid.*, **88**, 2759 (1966); (d) W. T. Ford, E. W. Graham, and D. J. Cram, *ibid.*, **89**, 4661 (1967).

of this *model* when ΔpK_a is low, $k_b \gg k_{-a}$ (eq 2 applies), and when ΔpK_a is high, $k_{-a} \gg k_b$ (eq 3 applies). The three trends in the data are consistent with the notion that in passing from the fluorene systems to the diarylmethane k_{-a}/k_b increases, and the balance of mechanistic components change. When eq 2 applies, the transition state of highest energy is $(A \rightarrow B)^{\neq}$, where a covalent bond is broken, and when eq 3 applies, the transition state of highest energy is $(B \rightarrow C)^{\neq}$, where one hydrogen bond is exchanged for its isotopic counterpart. The ground states of the medium are the same and the substrates are assumed to be comparable in solvation energy, and so the trends in data can be discussed in terms of the energies and structures of the two transition states.

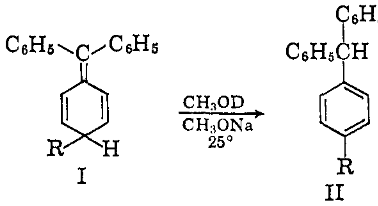

$(A \rightarrow B)^{\neq}$


$(B \rightarrow C)^{\neq}$

Change of Slope of Brønsted Plot with ΔpK_a. The Bronsted plot of Figure 1 shows curvature such that as ΔpK_a increases, the slope increases. For example, the slope defined by the two strongest acids is about 0.5, and by the three weakest acids is about unity. The slope, α, of a Brønsted plot lies within the range of zero and unity.[21] The magnitude of α has been interpreted as a semiquantitative measure of the degree of resemblance between the transition state and the final state in a proton-transfer process.[21] The closer the transition state resembles anion, the closer to unity α is expected to be. Transition state $(B \rightarrow C)^{\neq}$ actually involves the anion itself, and if it applies, should have an α of about unity, as is observed for the weaker carbon acids of the study. Transition state $(A \rightarrow B)^{\neq}$ involves a partially made anion and should be less than unity, as is observed for the stronger carbon acids investigated.

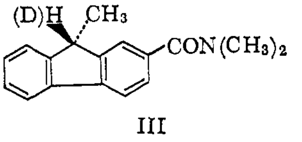
Change in $\Delta S^{\neq}$ for Isotopic Exchange with ΔpK_a. The data of Table VII describe a trend in which $\Delta S^{\neq}$ for isotopic exchange of the carbon acids changes from about -11 eu with the strongest carbon acid to close to $+11$ eu for the weakest carbon acid. In transition state $(B \rightarrow C)^{\neq}$ charge is highly delocalized into the aryl groups since the carbanion is the species involved. In transition state $(A \rightarrow B)^{\neq}$ charge is partially localized on oxygen. Thus, more solvent is expected to be "frozen out" in $(A \rightarrow B)^{\neq}$ than in $(B \rightarrow C)^{\neq}$. Thus, the carbon acid with the lower ΔpK_a has an entropy consistent with $(A \rightarrow B)^{\neq}$, and the carbon acid with the higher ΔpK_a an entropy consistent with $(B \rightarrow C)^{\neq}$. In this connection, potassium methoxide in methanol has an average solvation number of 9 at 25,[22] whereas the fact that the conversion of I → II occurs with 46% intramolecularity at 25° points to a solvation number of little more than one for a triarylmethyl anion.[20a]

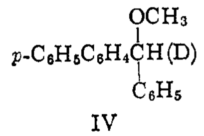
Change of Isotope Effect for Isotopic Exchange with ΔpK_a. The data provide kinetic isotope effects of $(k_H/k_D)_e \sim 6.7$ at 25° for carbon acid III and $(k_H/k_D)_e \sim 2.5$ at 126° for carbon acid IV. The *kinetic* isotope effect for a transition state such as $(B \rightarrow C)^{\neq}$ is expected to be close to or less than unity, whereas the kinetic isotope effect for $(A \rightarrow B)^{\neq}$ is expected to be higher and always positive.[18] The ΔpK_a for III is small compared to IV, and thus transition state $(A \rightarrow B)^{\neq}$ correlates again with carbon acids of low ΔpK_a, and $(B \rightarrow C)^{\neq}$ with carbon acids with high ΔpK_a's.


I II

The only trouble with this explanation is the fact that the isotope effect for IV is still not close to unity. In other work,[23] evidence for tunneling contributions to isotope effects in base-catalyzed proton-transfer reactions has accumulated. Proton tunneling enhances the kinetic isotope effect when eq 2 applies but should have no effect on either K or k_b when eq 3 applies. The value of k_{-a}/k_b should increase with proton tunneling; this would enhance the contribution of the mechanistic component described by eq 3. Thus, proton tunneling provides no reason why IV should exhibit a residual isotope effect. This residual isotope effect must reflect isotope effects associated either with k_b if eq 3 applies, or with k_1 if IV goes by a blend of the mechanisms represented by eq 1 and 3.

The three trends in the data can also be explained solely on the basis of changes in the character of transition state $(A \rightarrow B)^{\neq}$ with changes in ΔpK_a. The smaller the ΔpK_a, the lower the activation energy, and the more the transition state resembles the starting material. The larger the ΔpK_a, the higher the activation energy, and the more the transition state resembles the product.[24] The arguments parallel those developed above except that the scale for structural change of the transition states in question is compressed. Furthermore, proton tunneling is not required to explain the isotope effect for IV utilizing this single mechanism[10c,d,e] whose rate-determining transition state has a migrant reaction coordinate.


III


$p\text{-}C_6H_5C_6H_4CH(D)(OCH_3)C_6H_5$

IV

Experimental Section

General Comments. All physical measurements were made as described previously[14] unless otherwise stated. Deuterated reaction medium was prepared as before and base titer determinations were made the same way.[14] Fluorene, mp 115–116°, was obtained from Matheson Coleman and Bell. The synthesis of optically active and deuterated 2-(N,N-dimethylcarboxamido)-9-methylfluorene has been described previously.[17] The general procedure used for the exchange and racemization reactions has been described.[14]

9-Phenylxanthene. A known procedure to produce 9-phenylxanthydrol[15] was modified by substituting tetrahydrofuran (THF)

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[21] J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, pp 156–159.

[22] E. C. Steiner, J. D. Starkey, J. M. Tralmer, and R. O. Trucks, 153rd National Meeting of the American Chemical Society, April 1967, Miami Beach, Fla., Abstracts, Q33.

[23] (a) W. T. Ford and D. J. Cram, unpublished work; (b) R. P. Bell, J. A. Fendley, and J. R. Hulett, *Proc. Roy. Soc.* (London), **A235**, 453 (1956); (c) E. S. Lewis and L. H. Funderburk, *J. Am. Chem. Soc.*, **89**, 2322 (1967).

[24] G. S. Hammond, *ibid.*, 77, 334 (1955).

for ether as the reaction medium, which allowed addition of 9-xanthenone as a solution (not a solid) to phenylmagnesium bromide. The carbinol was obtained in 89% yield after recrystallization from benzene, mp 159–161°. This material (12.14 g) was reduced wih formic acid[25] to give, after two recrystallizations from ethyl acetate, 7.80 g of 9-phenylxanthene,[26] mp 145–146.5°; nmr (deuteriochloroform): τ 2.81–2.98 (13 H, multiplet, aromatic) and 4.80 (1 H, singlet, methine). *Anal.* Calcd for $C_{19}H_{14}O$: C, 88.34; H, 5.46. Found: C, 88.57; H, 5.27.

4-Biphenylyldiphenylmethane. A solution of 4-biphenylylmagnesium bromide in THF (0.050 mol) was added to benzophenone (0.050 mol) in THF. After 1.5 hr, the excess solvent was evaporated, and the syrupy residue was hydrolyzed with ice-cold aqueous ammonium chloride. The white solid was filtered and washed with 50% aqueous acetic acid and then with water. It was dissolved in benzene, filtered, dried, and evaporated. The residue was redissolved in hot glacial acetic acid and refiltered to remove traces of a white, voluminous substance. Crystallization by addition of water gave 11.6 g (77%) of 4-biphenylyldiphenylmethanol, mp 132–134.5° (lit. mp 136.4–137.2°).[16] This material, 11.25 g, was reduced with formic acid[25] to give, after recrystallization from methanol, 8.88 g (82%) of product with mp 109.5–114° (lit. mp 112–113°).[27] The melting point remained unchanged after column chromatography of the material on silica gel; nmr spectrum in deuteriochloroform: τ 2.42–2.90 (19 H, multiplet, aromatic) and 4.43 (1 H, singlet, methine). *Anal.* Calcd for $C_{25}H_{20}$: C, 93.71; H, 6.29. Found: C, 93.80; H, 6.03.

9,9-Dideuteriofluorene. The following method is longer than the method reported.[28] A mixture of 1.27 g of fluorene, 1.00 g of sodium methoxide, 11.05 ml of 99.8% deuterium oxide, and 50 ml of dimethoxyethane was refluxed under dry nitrogen for 20 hr, cooled, and poured into 100 ml each of water and ether. The organic layer was dried and evaporated. The crude product (1.20 g) was submitted to a second and similar exchange but with 0.43 g of catalyst. The product was recrystallized from methanol to give 0.90 g (71%) of product, mp 113.5–114.5°; nmr in deuteriochloroform: τ 2.17–2.92 (multiplet, aromatic). The infrared spectrum in carbon tetrachloride showed the absence of any bands attributable to methylene protons (2930, 1400, 1298, 952, and 692 cm^{-1}).[28] Deuterium analysis by the combustion and falling-drop method gave 96% of two atoms of deuterium per molecule.

9-Deuterio-9-phenylxanthene. Under dry nitrogen, 7.40 g of 9-phenylxanthene in 500 ml of dry ether was mixed with 21 ml of 1.6 *M n*-butyllithium, and the mixture was stirred for 2 hr at 25°. The mixture was quenched with 0.8 ml of 99.8% deuterium oxide. The ethereal solution was washed with 1 *N* hydrochloric acid and twice with water, dried, and evaporated. The residue was recrystallized from ethyl acetate. The product, 6.14 g (83%), had mp 145.5–146.5°. The infrared spectrum in chloroform exhibited a band at 985 cm^{-1} which was not observed in the protio compound. In addition, the protio compound had the following bands which were not present in the deuterated compound: 2880, 2020, 1320, 1180, 880, 840, and 590 cm^{-1}. Deuterium analyses (combustion and falling-drop method) revealed 77.7% of one atom of deuterium per molecule.

4-Biphenylyldeuteriodiphenylmethane. Into a dry, heavy-walled ampoule were placed 1.50 g of 4-biphenylyldiphenylmethane, 15.0 ml of 0.64 *N* potassium methoxide in methanol-O-*d*, and 5.0 ml of dimethyl-d_6 sulfoxide. The tube was sealed under vacuum and placed in a 100° bath for 6 days. The contents were poured into 100 ml each of 1 *N* hydrochloric acid and ether. The organic layer was washed twice with water, dried, and evaporated. The residue was recrystallized from ethanol; this procedure produced 1.35 g of product with mp 110–113°. Deuterium analysis (combustion and falling-drop method) revealed 95.0% of one atom of deuterium per molecule. The infrared spectrum (carbon tetrachloride) showed a C–D band at 2120 cm^{-1}.

Deuterium Analyses for Fluorene. The deuterium content at the benzylic position was determined from the nmr integration ratio of aromatic to benzylic protons. Each ratio was calculated from the average of ten or more integrations of each peak. The recovered kinetic samples, *ca.* 60–70 mg, were dissolved in 0.28 ml of carbon disulfide; these solutions were used in the nmr analyses. The analyses for a kinetic run were all obtained at the same session without intervening adjustments of the spectrometer.

Deuterium Analyses of 9-Phenylxanthene. The analyses made use of an infrared band at 985 cm^{-1} which was present in the deuterated compound and absent in the protio compound. Solutions of isolated and purified substrate were composed of *ca.* 15–20 mg in 0.100 ml of bromoform. Absorbances were measured with the following instrument settings: scale 5×, slit program 2×, gain 5, attenuator speed 600, suppression 5, scan speed 32 mn, and source current 0.30 amp. A calibration curve of absorbance/milligram *vs.* mole % exchangeable protium was constructed. The analyses of kinetic points were obtained by comparison to this curve. Analytical spectra for the calibration curve and kinetic points were always measured during the same session.

Deuterium Analyses of 4-Biphenylyldiphenylmethane. The analyses made use of an infrared C–D band at 2120 cm^{-1}. Solutions of isolated and purified substrate were composed of *ca.* 25 mg of 0.100 ml of bromoform. Absorbances were measured with the following instrument settings: scale 5×, slit program 2×, gain 5, attenuator speed 450, suppression 5, scan speed 32 min, and source current 0.30 amp. A calibration curve of absorbance/milligram *vs.* mole % exchangeable protium was constructed. The analyses of kinetic points were obtained by comparison to this curve. Analytical spectra for the calibration curve and kinetic points were always measured during the same session.

Deuterium Analyses of 2-(N,N-Dimethylcarboxamido)-9-methylfluorene. The procedure has been reported.[17]

Fluorene Exchange Runs. A typical experiment, run 6, involved 0.8030 g of substrate, 45.00 ml of basic methanol-O-*d*, and 15.00 ml of dimethyl-d_6 sulfoxide. Approximately 7-ml aliquots were placed in tubes, which were sealed with rubber septum caps and placed directly in the constant temperature bath. The appreciable exchange rate at room temperature required rapid action from the time the dimethyl-d_6 sulfoxide was added until the rate tubes were placed in the 0 or 15° bath. Aliquots were quenched in a Dry Ice–acetone mixture and then poured into an equally chilled and magnetically stirred mixture of 50 ml of ether and 0.3 ml of acetic acid. The organic solution was washed in succession with 50-ml portions of water, 0.1 *N* sodium bicarbonate solution, and water and then dried and evaporated. Residual ether was evaporated under vacuum. The exchanged substrate was dissolved in 0.28 ml of carbon disulfide and analyzed by nmr.

Several one-point rate constants were obtained at 25 and 50° by use of an inverted Y-shaped tube. In one arm of the tube was placed 133 mg of fluorene, 1.00 ml of dimethyl-d_6 sulfoxide, and 3.00 ml of methanol-O-*d*. In the other arm was placed 3.00 ml of 0.251 *N* potassium methoxide in methanol-O-*d* and 1.00 ml of dimethyl-d_6 sulfoxide. The tube was sealed with a rubber septum cap, removed from a drybox, and placed in the 25 or 50° bath. The reaction was initiated by pouring the contents of one arm into the other several times in rapid succession. After a timed interval the solution was quenched, worked up, and analyzed as before. In this manner one can assume 100% protio content in the substrate at the time of mixing. This value coupled with the protium content determined at the time of quenching allows calculation of the rate constant for reactions with very short half-lives.

9-Phenylxanthene Exchange Runs. A typical experiment, run 15, involved 0.2016 g of substrate, 15.00 ml of basic methanol-O-*d*, and 5.00 ml of dimethyl-d_6 sulfoxide. In runs 16 and 17 each ampoule contained *ca.* 2.2 ml and was worked up as follows. The contents were poured into 15 ml each of 1 *N* hydrochloric acid and ether. The organic layer was washed twice with water, dried, and evaporated. The residue was recrystallized from 0.50 ml of ethanol. The weighed sample, *ca.* 15–20 mg, was dissolved in 0.100 ml of bromoform for isotopic analysis. In runs 14 and 15 ampoules were not used. The kinetic solution was placed in a 50-ml flask which was sealed with a rubber septum cap and then placed in the 60.90° bath. During the temperature equilibration period, solvent pressure was vented by piercing the septum cap with a fine gauge syringe needle. The exchange rate at 60.90° was sufficiently slow so that the substrate was safely assumed to be 0.0% exchanged after this time. At kinetic time zero, the 100.0% protium value was assumed without actually working up a point. At timed intervals *ca.* 2.2-ml aliquots were removed with a dry, nitrogen-filled syringe. These aliquots were worked up as before.

4-Biphenylyldiphenylmethane Exchange Runs. Two typical experiments, runs 18 and 19, involved 0.5996 g of substrate, 30.00 ml of basic methanol-O-*d*, and 10.00 ml of dimethyl-d_6 sulfoxide. Two sets of ampoules, *ca.* 2 ml each, were prepared. In runs 18–21, the solutions were made up to initially contain about 20% deuterio

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[25] H. Kauffman and P. Pannwitz, *Ber.*, **45**, 766 (1912).

[26] F. Ullman and G. Engi, *ibid.*, **37**, 2367 (1904).

[27] W. Schlenk, T. Weickel, and A. Herzenstein, *Ann.*, **372**, 1 (1910).

[28] G. W. H. Scherf and R. K. Brown, *Can. J. Chem.*, **38**, 697 (1960).

substrate. The analytical error would have been excessively large for lesser deuterium content. The aliquots were worked up in the manner described for 9-phenylxanthene. The recovered material was recrystallized from 1 ml of ethanol. The weighed sample, *ca.* 25 mg, was dissolved in 0.100 ml of bromoform and analyzed by the infrared method.

2-(N,N-Dimethylcarboxamido)-9-methylfluorene Exchange and Racemization Runs. The following experiment measured the ratio of first-order rate constants for exchange and racemization of the protio substrate (runs 22 and 23). In 10.00 ml of 3:1 (by volume) methanol-O-*d*–dimethyl-d_6 sulfoxide, which was approximately 0.0026 *N* in potassium methoxide, was dissolved 0.2124 g of protio substrate with $[\alpha]^{26}{}_{546}$ +34.0° (*c* 6.00, dioxane).[17] Nine 1.00-ml aliquots were placed in clean 3-ml test tubes, sealed with rubber septum caps, placed in the 24.80° bath, and quenched at timed intervals as follows. A Hamilton syringe equipped with a Chaney adaptor delivered a highly reproducible volume (±0.5% precision) of about 0.25 ml of 9:1 (by volume) methanol–12 *N* hydrochloric acid into each test tube. The quenched aliquots were then used as such to determine the optical rotation at 25° and 436 mμ. Each aliquot was retrieved from the polarimeter cell and worked up for isotopic content. The aliquot was poured into 25 ml each of water and ether, washed twice with water, dried, and evaporated. The residue was chromatographed on silica gel in a small tube of 15-cm length and 0.7-cm inner diameter. About 20 ml of ether was used as the eluent. The eluent was evaporated and residual ether was pumped off under vacuum. The purified material was analyzed according to an established procedure.[17]

The following experiment measured the first-order rate constants for racemization of optically active protio and deuterio substrates (runs 24 and 25). In 1.00 ml of 3:1 by volume methanol-O-*d*–dimethyl-d_6 sulfoxide, which was *ca.* 0.0067 *N* in potassium methoxide, was dissolved 21.1 mg of the optically active protio substrate. This solution was placed in a polarimeter cell and removed from the drybox. The optical rotation was observed at 24.80° and 436 mμ. An identical experiment was performed with 19.3 mg of optically active deuterio substrate dissolved in 1.00 ml of the same solvent.

Control on Isotopic Fractionation during Crystallization of Partially Deuterated 9-Phenylxanthene. A sample of 22.7 mg of 9-phenylxanthene and 127.2 mg of 9-deuterio-9-phenylxanthene (77.7% of one atom of deuterium per molecule) was dissolved in carbon tetrachloride, divided into two equal aliquots, and evaporated to dryness. One aliquot was recrystallized from ethanol. Both samples were weighed and dissolved in 0.200 ml of bromoform. The infrared absorbance was measured at 985 cm^{-1}. The two samples, recrystallized and untreated, gave values of 1.79 and 1.80, respectively, for (absorbance × 10^3/mg of sample). Estimated errors of ±0.2 mg in sample weights and ±0.5% in absorbances indicate that the two values are identical within experimental error.

Intramolecular Nucleophilic Participation. V. The Role of the *ortho* Substituent in the Solvolysis of *o*-Nitrobenzhydryl Bromide and *o*-Nitrobenzyl Tosylate

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Abstract: The capacity of the *o*-nitro group to serve as an internal nucleophile in the hydrolysis of *o*-nitrobenzhydryl bromide and of *o*-nitrobenzyl tosylate has been investigated. Two experimental observations lead to the conclusion that it is a highly effective participant in the reaction of the former compound: (a) *o*-nitrobenzhydryl bromide solvolyzes considerably more rapidly in 90% aqueous acetone than does its *para* isomer; (b) its hydrolysis product is *o*-nitrosobenzophenone. *o*-Nitrobenzyl tosylate hydrolyzes somewhat less rapidly than its *para* isomer, and the evidence is strong that the *o*-nitro group participates much less extensively in reactions of benzyl than of benzhydryl systems. Good yields of *o*-nitrobenzhydryl bromide are obtained from the reaction of *o*-nitrodiphenylmethane and N-bromosuccinimide in carbon tetrachloride only if the temperature of the reaction is controlled. Otherwise a mixed product is obtained, from which 5-bromo-3-phenyl-2,1-benzisoxazole can be isolated. The reaction paths for production of the benzisoxazole and for formation of *o*-nitrosobenzophenone by hydrolysis of *o*-nitrobenzhydryl bromide are considered to have certain features in common.

There is a considerable accumulation of evidence, varying in credibility from mildly suggestive[1,2] to virtually conclusive, that *o*-nitro groups may function as internal nucleophiles in polar reactions at aromatic side chains. The fact that in acetic acid *o*-nitroiodobenzene dichloride dissociates to the component iodo compound and chlorine much faster than does its *para* isomer[3] is of particular significance in this regard. Also of fundamental importance in the same connection is the observation that *o*-nitrobenzhydrol is converted to *o*-nitrosobenzophenone when it reacts with formic acid or with *o*-toluenesulfonyl chloride in pyridine and yields 5-chloro-3-phenyl-2,1-benzisoxazole on treatment with thionyl chloride in chloroform.[4]

An attempt has been made previously to explore the possibility that the nitro group may participate in solvolysis reactions of *o*-nitrobenzhydryl bromide.[5] Until the present investigation a crystalline sample of this bromide has not successfully been prepared. In the earlier study[5] the crude oily product of the reaction of N-bromosuccinimide with *o*-nitrodiphenylmethane was employed (as the *ortho*-substituted isomer) in comparing the hydrolysis rates of *o*- and *p*-nitrobenzhydryl bromides. On the basis of the results of those measure-

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