with hydrochloric acid a commercial 40% aqueous solution of the corresponding hydroxide. The sample was dried at 100° (0.01 mm) for 6 hr, recrystallized from a mixture of anhydrous ethanol and ether, and again dried *in vacuo* at 100°. It was stored in a desiccator.

Kinetic Measurements. The reactions in ethanol were carried out essentially by the procedure of Saunders and Williams[2] for the reactions of the corresponding sulfonium bromides with sodium ethoxide in absolute ethanol. Aliquots were taken periodically with a 1.0-ml calibrated hypodermic syringe and diluted twice to 25.0 ml with 95% ethanol (625-fold dilution). The optical density was determined at the absorption maximum for the styrene[2] and the concentration of the styrene calculated. Initial concentrations in the reaction mixtures were near 0.1 *M* in the sodium ethoxide and 0.05 *M* in the ammonium salt. Rate constants were calculated point by point, using the integrated form of the second-order rate law for unequal initial concentrations. Values in Table I are averages of at least two separate runs. Reactions were followed to at least two half-lives.

The runs in *t*-butyl alcohol were carried out in the thermostated cell compartment of a Beckman DU or Unicam S.P. 800 spectrophotometer as described by Cockerill, Rottschaefer, and Saunders[6] for the corresponding reactions of the 2-arylethyl bromides. Reagents and solutions were prepared in the same fashion as well. Substrate concentrations of 3–8 $\times 10^{-5}$ *M* were used, and the base concentration was always at least ten times the substrate concentration, though the high speeds of these reactions made necessary lower base concentrations than in the previous work. The pseudo-first-order rate constants were determined as before[5] from the experimental data. The pseudo-1.5-order rate constants were determined from a plot of $[(D_\infty - D)C_0/D_\infty]^{-0.5}$, which is equivalent to $C^{-0.5}$.

Conductivity Measurements. A Mullard conductivity cell (type E 7591/B) with platinized platinum electrodes was used. The cell was connected to a Pye conductance bridge (No. 11,700) with screened coaxial cable. Errors in the conductances given in Table III are $\pm 0.003 \times 10^6$ mho/cm. We thank Mr. G. R. Taylor for use of this equipment.

Electrophilic Substitution at Saturated Carbon. XXXV. Mechanistic Components in Base-Catalyzed Racemization and Isotopic Exchange of 4-Biphenylylmethoxyphenylmethane in *t*-Butyl Alcohol-O-*d*[1]

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Abstract: The syntheses of optically active 4-biphenylylmethoxyphenylmethane (I-*h*) and 4-biphenylyldeuteriomethoxyphenylmethane (I-*d*) are described. The kinetics of racemization and isotopic exchange of (−)-I-*h* in *t*-butyl alcohol-O-*d*–potassium *t*-butoxide have been studied, as well as of racemization of (+)-I-*d* in the same medium. Rate constants for isotopic exchange of (±)-*I-h* and for racemization of (+)-I-*d* in this medium were determined. The variation with time of the optical activity of (−)-I-*h* was followed, and the results were demonstrated to be compatible with a kinetic model which provides for dissection of data into mechanistic pathways for isotopic exchange with retention and with inversion of configuration. The kinetic isotope effect for racemization in deuterated solvent at 116° was $(k^{\mathrm{H}}/k^{\mathrm{D}})_\alpha = 2.7$. At this temperature, the rate constant for isotopic exchange with retention exceeded that for isotopic exchange with inversion by a factor of 33. The mechanisms of the exchange and racemization reactions are discussed.

A kinetic model has recently been developed[2] that allows dissection into specific components of rate data for base-catalyzed isotopic exchange and racemization reactions of carbon acids in proton-donating solvents. As applied to behavior of a starting protio acid in a deuterated solvent, the components are defined by the equations. The symbol H_+ refers to dextrorotatory protio carbon acid, and similar meanings extend to the other symbols. Exchange of *starting material* with retention of configuration (k_1), exchange with inversion (k_2), inversion without exchange or isoinversion (k_3), and inversion of *exchanged product* (k_4) are the four potentially identifiable components.

$$\begin{array}{ll}
H_+ \xrightarrow{k_1} D_+ & H_- \xrightarrow{k_1} D_- \\
H_+ \xrightarrow{k_2} D_- & H_- \xrightarrow{k_2} D_+ \\
H_+ \xrightarrow{k_3} H_- & H_- \xrightarrow{k_3} H_+ \\
D_+ \xrightarrow{k_4} D_- & D_- \xrightarrow{k_4} D_+
\end{array}$$

This model was tested by two experimentally independent methods with optically active and isotopically labeled 2-(N,N-dimethylcarboxamido)-9-methylfluorene. In the first method, partially exchanged and racemized carbon acid was reresolved and the mole fractions of H_+, H_-, D_+, and D_- were calculated. From these mole fractions and experimentally determined values of k_4, values of k_1, k_2, and k_3 were calculated. In a second method, values of k_1, k_2, k_3 were calculated solely from kinetic data. The two methods gave excellent agreement. This kinetic model has been applied only to cases in which net inversion or racemization was the observed result.[2,3] The present paper reports results of a study in which the kinetic model is applied to a system that undergoes isotopic exchange with high net retention of configuration.

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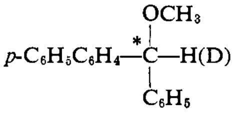
(1) This research was sponsored by the U. S. Army Research Office, Durham, N. C. Our thanks are extended.

(2) (a) W. T. Ford, E. W. Graham, and D. J. Cram, *J. Am. Chem. Soc.*, **89**, 689, 690 (1967); (b) W. T. Ford, E. W. Graham, and D. J. Cram, *ibid.*, **89**, 4661 (1967).

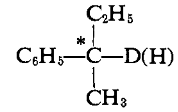
(3) D. J. Cram and T. A. Whitney, *ibid.*, **89**, 4651 (1967).

In previous studies, optically active 2-phenylbutane-2-*d* (II-*d*) and 1-phenylmethoxyethane-1-*d*[4] (III-*d*) were found to undergo potassium *t*-butoxide catalyzed deuterium–hydrogen exchange with net retention, but the high temperature required for the exchange precluded any other than gross kinetic measurements. In the present investigation, 4-biphenylylmethoxyphenylmethane (I-*h*) has been found to undergo rapid enough isotopic exchange with *t*-butyl alcohol-O-*d* to allow convenient kinetic measurements to be made at 116°.



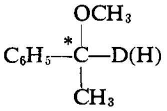
$p\text{-}C_6H_5C_6H_4\text{—}\overset{*}{C}(OCH_3)(C_6H_5)\text{—}H(D)$

I-*h*(*d*)



$C_6H_5\text{—}\overset{*}{C}(C_2H_5)(CH_3)\text{—}D(H)$

II-*d*(*h*)



$C_6H_5\text{—}\overset{*}{C}(OCH_3)(CH_3)\text{—}D(H)$

III-*d*(*h*)

Methods and Results

Starting Material. Racemic I was prepared by methylation of racemic 4-biphenylylphenylcarbinol with methyl iodide and barium oxide in dimethylformamide. The carbinol was prepared by reduction of 4-biphenylyl phenyl ketone with zinc and aqueous sodium hydroxide in dimethoxyethane. When deuterium oxide was substituted for ordinary water, the deuterated carbinol was produced, which led to deuterated ether (I-*d*), 0.98 atom of deuterium per molecule. Both deuterated and nondeuterated carbinol were resolved through the quinine salts of their respective acid phthalates, which were brought to maximum rotation through fractional crystallization.[5a] The acid phthalate of protonated alcohol gave $[\alpha]^{25}_{546}$ +10.4° (*c* 2.5, acetone) which in turn gave carbinol of $[\alpha]^{25}_{546}$ +7.5° (*c* 2.5, chloroform) which provided methyl ether (*I-h*) of $[\alpha]^{25}_{546}$ −6.3° (*c* 2.5, chloroform). The rotations of carbinol and ether could not be changed by fractional crystallization and may be maximal.

Kinetic Data. All kinetic experiments were carried out in *t*-butyl alcohol-O-*d* at identical substrate and potassium *t*-butoxide concentrations of 0.0616 and 0.233 *M*, respectively. At these concentrations the deuterium content of the solvent was 172 times that of the exchangeable hydrogen content in the substrate.

Table I records the first-order rate constants for isotopic exchange of (±)-I-*h* and the racemization of (+)-I-*d*. Both kinetic processes are first order in substrate. The rate constants were calculated from a minimum of 8 points taken over two half-lives by use of a linear least-squares program.[5b]

Table I. Isotopic Exchange of (±)-I-*h* and Racemization of (+)-I-*d* in *t*-Butyl Alcohol-O-*d*[a] with Potassium *t*-Butoxide at 115.80 ± 0.05°

Run	Substrate	Process	$k \times 10^2$, hr^{-1}
1	(±)-I-*h*	Exchange	112 ± 2.8%
2	(±)-I-*h*	Exchange	114 ± 3.2%
3	(+)-I-*d*	Racemization	2.42 ± 1.1%
4	(+)-I-*d*	Racemization	2.49 ± 1.6%

[a] >0.99 atom of deuterium per molecule.

The change in optical activity of (−)-I-*h* with time is given in Table II, and is not first order in substrate. Instantaneous first-order rate constants calculated from the data decrease with time. A qualitative interpretation is that optically active (−)-I-*h* produces (−)-I-*d* which racemizes slower than its protonated counterpart. An analytical interpretation is found in the next section.

Table II. Change of Optical Activity of (−)-I-*h* in *t*-Butyl Alcohol-O-*d*[a]–Potassium *t*-Butoxide with Time at 115.80 ± 0.05°

Time, hr	Run no. 5, $-\alpha_{\text{obsd}}$,[b] deg	Run no. 6, $-\alpha_{\text{obsd}}$,[b] deg
0.00	0.539[c]	0.524[d]
1.00	0.509	0.499
2.00	0.493	0.484
3.00	0.481	9.469
4.00	0.469	0.458
6.00	0.448	0.438
12.00	0.383	0.373
24.00	0.288	0.280

[a] >0.99 atom of deuterium per molecule. [b] Rotations were measured in 1-dm cells at 35.0° and 356 mμ. [c] The observed rotation before temperature equilibration was −0.545°. [d] The observed rotation before temperature equilibration was −0.533°.

Kinetic Model. Equation 1[2] [where $\phi = k_4/(k_2 + k_3)$, the reciprocal of kinetic isotope effect for racemization; $\theta = 2(k_2 + k_3)$, the rate constant for racemization at zero time; and $\psi = (k_2 - k_1)/2(k_2 + k_3)$] expresses α in terms of α_0 and k_1, k_2, k_3, and k_4 defined in the introduction. The model has been simplified by assuming the

$$\alpha = \alpha_0\left[\frac{(\phi - 1)e^{-\theta(1-\psi)t} + \psi e^{-\theta\phi t}}{(\phi - 1) + \psi}\right] \tag{1}$$

absence of an isoinversion component, or $k_3 = 0$ (this assumption is later tested), and eq 2 results. This equation

$$\alpha = \alpha_0\left[\frac{2(k_4 - k_2)e^{-(k_1+k_2)t} + (k_2 - k_1)e^{-2k_4t}}{2k_4 - (k_1 + k_2)}\right] \tag{2}$$

predicts the optical rotation of a carbon acid at time *t* in terms of initial rotation (α_0) and component rate constants for exchange with retention (k_1), with inversion (k_2), and with inversion of the exchange product (k_4). The average exchange rate constant from Table I is 1.13 hr^{-1}, and is equal to $k_1 + k_2$. The average rate constant for racemization of (+)-I-*d* (Table I) is 2.46×10^{-2} hr^{-1}, and this is $2k_4$. Assumed values of k_2/k_4 (kinetic isotope effect for racemization) coupled with these data provided a series of theoretical plots of α/α_0 *vs.* *t*, which were compared with the actual plot of α/α_0 *vs.* *t* computed from the average of runs 5 and 6 of Table II. Figure 1 records the theoretical curves with assumed isotope effects of 0.5, 2.7, and 5.0, and the actual values from runs 5 and 6. The best fit of the experimental data to calculated curves was achieved by a least-squares technique. The value of the sum of the squares deviations (eq 3) for various choices of k_2/k_4 was computed

$$\sum_{t=0}^{t=t} \Delta_t^{\,2} = \sum_{t=0}^{t=t} (f_{\text{calcd}} - f_{\text{obsd}})^2{}_{\text{at }t} \tag{3}$$

where f = fraction of the initial optical activity.

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[4] D. J. Cram, C. A. Kingsbury, and B. Rickborn, *J. Am. Chem. Soc.*, **89**, 3688 (1961).

[5] (a) The authors wish to thank Dr. A. Ratajczak who first performed this resolution. Earlier attempts at resolution were unsuccessful; *cf.* M. P. Balfe, J. Kenyon, and G. E. Searle, *J. Chem. Soc.*, 3309 (1950). (b) We thank Dr. P. Haake for the use of his computer program.

Table III records values of the sums of the squared deviations that correspond to changes in values for the kinetic isotope effect (k_2/k_4) that range fom 2.5 to 3.0.

Table III. Sum of Squared Deviations for Calculated and Observed Optical Activity[a] of (−)-I-*h* at Various Times

k_2/k_4	$10^4 \times \Sigma\Delta t^2$	k_2/k_4	$10^4 \times \Sigma\Delta t^2$
2.5	1.776	2.8	0.480
2.6	0.895	2.9	0.866
2.7[b,c]	0.478	3.0	1.774

[a] Average of runs 5 and 6. [b] The standard deviation produced by this value is ±0.003°. [c] Equivalent to *ca.* 3.7 at 25° (see ref 7).

The best fit ($k_2/k_4 = 2.7$) produced a standard deviation of ±0.003°, which is approximately the limit of error for any observed rotation for the polarimeter employed.

This procedure produced the following values for the rate constants for the various reactions that occurred when (−)-I-*h* underwent isotopic exchange and racemization in *t*-butyl alcohol-O-*d*-potassium *t*-butoxide at 116°. These values depend on the assumption that isoinversion is negligible ($k_3 = 0$). In previous applications of the kinetic model exchange was observed to occur with net inversion or with racemization, and values of $k_2 \sim 10\text{–}12k_3$ were demonstrated.[2,3] To test the assumption that $k_3 = 0$ in the present study, calculations were repeated using eq 1, the above values of k_1, k_2, and k_4, and values for $k_2 = 12k_3$ and $k_2 = k_3$. The assumption that $k_2 = 12k_3$ produced a standard deviation of ±0.008° while the assumption that $k_2 = k_3$ gave a standard deviation of ±0.048°. These values are much worse than the standard deviation of ±0.003° observed with the assumption that $k_3 = 0$, and indicate that k_3 is either very low valued or is zero.

k_1, exchange with retention	1.10 hr^{-1}
k_2, exchange with inversion	0.033 hr^{-1}
k_4, product exchange with inversion	0.012 hr^{-1}

Discussion

Retention Mechanism for Isotopic Exchange. This kinetic analysis leads to the same qualitative conclusion derived earlier from one-point rate constant determinations on other systems (II and III), namely, that base-catalyzed isotopic exchange in *t*-butyl alcohol–potassium *t*-butoxide occurs with high retention of configuration.[4] A measure of the stereospecificity of the reaction as applied to I is provided by the ratio of k_1/k_2 which equals 33. In other words, the rate constant for exchange with retention exceeds that for exchange with inversion by a factor of 33.

The simplest mechanism for isotopic exchange consistent with the results is contained in Chart I. In this scheme, (−)-I-*h* ionizes (reversibly) by a slow reaction with solvated potassium *t*-butoxide to produce an asymmetric ion pair (A) whose anion is planar or near planar due to delocalization of negative charge into the aryl groups. This first ion pair undergoes reorganization to provide a new ion pair B by *rotation of the potassium ion with its ligands* of deuterated and nondeuterated *t*-butyl alcohol. Thus, to produce B from A, C⁻···HOR goes to C⁻···DOR, the hydrogen bonds being made and broken in the same transition state at the "front side" of the carbanion. Collapse of ion pair B to the covalent state gives (−)-I-*d*, product of exchange with retention. This last step is irreversible, since the ROH produced must be "drowned" in the large deuterium pool of ROD. In principle, A → B is reversible, but it is possible that the potassium ion of B exchanges its ROH for ROD irreversibly and faster than B → A. All of the intermediates of this mechanism for isotopic exchange involve ion pairs, and the transition states do not involve large changes in charge separation. Particularly at 116°, *t*-butyl alcohol is a solvent of low dielectric constant.

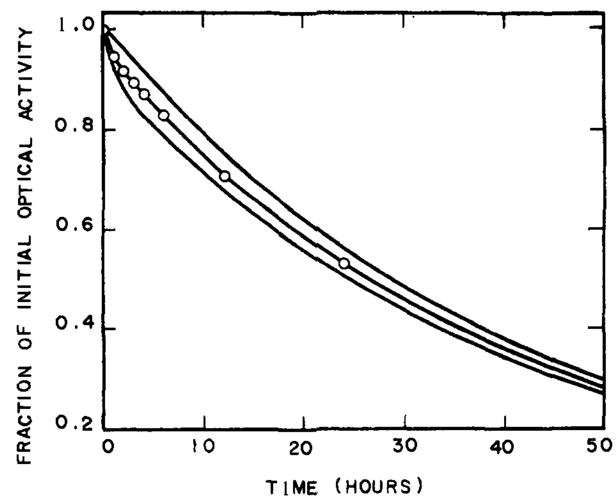
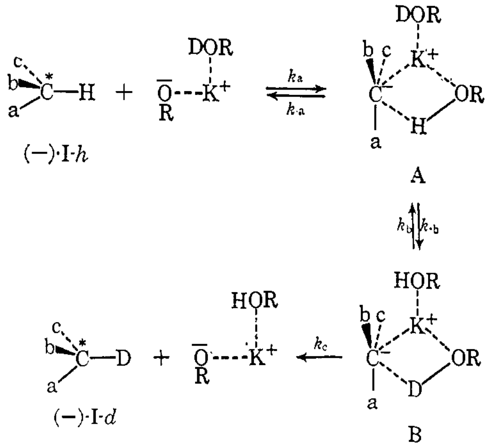


Figure 1. Calculated and observed changes in the optical activity of 4-biphenylylmethoxyphenylmethane, (−)-I-*h*, with time. Upper curve, $k_2/k_4 = 0.5$; middle curve, $k_2/k_4 = 2.7$; lower curve, $k_2/k_4 = 5.0$.

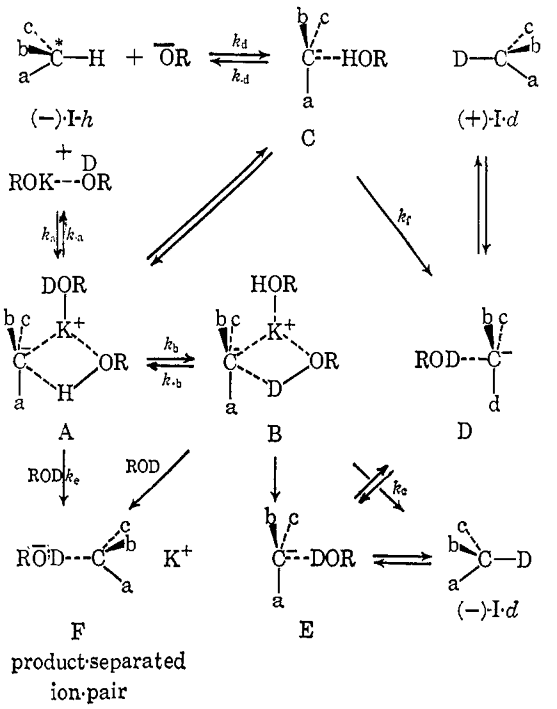
Chart I. Mechanism for Isotopic Exchange with Retention



Isotopic exchange with inversion of configuration was slower by a factor of 33 than exchange with retention. The absence of an isoinversion component ($k_3 \sim 0$) suggests that exchange with inversion does not involve *carbanion rotation* within the ion pair, although such a process can be visualized with the methoxyl group of I-*h* remaining as a ligand of the potassium ion during such rotation. More probable are mechanisms which involve dissociated ion pairs and carbanions hydrogen bonded at the back face as immediate precursors to inverted-exchanged material.

In Chart II, possible mechanisms for isotopic exchange with inversion are outlined. In this scheme, C, D, and E are hydrogen-bonded carbanions with

Chart II. Possible Mechanisms for Isotopic Exchange with Inversion



different configurations and isotopic labels. Only one hydrogen bond per carbanion is drawn since the degree of intramolecularity observed in base-catalyzed 1,5-proton-transfer reactions were incompatible with many hydrogen bonds per benzyl carbanion.[6] Intermediate C might be formed either by reversible reaction of dissociated *t*-butoxide anion with (−)-I-*h*, or by reversible dissociation of ion pair A. Intermediate E might be formed by irreversible dissociation of B, and D either by reversible reaction of E with solvent, or by irreversible reaction of C with solvent. Collapse of D to the covalent state produces inverted exchanged material, and collapse of E, retained exchange material.

Possible capture of either ion pairs A or B by solvent from the back face of the carbanion would lead to *inverted-product-separated* ion pairs F in a medium of low dielectric constant. Such reactions might occur at rates lower than those of Chart I that involve only ion-pair reorganization and collapse to the covalent state without charge separation, but possibly comparable to those of Chart II that involve dissociative processes.

Isotope Effects. The kinetic isotope effect for racemization of (−)-I-*h* and (−)-I-*d* in *t*-butyl alcohol-O-*d*-potassium *t*-butoxide at 116° was $(k_\alpha{}^{\rm H}/k_\alpha{}^{\rm D})_{\rm ROD}$ = 2.7 In the absence of complicating factors such as proton tunneling, this factor should be about 3.7 at 25°.[7] This value is intermediate between extreme values found in the literature. Several studies have reported isotope effects that were either less or slightly greater than unity[4,8,9] for base-catalyzed isotopic exchanges and racemizations of carbon acids. These low values have been explained on the basis of equilibria which precede the transition state of highest energy in which no covalent bonds (only hydrogen bonds) are made or broken.[4,8]

In the mechanism for isotopic exchange with retention envisioned in Chart I, A → (−)-I-*h* and B → (−)-I-*d* are processes that differ only in the type of isotope captured. If collapse of A or B to covalent material has an appreciable isotope effect, then $k_{-a} \gtrsim k_c$. Since exchange with retention occurs at least an order of magnitude faster than exchange with inversion, then k_{-a} and k_c must be higher valued than any rate constant at which intermediates A or B go to inverted-exchanged products. For example, if inverted product should arise by A → F at rate constant k_e, then $k_{-a} > k_e$, and the isotope effect for racemization of (−)-I-*h* *vs.* racemization of (−)-I-*d* in *t*-butyl alcohol-O-*d* can with the steady-state approximation be represented by eq 4 where $K_b{}^{\rm H} = (k_a/k_{-a})^{\rm H}$; $K_b{}^{\rm D} = (k_a/k_{-a})^{\rm D}$.

$$\left(\frac{k_{\rm obsd}{}^{\rm H}}{k_{\rm obsd}{}^{\rm D}}\right)^{\alpha}_{\rm ROD} = \frac{K_b{}^{\rm H}k_e{}^{\rm H}}{K_b{}^{\rm D}k_e{}^{\rm D}} \qquad (4)$$

Since O–H(D) bonds have greater zero-point energy differences than C–H(D) bonds, $K_b{}^{\rm D} \gtrsim K_b{}^{\rm H}$ and $K_b{}^{\rm H}/K_b{}^{\rm D} \lesssim 1$. The only difference in the transformation, A → F, for the two isotopic starting materials is that $k_e{}^{\rm H}$ involves breaking a hydrogen bond between carbanion and ROH, and $k_e{}^{\rm D}$ between carbanion and ROD. Thus, $k_e{}^{\rm H}/k_e{}^{\rm D} \gtrsim 1$, and the net kinetic isotope effect should be close to unity. This argument suggests that exchanged-inverted product arises by some mechanism not involving A or B as intermediates. Mechanism (−)-I-*h* → C → D → (+)-I-*d* provides a possible route, and this mechanism might be expected to provide a substantial kinetic isotope effect for inversion provided $k_f > k_{-d}$ (Chart II).

Experimental Section

General Comments. Deuterium analyses by the combustion and falling-drop method were performed by J. Nemeth of Urbana, Ill. Melting points were taken on a Mel-Temp melting point block apparatus and are uncorrected. Infrared spectra for deuterium analyses were obtained with a Perkin-Elmer 421 spectrophotometer, all others with a Beckman IR-5 spectrophotometer. Proton nuclear magnetic resonance (nmr) spectra and integrations were obtained with a Varian A-60 instrument. Tetramethylsilane was used as an internal standard. Optical rotations were measured with a Perkin-Elmer 141 polarimeter and a 1-dm, thermostated cell. Sodium sulfate was used as a drying agent unless otherwise stated. All kinetic solutions were prepared in a drybox filled with purified nitrogen.

Racemic 4-Biphenylyldeuteriophenylmethanol (IV-*d*). Benzoylation of biphenyl in 125-g batches gave *ca.* 85% yields of 4-biphenylyl phenyl ketone, mp 102–103° (lit.[10] mp 106° cor). Reduction was accomplished by a modification of a known procedure.[11] To a stirred mixture of 400 ml of dry dimethoxyethane, 81.2 g of ketone, and 60 g of dry zinc dust in a dry atmosphere was added a sodium deuterioxide solution prepared from 23 g of sodium and 62 g of 99.8% deuterium oxide. The mixture was stirred for 2 hr. The organic layer was decanted into 3 *N* hydrochloric acid solution. *Caution:* the residual zinc paste may spontaneously ignite if allowed to dry! The crude product was filtered, air dried, and recrystallized from hexane-benzene. The purified material weighed 74.2 g (90%) and had mp 94–95° (lit.[12] mp 95–96° for IV-*h*). In deuteriochloroform (15% solution by weight), IV-*d* gave bands at τ 2.65 (14 hydrogens, multiplet, aromatic) and at 7.28 (1 hydrogen,

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[6] D. J. Cram, F. Willey, H. P. Fischer, H. M. Relles, and D. A. Scott, *J. Am. Chem. Soc.*, **88**, 2759 (1966).

[7] K. B. Wiberg, *Chem. Rev.*, **55**, 713 (1955).

[8] D. J. Cram, D. A. Scott, and W. D. Nielsen, *J. Am. Chem. Soc.*, **83**, 3696 (1961).

[9] J. E. Hoffmann, A. Schriesheim, and R. E. Nickols, *Tetrahedron Letters*, 1745 (1965).

[10] H. R. Henze and L. M. Long, *J. Am. Chem. Soc.*, **63**, 1939 (1941).

[11] F. Y. Wiselogle and H. Sonneborn, "Organic Syntheses," Coll. Vol. 1, John Wiley and Sons, Inc., New York, N. Y., 1941, p 90.

[12] E. Bergmann, *Ber.*, **63**, 1617 (1930).

singlet hydroxyl). No signal was observed for the benzhydryl hydrogen. The infrared spectrum in carbon tetrachloride showed O–H absorption at 3600 and 3400 cm^{-1} and a weak C–D band at 2140 cm^{-1} which was absent in the corresponding protio compound.

The protonated analog IV-*h* was similarly prepared in 87% yield, mp 94–95°. Its nmr spectrum in deuteriochloroform (15% solution by weight) gave bands at τ 2.65 (14 hydrogens, multiplet, aromatic), 4.22 (1 hydrogen, doublet, J = 3 cps, methine), and 7.47 (1 hydrogen, doublet, J = 3 cps, hydroxyl).

Resolution of 4-Biphenylyldeuteriophenylmethanol (IV-*d*). A mixture of 64.7 g (0.437 mol) of phthalic anhydride, 114.5 g (0.437 mol) of racemic IV-*d*, and 71 ml of pyridine was heated at 75° overnight and then poured with stirring into ice-cold 1.3 *N* hydrochloric acid. The acid was decanted, and the gummy residue was washed repeatedly with water. The organic material was dissolved in 600 ml of nitromethane, dried, concentrated to 400 ml, and chilled overnight. This afforded 72.4 g of acid phthalate ester, mp 162–165°. The mother liquors were concentrated, dissolved in 250 ml of methanol, and chilled. The second crop of 78.8 g had mp 164–166°. Both crops were separately recrystallized from hot acetonitrile (15 ml/g) to give a total amount of 133 g with mp 168°. This acid phthalate ester was resolved *via* the diastereomeric quinine salts (see Table IV). The resolved salt from the eighth crystallization was dissolved in a minimum volume of acetone and treated with excess 10% sulfuric acid. The resulting oil crystallized and was collected, well washed, and air dried to give 24.5 g (82%) of acid phthalate ester with the indicated rotation. The mother liquors from the first crystallization gave 75.5 g of acid phthalate ester enriched in the opposite enantiomer, $[\alpha]^{25}_{546}$ −4.2° (*c* 2.5, acetone).

Table IV. Resolution of 4-Biphenylyldeuteriophenylcarbinyl Acid Phthalate with Quinine

No.	Input (g of salt)	Methanol, ml	Output (g of salt)	Rotation of ester[a]
1	310.8[b]	1200	160.0	. . .
2	160.0	1000	124.5	. . .
3	124.5	750	81.1	. . .
4	81.1	500	68.5	8.7 ± 0.2
5	68.5	450	61.9	9.6 ± 0.2
6	61.9	450	56.1	9.8 ± 0.3
7	56.1	450	51.4	10.1 ± 0.3
8	51.4	450	46.2	10.4 ± 0.3[c]

[a] $[\alpha]^{25}_{546}$ (*c* 2.5, acetone). [b] Prepared from 0.424 mol each of acid phthalate ester and quinine. [c] An additional recrystallization of *ca.* 200 mg of salt gave no further increase in the optical rotation.

Acid phthalate ester, 8.9 g, with $[\alpha]^{25}_{546}$ − 4.2° (*c* 2.5, acetone), was added to an aqueous sodium ethoxide solution prepared from 10.8 g of sodium, 6 g of water, and 293 ml of absolute ethanol. The solution was heated on a steam bath for 12 min and poured into ice-water. The fluffy precipitate was filtered, dissolved in ether, dried, and concentrated. Recrystallization of the residue from 3:1 (by volume) cyclohexane-benzene afforded 5.5 g (96%) of IV-*d* with mp 86–92° and $[\alpha]^{25}_{546}$ −5.0° (*c* 2.5, chloroform). This material was converted to optically active III-*d* and used in kinetic experiments (see below).

Optically active IV-*h* was similarly prepared by resolution and hydrolysis of racemic acid phthalate, mp 169° (lit.[13] mp 166–167°). From 134 g of quinine salt was obtained after five recrystallizations 19.8 g of salt, whose acid phthalate gave $[\alpha]^{25}_{546}$ 10.4 ± 0.3° (*c* 2.5, acetone), mp 115–170° (with discoloration). The rotation did not change with further recrystallization of the salt. The mother liquors from the first crystallization of the quinine salt gave acid phthalate (34.8 g) of $[\alpha]^{25}_{546}$ −3.8° (*c* 2.5, acetone). Saponification of the acid phthalate of maximum rotation (see above) gave (+)-IV-*h* in 93% yield, mp 93–94°, $[\alpha]^{25}_{546}$ + 7.5° (*c* 2.5, chloroform). Three recrystallizations of this material from 3:1 cyclohexane–benzene left the rotation and melting point unaltered. *Anal.* Calcd for $C_{19}H_{16}O$: C, 87.66; H, 6.19. Found: C, 87.65; H, 6.21.

Racemic 4-Biphenylylmethoxyphenylmethane (I-*h*). A mixture of 10.0 g of racemic IV-*h*, 30 g of barium oxide, 30 ml of methyl iodide, and about 100 ml of dimethylformamide and 0.4 g of water was stirred. The mixture warmed spontaneously and required ice cooling, and after stirring for 12 hr was poured into a mixture of 500 ml each of saturated aqueous ammonium chloride, water, and pentane. The organic layer was washed with aqueous sodium thiosulfate and twice with water, dried, and concentrated. Crystallization of the resulting crude white solid from methanol gave 10.1 g (96%) of purified material, mp 78–79° (lit.[12] mp 80°). This material in deuteriochloroform gave an nmr spectrum as follows: τ 2.3–2.8 (14 hydrogens, multiplet, aromatic), 4.75 (1 hydrogen, singlet, methine), and 6.63 (3 hydrogens, singlet, methoxyl). The infrared spectrum of the substance in carbon tetrachloride gave no OH absorption. *Anal.* Calcd for $C_{20}H_{18}O$: C, 87.56; H, 6.61. Found: C, 87.68; H, 6.59.

Optically Active and/or Deuterated 4-Biphenylylmethoxyphenylmethane (I). Repetition of the above methylation procedure with IV-*h* of maximum rotation $[\alpha]^{25}_{546}$ +7.5° (*c* 2.5, chloroform), mp 93–94°, gave (−)-I-*h* with $[\alpha]^{25}_{546}$ −6.3° (*c* 2.5, chloroform), mp 100–101°. After three recrystallizations from methanol, identical melting point and rotation were observed. *Anal.* Calcd for $C_{20}H_{18}O$: C, 87.56; H, 6.61. Found: C, 87.59; H, 6.54.

Conversion of partially optically active IV-*h* with rotation $[\alpha]^{25}_{546}$ +6.4° (*c* 2.5, chloroform), and mp 86–91°, to I-*h* gave material in 88% yield, $[\alpha]^{25}_{546}$ − 5.7° (*c* 2.5, chloroform), mp 98–101°. This material was spectrally identical with racemic material and material of maximum rotation, and was used in the kinetics.

Conversion of partially optically active IV-*d* with rotation $[\alpha]^{25}_{546}$ −5.0° (*c* 2.5, chloroform) and mp 86–92° gave an 88% yield of (+)-I-*d* with $[\alpha]^{25}_{546}$ +3.3° (*c* 2.5, chloroform) and mp 92–99°. The nmr spectrum of this substance in deuteriochloroform (15% by weight) gave bands at τ 2.3–2.8 (14 hydrogens, multiplet, aromatic) and 6.63 (3 hydrogens, singlet, methoxyl). The infrared spectrum of this material showed no absorption in the O–H region (3300–3600 cm^{-1}), but revealed a weak C–D bond which appeared as a doublet under high resolution at 2100 and 2120 cm^{-1}. This product contained 98.0 ± 0.1% of one atom of deuterium per molecule. The amount was determined from the nmr spectrum of a 19% by weight solution of (+)-I-*d* in deuteriochloroform through use of a Varian Model C-1024 time-averaging computer attached to a Varian A-60 nmr spectrophotometer. A comparison was made of the intensity of the residual protium peak at τ 4.75 (methine hydrogen) and the low-field $^{13}CH_3$ satellite of the methoxy group at τ 5.45.

General Procedures for Isotopic Exchange and Racemization Runs. The *t*-butyl alcohol-O-*d* used[14] contained 0.99 atom of deuterium per molecule (combustion and falling drop). The alcohol was purified by careful distillation in a very dry apparatus under pure nitrogen from dissolved potassium metal. The solvent was degassed by three freeze–thaw cycles under vacuum. Freshly sliced potassium metal was added and dissolved under a blanket of dry nitrogen. The basic solution was degassed as before and then stored in the drybox. Basic solvent prepared and stored in this manner did not discolor with time or cause any discoloration in kinetic samples. The base titer was determined to be 0.233 *N* by titration with aqueous 0.01 *N* hydrochloric acid to a phenolphthalein end point. This basic and deuterated solvent was used for all kinetic experiments.

All kinetic solutions were prepared in a drybox by the addition of 12.00 ml of the basic solvent to 200 mg of substrate. Complete dissolution of the substrate was facilitated by use of a hot plate. During this time the kinetic solution was kept in a tightly stoppered flask to avoid changes in base titer due to solvent evaporation. Measured aliquots, *ca.* 1.4 ml each, were placed in heavy-walled ampoules which had been cleaned with hot chromic acid, washed with ammonia, rinsed ten times with distilled water, and dried for 24 hr at 120°. The ampoules were stoppered with rubber septum caps, passed out of the drybox, and sealed under vacuum. Ten minutes was allowed for temperature equilibration after a set of ampoules were placed in the thermostated 115.80° bath. At timed intervals, ampoules were thermally quenched in ice-water and then analyzed for either deuterium content or optical activity as described below.

Racemization Runs. In runs 3 and 4, (+)-I-*d* with $[\alpha]^{25}_{546}$ +3.3° (*c* 2.5, chloroform), mp 92–99°, and 0.980 atom of D per molecule

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[14] D. J. Cram and B. Rickborn, *J. Am. Chem. Soc.*, **83**, 2182 (1961).

(nmr method) was used. The optical rotation of thermally quenched aliquots was measured at 25° and 356 mμ. In runs 5 and 6, (−)-I-*h* with $[\alpha]^{25}_{546}$ −5.7° (*c* 2.5, chloroform) and mp 98–101° was used. The optical rotation of thermally quenched aliquots was measured at 35° and 356 mμ. The higher temperature in the latter case was required to prevent crystallization of the substrate in the polarimeter tube. The use of shorter wavelength in both cases afforded higher valued observed rotations.

Exchange Runs and Isotopic Analyses. Runs 1 and 2 employed racemic VI-*h* with mp 78–79°. Thermally quenched aliquots were poured into 20 ml each of pentane and 1% (weight by weight) aqueous sodium chloride, washed with the salt solution and pure water, and then dried over anhydrous calcium chloride. The pentane layer was filtered through a glass wool plug, reduced in volume to *ca.* 3 ml, placed in a preweighed vial (±0.1 mg), and then stored in a vacuum desiccator at 1 mm or less overnight. The weight of substrate was determined by reweighing the vials. Errors were minimized by zeroing the balance before weighing every vial. To each vial was added 0.100 ml of carbon tetrachloride just prior to the infrared deuterium analysis which made use of the doublet CD band at 2100 and 2120 cm^{-1}. Absorbances were measured at both bands with the following instrument settings: scale 5×, slit program 2×, gain 5, attenuator speed 600, suppression 8, scan speed 32 min, and source current 0.30 amp. A calibration curve of absorbance/milligram *vs.* mole % exchangeable protium was constructed for both bands. The analyses of kinetic points were obtained by comparison to these curves. The average value was then used. The two values were normally within ±2% protium of each other. Analytical spectra for the calibration curves and kinetic points were measured during the same session.

Electrophilic Substitution at Saturated Carbon. XXXVI. Correlations between Rates of Potassium Methoxide Catalyzed Hydrogen–Deuterium Exchange Reactions of Carbon Acids and H_-[1]

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Abstract: Rate constants for isotopic exchange of triphenylmethane and diphenylmethane and racemization of (−)-4-biphenylylmethoxyphenylmethane and (+)-4-biphenylylmethoxyphenyldeuteriomethane in methanol-O-*d*-dimethyl sulfoxide-d_6 (75:25, by volume) catalyzed by potassium methoxide were measured. Increases in the apparent kinetic molecularity of the catalyst and observed second-order rate constants were noted as the catalyst concentration was raised. The rate data correlated with the reported thermodynamic behavior of methanolic potassium methoxide solutions as measured by the acidity function, H_-. The theoretical basis and qualitative limitations of such rate correlations with H_- are discussed. In an alternative treatment, the kinetic data were fitted to a rate equation of the form, rate = $k_2(\mathrm{RH})(\mathrm{B}) + k_3(\mathrm{RH})(\mathrm{B})^2$, where RH is the substrate, and B is the base. The two kinetic components were interpreted in terms of free carbanions and potassium carbanide ion pairs as reaction intermediates.

Correlations between acidity functions[2a] and rates of acid-catalyzed reactions[2b,3] have been extensively investigated. Although basic media have been less studied, data on the H_- acidity function for 29 basic solvent systems have been summarized.[4] This function measures the relative ability of a given solution to ionize a weak acid. A few reports on correlations between H_- and rates of base-catalyzed reactions have appeared in the literature, all but one[5] of which involve reactions in which base-catalyzed breaking of C–H bonds are involved.[6]

The present study reports results of potassium methoxide catalyzed isotopic exchanges of triphenylmethane (I) and diphenylmethane (II), and exchanges and racemizations of 4-biphenylylmethoxyphenylmethane (III-*h*(*d*), in deuterated methanol-O-*d*-dimethyl-d_6 sulfoxide. The pseudo-first-order rate constants for these reactions were empirically related to an H_- scale for methanolic potassium methoxide solutions. The kinetic data were also fitted to rate equations which possess terms both first and second order in base.

Methods and Results

Starting Materials and Media. Compounds (−)-III-*h* and (+)-III-*d* were available from another study.[7] Base titer determinations were routinely performed with an acidic titrant composed of benzoic acid dissolved in methanol–dimethyl sulfoxide (75:25, by volume). Comparison of a base concentration determination by this method with one made by potentiometric titration gave a negligible difference. In representative cases for every compound, the base titer was determined at the beginning and end of the kinetic run. With either long periods of time or high temperatures, noticeable decreases were detected. Typically, the decrease was less than 1%, and in the worst kinetic

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

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