Internally Competitive CH_3 *vs.* CD_3 Migration and Kinetic Isotope Effects. A Means of Determining Whether or Not Methyl Migration Occurs in the Rate-Controlling Step[1,2]

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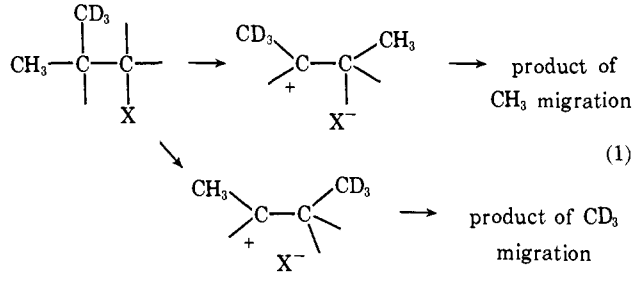
Abstract: A test has been made of the practical feasibility of a comparison between internally competitive CH_3–CD_3 migration and kinetic deuterium isotope effects as a relatively direct means of ascertaining whether or not the rate-controlling step of overall reaction and the migration step are one and the same. The test system is the rearrangement of $Ph_2COHCOH(CH_3)_2$ (I) and its mono-CD_3 (II) and di-CD_3 (III) derivatives in acidic media. A significant preference for CH_3 relative to CD_3 migration, 1.232, in the rearrangement of II has been found by mass spectral analyses of product mixtures. Kinetic isotope effects were $k_I/k_{III} = 1.18$ and $k_I/k_{II} = 1.07$. A correlation between the kinetic isotope effects and the extent of CH_3–CD_3 migration was found, indicating coincidence of rate-controlling and migration steps for this system. Fast exchange of ^{18}O at the benzhydryl carbon indicates that methyl migration follows after a reversible C–O heterolysis step. Phenyl migration occurred as a side reaction to the extent of 10–14%, dependent on the medium, and had a somewhat greater isotope effect than methyl migration.

This paper describes the beginnings of a study of a potential method for determining whether or not the alkyl migration step and the rate-controlling step of overall reaction are one and the same in rearrangement reactions of the type outlined in eq 1. The method involves measuring the extent of CH_3–CD_3 migration in the mono-CD_3 compound and comparing this with the kinetic isotope effects produced by successive replacement of CH_3 by CD_3 groups. That is, if the rate-controlling and migration steps are the same, then the ratio of CH_3 to CD_3 migration is theoretically related to the kinetic isotope effects (see later eq 9–12). On the other hand, if the rate-controlling and migration steps do not coincide, there is no relationship between the CH_3/CD_3 migration ratio and the kinetic isotope effects. These principles are of course applicable to any system having two or three equivalent migratable groups.



It is evident that in order to ascertain whether the method outlined also is practicable, it first must be determined whether internally competitive CH_3–CD_3 migration can differ significantly from unity. If that test can be met, then it is still necessary to obtain experimental verification of the relationship between product ratio and kinetic isotope effects that exist in principle for a reaction in which the rearrangement step and the rate-controlling step are the same. With these purposes in mind, the system chosen for first study was the acid-catalyzed pinacol rearrangement of 1,1-diphenyl-2-methyl-1,2-propanediol, reported to yield only 3,3-diphenylbutanone, the product of methyl rearrangement.[3] It appeared likely that methyl migration would be rate controlling, *i.e.*, that the relatively stable benzhydryl carbonium ion would be formed reversibly prior to rearrangement. Of course, the choice of system also was predicated on such considerations as ease of preparing CD_3 derivatives and accuracy and ease of measurement of rate constants and product ratios. A preliminary report of this work has been published.[2]

A long-range goal would be to accumulate enough data on methyl migrational isotope effects to allow a description of the nature of the bonding to the methyl in the transition state of migration. In a search of the literature, no examples of comparisons of CH_3 and CD_3 migration were found. However, studies on hydrogen *vs.* deuterium migration have been reported.[4]

Experimental Section

Rearrangement Products. The methyl ketone, 3,3-diphenyl-2-butanone, was prepared by pinacol rearrangement of 2,3-diphenyl-2,3-butanediol[5] and was recrystallized from pentane, mp 40–41.5° (lit.[5] 40°). It also was prepared by recrystallization of the rearrangement product of 1,1-diphenyl-2-methyl-1,2-propanediol. The phenyl ketone, α-phenylisobutyrophenone, was prepared by the method of Newman and Linsk[6] and recrystallized from hexane, mp 43–45° (lit.[5] 45–47°).

1,1-Diphenyl-2-methyl-$^2H_3$-1,2-propanediol. A mixture of 5 g of 1-hydroxy-1,1-diphenylpropanone,[7] 20 ml of purified dioxane, 10 g of D_2O and 0.02 g of dry potassium carbonate was heated to 50° for 15 hr. Dioxane and D_2O were removed by distillation under reduced pressure and the residue aspirated under 2 mm pressure for 10 min. Fresh dioxane–D_2O, in the same quantity, and a pinch of potassium carbonate were added and the procedure was

(1) Taken in part from the Ph.D. Thesis of P. H. LeFevre, University of Washington, 1967.

(2) Preliminary communication: W. M. Schubert and P. H. LeFevre, *J. Amer. Chem. Soc.*, **91**, 7746 (1969).

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repeated. After a total of six exchanges, the solid white residue was extracted several times with hot pentane and was twice recrystallized from pentane: yield 2.9 g; mp 64–64.5°.

To exchange the hydroxyl deuterium, a portion of the ketone (0.5 g) was dissolved in a neutral solution of methanol (8 ml) and water (7 drops), and then recovered by evaporation of the solvent under reduced pressure. The nmr spectrum in carbon tetrachloride was unchanged between three and five such exchanges. The per cent deuterium in the methyl group of the hydroxy ketone was determined to be 96.3 ± 0.5% by nmr analysis.

The deuteriomethyl compound (2.78 g) was added to a solution of methyl magnesium bromide (prepared from 8.0 g of methyl bromide) in 30 ml of purified tetrahydrofuran under nitrogen. The reaction mixture was poured into cold saturated ammonium chloride solution and extracted with ether. The ether solution was washed with 5% sodium bicarbonate and saturated sodium chloride and dried over magnesium sulfate. The ether was removed and the residue was recrystallized from heptane: yield 2.21 g; mp 89.5–90.0° (lit. mp of normal compound[8] 89.5–90.0°). Comparison of relative areas of methyl, hydroxyl, and aromatic protons in the nmr spectrum (Varian A-60, CCl_4 solvent) established the deuterium content of the labeled methyl group to be 96.9 ± 0.5%.

1,1-Diphenyl-2-methyl-$^2H_3$-propanediol-3-$^2H_3$. A solution of 6.95 g of methyl ester of benzylic acid in 40 ml of purified tetrahydrofuran was treated with 0.665 g of sodium metal. The resulting solution then was added over a period of 1 hr to a Grignard solution prepared from 5.0 g of deuteriomethyl bromide (Merck, Sharpe and Dohme, 99.8% D) and 1.27 g of magnesium in 30 ml of purified tetrahydrofuran under nitrogen. Isolation and recrystallization as above yielded 6.04 g, mp 90–91°. The nmr spectrum (Varian A-60, CCl_4 solvent) showed 99.0 ± 0.5% D in the methyl groups.

Rate Measurements. Rate constants were determined by continuous observation of the optical density of solutions of glycol substrate with either a Beckman Model DU or a Model DU-2 spectrophotometer. The stoppered quartz ultraviolet cells used as reaction vessels were placed in a self-contained constant temperature water bath which was mounted in place of the standard Beckman cell compartment. Temperature control to ±0.02° was maintained with the aid of a Sargent Model SW Thermoniter. For runs in mixed solvent, 1-cm cells were used and the glycol concentration was about 10^{-3} *M*. For runs in 50.3% aqueous H_2SO_4, 10-cm cells were used and the glycol concentration was about 10^{-4} *M*. The glycol was first dissolved in two drops of acetic acid before addition of H_2SO_4.

Product Extraction and Mass Spectral Analysis. Larger portions (about 50 ml) of kinetic solutions of compounds I, II, and III (about 10^{-3} *M*) were allowed to react for ten half-lives or more. The solutions were diluted with an equal volume of water and extracted continuously with purified pentane (30 ml) for about 15 hr. The pentane solution was concentrated by distillation to about 3 ml and then quantitatively transferred to the tube for introduction of sample into the hot inlet of the mass spectrometer. After evaporation of the remaining pentane, the residue was introduced into a Consolidated Electronics Model 103 mass spectrometer.

Oxygen Exchange Experiment. A sample of 1,1-diphenyl-2-methyl-1,2-propenediol (7 mg) was dissolved in 0.3 g of ethanol and the solution was diluted with 14.28 g of 30.0% sulfuric acid containing 1.17 atom % ^{18}O. The solution was allowed to stand for 5 min at 25°, and then was quickly extracted with pentane. The extract was washed with sodium bicarbonate and then dried, and the pentane was removed under reduced pressure. The residue was submitted to mass spectral analysis.

Phenyl *vs.* Methyl Migration Product. Quantitative ultraviolet spectra of 3,3-diphenylbutanone, α,α-dimethylpropiophenone, and reaction product solutions of glycols I and III were determined in three solvents at room temperature.

Results

Rate Constants for Compounds I–III. Rate constants were determined by the increase in optical density at λ values around 290 mμ, corresponding to a broad maximum in the n → π* absorption band of 3,3-diphenyl-2-butanone. Initial absorbances were around zero, and the final absorbances about 0.5 and stable from about nine to more than 25 half-lives. Plots of ln $(A_\infty - A)$ *vs.* time were linear throughout (three half-lives), except for a rare stray point, about one point in ten kinetic runs, which was discarded. Data over the interval about 0.3–2.0 half-lives or so, 15–20 points, were processed by computer and the least-squares slope $(-k_{obsd})$ and the standard deviation of the regression line was calculated. Runs with a standard deviation of greater than 1%, one run in about twenty, were arbitrarily discarded.

Phenyl *vs.* Methyl Migration. Extracts of product solutions from glycol I were subjected to glc analysis in an Aerograph HyFi Model 600 (3-ft SE-30 silicone rubber column at 130°). Only one peak was observed, with a retention time equal to that of authentic 3,3-diphenylbutanone. However, mass spectra and ultraviolet spectra of product mixtures established that the phenyl migration product, α,α-dimethylpropiophenone, also was formed in significant amounts.

The ratio of phenyl to methyl migration product was quantitatively determined for the normal glycol I and the di-CD_3 glycol III in three representative solvents, 50.3% aqueous sulfuric acid and the mixed solvents A and G. Equation 2 was applied to ultraviolet spectral data from 242.5 to 275 mμ, at 2.5-mμ intervals. In this equation, ϵ_∞ is the molar absorptivity of glycol solution after more than ten half-lives of reaction, ϵ_{Ph} is the molar absorptivity of authentic α,α-dimethylpropiophenone, and ϵ_{Me} is that of authentic 3,3-diphenylbutanone. Values obtained in solvent G are reproduced in Table I. The ratios of phenyl to methyl migration product determined in the three solvents are given in Table II.

Table I. Ultraviolet Spectral Data and [Ph]/[Me] Values for Glycols I and III in Solvent G[a]

λ, mμ	ϵ_{Ph}[b]	ϵ_{Me}[c]	ϵ_I^{∞}[d,f]	ϵ_{III}^{∞}[e,f]	[Ph]/[Me][g] I	[Ph]/[Me][g] III
242.5	8915	893	1700	1640	0.111	0.103
245	9410	747	1610	1540	0.110	0.100
247.5	9740	667	1560	1490	0.109	0.100
250	9850	625	1530	1470	0.109	0.102
252.5	9700	639	1530	1475	0.109	0.102
255	9130	626	1460	1410	0.109	0.103
257.5	8145	661	1400	1360	0.110	0.106
260	7190	661	1310	1290	0.110	0.107
262.5	6160	610	1160	1140	0.110	0.109
265	5480	590	1085	1070	0.114	0.109
267.5	4940	562	992	990	0.109	0.109
270	4290	468	853	847	0.112	0.110
272.5	3920	411	768	760	0.113	0.110
275	3430	400	708	700	0.113	0.109
					0.111 ±0.002[h]	0.105 ±0.004[h]

[a] Solvent G, H_2SO_4–HOAc–H_2O, 50.7:14.8:34.5. [b] Absorption spectrum of 3,3-diphenylbutanone. [c] Absorption spectrum of α,α-dimethylpropiophenone. [d] Product solution from glycol I. [e] Product solution from glycol III. [f] Spectra stable for several days. [g] Ratio of α,α-propiophenone to 3,3-diphenylbutanone obtained from glycols I and III; application of eq 2. [h] Average deviation.

$$\frac{k_{Ph}}{k_{Me}} = \frac{[Ph]}{[Me]} = \frac{\epsilon_\infty - \epsilon_{Me}}{\epsilon_{Ph} - \epsilon_\infty} \quad (2)$$

Product Mass Spectra. When pure 3,3-diphenylbutanone was subjected to mass spectral analysis, parent peaks were either absent or of extremely low intensity, even under an ionization voltage as low as 8 V.

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Table II. Values of k_{Ph}/k_{Me} for Glycols I and III[a]

Solvent	k_{Ph}^{I}/k_{Me}^{I}	$k_{Ph}^{III}/k_{Me}^{III}$
A[b]	0.167 ± 0.004	0.161 ± 0.003
G[b]	0.111 ± 0.002[c]	0.105 ± 0.004[c]
50.3% aq H_2SO_4	0.123 ± 0.004	0.119 ± 0.006

[a] Equation 2 applied to product spectrum at 2.5 mμ intervals between 242.5 and 275 mμ. Average deviation, as function of λ, is given. [b] Solvent A, H_2SO_4–HOAc–H_2O, 38.9:15.8:45.3; solvent G, see Table I, footnote *a*. [c] Data of Table I.

CO^+,[9] as well as weak ones due to $PhC(CL_3)_2^+$ and $PhCO^+$. The absolute intensity at mass 184 ($Ph_2CCD_3^+$) was usually around 1000, making for an accurate count of $Ph_2CCL_3^+$ fragments. The relative intensities of peaks at M − 180 through 186 obtained from the reaction products of the sample of glycol II are listed in Table III. The relative intensities of the peaks obtained from the samples of glycols I and III also are listed. There were no peaks immediately below M − 180 nor above M − 186.

Table III. Mass Spectra of $Ph_2CCL_3^+$ Fragments from Reaction Products of I, II, and III[a]

Compd		Solvent[b] H_2SO_4	HOAc	H_2O	Experimental mass ratios[c] 180	181	182	183	184	185	186
I	D	45.0	15.4	39.6	1.5	100	15.2	1.2	0	0	0
II	A	38.9	15.8	45.3	2.7	133.7	22.1	11.4	100	15.3	1.2
	B	41.1	15.7	43.2	2.5	133.3	22.6	11.7	100	15.3	1.2
	C	42.2	15.5	42.3	2.6	134.3	21.8	11.7	100	15.3	1.2
	D	45.0	15.4	39.6	2.6	130.9	22.3	11.7	100	15.3	1.2
	E	46.5	15.2	38.3	2.6	134.4	22.6	11.7	100	15.3	1.2
	F	49.1	15.0	35.9	2.7	133.7	22.1	11.4	100	15.3	1.2
	G	50.7	14.8	34.5	3.3	133.5	22.6	11.6	100	15.1	1.2
		50.3% aq H_2SO_4				132.5	24.6	11.7	100	15.9	
					Av 2.6	133.0	22.8	11.6	100	15.4	1.2
III	D	45.0	15.4	39.6	0	<0.05	3.3	2.8	100	15.1	1.2

[a] Most determinations at 8 V, Consolidated Electrons Model 103 mass spectrometer. [b] Weight per cents. The mixed solvents were prepared by dilution of 20 ml of HOAc to 100 ml with, respectively: 46.26, 48.75, 49.97, 53.14, 54.75, 57.37, and 58.95% aqueous H_2SO_4. [c] Values relative to 100 for M − 184, except for I. The most intense peak usually had an absolute intensity of greater than 1000.

Table IV. Values of k_{obsd} (sec^{-1}), $k_{obsd}^{I}/k_{obsd}^{II}$, and $k_{obsd}^{I}/k_{obsd}^{III}$ at 25°

Solvent[a]	No. of runs[b]	$10^4 k_{obsd}^{I}$[c]	$k_{obsd}^{I}/k_{obsd}^{II}$	$k_{obsd}^{I}/k_{obsd}^{III}$[d]
A	4	1.087 ± 0.011	1.065	1.149
B	2	2.499 ± 0.004	1.056	
C	2	3.309 ± 0.032	1.077	
D	2	8.258 ± 0.040	1.057	
E	4	16.27 ± 0.11	1.078	1.204
F	3	35.71 ± 0.11	1.062	
G	2	55.60 ± 0.45	1.080	
50.3% aq H_2SO_4	6	7.185 ± 0.051	1.078	1.177
			Av 1.071[e] ±0.009[f]	Av 1.177 ±0.019[f]

[a] Solvents described in Table III. [b] Number of individual rate constant determinations for glycols I and II. [c] See ref 14. [d] Three determinations in each solvent for glycol III. [e] Average weighted according to number of runs. [f] Average deviation.

However, the cracking pattern was very simple at low-ionization voltage, showing two intense peaks. One was at mass 181, corresponding to $Ph_2CCH_3^+$, with P + 1 and P + 2 satellites (^{13}C and natural ^2H). The other was at M − 43, corresponding to CH_3CO^+, with P + 1 and P + 2 satellites. There was a small peak at M − 42 (CH_2CO^+) of about 5% the intensity of the M − 43 peak and a very weak one at M − 180 ($Ph_2C\cdot{}^-CH_2^+$) of 1.5% the intensity of the M − 181 peak.

The mass spectra of product mixtures obtained in the rearrangement of nondeuterated 1,1-diphenyl-2-methyl-1,2-propanediol closely matched that of authentic 3,3-diphenyl-2-butanone except for additional weak peaks at M − 105, M − 118, and M − 119. These peaks, corresponding to $PhCO^+$, $PhC(CH_3)\cdot{}^-CH_2^+$, and $PhC(CH_3)_2^+$ must have arisen from α,α-dimethylpropiophenone, the phenyl migration product of the original glycol. Authentic α,α-dimethylpropiophenone showed the same pattern at M − 105 and M − 118 and M − 119, and no peaks in the region of M − 181.

The mass spectra of product mixtures obtained from the deuterium-labeled glycols II and III also showed the intense peaks corresponding to $Ph_2CCL_3^+$ and CH_3-

Mass Spectra of Starting Materials. The mass spectrum of 1,1-diphenyl-2-methyl-1,2-propanediol showed little or no parent peak, at ionization voltages that were varied from 7 to 70 V. Intense peaks were obtained at M − 182 (Ph_2CO^+), M − 181 ($Ph_2{}^+CCH)_3$, M − 105 ($PhCO^+$), M − 59 ($(CH_3)_2COH^+$), M − 58 ($(CH_3)_2CO^+$), and M − 43 (CH_3CO^+). Weaker, but not insignificant peaks were obtained at M − 42 (CH_2CO^+) and M − 57 ($CH_3COCH_2^+$). This precluded the use of methyl-containing fragments as a means of accurately counting the CD_3, CHD_2, CH_2D, and CH_3 distribution in the samples of II and III. Qualitatively, the mass spectrum of the sample of III indicated a predominance of di-CD_3 and negligible di-CH_3 compounds. In particular, there were no detectable peaks at M − 181 ($Ph_2CCH_3^+$) and M − 58 ($(CH_3)_2CO^+$), peaks of goodly intensity in the mass spectrum of unlabeled glycol I.

(9) Under the rearrangement reaction conditions, a highly dilute solution of glycol in strong proteo acids, deuterium atoms in the acyl methyl of methyl ketone product are essentially completely washed out by exchange with solvent protons. Thus, the product mass spectra in the region of CL_3CO^+ showed only CH_3CO^+.

The CL_3 isomer distribution in the sample of α-D labeled 1-hydroxy-1,1-diphenylpropane (the precursor of the sample of the glycol II) also could not be determined by mass spectral analysis. Again, the parent peaks were too weak and the cracking pattern for methyl-containing fragments too complex. At 8 V, the main peaks in the mass spectrum of normal 1-hydroxy-1,1-diphenylpropanone corresponded to Ph_2CO^+, $PhC(CH_3)OH^+$, $PhCO^+$, and CH_3CO^+, with significant peaks just below those of the main methyl-containing fragments.

Oxygen Exchange Results. Since the most well-defined peaks in the mass spectrum of 1,1-diphenyl-2-methyl-1,2-propanediol were at M − 105 ($PhCO^+$) and M − 43 (CH_3CO^+), these regions were used to determine the extent of ^{18}O exchange in a sample of glycol I that had been treated for 5 min in 30% sulfuric acid containing 1.17 atom % ^{18}O. Mass spectra were determined at 70 V. In the unexchanged glycol, (M − 107)/(M − 105) = 0.0068. In the exchanged glycol, (M − 187)/(M − 185) = 31.2/2580 = 0.0121, corresponding to 45% ^{18}O exchange in the $PhCO^+$ fragment. The ratio (M − 45)/(M − 43) suffered no significant change, from 20.4/1860 = 0.0109 in normal glycol to 15.3/1443 = 0.106 in exchanged glycol.

Discussion

Treatment of 1,1-diphenyl-2-methyl-1,2-propanediol (I) with strong sulfuric acid has been reported to yield only the product of methyl migration, 3,3-diphenylbutanone.[3] However, in this work, α,α-dimethylpropiophenone, the phenyl migration product, also was formed to a significant extent. This was revealed by both mass spectra and ultraviolet spectra of products obtained under kinetic conditions, although no separation was achieved by glc. Quantitative ultraviolet spectra of kinetic product solutions in three representative solvents show the ratio of phenyl to methyl migration product to range from 0.11 to 0.17, depending on solvent (Table II).

Cl_3 Product Ratios from Compound II. The relative extent of CH_3 to labeled methyl migration given under each of the kinetic conditions by the sample of the mono-CD_3 glycol II was determined by mass spectral analysis of the product mixtures. In principal, the parent peaks of product could be used to determine this, since any deuterium in the nonmigrating group of methyl rearrangement product was completely washed out under the reaction conditions.[9] However, it proved difficult to obtain sufficiently intense parent peaks for accurate counts to be made. Fortunately, the extent of CH_3 *vs.* CD_3 (and also CHD_2 and CH_2D) migration could be determined by the relative intensities of the peaks in the isolated and intense regions of the mass spectrum corresponding to the fragments $Ph_2CCL_3^+$. Furthermore, use of the $Ph_2CCL_3^+$ peaks has a distinct advantage over the use of parent peaks in that the latter would be contaminated by the phenyl migration product.

It is seen in Table III that the experimental mass ratios obtained for glycol II products are practically invariant with medium. Consequently, only the average values have been processed. Corrections for natural ^{13}C and the minute fraction of natural ^2H on aromatic ring positions were applied (P + 1 = 0.1357 and P + 2 = 0.0100 relative to P = 0.8543) giving for the ratio of migrated methyl groups: $CH_3:CH_2D:CHD_2:CD_3$ = 135.4:1.8:10.0:100. Since the mass spectra also show a small percentage of fragment of mass 180, corresponding to $Ph_2C\cdot^-CH_2^+$, a correction for this also was applied, setting $Ph_2C\cdot^-CL_2^+/Ph_2CCL_3^+ = 1.8 \times 10^{-2}$ and assuming no isotope effect in the cracking. This gives for the fully corrected ratio, used in further calculations, $CH_3:CH_2D:CHD_2:CD_3$ = 135.3:0.4:10.2:100. The fully corrected ratio differs significantly only in the minor CHD_2 component from that obtained by use of just P + 1 and P + 2 corrections. The total atom per cent of deuterium in the migrated CD_3, CHD_2, and CH_2D groups from glycol I is calculated from the CL_3 ratios to be 97.5%.[10] This compares favorably with the nmr determination of 96.9 ± 0.5 atom per cent deuterium in the labeled methyl group of the sample of glycol II.

For the doubly labeled glycol III in solvent D, application of the same corrections to the experimental mass ratios shown in the last row of Table III gives the ratio of migrated methyl groups: $CH_3:CH_2D:CHD_2:CD_3$ = 0–0.03:0.2:1.5:100. This distribution corresponds to 99.5% deuterium in the migrated methyl group, compared to the nmr value of 99.0 ± 0.5% in the two labeled methyl groups of the sample of glycol III.

The low atom fraction of hydrogen found in the total migrated CL_3 groups in the reaction product from the sample of III, and in the migrated CL_3 groups containing at least one deuterium in the product of the sample of II, shows that no hydrogen exchange has occurred in the methyl group that has migrated. This demonstrates that formation of methyl ketone migration product is rate controlled. That is, reversibility of the overall conversion of glycol to methyl ketone would have resulted in exchange at both *methyl* groups since the *acyl* methyl of methyl ketone does exchange rapidly with solvent protons.[9]

The Rate of CH_3–CD_3 Migration. A distinct preference for migration of CH_3 relative to CD_3 is indicated by the value $[Ph_2CCH_3^+]/[Ph_2CCD_3^+] = 1.353$. Here, $[Ph_2CCH_3^+]/[Ph_2CCD_3^+]$ is the ratio of the $Ph_2CCH_3^+$–$Ph_2CCD_3^+$ fragment determined as above from mass spectral analyses of the product mixtures obtained in the rearrangement of glycol labeled in one methyl group. However, only in the event of 100% deuterium incorporation in the labeled methyl of the glycol would $[Ph_2CCH_3^+]/[Ph_2CCD_3^+]$ be directly the same as $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$,[11] the latter ratio being defined as the rate constant ratio for competing CH_3 and CD_3 migration steps of fully deuterated compound II. Actually, $[Ph_2CCH_3^+]/[Ph_2CCD_3^+]$ is larger than $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$ since the sample of glycol used contained not only fully deuterated II but also some $Ph_2COHCOHCH_3CHD_2$, about 10%, and $Ph_2COHCCH_3OHCH_2D$, less than 1%. That is, CH_3 rearrangement of the latter glycols also contributes to the total $Ph_2CCH_3^+$ fragment, whereas the $Ph_2CCD_3^+$ fragment arises only from CD_3 rearrangement of fully deuterated II.

(10) Statistically, the percentage CH_3 in labeled methyl groups should be negligible.

(11) The subscript in the symbols $k_{CL_3}^{CL_3}$' and $k_L^{L'}$ refers to the migrating group; the superscript refers to the nonmigrating group.

The ratio $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$ can be extracted from the data available by application of eq 3, which expresses the relationship between $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$ and the relative amounts of all four $Ph_2CCL_3^+$ fragments. In eq 3, $k_{CH_3}^{CHD_2}/k_{CHD_2}^{CH_3}$ is the rate constant ratio for the steps of CH_3 *vs.* CHD_2 migration in the rearrangement of CHD_2 glycol and $k_{CH_3}^{CH_2D}/k_{CH_2D}^{CH_3}$ is the corresponding ratio for CH_2D glycol. Equation 3 is derived by combining the four separate velocity expressions for migration of CD_3, CHD_2, CH_2D, and total CH_3, respectively.

$$k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3} = \frac{[Ph_2CCH_3^+]}{[Ph_2CCD_3^+]} - \frac{k_{CH_3}^{CHD_2}[Ph_2CCHD_2^+]}{k_{CHD_2}^{CH_3}[Ph_2CCD_3^+]} - \frac{k_{CH_3}^{CH_2D}[Ph_2CCH_2D^+]}{k_{CH_2D}^{CH_3}[Ph_2CCD_3^+]} \quad (3)$$

Equation 3 can be solved for the desired $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$ value if a relationship between the various $k_{CH_3}^{CL_3}/k_{CL_3}^{CH_3}$ is known or assumed. A reasonable assumption is that per D in CL_3 there is an additive effect on the free energy of activation differences, $\Delta F^{\ddagger}_{CL_3}^{CH_3} - \Delta F^{\ddagger}_{CH_3}^{CL_3}$; *i.e.*, set $k_{CH_3}^{CHD_2}/k_{CHD_2}^{CH_3} = (k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3})^{2/3}$ and $k_{CH_3}^{CH_2D}/k_{CH_2D}^{CH_3} = (k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3})^{1/3}$. Solution of the resulting cubic equation gives $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3} = 1.232$, the value that will be used in subsequent treatment.

It is to be noted that the calculated value of $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$ is not very sensitive to assumptions regarding relationships between the various $k_{CH_3}^{CL_3}/k_{CL_3}^{CH_3}$ ratios. The lowest possible value of $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$ is obtained by application of the limiting assumption that CH_2D and CHD_2 have the same relative migration rates as CD_3; *i.e.*, set $k_{CH_3}^{CH_2D}/k_{CH_2D}^{CH_3} = k_{CH_3}^{CHD_2}/k_{CHD_2}^{CH_3} = k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$. The highest possible value of $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$ is obtained by application of the limiting assumption that CH_2D and CHD_2 have the same relative migration rate as CH_3; *i.e.*, set $k_{CH_3}^{CH_2D}/k_{CH_2D}^{CH_3} = k_{CH_3}^{CHD_2}/k_{CHD_2}^{CH_3} = 1$. The values of $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$ thus obtained are 1.223 for the lower limit and 1.247 for the upper limit.

The ratio $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$ is not, of course, purely an isotope effect in the migrating group. Rather, it is the product of a migrational isotope effect (CH_3 *vs.* CD_3 migrating) and the inverse of a nonmigrational isotope effect (CD_3 *vs.* CH_3 nonmigrating). Of special interest and importance is that the ratio differs significantly from unity. In other words, the method for determining whether or not migration and rate-controlling steps coincide has survived its first test of practicability.

Kinetic Isotope Effects. Listed in Table IV are the values in various acidic media of k_{obsd}^{I}, the observed first-order rate constant for the total reaction of the normal glycol I. Also listed are values of the directly measured kinetic isotope effects, $k_{obsd}^{I}/k_{obsd}^{II}$ and $k_{obsd}^{I}/k_{obsd}^{III}$. Each observed rate constant is of course a sum of the first-order rate constant for *total* methyl migration, labeled k_{Me}, and a first-order rate constant for phenyl migration, k_{Ph} (eq 5–7). The presence of a small percentage of hydrogen in the labeled methyl group of II (3 atom %) and both methyl groups of III (<1 atom %) negligibly affects k_{obsd}^{II} and k_{obsd}^{III} and no correction for this was attempted.[12]

(12) The velocity of reaction of the sample of II is at most (*i.e.*, at time zero) only 0.3% greater than of fully deuterated II.

To accurately obtain the kinetic isotope effect for just methyl rearrangement, it was necessary to determine the relative extent of phenyl to methyl migration. The rate constant ratios k_{Ph}^{I}/k_{Me}^{I} and $k_{Ph}^{III}/k_{Me}^{III}$ for glycols I and III, respectively, were determined in three representative solvents by ultraviolet spectral analysis of products (Table II). Although the phenyl to methyl migration ratio is sensitive to solvent, it is seen that in each individual solvent k_{Ph}^{I}/k_{Me}^{I} and $k_{Ph}^{III}/k_{Me}^{III}$ are very nearly the same. In other words, the ratio of phenyl to methyl migration is very nearly isotope independent, with the kinetic isotope effect for phenyl migration being only slightly greater than that for methyl migration.[13] Since also the extent of phenyl migration is small, this means that the kinetic isotope effects for total methyl migration alone, k_{Me}^{I}/k_{Me}^{III} and k_{Me}^{I}/k_{Me}^{II}, differ insignificantly from the observed ratios $k_{obsd}^{I}/k_{obsd}^{III}$ and $k_{obsd}^{I}/k_{obsd}^{II}$, respectively.[14]

Examination of the values of Table IV reveals no trend with changing solvent in the experimental $k_{obsd}^{I}/k_{obsd}^{II}$ and $k_{obsd}^{I}/k_{obsd}^{III}$ values. Consequently, only the statistically more significant average values will be used in the correlation of the kinetic isotope effects with the $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$ value, also an average.

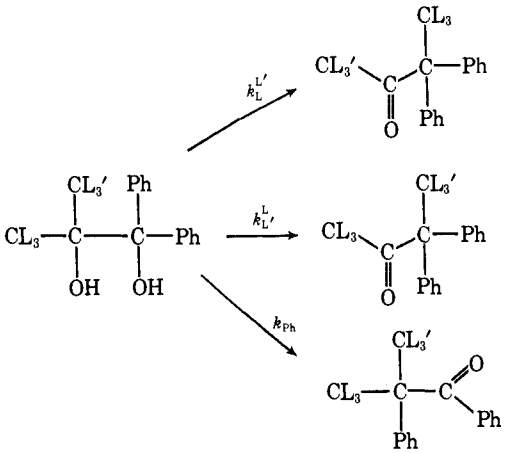
Correlation of $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$ with Kinetic Isotope Effects. The rate constants k_{Me}^{I}, k_{Me}^{II}, and k_{Me}^{III} of eq 4–6 are first-order rate constants for total methyl ketone formation from the glycols I, II, and III, respectively. In other words they are rate constants governed by the free-energy change from initial ground state to transition state of the rate-controlling step. On the other hand, the ratio $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$, obtained by product analysis, is the rate constant ratio *just* for the internally competing CH_3 and CD_3 migration steps alone, in the reaction of the glycol II. A relationship between the kinetic isotope effects and $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$ will exist theoretically if and only if the rate-controlling and migration steps are one and the same. Coincidence of rate-controlling and migration steps of course includes the inherent requirement that the immediate reactant in the migration step be in conformational equilibrium. Such a requirement may not necessarily be met since the barrier to the further chemical transformation of a high energy intermediate may be quite low and hence conceivably lower than even an ordinary conformational barrier.

Equations 9–12 are forms of the relationships that exist between the kinetic isotope effects and the CH_3/CD_3 product ratio from II (*i.e.*, $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$) if and only if the rate-controlling and migration steps coincide. In these equations, k_H^H/k_D^H is a purely migrational isotope effect, *i.e.*, the isotope effect exerted in the migrating group (CD_3 *vs.* CH_3 migrating) when CH_3 is the constant nonmigrating group; k_H^D/k_D^D is the migrational isotope effect when CD_3 is the nonmigrating group.[11] The secondary isotope effect exerted in the nonmigrating group (CH_3 *vs.* CD_3 nonmigrating) is

(13) The slightly greater phenyl to methyl product ratio from glycol I as compared to glycol III (values of Table II) is probably real. The molar absorptivities of product solutions from I were invariably higher than those from III at wavelengths corresponding to relatively high molar absorptivity of phenyl migration product (*e.g.*, see Table I).

(14) If the greater isotope effect for phenyl migration were taken into account, k_{Me}^{I}/k_{Me}^{III} would differ from $k_{obsd}^{I}/k_{obsd}^{III}$ by at most 5 in the fourth figure. Although the values of Table IV are reported to the fourth figure, for calculation purposes, the experimental accuracy is significant only to the third figure (compare the average deviations listed).

expressed by k_H^H/k_H^D when CH_3 is the migrating group and by k_D^H/k_D^D when CD_3 is the migrating group. Equations 8–11 are derived as follows. When rate-controlling and migration steps coincide, the first-order rate constant for total methyl migration of compound II, k_{Me}^{II}, can be set equal to the sum $k_H^D + k_D^H$, where k_H^D is the first-order rate constant for II → $Ph_2CCH_3COCD_3$ and k_D^H is the first-order rate constant for II → $Ph_2CCD_3COCH_3$. Hence, also, $k_{Me}^{I} = 2k_H^H$ and $k_{Me}^{III} = 2k_D^D$. These three equations, together with the equality of eq 8, are then combined to generate the set 9–12. Equation 8 holds when rate-controlling and migration steps coincide, since under this proviso both the *ratio* k_H^D/k_D^H and the *ratio* $k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3}$ are governed by the same free-energy difference, *i.e.*, the free-energy difference between the transition state of the CH_3 migration step and the transition state of the CD_3 migration step in the reaction of glycol II.



(4)

I, $CL_3' = CL_3 = CH_3$
II, $CL_3' = CD_3$; $CL_3 = CH_3$
III, $CL_3' = CL_3 = CD_3$

$$k_{Me}^{I} = k_{obsd}^{I} - k_{Ph}^{I} = 2k_H^H \quad (5)$$

$$k_{Me}^{II} = k_{obsd}^{II} - k_{Ph}^{II} = k_H^D + k_D^H \quad (6)$$

$$k_{Me}^{III} = k_{obsd}^{III} - k_{Ph}^{III} = 2k_D^D \quad (7)$$

If rate-controlling and migration steps coincide, then

$$k_H^D/k_D^H = k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3} \quad (8)$$

Hence, also

$$k_H^H/k_D^H = \frac{k_{Me}^{I}(1 + k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3})}{2k_{Me}^{II}} \quad (9)$$

$$k_H^D/k_D^D = \frac{2k_{Me}^{II}}{k_{Me}^{III}(1 + k_{CD_3}^{CH_3}/k_{CH_3}^{CD_3})} \quad (10)$$

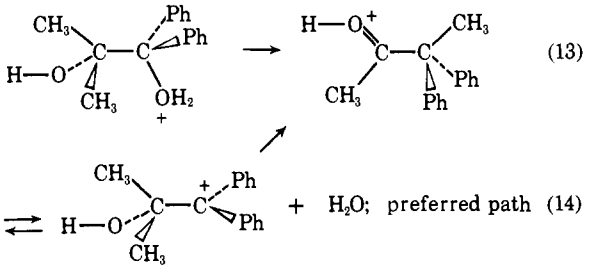
$$k_H^H/k_H^D = \frac{k_{Me}^{I}(1 + k_{CD_3}^{CH_3}/k_{CH_3}^{CD_3})}{2k_{Me}^{II}} \quad (11)$$

$$k_D^H/k_D^D = \frac{2k_{Me}^{II}}{k_{Me}^{III}(1 + k_{CH_3}^{CD_3}/k_{CD_3}^{CH_3})} \quad (12)$$

Application of eq 9–12, based on the assumption of coincidence of rate-controlling and migration steps, allows solution for the complete set of $k_L^{L'}$ ratios. The internal consistency of these ratios then constitutes a check on the validity of the assumption. In the solution of eq 9–12, kinetic isotope effects for total methyl migration were taken as equal to those on k_{obsd}, and only the average values listed in Table IV were used, as discussed above.[14] For k_H^H/k_D^H, the purely migrational isotope effect for CH_3 *vs.* CD_3 migrating and CH_3 as the nonmigrating group,[11] one obtains the value 1.195. The value 1.214 is obtained for k_H^D/k_D^D, the migrational isotope effect with CD_3 as the nonmigrating group. The nonmigrational isotope effects are k_H^H/k_H^D = 0.970 (CH_3 migrating) and k_D^H/k_D^D = 0.985 (CD_3 migrating).

The reasonable agreement between the values for the two migrational isotope effects, and between the values for the two nonmigrational isotope effects, constitutes good evidence that the rate-controlling and migration steps are indeed one and the same. That is, the relative migratory aptitude of CH_3 and CD_3 should be practically uninfluenced by whether the nonmigrating group is CH_3 or CD_3. Similarly, the secondary isotope effect in the nonmigrating group should be practically the same for either CH_3 or CD_3 migrating. If, however, the rate-controlling and migration steps are not the same, the results obtained would require the unlikely fortuity that net zero-point changes between the initial state and the transition state of the rate-controlling step be practically the same as those between the initial state and a different transition state, that of the migration step.

The deuterium isotope results, while strongly indicative of a coincidence of rate-controlling and migration steps, do not establish whether methyl migration is synchronous with C–O heterolysis of protonated glycol, eq 13, or occurs after a step of simple unassisted heterolysis of the C–O bond, eq 14. On the basis of the stabilizing influence of the phenyl substituents on the classical carbonium ion, methyl participation in the loss of the water molecule would appear to be less likely *per se*. That migration does occur only after C–OH_2^+ bond cleavage is supported by the finding that in ^{18}O enriched 30% sulfuric acid at 25° about 45% ^{18}O exchange had occurred at the benzhydryl oxygen in 5 min, conditions under which there is no rearrangement. There also was no experimentally detectable exchange of the other oxygen under these conditions.



(13)

+ H_2O; preferred path (14)

Although rearrangement in 30% H_2SO_4 at 25° was too slow to conveniently measure, k_{Me}^{I} is estimated to lie between 10^{-5} and 10^{-6} sec^{-1}, based on the value of k_{Me}^{I} in 50.3% H_2SO_4 and $-d \log k_{Me}^{I}/dH_0'$ lying between 1 and 2 (see below). The rate constant for ^{18}O exchange is 2×10^{-3} sec^{-1}, based on 45% exchange in 5 min. Thus, k_{exch}/k_{Me}^{I} is 10^2–10^3.

The reasonably large migrational isotope effect indicates an appreciable "loosening" of zero-point vibrations in the migrating methyl, consistent with a decrease in electron density within the migrating group. The nonmigrational isotope effect is small, and the experimental value may not differ significantly from unity. It appears that the positive charge in the activated com-

plex is not greatly shared by the nonmigrating methyl. This does not necessarily imply that methyl migration has proceeded only slightly in the activated complex, since any positive charge developed at the site being vacated may be efficiently dispersed to the conjugating hydroxyl group.

A main conclusion of these studies is that a comparison of CH_3/CD_3 product ratios with kinetic isotope effects has promise as a general practicable method of determining whether or not the rate-controlling and migration steps are coincident in other rearrangements in which there are two or three alkyl groups at the migrating origin. In particular, the practical requirement that there be a significant product isotope effect has been met by the system under study here. It remains to be seen how the product ratio is affected by substituents, as related, for example, to their influence on the degree of transfer of the migrating group in the transition state of migration. It also remains to be seen whether a process of synchronous migration and carbon–nucleophile bond heterolysis could give comparable migrational isotope ratios.

Acidity Dependence. The rearrangement of 1,1-diphenyl-2-methyl-1,2-propanediol is of course acid catalyzed and undoubtedly proceeds *via* reversibly formed oxygen conjugate acid. Because of the limited solubility of glycol and rearrangement products, the bulk of the rate constants was determined in mixed H_2SO_4–H_2O–HOAc solvents (solvents A–G of Table III), for which there is unfortunately no acidity function data. However, it can be concluded that the acidity dependence of the first-order rate constants is quite steep. The solvents A–G all had close to 15% by weight of acetic acid in them, but greater than 34% water. Therefore, in the absence of direct acidity function data, the next best thing was tried. That is, log $k_{obsd}{}^{I}$ was plotted against the acidity functions for purely aqueous sulfuric acid, H_0' and H_R,[15,16] at matching H_2SO_4 percentages in the two media. These plots are shown in Figure 1. Against $-H_0'$, the acidity function for protonation of primary anilines,[15] the slope of the arbitrary plot is 1.64. Against $-H_R$, the acidity function for ionization of triarylcarbinols,[16] the slope is 0.82.[17]

The steepness of the acidity dependence of the rate constant is consistent with the mechanism of eq 13. That is, the process from glycol to transition state of the second step formally resembles the ionization of triarylcarbinols (H_R function) and not the protonation of aniline indicators (H_0' function). One outstanding difference, however, is that the activated complex contains a site for specific hydrogen-bonding solvation, *i.e.*, the hydroxyl hydrogen, whereas the triarylcarbonium ion does not. One might, therefore, expect log $k_{obsd}{}^{I}$ to increase with acidity less than does $-H_R$ (*e.g.*, see ref 18 and references cited therein).

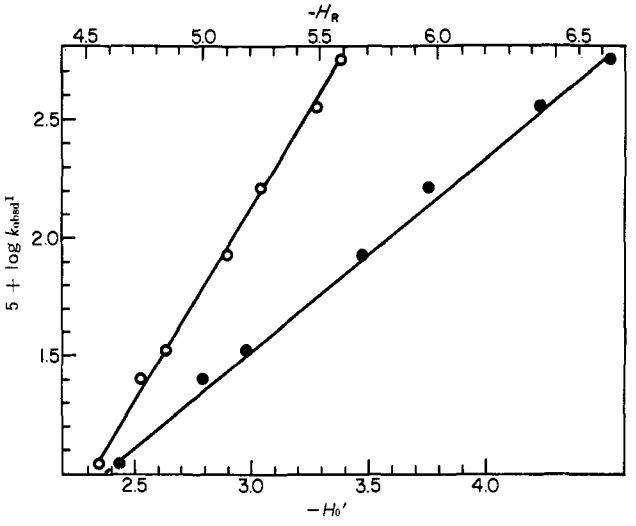
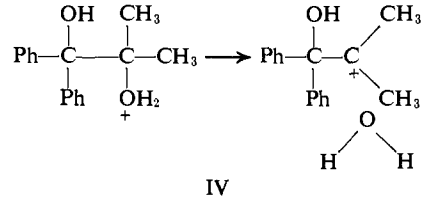


Figure 1. Plot of log $k_{obsd}{}^{I}$ in solvents A–G against $-H_0'$ (○) and $-H_R$ (●) in aqueous H_2SO_4.

Phenyl Migration. The average kinetic isotope effect in phenyl migration, $k_{Ph}{}^{I}/k_{Ph}{}^{III}$, is 1.23, calculated from the isotope effect in three solvents on the phenyl to methyl product ratio (Table II) and the average value of $k_{obsd}{}^{I}/k_{obsd}{}^{III}$ (Table IV). This is a fairly substantial β deuterium isotope effect and indicates that the transition state of the rate-controlling step of phenyl migration has a considerable amount of the character of the tertiary cation IV.[19] This, together with the finding of no ^{18}O exchange at the tertiary aliphatic oxygen of the glycol I, coupled with exchange at the benzylic oxygen,[20] is consistent with the formation of the tertiary cation IV, eq 15, rather than the bridged phenonium ion in the rate-controlling step of phenyl ketone formation.



(15)

IV

Since the extent of phenyl–methyl migration decreases with increasing acidity of the medium (Table II), the acidity dependence of the phenyl migration reaction is somewhat less than that of the methyl migration reaction.[21] This is consistent with the rate-controlling transition data for phenyl migration having more oxonium ion character than that for methyl migration.[18]

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(15) (a) M. J. Jorgenson and D. R. Hartter, *J. Amer. Chem. Soc.*, **85**, 878 (1963); (b) E. M. Arnett and G. W. Mach, *ibid.*, **86**, 2671 (1964).

(16) N. C. Deno, J. J. Jaruzelski, and A. Schriesheimer, *ibid.*, **77**, 3044 (1955).

(17) Alternatively, one may apply the working assumption, probably a limiting one, that the H_0' and H_R functions for solvents A–G change the same as for aqueous sulfuric acid solutions of the same stoichiometric H_2SO_4/H_2O ratios. This gives a slope of log $k_{obsd}{}^{I}$ against $-H_0'$ of 1.31, and 0.64 against $-H_R$.

(18) (a) W. M. Schubert, H. Burkett, and A. L. Schy, *J. Amer. Chem. Soc.*, **86**, 2520 (1964); (b) W. M. Schubert and R. H. Quacchia, *ibid.*, **85**, 1278 (1963).

(19) V. J. Shiner, Jr., W. E. Buddenbaum, B. L. Murr, and G. Lamaty, *ibid.*, **90**, 418 (1968).

(20) In the ^{18}O exchange experiment that was carried out, a small percentage of exchange at the tertiary aliphatic oxygen could have escaped experimental detection.

(21) From the experimental values of $k_{Ph}{}^{I}$ and $k_{Me}{}^{I}$ in solvents A and G, one calculates that the magnitude of the "slope" of a plot log $k_{Ph}{}^{I}$ against an appropriate acidity function would be 90% of the magnitude of the slope of the corresponding plot for log $k_{Me}{}^{I}$, *i.e.*, $\Delta \log k_{Ph}{}^{I}/\Delta \log k_{Me}{}^{I} = 0.90$.