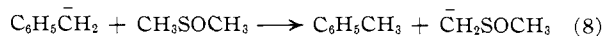


least acidic of all species present and it is reasonable to



assume that the rate-determining step is the initial abstraction of a proton. The rate expression would then be given by

$$R = k_i(T)(\text{B}^-) \quad (9)$$

where k_i = rate constant for ionization.

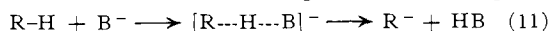
This expression is essentially equivalent to eq. 5 except for the base concentration. It has been proposed that rates become independent of base because of agglomeration.^{3a,9} Such a condition provides a constant concentration of active catalytic species even though the bulk concentration of base is changed. For these reasons, the first-order slope is, therefore, a direct measure of the rate constant for ionization (eq. 10).

$$\text{slope} = k_i/\beta \quad (10)$$

For the comparison of rates of toluene exchange at different conditions, the value of the isotope effect, β , will be essentially constant and the comparison will be related directly to the rate constants for ionization. Future work will be aimed primarily at comparing the ionization rate of toluene with other similar hydrocarbons where the ratio of β values can again be assumed to be close to unity.

The existence of an equilibrium isotope effect between toluene and dimethyl sulfoxide will not have a significant effect on the measurement of relative ionization rates. Essentially, this means a slightly higher kinetic isotope effect for the abstraction of a proton from toluene as compared to dimethyl sulfoxide. However, as previously discussed, comparisons will be made among similar compounds where all effects should be about equivalent. The isotope effect itself most likely arises because of a stronger C-H bond in the methyl group of toluene as compared to dimethyl sulfoxide, but it is not the purpose of this work to give a rigorous explanation for this observation.

The similar activation parameters for base-catalyzed olefin isomerization and isotope exchange are not unusual in view of the similarity of the proposed transition states. In both cases the rate-determining step is the initial ionization. The fraction of the initial complex that becomes free enough to abstract a proton



from the solvent or another hydrocarbon molecule has not been rigorously determined, but indications from olefin isomerization work are that the fraction is

fairly small.¹³ For exchange with alkyl aromatics there is, of course, no way of detecting how much complex is formed for each exchange measured.

Experimental

Reagents.—Baker analyzed reagent grade toluene was used as obtained from the bottle.

Potassium *t*-butoxide was obtained from Mine Safety Appliances, Inc., as the sublimed powder. Analyses showed this material to be 98.5% pure with the major impurity being potassium carbonate.

Tritiated dimethyl sulfoxide was obtained from Niche Inc. and as received had a specific activity of approximately 50 mc./g. Before use, this material was diluted 100-fold with straight DMSO that had been freshly distilled from Linde 13X Molecular Sieves. A 0.56 *M* solution of potassium *t*-butoxide in this solution was checked for catalytic activity by comparing the rate of isomerization of 2-methyl-1-pentene to 2-methyl-2-pentene with that observed for a corresponding solution of potassium *t*-butoxide in straight dimethyl sulfoxide. The rates in both solvent media agreed within experimental error.

Kinetic Procedure.—A 0.56 *M* solution of potassium *t*-butoxide in tritiated dimethyl sulfoxide was prepared in a nitrogen-blanked drybox equipped with a moisture conductivity cell. The exchange reactions were carried out using 7.0 ml. of solvent solution in small vials, capped with self-sealing neoprene stoppers in a Fisher constant temperature bath ($\pm 0.2^\circ$). After allowing sufficient time for the vial to equilibrate to bath temperatures, approximately 2.5 mmoles of toluene was injected into the solution by means of a hypodermic syringe. Aliquots were withdrawn periodically with a hypodermic syringe and injected into a small bottle containing water (to stop the reaction) and a small amount of 2,3-dimethylbutane for extraction. After shaking, the hydrocarbon phase was allowed to separate and the aqueous phase was frozen out over Dry Ice. The hydrocarbon was then analyzed on a radio-assaying gas chromatograph that has been described previously.¹⁴ A 10-ft. Dow Corning silicon oil (DC-200) column at 100° and helium pressure at 10 p.s.i.g. was employed for the chromatographic analysis. The specific activity of toluene was calculated by dividing the total counts registered (corrected for background) by the chemical peak area corrected for molar response.¹⁵ The first-order rate constants were calculated on an IBM 1620 computer, using a least squares program devised by Dr. S. Bank of this Laboratory.

The equilibrium distribution of tritium between dimethyl sulfoxide and toluene was determined by equilibrating methyl labeled toluene (obtained from New England Nuclear Corp. with a specific activity of 0.0225 mc./mmole) with unlabeled dimethyl sulfoxide. The activity of the toluene at equilibrium was measured on the radio-assaying gas chromatograph and the activity of the dimethyl sulfoxide was calculated by difference from the initial and final activities of the toluene.

Acknowledgment.—The authors wish to acknowledge helpful discussions with Professors H. C. Brown and S. J. Cristol and the Esso Research and Engineering Co. for permission to publish this work.

(13) S. Bank, C. A. Rowe, Jr., and A. Schriesheim, *J. Am. Chem. Soc.*, **85**, 2115 (1963).

(14) J. E. Hofmann and A. Schriesheim, *ibid.*, **84**, 957 (1962). Note: propane was employed for the counter in place of methane.

(15) A. E. Messner, D. M. Rosie, and P. A. Argabright, *Anal. Chem.*, **31**, 230 (1959).

[CONTRIBUTION FROM THE ESSO RESEARCH AND ENGINEERING CO., LINDEN, N. J.]

Ionization Rates of Weak Acids. II. Base-Catalyzed Proton Exchange between Polyalkylbenzenes and Tritiated Dimethyl Sulfoxide

By J. E. HOFMANN, RENE J. MULLER,¹ AND A. SCHRIESHEIM

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The base-catalyzed hydrogen isotope exchange between polyalkylbenzenes and tritiated dimethyl sulfoxide has been carried out according to the procedures outlined in the previous paper.² It has been found that only hydrogens α to the aromatic ring undergo exchange and that ring substituents have a pronounced effect on ionization rates. Partial rate factors, defined from rate measurements with *o*-, *m*-, and *p*-xylene, have been employed to predict rate constants for benzenes containing three to six methyl groups.

Introduction

The preceding paper described the base-catalyzed proton exchange between toluene and tritiated di-

methyl sulfoxide.² The present paper gives the results for exchange with a number of polyalkylbenzenes and

(1) Summer employee of Esso Research & Engineering Co. (1962).

(2) J. E. Hofmann, R. J. Muller, and A. Schriesheim, *J. Am. Chem. Soc.*, **85**, 3000 (1963).

shows the effects of both ring substituents and side-chain substituents on the ionization rates of benzylic C-H bonds.

An ultimate goal of these studies would be to establish correlations between rates of ionization and pK_a values as has been done in the past for more acidic compounds.³ The present work, however, covers only a narrow range in rate constants (100-fold variation) which is not sufficient at this point to develop such a correlation.

Results

As outlined in the preceding paper,² first-order slopes for a hydrocarbon containing equivalent benzylic hydrogens yield directly the ionization constant, per hydrogen, for the molecule in question. However, for molecules with nonequivalent benzylic hydrogens (*p*-cymene or pseudocumene, for example), the isotope exchange technique yields an average rate constant, per hydrogen, for all the exchangeable positions.⁴

The rate constants for proton exchange with a number of alkylaromatics and the rate constant for the toluene standard at 30° are given in Table I. From the series of first-order rate constants to toluene, the two σ -limit of a single rate constant determination was found to be about $\pm 10\%$. The average of the rate constants for toluene was used in computing the rela-

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

(4) A plot of $\ln\left(1 - \frac{X}{X_\infty}\right)$ vs. time for a molecule containing nonequivalent hydrogens will not yield a straight line but will be the average of several individual lines depending on the number of nonequivalent positions. However, it can be shown that the initial slope, which approaches a straight line, will be the average rate constant for all hydrogens. The over-all rate of exchange for a molecule having nonequivalent hydrogens, neglecting the kinetic isotope effect, can be written as the sum of the individual rates

$$R = R_1 + R_2 + \dots + R_n \quad (1)$$

or in terms of the expression for isotope exchange

$$Rt = a_1 \ln\left(1 - \frac{X_1}{X_\infty}\right) + a_2 \ln\left(1 - \frac{X_2}{X_\infty}\right) + \dots + a_n \ln\left(1 - \frac{X_n}{X_\infty}\right) \quad (2)$$

a_1, a_2, \dots , etc. = concentration of reactive hydrogens in various positions
 X_1, X_2, \dots , etc. = specific activity at time t , per hydrogen
 X_∞ = specific activity at equilibrium, per hydrogen (in the absence of an equilibrium isotope effect, this is a constant for all positions)

This rate expression yields a curved line on semilog paper but can be simplified at low conversions. If a factor (f) is defined as the ratio of protons in one position to the total number of protons, eq. 2 can be rewritten as

$$Rt = a \ln\left(1 - \frac{X_1}{X_\infty}\right)^{f_1} \left(1 - \frac{X_2}{X_\infty}\right)^{f_2} \dots \left(1 - \frac{X_n}{X_\infty}\right)^{f_n} \quad (3)$$

At small values of X/X_∞ , the first term of the binomial series can be substituted and eq. 3 becomes

$$Rt = a \ln\left(1 - \frac{f_1 X_1}{X_\infty}\right) \left(1 - \frac{f_2 X_2}{X_\infty}\right) \dots \left(1 - \frac{f_n X_n}{X_\infty}\right) \quad (4)$$

Upon expansion and elimination of second-order and higher terms, eq. 4 reduces to

$$Rt = a \ln\left(1 - \frac{f_1 X_1 + f_2 X_2 + \dots + f_n X_n}{X_\infty}\right) \quad (5)$$

It can readily be shown that the average specific activity per hydrogen of the entire molecule (X) is equivalent to the sum of ($f_1 X_1 + f_2 X_2 + \dots + f_n X_n$). Substitution of this into eq. 5 yields eq. 6 which is essentially identical with the case for equivalent hydrogens. A plot of t vs. $\ln\left(1 - \frac{X}{X_\infty}\right)$

$$Rt = a \ln\left(1 - \frac{X}{X_\infty}\right) \quad (6)$$

at low conversion will yield a straight line of slope R/a . As was the case with toluene, it is assumed that ionization is the rate-determining step so that

$$R = k'_{i(av)} a \quad (7)$$

or

$$\text{slope} = \frac{k'_{i(av)}(a)}{a} = k'_{i(av)} \quad (8)$$

TABLE I

RATE CONSTANTS, RELATIVE RATES, AND EQUILIBRIUM SPECIFIC ACTIVITIES RELATIVE TO TOLUENE FOR PROTON EXCHANGE IN POLYALKYLBENZENES

Hydrocarbon	—Rate constant, sec. ⁻¹ —		k , rel. to tolu- ene ^b	K_{eq} , rel. to tolu- ene ^b
	Toluene	Hydro- carbon		
<i>o</i> -Xylene	2.8×10^{-4}	3.9×10^{-4}	1.40	1.005
<i>m</i> -Xylene	2.9×10^{-4}	1.4×10^{-4}	0.51	0.98
<i>p</i> -Xylene	2.6×10^{-4}	9.1×10^{-5}	0.33	0.95
Ethylbenzene	3.0×10^{-4}	6.2×10^{-5}	.22	1.14
Cumene	2.8×10^{-4}	6.3×10^{-5}	.023	1.22
<i>t</i> -Butylbenzene ^c	3.3×10^{-4}	0.0	0.0	0.0
1,2,4-Trimethylbenzene	3.2×10^{-4}	7.1×10^{-5}	.26	.96
1,3,5-Trimethylbenzene	2.8×10^{-4}	6.2×10^{-5}	.22	.99
1,2,3-Trimethylbenzene	2.7×10^{-4}	3.1×10^{-4}	1.12	.99
1,2,4,5-Tetramethylbenzene	2.7×10^{-4}	4.9×10^{-5}	0.018	^c
1,2,3,5-Tetramethylbenzene	2.9×10^{-4}	3.2×10^{-5}	.12	0.97
1,2,3,4-Tetramethylbenzene ^d	3.2×10^{-4}	1.5×10^{-4}	.46	0.96
Pentamethylbenzene	2.7×10^{-4}	1.5×10^{-5}	.056	1.05
Hexamethylbenzene ^d	2.8×10^{-4}	2.8×10^{-6}	.010	1.01
<i>o</i> -Ethyltoluene ^e	3.4×10^{-4}	1.7×10^{-4}	.51	1.10
<i>m</i> -Ethyltoluene ^e	2.9×10^{-4}	7.0×10^{-5}	.24	1.05
<i>p</i> -Ethyltoluene	2.7×10^{-4}	7.2×10^{-5}	.026	0.98
<i>p</i> -Cymene	2.7×10^{-4}	6.2×10^{-5}	.023	^c
<i>p</i> - <i>t</i> -Butyltoluene ^e	3.0×10^{-4}	1.0×10^{-5}	.033	1.03

^a Third batch of stock solvent solution which showed slightly higher activity. ^b Per benzylic hydrogen. ^c Not run to equilibrium. ^d Some hexamethylbenzene did not go into solution.

tive rate constants shown in column 4. Column 5 gives the specific activity per benzylic hydrogen at equilibrium relative to the equilibrium value of toluene. In all cases the equilibrium ratio of specific activity is quite close to unity.

The largest deviations in the equilibrium isotope effects are observed with compounds having alkyl substituents on the benzylic carbon. To verify this point and to avoid the possibility of contamination during kinetic sampling, several experiments were carried out where the substrates were allowed to equilibrate before the first sample was withdrawn. A second sample was taken several days later and then four determinations of specific activity were made on each sample. The averages of these determinations are given in Table II. Once again, the only compounds showing significant deviations from unity are those with benzylic alkyl substituents, ethylbenzene, and cumene.

TABLE II

RELATIVE EQUILIBRIUM SPECIFIC ACTIVITIES

Hydrocarbon	K_{eq} ^a rel. to toluene
Toluene	1.0
<i>o</i> -Xylene	0.995
<i>p</i> -Xylene	0.975
Ethylbenzene	1.10
Cumene	1.30
1,2,3-Trimethylbenzene	1.012
1,3,5-Trimethylbenzene	0.987

^a Equilibrium expressed per reactive hydrogen.

TABLE III

RATE CONSTANTS AND RELATIVE RATES FOR *p*-XYLENE AND ETHYL BENZENE AT 30, 55, AND 80°

Hydrocarbon	Temp., °C.	—Rate constant, sec. ⁻¹ —		k , rel. to toluene
		Toluene	Hydrocarbon	
<i>p</i> -Xylene	30.0	1.4×10^{-4}	4.6×10^{-6}	0.033
<i>p</i> -Xylene	55.0	1.7×10^{-3}	8.7×10^{-5}	.051
<i>p</i> -Xylene	80.0	9.2×10^{-3}	7.2×10^{-4}	.078
Ethylbenzene	30.0	1.4×10^{-4}	2.8×10^{-5}	.20
Ethylbenzene	55.0	1.6×10^{-3}	3.0×10^{-4}	.19
Ethylbenzene	80.0	10.0×10^{-3}	2.0×10^{-3}	.20

^a Fourth batch of stock solvent solution which showed about one-half the activity of batches one and two over the entire temperature range.

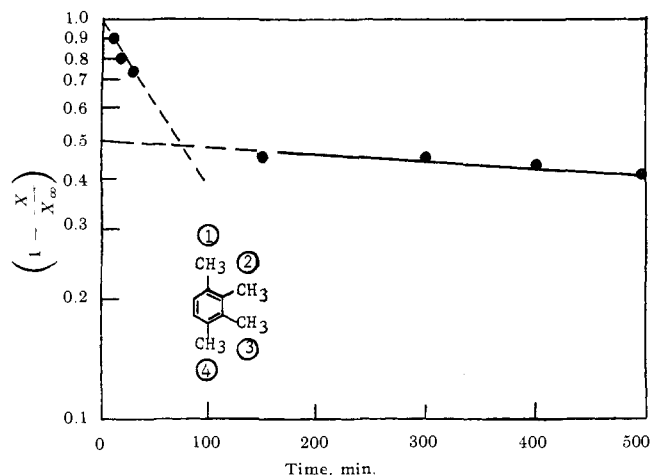


Fig. 1.—Isotope exchange with 1,2,3,4-tetramethylbenzene: $k_0 = 1.48 \times 10^{-4}$; $k_{2,3} = 2.9 \times 10^{-4}$; $k_{1,4} = 4.6 \times 10^{-6}$.

The significance of the fact that *p*-xylene exchanges more slowly than ethylbenzene will be discussed later. This surprising result prompted a brief investigation of these hydrocarbons at several temperatures. These data are shown in Table III.

A plot of $\ln(1 - X_1/X_\infty)$ for a hydrocarbon containing nonequivalent hydrogens, 1,2,3,4-tetramethylbenzene, is shown in Fig. 1. It is apparent that there are two independent straight lines representing the two nonequivalent pairs of methyl groups. Assignment of a rate constant to the 1- and 4-methyl groups and the 2- and 3-methyl groups is based on substituent factors outlined in the discussion. These individual rate constants are calculated as follows.

The over-all rate of exchange for 1,2,3,4-tetramethylbenzene is given by

$$R = \frac{a_1}{t} \ln \left(1 - \frac{X_1}{X_\infty} \right) + \frac{a_2}{t} \ln \left(1 - \frac{X_2}{X_\infty} \right) \quad (9)$$

At low conversions, this may be reduced⁴ to

$$R = \frac{a}{t} \ln \left(1 - \frac{X}{X_\infty} \right) \quad (10)$$

where R can be expressed by

$$R = k'_1 a_1 + k'_2 a_2 \quad (11)$$

The slope of the initial portion of Fig. 1 is given by

$$\text{slope} = k'_{i(\text{av})} = \frac{k'_1 a_1 + k'_2 a_2}{a} \quad (12)$$

Beyond the time required for equilibration of the more reactive hydrogens, the rate expression reduces to

$$R = \frac{a_2}{t} \ln \left(1 - \frac{X}{X_\infty} \right) \quad (13)$$

and for this portion of the reaction

$$R = k'_2 a_2 \quad (14)$$

$$k'_2 a_2 = \frac{a_2}{t} \ln \left(1 - \frac{X_2}{X_\infty} \right) \quad (15)$$

where X_2 is obtained from the fact that

$$X = \frac{X_1 + X_2}{2} \quad (16)$$

where X_1 is essentially equal to X_∞ . A plot of these data is shown in Fig. 2. The values of k'_1 are calculated from eq. 12.

Discussion

That only benzylic hydrogens participate in the exchange reaction is indicated by the fact that neither benzene nor *t*-butylbenzene undergoes exchange with tritiated dimethyl sulfoxide and that the equilibration of perdeuteriotoluene with unlabeled DMSO results ex-

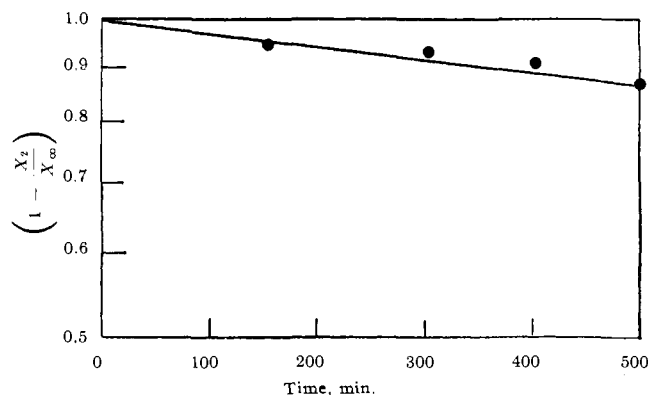


Fig. 2.—Exchange of 1 and 4 methyl groups on 1,2,3,4-tetramethylbenzene: $k_{1,4} = 4.6 \times 10^{-6}$ sec.⁻¹.

clusively in the formation of methyl C-H bonds.² The near-unity values of the equilibrium specific activities relative to toluene (K_{eq} , Tables I and II) indicate that the equilibrium isotope effect between each hydrocarbon and dimethyl sulfoxide is the same as that between toluene and dimethyl sulfoxide.⁵ Although the isotope effect is a thermodynamic rather than a kinetic phenomenon, it does lend some credence to the assumption that the kinetic isotope effect for ionization will not vary appreciably for a series of similar hydrocarbons.⁶ Thus, if the first-order slope is taken as

$$\text{slope} = k'_1 \beta^7 \quad (17)$$

$$k'_1 = \text{rate constant for ionization}$$

$$\beta = \text{kinetic isotope effect}$$

and the value of β is assumed to be fairly constant, a relative value based on ratios of slope will give directly the relative rates of ionization. In those cases where there is a deviation from unity in the equilibrium distribution of tritium—those compounds having α -methyl substituents—the deviation is not large enough to significantly alter the conclusions.

Effect of Position of Substituent on Rate.—The relative rates of exchange for *o*-, *m*-, *p*-xylene, ethylbenzene, and cumene are shown in Table IV and compared with values obtained by Streitwieser, *et al.*,⁸ using lithium

TABLE IV
RELATIVE RATES FOR PROTON EXCHANGE IN
DIFFERENT BASE-SOLVENT SYSTEMS

Hydrocarbon	This work, 30°	Streitwieser, ^a 50°	Shatenshtein, ^b 10°
Toluene	1.0	1.0	1.0
<i>o</i> -Xylene	1.4
<i>m</i> -Xylene	0.51	0.6	...
<i>p</i> -Xylene	.033	.29	...
Ethylbenzene	.22	.116	0.14
Cumene	.023	.0079	.029

^a See ref. 8. ^b See ref. 9.

cyclohexylamide in cyclohexylamine, and Shatenshtein,⁹ using potassium amide in liquid deuterioammonia. Comparison of rates of exchange of toluene with ethylbenzene and cumene in all cases shows the expected behavior, *i.e.*, ease of carbanion formation increasing in the order, primary > secondary > tertiary. There are some differences in absolute value, the largest of which arises

(5) It will be recalled from the previous paper² that an equilibrium isotope effect of about 1.5 exists between toluene and dimethyl sulfoxide.

(6) This arises from the fact that the kinetic isotope effect in the reverse direction, abstraction of a solvent proton by a very reactive hydrocarbon carbanion, would be expected to be very similar for similar carbanions.

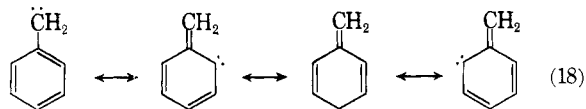
(7) See eq. 10 of previous paper.²

(8) A. Streitwieser, Jr., and D. E. Van Sickle, *J. Am. Chem. Soc.*, **84**, 249 (1962).

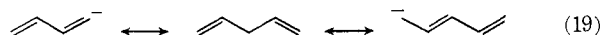
(9) A. I. Shatenshtein and E. A. Izrealevich, *Zh. Fiz. Khim.*, **32**, 2711 (1958).

in comparison of this work with that of Streitwieser. The most striking difference is the reversal of the relative rates of ethylbenzene and *p*-xylene. The strong rate-retarding tendency of the *p*-methyl group holds over the entire range of 30 to 80° and *p*-xylene shows an activation energy of 21.6 kcal. as compared to about 18 kcal. for toluene and ethylbenzene. The other *p*-alkyl derivatives also show surprisingly small relative rates (Table I). The most likely explanation for these data is a greater degree of charge delocalization through the aromatic ring for the transition state in dimethyl sulfoxide as compared to cyclohexylamine. This is not unreasonable in that dimethyl sulfoxide is considerably more polar than cyclohexylamine.

The canonical forms for charge delocalization in the benzyl system (eq. 18) distribute the negative charge in the *o*- and *p*-positions. Simple molecular orbital

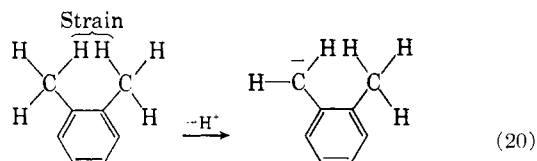


calculations for this odd-alternate system lead to the same results. The exceptionally small relative rate for *p*-xylene (and the other *para* substituted compounds) as compared to *o*-xylene suggests not only considerable delocalization of charge into the ring but also preferential charge localization in the *para* position. Zimmerman¹⁰ recently completed modified LCAO calculations to account for the position of protonation in metal ammonia reductions, which indicate that there may be preferential charge localization on the central



carbon in a five-carbon carbanion. If such were also the case for the benzyl carbanion, the inductive effect of a *p*-methyl group would be more pronounced than that of a *o*-methyl group.

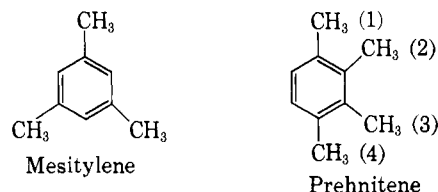
Although this may be part of the explanation, there must be an additional reason for the fact that ionization of *o*-xylene is actually faster than toluene. Brown and Kahn¹¹ observed similar results in measuring the acidity of the unsubstituted and the *o*-, *m*-, and *p*-methyl anilinium ions. The explanation offered involved relief of steric strain (nonbonded hydrogen interactions) upon ionization. Since the benzyl carbanion is isoelectronic with and approximately the same size as aniline, it is possible that relief of strain also occurs during ionization of *o*-xylene.



Unfortunately, since the actual inductive effect of the *o*-methyl group is unknown, it is impossible to estimate just how much relief of strain is required to explain the observed results. An alternate or, perhaps, co-explanation is the possibility of hydrogen bonding between the incipient carbanion and hydrogens on the *o*-methyl group. It has been suggested that carbanions should be excellent hydrogen bonding bases¹² and this may in turn lower the activation barrier for ionization.

The Additive Effect of Ring Substituents.—Linear free-energy relationships have been used to correlate a number of reactions where the reaction center is effected

by several groups.¹³ In the present work, the rates of proton exchange for all of the higher methylbenzenes can be broken down into substituent effects of *o*-, *m*-, and *p*-methyl derivatives. Thus, in mesitylene, each methyl group is effected by two *m*-methyl groups, and in prehnitene there are two pairs of methyl groups, one



effected by one *o*-, one *m*-, and one *p*-methyl and the other effected by two *o*- and one *m*-methyl. If substituent factors are defined as the log of the rate constants of the three xylene isomers relative to toluene, then the relative rate constant for any of the higher methyl benzenes can be predicted by addition of the proper

$$f_o = \ln k_o/k_t \quad (21)$$

$$f_m = \ln k_m/k_t \quad (22)$$

$$f_p = \ln k_p/k_t \quad (23)$$

factors. As an example, calculations for the two compounds previously mentioned are shown below.

$$\ln \frac{k_{\text{mesitylene}}}{k_{\text{toluene}}} = 2f_m \quad (24)$$

$$\ln \frac{k_{\text{prehnitene}}}{k_{\text{toluene}}} = 0.5(f_o + f_m + f_p) + 0.5(2f_o + f_m) \quad (25)$$

Comparison of predicted and observed values are shown in Table V. Agreement is excellent for the tri-

TABLE V
PREDICTED AND OBSERVED RELATIVE RATES FOR PROTON EXCHANGE IN POLYMETHYLBENZENES

Hydrocarbon	—Rate constant rel. to toluene—	
	Pred.	Obsd.
1,2,3-Trimethylbenzene	1.13	1.12
1,2,4-Trimethylbenzene	0.26	0.26
1,3,5-Trimethylbenzene	.26	.22
1,2,3,4-Tetramethylbenzene	.51	.46
1,2,3,5-Tetramethylbenzene	.20	.12
1,2,4,5-Tetramethylbenzene	.024	.018
Pentamethylbenzene	.12	.056
Hexamethylbenzene	.017	.010

methylbenzenes, but discrepancies between observed and calculated rate constants increase among the higher methylbenzenes, most likely due to increased steric requirements in solvating the incipient carbanion as the number of methyl groups increases.¹⁴

For prehnitene it was possible to measure the rate constant for each pair of equivalent methyl groups. These are compared with predicted values in Table VI. The agreement is certainly good enough to justify

TABLE VI
PREDICTED AND OBSERVED RATE CONSTANTS FOR EACH PAIR OF EQUIVALENT METHYL GROUPS IN 1,2,3,4-TETRAMETHYLBENZENE

Methyl groups	—Rate constant, sec. ⁻¹ —	
	Pred.	Obsd.
1 and 4	7.0×10^{-6}	4.6×10^{-6}
2 and 3	3.1×10^{-4}	2.9×10^{-4}

the approach of linear combination of free energies. Determination of the slower rate constant of the 1- and 4-methyl groups is the less accurate of the two since

(13) See F. E. Condon, *ibid.*, **70**, 1963 (1948). Also, extensive work of H. C. Brown and co-workers, *J. Am. Chem. Soc.*

(14) Data on hexamethylbenzene are somewhat in doubt because of failure to reach a homogeneous solution.

(10) H. E. Zimmerman, *Tetrahedron*, **16**, 169 (1961).

(11) H. C. Brown and A. Kahn, *J. Am. Chem. Soc.*, **72**, 2939 (1950).

(12) L. L. Ferstandig, *ibid.*, **84**, 3553 (1962).

it must be measured against a background of the fully tritiated 2- and 3-methyl groups.

Effect of Alkyl Group Size on Rate.—A question that has received little attention in carbanion reactions is the relative inductive effects of different alkyl substituents. For instance, what is the rate of exchange of a methyl group when it is effected by a methyl, ethyl, isopropyl, or *t*-butyl group? The most reliable data will be obtained with these substituents in the *meta* or *para* positions where steric effects are not significant. Relative rate constants for several compounds are summarized in column 1 of Table VII.

TABLE VII
RELATIVE INDUCTIVE EFFECTS OF ALKYL GROUPS

Hydrocarbon	—Rate constant rel. to toluene—	
	Exptl.	Calcd. for CH ₃ group
<i>p</i> -Xylene	0.033	0.033
<i>p</i> -Ethyltoluene	.026	.041
<i>p</i> -Cymene	.023	.03
<i>p</i> - <i>t</i> -Butyltoluene	.033	.033
<i>m</i> -Xylene	.51	.51
<i>m</i> -Ethyltoluene	.24	.33

For those compounds containing nonequivalent hydrogens, *p*-ethyltoluene and *p*-cymene, the experimental rate constant is, as before, an average value. The rate constant for the methyl group of each hydrocarbon can be calculated if the rate of exchange of all other hydrogens is backed out. This was accomplished by assuming that a methyl substituent has the same effect on all other alkyl groups as it does on another methyl group. These data are presented in column 2. Within a given series there appears to be little or no difference in the inductive effect as the size of the alkyl group is varied. The largest deviation occurs with the *meta* isomers. Data on other *meta* alkyl substituents are not yet available, so it is impossible to tell if this is a general phenomenon.

The preceding data have demonstrated the usefulness of dimethyl sulfoxide as a solvent for determining relative acidities. It is clear that over a small range of acidities, any relative order of acidity will be solvent dependent. We hope to extend the present work to include the effect of solvent polarity on relative acidities, particularly with the xylenes, ethylbenzene, and cumene. Finally, it has been shown that substituents

behave in an additive manner, from a free-energy standpoint, and that cumulative effects can be predicted from simple models.

Experimental

Procedures employed during this study were essentially identical with those described in the previous paper.² Approximately 50–50 mole % blends were prepared for each hydrocarbon with toluene. These mixtures were then injected into prethermostated base–solvent solutions as described previously. Each hydrocarbon was used as received from the source given below.

Toluene	Baker (Analyzed Reagent)
<i>o</i> -Xylene	Matheson Coleman and Bell (Reagent)
<i>m</i> -Xylene	Matheson Coleman and Bell (Reagent)
<i>p</i> -Xylene	Matheson Coleman and Bell (Reagent)
1,2,4,5-Tetramethylbenzene	Matheson Coleman and Bell (Reagent)
Cumene	Matheson Coleman and Bell (Reagent)
<i>p</i> -Cymene	Matheson Coleman and Bell (Reagent)
1,2,3-Trimethylbenzene	Aldrich (Puriss.)
1,2,4-Trimethylbenzene	Aldrich (Puriss.)
1,3,5-Trimethylbenzene	Aldrich (Puriss.)
1,2,3,4-Tetramethylbenzene	K & K Laboratories
1,2,3,5-Tetramethylbenzene	K & K Laboratories
<i>o</i> -Ethyltoluene	K & K Laboratories
<i>m</i> -Ethyltoluene	K & K Laboratories
<i>p</i> -Ethyltoluene	K & K Laboratories
<i>p</i> - <i>t</i> -Butyltoluene	Fisher
Pentamethylbenzene	Eastman
Hexamethylbenzene	Eastman

Radio-assaying gas chromatographic analyses were carried out on a 10-ft. Dow Corning silicone oil column (DC-200) at 100–135° for all compounds except the tetra-, penta- and hexamethylbenzenes. For these compounds, a 2-ft. silicone rubber column was used at 125°. Mole response factors given by Messner¹⁵ were employed in the calculation of chemical peak areas when available. Other mole response factors were extrapolated from the data of Messner and are given below.

Tetramethylbenzenes	1.66
Pentamethylbenzenes	1.82
Hexamethylbenzene	1.99
1,2,3-Trimethylbenzene	1.50
<i>o</i> -Ethyltoluene	1.50
<i>m</i> -Ethyltoluene	1.50
<i>p</i> -Cumene	1.6
<i>p</i> - <i>t</i> -Butyltoluene	1.8

After sampling for the kinetic portion of each experiment was complete, the samples were allowed to remain in the temperature bath for a time equivalent to at least ten half-lives of the slower of the two reactions. At this time final samples were withdrawn and equilibrium specific activities were determined.

(15) A. E. Messner, E. M. Rosie, and P. A. Argabright, *Anal. Chem.*, **31**, 230 (1959).

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The Hydrolysis of Substituted 2-Phenyl-1,3-dioxanes^{1a}

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A series of 2-(substituted phenyl)-1,3-dioxanes have been prepared and the pH–rate profiles of their hydrolyses determined. All the acetals show the usual hydronium ion-catalyzed hydrolyses. In addition, those acetals containing an *o*- or *p*-phenolic substituent exhibit a hydrolytic reaction which is independent of external hydronium ion but which is dependent on the un-ionized form of the acetal. The hydrolyses of those acetals containing *o*-phenolic substituents could formally be attributed to intramolecular general acid catalysis. However, the comparable hydrolysis of acetals containing *p*-phenolic substituents and the effect of deuterium oxide on the kinetics indicates that the best interpretation of the spontaneous hydrolysis of the phenolic acetals is the hydronium ion-catalyzed hydrolysis of the phenolate ion form of the substrates.

The cleavage of the acetal linkages of polysaccharides is catalyzed by enzymes which appear to contain no prosthetic groups² and which therefore presumably

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(2) E. H. Fischer and E. A. Stein in "The Enzymes," 2nd Ed., Vol. 4, Academic Press, Inc., New York, N. Y., 1960, Chapter 18.

utilize acidic and/or basic sites of the constituent amino acids as the catalytic functions. On the other hand, the hydrolysis of acetals has been cited as an example of a hydrolytic reaction that is subject to specific hydronium ion catalysis.^{3,4} The failure^{4–6} to detect general

(3) P. D. Bartlett in H. Gilman "Organic Chemistry, an Advanced Treatise," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1953, pp. 115–116.