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Acidity of Hydrocarbons. X. Exchange Rates of Ring-Substituted Toluene- α - t 's with Lithium Cyclohexylamide in Cyclohexylamine^{1,2}

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Relative exchange rates at 50° toward lithium cyclohexylamide in cyclohexylamine of substituted α -tritio-toluenes and some α -deuteriotoluenes are: H, 1.00; *o*-CH₃, 0.60; *m*-CH₃, 0.60; *p*-CH₃, 0.31; *o*-CH(CH₃)₂, 0.41; *m*-CH(CH₃)₂, 0.61; *p*-CH(CH₃)₂, 0.29; *o*-F, 12; *m*-F, 22; *p*-F, 0.73; *m*-CF₃, 60; *p*-CF₃, ~180; *m*-OCH₃, 2.1; *p*-OCH₃, 0.091. These values fit a Hammett $\sigma\rho$ correlation with $\rho = 4.0$, a value higher than that for phenol or anilinium dissociations. The extension to polycyclic systems is discussed.

Previous work from these laboratories on the exchange reaction of deuterated and tritiated methylarenes with lithium cyclohexylamide in cyclohexylamine has indicated that the relative rates may be useful measures of relative acidities. This research has encompassed results from the reaction kinetics,^{1,3} isotope effects,^{4,5} effects of methyl substituents,⁶ stereochemistry,⁷ and the effect of arene ring size.⁸ In this paper, we explore the effect of various ring substituents on the exchange rate of toluene- α - t or toluene- α - d .

The kinetic procedure was similar to that developed in the earlier work. The solution of substrate and lithium cyclohexylamide was prepared in a reaction vessel on the vacuum line and aliquots were isolated in the usual way. Most of the compounds examined were labeled with both deuterium and tritium. The analysis of deuterium content by infrared followed our customary procedure. The tritium analysis, however, was accomplished using a radioassay gas chromatography apparatus, and the ratio of counts in the proportional flow counter to area of the g.c. peak was used as the measure of specific activity as a function of time. By this procedure, several compounds could be run simultaneously in a kinetic run.

Experimental

Chemicals.—The labeled toluenes were prepared generally by quenching the Grignard reagent from the corresponding benzyl halide with tritium-enriched D₂O. Purity of the distilled products was established by gas chromatography. The products had a tritium activity generally of 10⁴–10⁸ d.p.m. per λ . The ultimate starting materials were commercially available benzyl chlorides, bromides, or alcohols. The trifluoromethyltoluenes were obtained from the corresponding benzoyl chlorides by conversion to the methyl esters, reduction with lithium aluminum hydride, and conversion to the benzyl bromides with hydrobromic acid.

A mixture of the three isopropyltoluene- α - t 's was prepared by alkylation of toluene- α - t with isopropyl alcohol and boron fluoride. This method gives a cyrene mixture that is 41% *ortho*, 22% *meta*, and 37% *para*.⁹

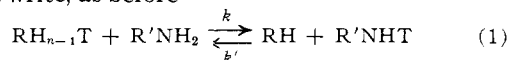
Kinetics.—The exchange experiments were carried out between the labeled hydrocarbons and lithium cyclohexylamide in cyclohexylamine in a manner similar to procedure B described earlier.³ The aliquots were analyzed for deuterium by the infrared spectra of CCl₄ solutions. When both deuterium and tritium analyses were carried out, the infrared spectra were taken on isoctane solutions. In each case, a semilog plot of the deuterium content minus the infinity value gave a good straight

line whose slope was used for $k_{D, \text{exptl}}$. A portion of each isoctane solution was used for tritium analysis as follows: The tritium analysis utilized a radioassay gas chromatograph. An Aerograph A-90P was used in conjunction with proportional counter tubes and electronics similar to that described by Wolfgang and co-workers.^{10,11} A kinetic aliquot was washed with dilute hydrochloric acid to remove the amine and extracted with isoctane. A portion of the isoctane solution was used for infrared analysis of deuterium in some runs. For the tritium analyses, a portion was injected into the Aerograph. The g.c. area, measured with a planimeter, gave a measure of the amount of compound injected, and the printout of radioactivity counts from the proportional counter gave a measure of the total activity during the time corresponding to the g.c. peak. The total counts (C) for a given peak (corrected for background) was divided by the g.c. area (A) to yield a number proportional to the specific activity ($C/A = y$). Corrections can be applied to the thermal conductivity response for different compounds¹² in order to obtain true relative specific activities, but such corrections are not required for the kinetics of single compounds. Semilog plots of ($y_t - y_\infty$) vs. time gave good straight lines whose slopes gave $k_{T, \text{exptl}}$.

We found in our work that we were able to use methane as both the carrier gas for the g.c. and for the proportional counter. Most of our runs used this technique. Alternatively, helium could be used for greater g.c. sensitivity and methane is then added to the carrier gas before entry into the counter tube. A few runs with this method gave rate constants that agreed within 10% of those obtained by the preceding method. Using only methane, one is able to obtain broader operating plateaus with the counter and the operation is simplified. We normally used counter temperatures of 130–150° (about 20–40° higher than the g.c. temperatures) with a voltage of 2.5–3.0 kv. and flow rates of 90–120 ml./min. The following substituents were found to give satisfactory response in the counter: CH₃, CF₃, F, Cl, and OCH₃. The substituents, Br, I, and CCl₃ gave serious quenching in the counter and were unsuitable for this analysis. Chlorinated solvents and highly fluorinated aliphatic compounds also gave serious quenching in the counter. Figure 1 gives a representative sample plot of $k_{D, \text{exptl}}$ and $k_{T, \text{exptl}}$ with a mixture of toluene- α - d and toluene- α - t . The g.c. analysis was run on a 10-ft. DEGS column at 92° with 63 ml./min. of methane. The counter tube was maintained at about 130° and counts were printed every 20 sec.

The real virtue of the radioassay gas chromatograph is its ability to provide analyses of mixtures. In many of our kinetic runs, two or more components were mixed together. From each kinetic aliquot (C/A) ratios (y_i) are obtained for each component so that several rate constants are determined in a single run. In addition to saving of time—each kinetic run on the vacuum line represents several days of work—this procedure provides relative rates directly, independent of the base concentration.

Kinetic Analysis.—For the deuterium rates, a correction for the back reaction was applied to $k_{D, \text{exptl}}$ to obtain k_D as described earlier.³ In our previous paper on k_D/k_T isotope effects,⁴ we implied that the same correction applies to the tritium rates. This is incorrect, because of the minute amount of tritium actually present. We write, as before



(10) We are deeply indebted to Irving Whitemore for suggesting this method and for much technical assistance and advice.

(11) R. Wolfgang and C. F. Mackay, *Nucleonics*, **16**, No. 10, 69 (1958); R. Wolfgang and F. S. Rowland, *Anal. Chem.*, **30**, 903 (1958). Our apparatus is patterned closely after that described by R. T. Mullin, UCRL Report No. 9603 (1961).

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

(1) Paper IX: A. Streitwieser, Jr., and R. G. Lawler, *J. Am. Chem. Soc.*, **85**, 2854 (1963).

(2) This work was supported by a grant from the United States Air Force Office of Scientific Research of the Air Research and Development Command. This work was presented in part at the 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., Sept. 10, 1962.

(3) A. Streitwieser, Jr., D. E. Van Sickle, and W. C. Langworthy, *J. Am. Chem. Soc.*, **84**, 244 (1962).

(4) A. Streitwieser, Jr., W. C. Langworthy, and D. E. Van Sickle, *ibid.*, **84**, 251 (1962).

(5) A. Streitwieser, Jr., and D. E. Van Sickle, *ibid.*, **84**, 254 (1962).

(6) A. Streitwieser, Jr., and D. E. Van Sickle, *ibid.*, **84**, 249 (1962).

(7) A. Streitwieser, Jr., D. E. Van Sickle, and L. Reif, *ibid.*, **84**, 258 (1962).

(8) A. Streitwieser, Jr., and W. C. Langworthy, *ibid.*, **85**, 1757 (1963).

(9) Unpublished results from this laboratory.

$$d[\text{RH}_{n-1}\text{T}]/dt = k[\text{RH}_{n-1}\text{T}](1 - \rho) - nk'[\text{RH}_n]\rho \quad (2)$$

ρ = fraction of tritium in solvent = $(x_0 - x)a/2b$
 a = $[\text{RH}_{n-1}\text{T}] + [\text{RH}_n] \cong [\text{RH}]$
 b = $[\text{R}'\text{NH}_2] + [\text{R}'\text{NHT}] \cong [\text{R}'\text{NH}_2]$
 x = $[\text{RH}_{n-1}\text{T}]/a$ = fraction of tritium in substrate
 $-\frac{dx}{dt} = kx - nk' \frac{a(x_0 - x)}{2b} \quad (3)$

We take $k = k'$,³ and solve this first-order equation to obtain

$$\ln \frac{x_0 - x_\infty}{x_t - x_\infty} = k_{\text{expt}} t = \frac{2b + na}{2b} kt \quad (4)$$

Therefore, the true first-order rate constant

$$k_T = \frac{2b}{2b + na} k_{\text{Texptl}} \quad (5)$$

In practice, for the values of a we usually use (~ 0.1 – $0.2 M$); this correction is close in magnitude to the numerically different correction that applies to the deuterium kinetics. Thus the magnitudes of isotope effects reported previously are not changed significantly.

The foregoing corrections apply because the proton pool in the solvent is not effectively infinite compared to the exchangeable hydrogens in the substrate. A further kinetic complication arises in such cases when a mixture of two or more substrates is studied. Consider a "fast" and a "slow" substrate. The fast compound releases its isotope rather quickly to the solvent until an equilibrium is reached. As the slow compound releases its additional isotope to solvent, the first equilibrium is displaced and isotope returns progressively to substrate. The effective "infinity" value to be used in the equation for first-order kinetics (eq. 4) varies with time and is a function of the various substrates present. This effect can be minimized by keeping the substrate concentrations low or by using substrates that have either identical rates or differ in reactivity by a large factor. For intermediate situations, a complete kinetic analysis is necessary. An analytical treatment is possible, but the resulting equations are cumbersome and are best handled with a high speed computer.¹³ The following treatment involves instead a graphical integration and may be applied readily.¹⁴

In the kinetic treatment above, ρ , the fraction of isotope in the solvent, is related simply to that in the hydrocarbon. If we retain ρ as an explicit quantity and include the simplifications inherent in the small amount of tritium actually present, eq. 2 leads to

$$-\ln x/x_0 = k \left(t - na \int_0^t \frac{\rho}{x} dt \right) = k\theta \quad (6)$$

The quantity ρ/x may be evaluated by the conservation of tritium

$$[\text{R}'\text{NHT}] = \sum_i a_i (x_i^* - x_i) = 2b\rho \quad (7)$$

in which the x^* refers to the activity before any reaction has taken place—zero time is usually taken some time after the reaction solution has been prepared. This equation requires relative molar activities; in the present case in which $C/A = y$ is used as the measure of radioactivity, it is necessary to use relative thermal conductivities, η_i

$$x_i = a_i \eta_i y_i \quad (8)$$

$$\frac{\rho}{x_i} = \frac{[\text{R}'\text{NHT}]}{2bx_i} = \frac{\sum_i (y_i^* - y_i) \eta_i a_i}{2by_i \eta_i a_i} \quad (9)$$

(13) We are indebted to Dr. C. Perrin for the analytical solution.

(14) We are pleased to acknowledge the assistance of R. A. Caldwell in this treatment.

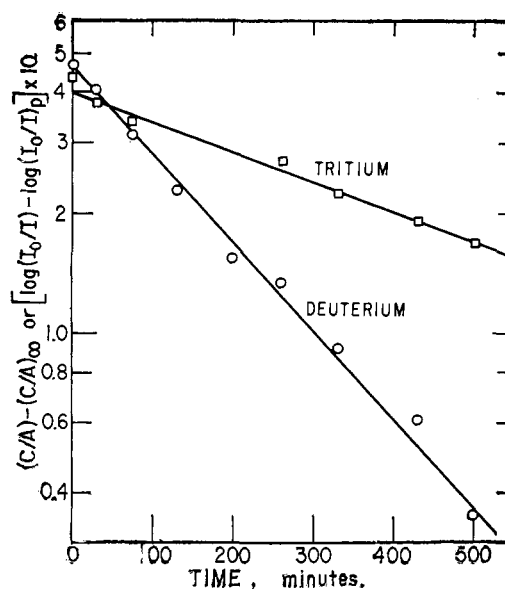


Fig. 1.—A kinetic plot of run 67, 0.50 M in a mixture of toluene- α - d and toluene- α - t and 0.027 M in lithium cyclohexylamide: $k_{\text{Dexptl}} = 8.3 \times 10^{-6} \text{ sec.}^{-1}$; $k_{\text{Texptl}} = 2.9 \times 10^{-5} \text{ sec.}^{-1}$.

ρ/x_j is obtained directly from the experimental data for each time aliquot and is plotted vs. time. Graphical integration is used to define the new time parameter, θ , as in eq. 6. A semilog plot of y_j vs. θ then gives k_j directly. Note that by this procedure, the back reaction has been taken into account and the resulting rate constants are directly the corrected rate constants, k_T .

The kinetic run with the cymenes exemplifies the power of this technique. The mixture of *o*-, *m*-, and *p*-isopropyltoluene- α - t as synthesized was used directly together with toluene- α - t and *o*- and *p*-xylene- α - t in kinetic run 151. In this case, *m*- and *p*-cymene could not be separated completely by g.c.; however, partial separation was obtained and reproducible estimates could be made of the radioactivities of the two components. All of the other hydrocarbons in the reaction mixture could be separated cleanly. The toluene- α - t used in this run was a sample of the same material which was alkylated to prepare the cymenes—all, therefore, have the same molar activity (412,000 d.p.m./mg.). The xylenes, unfortunately, had substantially lower specific activity (23,000 d.p.m./mg.). Consequently, the tritium content of the solvent rapidly became comparable to that in the xylenes and only order-of-magnitude rate constants could be obtained for the xylenes. This example emphasizes a further demand of this method, namely, that all components have comparable levels of isotope content. The results for the other four components are illustrated in Fig. 2. The cymene rate constants have an estimated uncertainty of 10–15% and are less precise than the other values in Table I.

The trifluoromethyl substituents presented another problem. *m*-Trifluoromethyltoluene is stable to lithium cyclohexylamide and rate constants could be obtained in the normal manner. The *o*- and *p*-isomers are decomposed by the reaction mixture and produce tars. Two to three moles of lithium cyclohexylamide are destroyed simultaneously; this destruction of base permitted a competitive reaction study. *p*-Trifluoromethyltoluene- α - d_3 was prepared by reduction of *p*-trifluoromethylbenzoyl chloride with lithium aluminum deuteride, treatment of the product with hydrobromic acid, and reduction with lithium deuteride–lithium aluminum deuteride using normal procedures. A com-

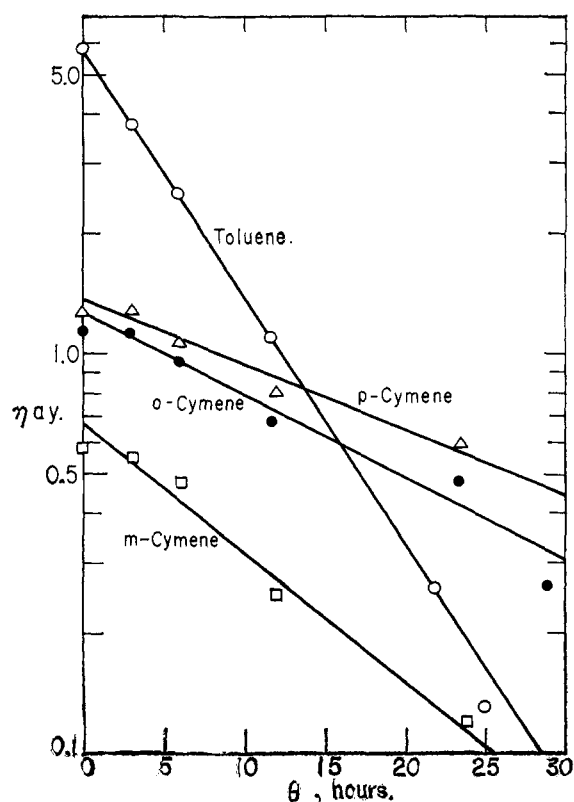


Fig. 2.—Kinetic plots of exchange of toluene- α - t and o -, m -, and p -isopropyltoluene- α - t from run 151.

petitive reaction was run with 1-methylpyrene- α - d .⁸ In each of two experiments, a mixture of toluene, trifluoromethyltoluene- α - d_3 , and 1-methylpyrene- α - d in cyclohexylamine was treated with an insufficient amount of lithium cyclohexylamide. When reaction was complete, the amount of undecomposed trifluoromethyltoluene- α - d_3 was determined by g.c. using the toluene as an internal standard, and the amount of deuterium lost from 1-methylpyrene- α - d was determined by infrared analysis. In the first experiment, 14% of the trifluoromethyltoluene, F, had decomposed and the methylpyrene, P, lost 6% of its deuterium. Assuming that each reaction of trifluoromethyltoluene with base destroys base, the relative rate is given by

$$k(F)/(k_D)(P) = \log [(F)_0/(F)_\infty] / \log [(P)_0/(P)_\infty] \quad (10)$$

This first experiment gives $k(F)/k_D(P) = 2.4$. In the second experiment, 23% of the trifluoromethyl was destroyed and the 1-methylpyrene- α - d lost 12% of its deuterium. This gives a relative rate of 2.0. Despite this reproducibility, we consider the result to be approximate.

The kinetic results are summarized in Table I.

Discussion

The aggregation of lithium cyclohexylamide in this system prevents the assigning of accurate, true second-order rate constants³; however, relative rates can be meaningfully assigned from the known exchange rates of toluene- α - d and - α - t as a function of the concentration of lithium cyclohexylamide or from those kinetic runs which included toluene- α - t as one component. Such relative rates are given for each kinetic run in Table I and are summarized for each substituent in Table II. The value for p -CF₃ is derived from competition experiments of p -trifluoromethyltoluene- α - d_3 with 1-methylpyrene- α - d . When a known mixture of the two is brought together with a limited amount of lithium cyclohexylamide in cyclohexylamine, the base causes loss of deuterium from the pyrene com-

TABLE I
EXCHANGE RATES OF SUBSTITUTED TOLUENE- α - t 'S WITH LITHIUM CYCLOHEXYLAMIDE IN CYCLOHEXYLAMINE AT 50.0 \pm 0.1°

Run	Substituent	a , ^a mole/l.	c , ^b mole/l.	$10^3 k_T$, sec. ⁻¹	Rel. rate toluene- α - t = 1
37	o -CH ₃	0.48	0.029	4.3 ^c	0.57
39	o -CH ₃	.47	.029	4.5 ^c	.60
41	m -CH ₃	.47	.031	4.7 ^c	.60
67	H	.50	.027	7.2 ^c	(2.9) ^d
81	m -F	.25	.023	43	19
87	p -F	.14	(.034) ^e	1.9	0.68
	H	.11		2.8	
91	p -F	.11	0.023	2.1	0.78
	H	.11		2.7	
95	o -F	.25	0.019	23	11
105	m -CF ₃	.07	.019	142	68
113	o -CH ₃	.14	.016	1.22	.64
	p -CH ₃	.17		0.58	.31
	p -OCH ₃	.09		Slow ^f	
117	p -OCH ₃	.12	0.046	0.27	.090
				0.74 ^c	(2.7) ^d
121	m -CF ₃	0.15	0.010	85	57
129	o -F	.25	.045	38	13
131	m -F	.25	.032	64	25
133	p -OCH ₃	.12	.064	0.31	0.091
135	m -CF ₃	.13	.053	178	56
137	m -OCH ₃	.12	.062	7.2	2.1
139	m -OCH ₃	.13	.064	7.2	2.1
151	H	.046	.06	3.4	
	p -CH ₃	.091	
	o -CH ₃	.075	
	o -CH(CH ₃) ₂	.014		1.4	0.41
	m -CH(CH ₃) ₂	.007		2.1	.61
	p -CH(CH ₃) ₂	.012		1.0	.29

^a Concentration of substrate. ^b Formal concentration of lithium cyclohexylamide. ^c k_D for α -deuterio compounds. ^d k_D/k_T isotope effect. ^e This value may be in error. ^f Kinetic points corresponded to too little reaction to permit derivation of a rate constant. ^g Tritium activity too low; see Experimental.

ound but is destroyed by the trifluoromethyl compound. The p -trifluoromethylbenzyl lithium, presumed as an intermediate, is apparently unstable and loses lithium fluoride to produce the corresponding difluoroquinodimethane which, in turn, polymerizes. From the amount of deuterium lost from the 1-methylpyrene- α - d , we derive a relative rate of ~ 2.2 . This number is converted to a relative exchange rate of p -trifluoromethyltoluene- α - d to toluene- α - d of ~ 180 by applying a statistical factor of 3, and a secondary deuterium isotope effect of 1.3⁵ to the known relative reactivity of 1-methylpyrene. 190.⁸

TABLE II
RELATIVE REACTIVITIES OF SUBSTITUTED TOLUENES

Substituent	Relative rate ($H = 1$)		
	ortho	meta	para
CH ₃	0.60	0.60 ^a	0.31 ^b
CH(CH ₃) ₂	0.41	0.61	.29
F	12	22	.73
CF ₃		60	~ 180 ^c
CH ₃ O		2.1	0.091

^a Reported previously (ref. 6): 0.60. ^b Reported previously (ref. 6): 0.29. ^c See text.

The rates of o - and p -xylene- α - t relative to toluene- α - t agree very well with those of o - and p -xylene- α - d relative to toluene- α - d . There is no important change in primary isotope effect for this group of compounds. A direct measurement of k_{11}/k_T for p -methoxytoluene^{2,7} is also in good agreement with the corresponding values for toluene (2.8 ± 0.2).⁴

The relative rates in Table II give the Hammett plot in Fig. 3.¹⁵ A good correlation is obtained with $\rho = 4.0$, a value which confirms the relatively high degree of carbanionic character of the transition state inferred from our previous studies. This value is similar to the value, 5.0, found recently for an anionic polymerization¹⁶ and may also be compared with the value ~ -4 obtained for many carbonium ion solvolysis reactions¹⁷; that is, it would appear that about as much benzyl anion character is developed in our exchange reaction as there is benzyl cation character developed in many solvolytic reactions. These results add strength to the case that these exchange rates are valid measures of relative hydrocarbon acidities.

The individual functional groups merit further discussion.

Alkyl Groups.—The results obtained in this work for *m*- and *p*-methyl substituents, 0.60 and 0.31, respectively, agree well with those we reported earlier, 0.60 and 0.29, respectively.⁶ The rate of *o*-xylene is of interest. Its rate-retarding electronic effect should be at least comparable to a *p*-methyl and any steric hindrance to coplanarity of the benzylic methylene group at the transition state should be an additional rate-retarding factor. In polycyclic methylenes, a *peri*-hydrogen causes a rate reduction of ~ 20 -fold attributed to such steric hindrance.⁸ Although steric hindrance of an *o*-methyl hydrogen is expected to be substantially less than that of a *peri*-hydrogen, it seems clear that a relative rate of < 0.3 is to be expected from these factors alone. The actual relative rate (0.6) is double that of a *p*-methyl and corresponds to a substantial rate acceleration over that expected. One of the most interesting interpretations of this phenomenon that we have encountered is that offered by Dr. E. Grunwald, who suggested¹⁸ that the rate enhancement may result from reduced rotational entropy of *o*-xylene. In the reaction of toluene, a freely rotating methyl group is converted to a rotationally rigid methylene group in the transition state. If rotation of the methyl groups in *o*-xylene is already restricted, there is less consequent reduction of rotational entropy in going to the transition state. This effect could introduce a factor of 3 into the relative rate or just about enough to account for the observed relative rate.

As expected, the *m*- and *p*-isopropyl groups behave similarly to methyl groups. The *o*-isopropyl group causes a small rate reduction relative to an *o*-methyl, but it is still somewhat more reactive than a *p*-isopropyl.

These results should be compared to those reported by Hofmann, Muller, and Schriesheim¹⁹ for the tritium exchange of substituted toluenes with potassium *t*-butoxide in tritiated dimethyl sulfoxide. Their relative rate for a *m*-methyl group, 0.51, compares well with our result of 0.60; however, their relative rate for a *p*-methyl group, 0.033, is ninefold smaller than our 0.3. The trend for an *o*-methyl is the same, although the relative rate in dimethyl sulfoxide, 1.4, is considerably higher than that in cyclohexylamine, 0.6. It seems clear that there are important and deep-seated differences between the dimethyl sulfoxide and cyclohexylamine solvent systems for carbanions. This

(15) σ -Values were taken from Table VII of D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958); σ for *m*-CH(CH₃)₂ was estimated as -0.08 .

(16) M. Shima, D. N. Bhattacharyya, J. Smid, and M. Szwarc, *J. Am. Chem. Soc.*, **85**, 1306 (1963).

(17) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 180.

(18) During a discussion of preliminary results at the Bell Laboratories, Murray Hill, N. J., Feb. 19, 1962.

(19) J. E. Hofmann, R. J. Muller, and A. Schriesheim, *J. Am. Chem. Soc.*, **85**, 3002 (1963). We are indebted to Dr. Schriesheim for a copy of his manuscript in advance of publication.

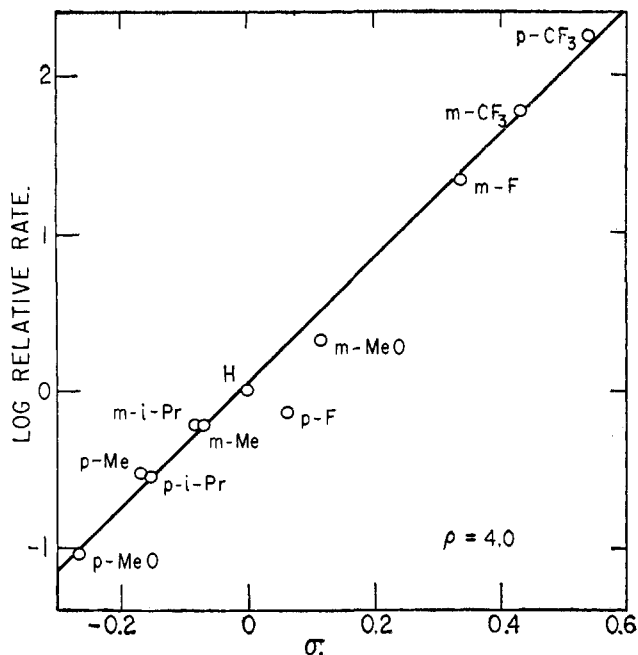


Fig. 3.—Hammett $\sigma\rho$ plot for proton exchange of substituted toluene- α - t 's with lithium cyclohexylamide.

difference is further emphasized by the exchange of aryl hydrogens. The report of a millionfold rate difference between the α -hydrogens of toluene and the ring-hydrogens of benzene with potassium *t*-butoxide and dimethyl sulfoxide¹⁹ contrasts strikingly with our finding¹ of a 200-fold rate difference with lithium cyclohexylamide and cyclohexylamine.

In private discussion,²⁰ Dr. D. J. Cram has offered an important and suggestive explanation for these differences, based on his observations of small primary isotope effects in proton exchanges in dimethyl sulfoxide.²¹ He suggests that when potassium *t*-butoxide in dimethyl sulfoxide removes a hydrogen isotope from a hydrocarbon, the return of that hydrogen to the resultant carbanion is an important competing step; that is, the diffusion away of the labeled alcohol is an important component of the rate-determining step.²¹ The net exchange reaction is thus determined both by the rate of initial proton removal and by the competition between return and diffusion. A change in structure could affect both of these quantities; for example, if the return step for benzene in dimethyl sulfoxide competes more effectively than for the benzyl position of toluene, an "abnormally" low relative rate for benzene would result. If Cram's interpretation is sustained by further work, it will mean that *kinetic* measurements in dimethyl sulfoxide have only limited significance as measures of acidity. The high isotope effects obtained in the cyclohexylamine system indicate that the problem of return is not important here; nevertheless, we are currently examining other corollaries of Cram's hypothesis in our system. We may mention at this time that to the extent that the investigations overlap, our relative rates in cyclohexylamine agree very well with those of Shatenshtein²² who is studying exchanges with potassium amide in liquid ammonia. The significance of these comparisons will be discussed in more detail later.

Halogens.—Aryl bromides and chlorides are rapidly decomposed by lithium cyclohexylamide, presumably *via* an aryne mechanism. The fluoro group, however,

(20) During the I.U.P.A.C. Meeting, London, July, 1963.

(21) D. J. Cram, C. A. Kingsbury, and B. Rickborn, *J. Am. Chem. Soc.*, **83**, 3688 (1961).

(22) A. I. Shatenshtein, *Tetrahedron*, **18**, 95 (1962).

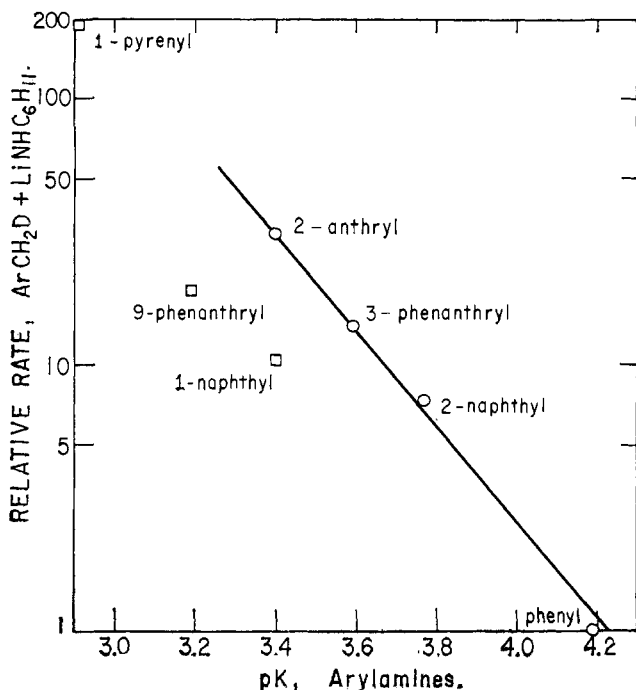


Fig. 4.—Comparison of lithium cyclohexylamide exchange rates of polycyclic methylarenes- α -*d* with pK 's of the corresponding arylamines.

is stable and reproducible kinetics were obtained for *o*-, *m*-, and *p*-fluorotoluene- α -*t*.

Fluoro.—The *m*-fluoro group is electron-attracting and is as rate enhancing as one expects from its normal σ -value. The *p*-fluoro group deviates farthest from the Hammett plot of any of the functions studied; indeed, instead of being rate enhancing as expected from its positive σ -value, the *p*-fluoro group is rate retarding. Actually, this effect was presaged by phenol and anilinium ion acidities. The pK of *p*-fluorophenol is 0.09 less than that of phenol in water at 25°,^{23,24} somewhat smaller than the 0.14 expected from the σ -values of *p*-F and ρ for phenol ionization, 2.23.²³ Moreover, the pK of *p*-fluoroanilinium ion is 0.05 higher than that for aniline.^{23,27} In these cases, the effects are small and there are differences with different investigators. It seems clear, however, that *p*-fluoro is more electron donating in phenol and anilinium ionizations than in benzoic acid dissociation, undoubtedly because of the higher electron density produced in the ring in the conjugated systems. In our case, the charge distribution into the ring is greater (ρ is higher) and the effect of *p*-fluoro is more pronounced. This result emphasizes the uniqueness of fluorine in combining the characteristics of high electronegativity and consequently a strong electron-withdrawing inductive effect, with the high double-bonding tendency characteristic of first-row elements. We should, perhaps, add to the normal σ for *p*-fluorine a σ^- component similar to the composite $\sigma + \sigma^+$ treatment helpful in many cationic reactions.²⁹

In the *o*-position, both the inductive and conjugative influences should also be operative; now, however,

(23) A. I. Biggs and R. A. Robinson, *J. Chem. Soc.*, 388 (1961).

(24) Other ΔpK 's reported are: -0.14 (ref. 25) and -0.10 (in 30% ethanol; ref. 26).

(25) C. M. Judson and M. Kilpatrick, *J. Am. Chem. Soc.*, **71**, 3110 (1949).

(26) G. M. Bennett, G. L. Brooks, and S. Glasstone, *J. Chem. Soc.*, 1821 (1935).

(27) Other ΔpK 's reported are: -0.06 (ref. 28) and $+0.02$ (in 30% ethanol; ref. 26).

(28) M. Kilpatrick and C. A. Arenberg, *J. Am. Chem. Soc.*, **75**, 3812 (1953).

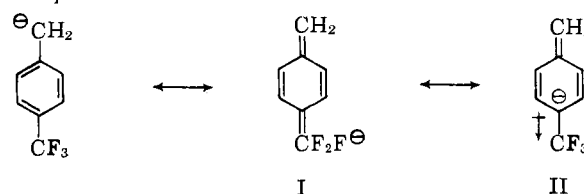
(29) Y. Yukawa and Y. Tsuno, *Bull. Chem. Soc. Japan*, **32**, 971 (1959).

the substituent is so close to the reactive center that the inductive (field) effect is dominating. Nevertheless, the relative rate of the *o*-fluoro (12) is still substantially less than *m*-fluoro (22).

The dichotomy of an electron-withdrawing inductive effect and an electron-donating conjugative effect has long been apparent with oxygen and is clearly reflected in our results with *m*- and *p*-methoxy groups. Oxygen is less electronegative than fluorine and probably has better π -bonding; hence, these relative rates are both shifted downward by about one log unit from *m*- and *p*-fluoro, respectively.

Trifluoromethyl.—*m*-Trifluoromethyltoluene is stable to lithium cyclohexylamide and gives an exchange rate completely in accord with that expected for $\sigma(m-CF_3)$. Both *o*- and *p*-trifluoromethyltoluenes, however, are rapidly decomposed by lithium cyclohexylamide, giving polymers which have not yet been studied further. In these cases, the trifluoromethylbenzyl lithium, presumably formed as an intermediate, appears to eliminate lithium fluoride to produce the corresponding difluoroquinodimethane which react further with lithium cyclohexylamide. It is noteworthy that *o*- and *p*-trifluoromethylphenols are extremely labile toward base and give polymers which appear to be derived from the corresponding difluoroquinomethane.³⁰

Although this decomposition prevented us from determining the reactivity of *p*-trifluoromethyltoluene by our usual techniques, we were able to obtain a relative rate by competition between *p*-trifluoromethyltoluene- α -*d*₃ and 1-deuteriomethylpyrene. The trideuteriomethyl compound was used in order that the primary isotope effect be utilized to reduce the relative reactivity. Despite the good reproducibility obtained in two experiments, we regard the result as having a relatively high probable error. The observed agreement of the relative reactivity found with the σ -value for *p*-CF₃ determined from benzoic acid ionizations cannot yet be taken seriously. In particular, our results cannot be used to distinguish between anionic hyperconjugation structures such as I or inductive structures such as II to interpret the observed electrical effects of trifluoromethyl groups.³¹ We are currently carrying out additional experiments that we hope will bear on this question.



Finally, we may develop a further comparison between the acidities of methylarenes as measured by our exchange rates and those of phenols and amines. Since these quantities all correlate with σ , they will clearly all correlate with each other—to this extent, data from other anilinium and phenol dissociations may be used to predict exchange rates of other substituted toluenes. It is of interest to attempt to extend this intercorrelation to polycyclic hydrocarbons. Unfortunately, pK values are available only for the naphthols and anthrols and cover a range of only 0.14 pK unit³²; no correlation with our results⁵ is possible.

Recent data are available for some polycyclic aminoarenes in 50% aqueous ethanol.³³ From the ρ -values of

(30) R. G. Jones, *J. Am. Chem. Soc.*, **69**, 2346 (1947).

(31) For example, see J. D. Roberts, R. L. Webb, and E. A. McElhill, *ibid.*, **72**, 408 (1950).

(32) K. Lauer, *Ber.*, **70**, 1288 (1937); H. Schenkel, *Experientia*, **4**, 383 (1948).

(33) J. J. Elliott and S. F. Mason, *J. Chem. Soc.*, 2352 (1959).

anilinium ions in 50% aqueous ethanol, ~ 3.5 ,³⁴ and that for the exchange reaction in this paper, 4.0, we would anticipate that a plot of $\log k$ for the exchange reaction of polycyclic methylarenes with lithium cyclohexylamide *vs.* the pK values for the corresponding amines would have a slope of ~ 1.1 . In such a plot, Fig. 4,

(34) Jaffé (ref. 35) gives $\rho = 3.435$ in 30% aq. ethanol and 3.535 in ethanol.

(35) H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953).

the non-*peri*-positions do give a good straight line but with a slope of 1.8. The difference in slopes is undoubtedly due to the prevailing importance of inductive effects in the substituted anilines and toluenes and to the enhanced importance of conjugative charge distribution in the polycyclic systems. We conclude that for other than broad qualitative purposes, amines are not good models for carbanions.

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Solvent Effects in Organic Chemistry. II. Sulfolane¹—A Weakly Basic Aprotic Solvent of High Dielectric Constant²

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Indicator and cryoscopic studies have been performed on solutions of sulfuric acid in sulfolane.¹ All of the evidence presented here indicates that this is a very weakly basic solvent in which ions are poorly solvated so that highly acidic solutions are obtained even at low acid concentration. In spite of ion-pair complications, a fairly good H_0 acidity function scale is developed in this solvent. In all of these ways sulfolane is very similar to nitromethane^{3,4} but has the great advantage of being far easier to handle.

Introduction

The three most important properties of a solvent that determine its behavior as a medium for acid-base reactions are: (1) its acidity and basicity; (2) its ability to function as a hydrogen bond donor, especially through hydroxyl groups; (3) its dielectric constant. Interesting effects have been observed by the shrewd variation of these properties. One of the most enlightening studies of this kind is that of Hammett and his students on nitromethane as a diluent for sulfuric acid.^{3a,b} Nitromethane is an aprotic dipolar solvent of very low basicity^{4,5} and relatively high dielectric constant (38). Hammett found it to be an extraordinarily poor medium for the solvation of ions^{3b} although a reasonably good acidity function could be developed in nitromethane solutions of sulfuric acid. Furthermore, because nitromethane is such a poor proton acceptor, sulfuric acid itself acts as the acid in this medium instead of the protonated solvent serving in this role as is usually the case. The result is that sulfuric acid solutions in nitromethane have an enormously greater effective acidity at low acid concentrations than do aqueous ones of the same acid concentration.

In the course of an investigation of ion solvation which will be described at a later time we were prompted to examine the properties of sulfolane.¹ Although our study is by no means as complete as that of Hammett for nitromethane, we believe that it will be of value to other workers.

Sulfones are almost as weakly basic as aliphatic nitro compounds⁶ and since sulfolane has a dielectric constant of 44 one might expect that if Hammett's conclusions are correct it should behave in a way similar to nitromethane as an acid-base medium. There are other properties of sulfolane that make it even more at-

tractive than nitromethane for such studies: it is much more easily purified and also has a large cryoscopic constant⁷ with a melting point close to room temperature so that dissociation or association measurements in it are especially convenient to perform. In the work to be described here we will show that sulfolane is probably not protonated by sulfuric acid and that its behavior is very similar to that found for nitromethane by Hammett and his students.

Experimental

Sulfolane was supplied through the generosity of the Shell Development Company of Emeryville, Calif. It was vacuum distilled repeatedly from sodium hydroxide pellets⁸ until a 1-ml. sample in a small test tube did not show development of visible color within 5 min. after the addition of an equal volume of 100% sulfuric acid. This usually required two or three distillations. It was then distilled again from calcium hydride to remove traces of water, which it holds tenaciously, and stored briefly under vacuum or dry air. Following the use of a batch of sulfolane for the cryoscopic or indicator studies to be described, it was usually found possible to remove most of this valuable solvent from the less acidic solutions by neutralization of the sulfuric acid content with sodium hydroxide pellets. The high viscosity of the solutions prevented the reaction from becoming violent and, after cooling, the remaining sulfolane could be decanted from the residual salts to produce material with the desired physical properties (freezing point 28.37°⁹ and optically clear) after several distillations.

Sulfuric acid (100%) was prepared by mixing Baker and Adamson 96% sulfuric acid (C.P. reagent) with Baker analyzed reagent 21% oleum until a maximum freezing point was reached. A small excess of oleum, corresponding to 0.02% sulfur trioxide, was then added to assure the use of anhydrous material. All glassware was baked out prior to use.

Cryoscopic Measurements in Sulfolane.—A sealed freezing point apparatus of the Beckmann type was attached through a ground glass joint to the fraction collector of the vacuum distillation apparatus used for purification of the sulfolane. It could thereby be filled to a suitable level with solvent without exposure to the atmosphere. Material that was handled in this way maintained a steady freezing point of 28.37° over a number of hours, but when the apparatus was vented to the atmosphere the freezing point dropped to 28.23° within an hour due to absorbance of atmospheric moisture. The thermometer used could be estimated to the nearest 0.01° and was calibrated against a National Bureau of Standards one.

A small side arm fitted with a silicone rubber serum plug was attached to the freezing point tube in such a way that solute

(7) R. L. Burwell, Jr., and C. H. Langford, *J. Am. Chem. Soc.*, **81**, 3799 (1959).

(8) G. A. Olah, S. J. Kuhn, and S. H. Flood, *ibid.*, **83**, 4571 (1961).

(9) S. F. Birch and D. T. McAllan, *J. Chem. Soc.*, 2556 (1951), report a melting point of 28.86°, but this was based on an estimate which led them to the erroneous conclusion that the cryoscopic constant of sulfolane was very low.

(1) Tetramethylene sulfone; thiophene, tetrahydro-1,1-dioxide.

(2) This work was generously supported by the National Institutes of Health through Grant Number G. M. 10872-04 in the Division of General Medical Sciences.

(3) (a) L. C. Smith and L. P. Hammett, *J. Am. Chem. Soc.*, **67**, 23 (1945);

(b) H. Van Looy and L. P. Hammett, *ibid.*, **81**, 3872 (1959).

(4) E. M. Arnett, "Quantitative Comparisons of Weak Organic Bases," in "Progress in Physical Organic Chemistry," A. Streitwieser, Jr., R. W. Taft, Jr., and S. G. Cohen, Eds., Interscience Publishers, Inc., New York, N. Y., 1963.

(5) For an extensive discussion of the physical properties of dipolar aprotic solvents and their applications to organic chemistry see A. J. Parker, *Quart. Rev. (London)*, **16**, 163 (1962).

(6) R. J. Gillespie and J. A. Leisten, *ibid.*, **8**, 40 (1954).