tensive data of Cram and co-workers on the stereochemical capabilities of carbanions. Few data from Cram's work are available for amine solvents. However, data in N-methylaniline and ethylenediamine suggest that amines are retention solvents.[25] From data in t-butyl alcohol, a retention solvent, it appears that more racemization occurs with sodium and potassium carbanides than with lithium carbanides,[26] although high retention occurs with all three cations. The available data in amine solvents[25] indicate that stereoselectivity is less for amines than for t-butyl alcohol; hence, cesium salts in amine solvents should exhibit the least stereoselectivity of any of the systems mentioned above.

Perhaps the pertinent point when comparing amines with t-butyl alcohol is that amines in general are less acidic than t-butyl alcohol, and hence are presumably

less reactive in protonating the carbanion. This implies directly a longer lifetime for the alkali metal carbanide in amine solvents, e.g., k_{-1} for amines $<$ k_{-1} for alcohols. If the values for k_{rac} are comparable in the two types of solvents, amines are necessarily less stereoselective than alcohols.

Of particular importance is the assumption in I that the central carbon atom has much of the carbanion character expected for organocesium compounds. Relative exchange rates in this system may be expected to be useful measures of carbanion stabilities and of hydrocarbon acidities, subject to the general limitations of such rate–equilibrium correlations.[27]

Cesium cyclohexylamide gives exchange rates for weakly acidic hydrocarbons which are considerably greater than for any other convenient system studied. Consequently this system is now being used to study still weaker acids.

(25) D. J. Cram, J. Allinger, and A. Langemann, Chem. Ind. (London), 919 (1955).
(26) D. J. Cram, F. Hauck, K. R. Kopecky, and W. D. Nielsen, J. Am. Chem. Soc., 81, 5767 (1959).

(27) M. Eigen, Angew. Chem. Intern. Ed. Engl., 3, 1 (1964).

Acidity of Hydrocarbons. XX. Comparison of Relative Proton Exchange Rates of Hydrocarbons with Lithium Cyclohexylamide and Cesium Cyclohexylamide[1]

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Absolute rate constants for exchange of aryl hydrogens in toluene vary over a wide range with LiCHA or CsCHA in cyclohexylamine or with KNH$_2$ in liquid ammonia but relative rates are much the same in the different systems. There is little steric hindrance to exchange ortho to the methyl group. The relative rates of some benzylic positions are also comparable for these exchange systems. The results justify the use of such relative rates as measures of hydrocarbon acidity.

In our studies of proton exchange rates in cyclohexylamine we have reported the use of lithium cyclohexylamide[3] (LiCHA) and cesium cyclohexylamide[1b] (CsCHA). The latter catalyst gives exchange rates $\sim 10^4$ faster than LiCHA and allows the convenient extension of exchange kinetics to less reactive hydrocarbons.[1b] Since these exchange rates are being used as relative measures of acidity, it is important to compare the relative reactivities of different hydrocarbons with both catalysts. In this paper we compare such reactivities for the ring positions of toluene and mesit-

ylene and for the benzylic positions of cumene and 2-phenylbutane.

Experimental Section

The experimental procedures follow closely those of the proceeding three papers.[1b,4]

Materials. Ring-deuterated and -tritiated toluenes were prepared from the corresponding bromides by quenching the Grignard reagent with tritium-enriched D$_2$O. The starting bromides were shown to be pure by gas chromatography (g.c.) and the products were fractionally distilled. Toluene-2-$d(t)$, b.p. 107.8–108.8°, had a C–D band at 2262 cm.$^{-1}$. Toluene-3-$d(t)$, b.p. 108.9–109.4°, had a C–D band at 2268 cm.$^{-1}$. Toluene-4-$d(t)$, b.p. 108.9–109.4°, had a C–D doublet at 2264, 2287 cm.$^{-1}$. Other bands also serve to distinguish these isomers in the infrared: only the ortho has a band at 1130 cm.$^{-1}$; a band at 950 cm.$^{-1}$ was present for the ortho and para but not for the meta. A 1670-cm.$^{-1}$ band in the meta is absent in para. These bands show that the compounds prepared are specifically labeled to the limit of infrared analysis ($\sim$5%).

Mesitylene-2-t was prepared by quenching the Grignard reagent from the bromide with tritiated water followed by fractional distillation, b.p. 162–163°.

Table I. LiCHA Exchange Rates at 49.9°

Run no.	Hydrocarbon, R–D(T)	Concn., mole/l.	[LiCHA],[a] mole/l.	$10^7 k_T$, sec.$^{-1}$	$k_T/k_{\phi T}$
L25[b]	2-Toluene	0.20	0.052[c]	0.355 ± 0.016[d]	0.13
L34[b]	2-Toluene	0.28	0.066	0.409 ± 0.008	0.11
L30[b]	3-Toluene	0.20	0.039	1.56 ± 0.02	0.52
L37[b]	3-Toluene	0.059	0.057	1.89 ± 0.13	0.56
	α-sec-Butylbenzene	0.080		1.06 ± 0.04	0.31
L27[b]	4-Toluene	0.20	0.068	1.61 ± 0.03	0.48
L31[b]	4-Toluene	0.28	0.069	1.52 ± 0.03	0.45

[a] Formal concentration. [b] Benzene-d,t was also present; see ref. 4a. [c] Base concentration may be in error. [d] $k_D = 0.435 \pm 0.23 \times 10^{-7}$ sec.$^{-1}$, $k_D/k_T = 1.23 \pm 0.09$, $k_D/k_{\phi D} = 0.11$.

2-Phenylbutane-2-$d(t)$ was described previously.[1b] Cumene-α-$d(t)$ was prepared as described previously,[5] except that quenching was with tritium-enriched D_2O.

Kinetics. The lithium cyclohexylamide (LiCHA) exchange reactions are relatively slow with these hydrocarbons and the "hexapus" apparatus[4a] was used in which the reaction mixture was transferred in an inert atmosphere into sealed tubes. The cesium cyclohexylamide (CsCHA) runs followed the procedure of the preceding paper.[1b] In all cases, a mixture containing two or more hydrocarbons was used in order to obtain relative rates directly and to avoid error associated with determining the base concentration. Tritium content was determined with the g.c.–proportional counter method described earlier.[6]

For deuterium kinetics the hydrocarbons were separated in each kinetic aliquot by g.c. and examined in the infrared. Rate constants were obtained using Perrin's program.[4a] The errors assigned are determined from the standard deviation of experimental and calculated data. Results are summarized in Tables I and II.

Table II. CsCHA Exchange Rates at 25.0°

Run no.	Hydrocarbon,[a] R–D(T)	[CsCHA],[b] mole/l.	$10^4 k_T$, sec.$^{-1}$	$k_T/k_{\phi T}$
C11	2-Toluene	0.020[c]	2.04 ± 0.16	0.208
C32	2-Toluene	0.0098	1.78 ± 0.04	0.197
C13	3-Toluene	0.032[c]	5.4 ± 0.1[d]	(0.67)[e]
C15	3-Toluene	0.043	11.3 ± 0.6	0.56
C18	3-Toluene	0.034	1.57 ± 0.15[f]	
C14	4-Toluene	0.048	1.04 ± 0.3	0.49
C23	4-Toluene	0.020	5.86 ± 0.31	0.56
C25	α-Cumene	0.013	4.74 ± 0.07	1.36
C26	α-Cumene	0.0044	1.63 ± 0.11	
Z215	2-Mesitylene[g]	0.08	0.59 ± 0.04	0.013
Z231	2-Toluene[h]	0.037	4.12 ± 0.17	
Z237	2-Toluene[h]	0.043	36.7 ± 2.1[i]	

[a] Hydrocarbon concentrations were less than 0.4 M. Except where noted benzene-d,t and/or 2-phenylbutane-2-d,t were also present; see ref. 1b. [b] Active concentration by bromobenzene titration (ref. 1). [c] Total base concentration obtained by evaporating an aqueous solution and titrating with acid. [d] $k_D = 10.6 \pm 0.5 \times 10^{-4}$ sec.$^{-1}$; $k_D/k_T = 2.0$. [e] The experimental data were less reproducible in run C13 and this result is given lower weight. [f] $k_D = 3.67 \pm 0.07 \times 10^{-4}$ sec.$^{-1}$; $k_D/k_T = 2.3$. [g] Mixture contained benzene-t and ethylbenzene-β-d. [h] Contained triptycene derivatives. [i] At 50.0°.

(5) A. Streitwieser, Jr., and D. E. Van Sickle, J. Am. Chem. Soc., 84, 249 (1962).
(6) A. Streitwieser, Jr., and H. F. Koch, ibid., 86, 404 (1964).

Discussion

In one of the initial papers in this series[7] we pointed out the similarity in relative exchange rates of the α-positions of toluene, ethylbenzene, and cumene with our LiCHA–cyclohexylamine and with Shatenshtein's potassium amide–liquid ammonia. The comparison was made even closer in the preceding paper[1b] in which it was shown that second-order rate constants for exchange of benzene are not much different in order of magnitude with CsCHA–cyclohexylamine and with KNH_2–NH_3. This remarkable result is obtained despite the difference in polarity of the two solvents and the difference in reaction mechanism—CsCHA reacts as an ion pair in cyclohexylamine whereas the free amide ion appears to be active catalyst in liquid ammonia.[8] The comparison is extended in the summary in Table III. The agreement between the CsCHA and KNH_2[9] results is good. This result suggests that these are overlapping systems for which structural influences are comparable; the only reservation lies in the limited range of the relative rates. Shatenshtein's observation[9] that exchange rates for o-benzene derivatives correlate well with σ_I with a high ρ can apparently be carried over to the CsCHA system as well—both systems appear to be valid measures of carbanion stability or of the acidity of hydrocarbons.

Table III. Summary of Relative Rate Comparisons

Hydrocarbon	LiCHA, $k_T/k_{\phi T}$ at 50°	CsCHA, $k_T/k_{\phi T}$ at 25°	KNH_2–NH_3, $k_D/k_{\phi D}$[a]
Benzene	(1.00)	(1.00)	(1.00)
o-Toluene	0.12	0.20	0.22
m-Toluene	0.54	0.59	0.45
p-Toluene	0.47	0.52	0.41
α-Cumene	0.79[b]	1.36	3
α-sec-Butylbenzene	0.31	0.38	
Mesitylene ring		0.013	0.015

[a] See ref. 9. [b] From ref. 7 assuming that α-toluene and α-cumene have the same primary isotope effect.

The additional data of the present study justify a detailed look at the rate effects of a methyl substituent on the ring hydrogens. In agreement with the idea that the methyl group is effectively electron donating, all of

(7) A. Streitwieser, Jr., and D. E. Van Sickle, ibid., 84, 249 (1962).
(8) A. I. Shatenshtein and E. A. Izrailevich, Zh. Fiz. Khim., 28, 3 (1954).
(9) Summarized in A. I. Shatenshtein, Advan. Phys. Org. Chem., 1, 155 (1963).

the ring positions of toluene are less reactive than in benzene. The effect is greatest in the *ortho* position and the question arises as to the possible role of steric effects. Shatenshtein has pointed out[9] that the effect of methyl substituents on the ring reactivity of benzene follows a partial rate factor approximation. This result also carries over to the CsCHA system; thus, the rate data for toluene predicts a relative rate for the ring of mesitylene of $(0.20)^2(0.52) = 0.021$ in reasonable agreement with the experimental result, 0.013. If the comparatively low rate of *o*-toluene contained a steric effect component, we would expect such steric hindrance to be still greater for mesitylene—two *ortho*-methyl groups would then yield a relative rate much lower than that predicted by partial rate factors. The observed similarity of rates indicates strongly that an *ortho*-methyl group offers no appreciable steric hindrance to reaction of an aryl hydrogen with CsCHA.

The activation parameters for toluene-2-*t* are also worthy of note. Ziegler's runs (Z231 and 237 in Table II) made use of triply distilled cesium[1b] and the derived second-order rate constants, 0.0111 and 0.085 l. mole^{-1} sec.$^{-1}$ at 25 and 50°, respectively, should be reliable. These values lead to $\Delta H^* = 15.0$ kcal./mole and $\Delta S^* = -17$ e.u., numbers that are similar to those for benzene-*d* or -*t* with CsCHA or with KNH$_2$/NH$_3$.[1b] There is no dramatic change in the activation parameters as *might* be anticipated if steric effects were important.

The *para* position is somewhat less reactive than the *meta* and suggests the operation of a polarization effect as in I. Such polarization effects were found to be

CH$_3$

I
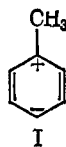
small in polycyclic aryl anions[4b] where a simple field effect was shown to dominate. The addition of a substituent seems clearly to introduce a perturbation such that the simple field effect concept taken by itself no longer suffices for a satisfactory interpretation. It may also be mentioned that the correlation established previously[4b] between the pK values of phenyl- and naphthylacetic acids and the corresponding aryl hydrogen exchange rates does not apply to toluene; this correlation predicts a relative rate for *p*-toluene of about 0.25 to be compared with an experimental number twice this high.
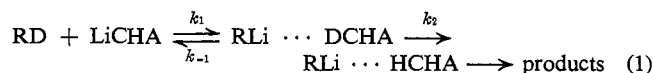
Some of these same comparisons extend to the LiCHA systems; thus, the *meta* and *para* positions of toluene show relative reactivities that are similar to those with CsCHA. Moreover, these relative rates are as close as could be expected considering the difference in reaction temperatures (50° for LiCHA, 25° for CsCHA). The somewhat lower rate for *o*-toluene with LiCHA may reflect some steric hindrance in this case. It should be recalled that the exchange of phenyl hydrogens with LiCHA has a much lower primary isotope effect $(k_D/k_T = 1.5)$[4a] than with CsCHA $(k_D/k_T = 2.5)$.[1b] Significant in this context may be the apparently lower isotope effect for *o*-toluene, $k_D/k_T = 1.2$ (Table I). As a consequence, the relative rates depend on the isotope used, *e.g.*, toluene-*o*-*d*/benzene-*d* = 0.10 compared to toluene-*o*-*t* = 0.12. For the deuterium exchange rates, the difference from CsCHA, 0.19, is in the direction to increase the apparent significance of steric hindrance.

The relative rates serve to eliminate one possible mechanism for ring exchange in toluene. Exchange of the methyl hydrogens is $\sim 10^2$ faster than exchange of the aryl positions; hence, on the time scale for aryl hydrogen exchange, the toluene is in mobile equilibrium with benzyl anion. Protonation of benzyl anion at the *ortho* or *para* positions gives nonaromatic isomers of toluene which on further reaction lead to aryl hydrogen exchange without ever involving an aryl carbanion. However, this mechanism cannot be applied to the *meta* position and, since this position exchanges even faster than the *ortho* and *para* positions, it seems clear that this alternative mechanism is not at all significant in our system. The conclusion that benzyllithium and benzylcesium are protonated by cyclohexylamine entirely at the α-position may be compared to the significant extent of ring protonation when stronger acids are used.[10]

The difference in isotope effects for benzylic and aryl positions with LiCHA makes meaningless any attempt to analyze in further detail the small differences in relative rates for such comparisons with the LiCHA and CsCHA catalysts. For example, $k_D/k_{\phi D}$ for α-cumene and α-*sec*-butylbenzene are 1.4 and 0.55, respectively, assuming that k_D/k_T for the benzylic positions have the α-toluene value, 2.8.[11] The corresponding tritium exchange relative rates are 0.79 and 0.31, respectively, from Table III. The important point is not that there are small variations in relative rates between aryl and benzylic positions as measured with LiCHA or with CsCHA, but that the relative rates are so comparable for the three catalyst systems summarized in Table III. Not only does this comparability enhance the usefulness of such exchange rates by allowing an expansion of structural changes that can be measured and compared conveniently, but significant conclusions also follow as regards the mechanism of exchange of aryl hydrogens with LiCHA.

One interpretation of the relatively low primary isotope effect in this system[4] is that internal return[12] is important; that is, that the mechanism is given by eq. 1. For such a mechanism, the experimental rate

$$\text{RD} + \text{LiCHA} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{RLi} \cdots \text{DCHA} \overset{k_2}{\longrightarrow}$$
$$\text{RLi} \cdots \text{HCHA} \longrightarrow \text{products} \quad (1)$$

constant, ignoring effects due to the finite proton pool in solvent, is given by eq. 2. Since the isotope effect

$$k_{\text{exptl}} = k_1 \frac{k_2}{k_{-1} + k_2} \quad (2)$$

for the diffusion reaction (k_2) is expected to be small, k_1 and k_{-1} could have large primary isotope effects and still lead to small isotope effects in k_{exptl} if $k_{-1} \cong$ or $> k_2$. For exchange of aryl deuterium with LiCHA,

(10) G. A. Russell, *J. Am. Chem. Soc.*, 81, 2017 (1959). Similar results have been found for di- and triphenylmethyl anions: unpublished work of M. R. Granger
(11) A. Streitwieser, Jr., W. C. Langworthy, and D. E. Van Sickle, *J. Am. Chem. Soc.*, 84, 251 (1962).
(12) D. J. Cram, C. A. Kingsbury, and B. Rickborn, *ibid.*, 83, 3688 (1961).

if k_1 (and k_{-1} since the equilibrium isotope effect is small) has $k_D/k_T = 2.8$, the observed values of $k_D/k_T = 1.2$–1.5 require that $k_{-1}/k_2 = 10$–3; that is, that $k_{-1}/k_{exptl} = 11$–4.

Internal return cannot be important for exchanges with CsCHA or for benzylic positions with LiCHA because the experimental primary isotope effects are too high. If the internal return explanation were correct for exchange of aryl deuterium with LiCHA, the derived values for $k_1(\alpha\text{-cumene})/k_1(\text{benzene})$ would be smaller than the experimental ratio by the 11–4 factors

given above; that is, the LiCHA relative rate, 0.13–0.35, would now be far lower than the CsCHA relative rate, 1.3. Although this is a logically permissible result, it seems more probable that the relative rates for the forward steps with the two catalysts are more nearly comparable and, consequently, that $k_2 \gg k_{-1}$ and $k_{exptl} = k_1$ for all of our systems. The latter alternative requires that the observed low isotope effect for exchange of aryl hydrogens with LiCHA be a real effect for k_1 and leads to the interpretation advanced earlier.[4a]

Acidity in Nonaqueous Solvents. I. Picolinium Ions in Methanol[1]

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Contribution from the Department of Chemistry, State University of New York at Buffalo, Buffalo 14, New York. Received July 27, 1965

Free energies, enthalpies, and entropies of ionization of a series of α-substituted 4-picolinium ions in pure anhydrous methanol have been determined by the differential potentiometric method. Three points of general interest emerge from the data. First, the effects of alkyl group substituents are remarkably small; second, pK values are very nearly equal to those found for aqueous solutions; and third, there is no correlation between free energies and enthalpies of ionization for these acids.

Introduction

Very little data exists on the free energies, enthalpies, and entropies of ionization of Brønsted acids in nonaqueous solutions. Such data must be acquired if any interpretation of solvent effects is to be complete. In a continuing study to shed light on the nature of solvent effects on reactivity, we have measured the dissociation constants of a series of α-substituted 4-picolinium ions in pure methanol solution at 0.1 and 25.0°. From these data, free energies, enthalpies, and entropies of ionization are evaluated.

Results

The data obtained are summarized in Table I. Reported pK values are not corrected for ionic strength, and, therefore, standard states are implicitly referred to ca. 10^{-3} M solution in methanol. Under the assumptions of Debye–Hückel theory, no corrections are necessary for reference to a standard state of infinitely dilute solution.

The limitations of the differential potentiometric method for determining pK values have been discussed by Grunwald.[2] The pK values for the picolines in methanol fall within the optimum range for this method, and the values reported in Table I should have an ac-

Table I. Thermodynamic Data for the Reaction
$4\text{-XCH}_2C_5H_4NH^+ \rightleftarrows 4\text{-XCH}_2C_5H_4N + H^+$

	pK		$\Delta G°$ (25°), kcal./ mole	ΔH (25°), kcal./ mole	$\Delta S°$ (25°), e.u.
	0.1°	25.0°			
H	6.541	6.090	8.300	6.7	−5.2
CH$_3$	6.550	6.090	8.300	6.9	−4.8
C$_2$H$_5$	6.534	6.073	8.280	6.9	−4.7
C$_6$H$_5$	6.228	5.794	7.900	6.5	−4.7
OH	6.333	5.846	7.970	7.3	−2.3
CN	5.002	4.565	6.220	6.5	+1.0
NH$_3^+$	4.13	3.77	5.13	5.5	+1.2

curacy approaching the precision of 0.01 unit reported in the Experimental Section of this paper.

The accuracy of the enthalpies and entropies reported is more difficult to evaluate. According to the analysis of Petersen, Margraf, and Ross,[3] however, the accuracy is certainly not worse than ±10%, and is quite probably better than ±5%. The enthalpies are thus constant within experimental error for all of the compounds studied except those with the hydroxyl and ammonium substituents.

Discussion

Three points of general interest emerge from the data of Table I.

First, the effects of alkyl group substituents are remarkably small. Several years ago, Brown[4] reported pK values for 4-methyl-, 4-ethyl-, and 4-isopropyl-pyridine in aqueous solution. The pK value was 6.02 for all three compounds. These two pieces of information may now be added to the growing body of data[5] in support of ourearlier suggestion that alkyl groups have negligible inductive effects.[6]

(1) Presented at the 149th National Meeting of the American Chemical Society, Detroit, Mich., April 1965.

(2) E. Grunwald, J. Am. Chem. Soc., 73, 4934 (1951).

(3) R. C. Petersen, J. H. Margraf, and S. D. Ross, ibid., 83, 3819 (1961).

(4) H. C. Brown and X. R. Mihm, ibid., 77, 1723 (1955).

(5) H. D. Holtz and L. M. Stock, ibid., 86, 5188 (1964), and other references cited therein.