

## Acidity of Hydrocarbons. XVII. Kinetics and Mechanism of Proton Exchange of Benzene and Naphthalene with Lithium Cyclohexylamide in Cyclohexylamine<sup>1</sup>

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*Benzene-*t* exchanges with lithium cyclohexylamide (LiCHA) 0.01 as fast as toluene- $\alpha$ -*t*. The  $k_D/k_T$  isotope effect is comparatively small (1.6). Kinetic studies are reported of the  $\alpha$  and  $\beta$  positions of naphthalene and the mechanism of the exchange reaction is discussed.*

As part of our continuing studies of proton exchanges of hydrocarbons in cyclohexylamine we have examined a number of aryl-hydrogen bonds. In this paper we present results for benzene and naphthalene which bear on the kinetics and mechanism of deuterium and tritium exchange catalyzed by lithium cyclohexylamide.

### Experimental Section

**Methods and Materials.** All melting points are uncorrected. Infrared spectra were taken on a Baird AB2 spectrophotometer and, later in the work, on a Perkin-Elmer Model 421 or 237G spectrophotometer. Radioactive counting of benzene-*t* was accomplished with a proportional flow counter attached to an Aerograph-A90P gas chromatograph.<sup>3</sup> Analyses were carried out by the Microanalytical Laboratory of the University of California. Deuterium analyses were based on drop-suspension density gradient determinations of combustion water.

Naphthalene-1-*d*<sup>4</sup> was prepared by quenching the Grignard reagent from 1-bromonaphthalene with D<sub>2</sub>O, followed by sublimation and recrystallization, m.p. 79.5–80°.

*Anal.* Calcd. for C<sub>10</sub>H<sub>7</sub>D: D, 12.5 atom %. Found: D, 12.2 atom %.

The infrared spectrum in CCl<sub>4</sub> showed a C–D band at 2260 cm.<sup>-1</sup> and absorption at 1880, 1050, and 931 cm.<sup>-1</sup> which is absent in naphthalene. Peaks at 1825 and 1802 cm.<sup>-1</sup> have the same intensity in both compounds and were used as reference bands in the kinetic analyses.

(1) This research was supported in part by the Directorate of Chemical Sciences, Air Force Office of Scientific Research, Grants No. 62-175 and 64-554. A preliminary communication of some of this work appeared in A. Streitwieser, Jr., and R. G. Lawler, *J. Am. Chem. Soc.*, **85**, 2854 (1963). Part XVI: A. Streitwieser, Jr., J. I. Brauman, J. H. Hammons, and A. H. Pudjaatmaka, *ibid.*, **87**, 384 (1965).

(2) (a) National Science Foundation Predoctoral Fellow, 1960–1963; Eastman Kodak Science Award in Chemistry, 1962–1963; (b) National Science Foundation Postdoctoral Fellow, 1963; author responsible for work presented in the appendix.

(3) A. Streitwieser, Jr., and H. F. Koch, *J. Am. Chem. Soc.*, **86**, 404 (1964).

(4) Prepared by Lawrence Craft.

Naphthalene-2-*d* was prepared by treating 2-bromonaphthalene in ether for 1 hr. with butyllithium (Lithium Corp. of America) followed by quenching with D<sub>2</sub>O. The sublimed and recrystallized white plates had m.p. 80.2–81°.

*Anal.* Calcd. for C<sub>10</sub>H<sub>7</sub>D: D, 12.5 atom %. Found: D, 12.3, 11.9 atom %.

The infrared spectrum in CCl<sub>4</sub> had a C–D band at 2280 cm.<sup>-1</sup> with additional peaks at 1675, 1602, 1190, and 1030 cm.<sup>-1</sup> not present in naphthalene. A band at 1805 cm.<sup>-1</sup> has the same intensity and was used as a reference in kinetic analyses.

Naphthalene-1-*t* was prepared in a similar manner except on a smaller scale and with quenching by tritiated water. The product was diluted with naphthalene and sublimed to give white plates, m.p. 78.5–79.1°, 6.4 × 10<sup>6</sup> d.p.m./mmole.

Benzene-1-*d* and -1-*t* were prepared<sup>5</sup> by quenching phenylmagnesium bromide with tritium-enriched D<sub>2</sub>O.

**Kinetics.** Kinetic studies were carried out in a manner similar to that described by Streitwieser and Langworthy<sup>6</sup> but with some modifications (method B). For the naphthalene runs the reaction vessel was similar to that described in Figure 1 of ref. 6 except that the stopcock on the capillary delivery tube was replaced by a three-way stopcock carrying a return tube to the flask. With the original design the solvent gradually channeled the stopcock during the longer reaction times of the present study; the new design equalized the levels between the taking of points and reduced this problem. Channeling was still important for reactions run for several weeks (e.g., benzene), and for these runs the reaction mixture was made up in a central flask connected to the vacuum line and to which were sealed a set of six tubes of about 4-ml. capacity (method C). After preparation of the solution in the usual way the tubes were filled by tipping the "hexapus" vessel and were sealed off under vacuum. The tubes were placed in a thermostat and withdrawn at intervals for kinetic analysis.

In most of the runs the cyclohexylamine was purified by bulb-to-bulb distillation from lithium cyclohexylamide (LiCHA).

Kinetics were generally carried out at 49.9 ± 0.1°. Kinetic aliquots were quenched with water and hydrochloric acid, and, for naphthalene were extracted into carbon tetrachloride. The solvent was evaporated to

(5) Prepared by Richard A. Caldwell.

(6) A. Streitwieser, Jr., and W. C. Langworthy, *J. Am. Chem. Soc.*, **85**, 1757 (1963).

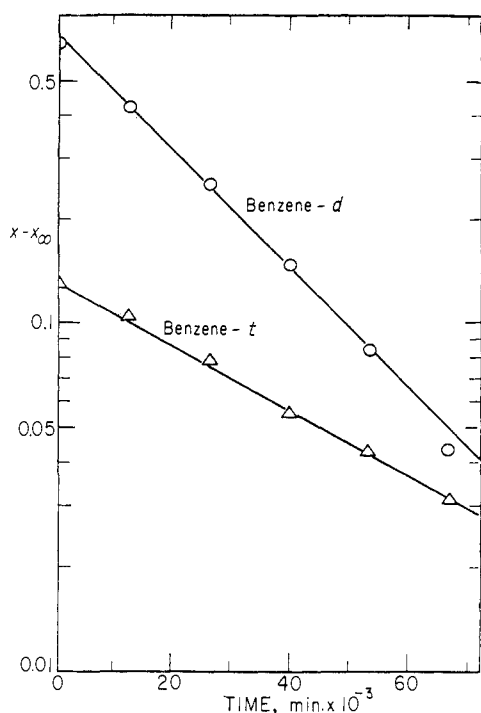


Figure 1. Representation of run 19. The ordinate is determined from the intensity of the C-D band for benzene-*d* and from the counts per minute per unit g.c. peak area for benzene-*t*.

give a 10 mole % solution, dried, and examined in the infrared. The C-D intensity was normalized using a reference absorption band. For benzene, a sample was isolated by g.c. and the infrared spectrum was taken on the neat liquid in a microcell. The extract was used directly for tritium analysis in the gas radiochromatograph and the value of the counts per unit area was obtained for each kinetic point as described previously.<sup>3</sup>

Base concentrations were determined, except where noted, by titration with acid after evaporation of amine.<sup>7</sup> This procedure gives base titers that are slightly high because it includes any catalytically inactive lithium hydroxide present. The effect on the rate comparisons is not significant (*vide infra*).

The equations used for converting experimental data to rate constants have been derived previously.<sup>3,7</sup> In the present study the kinetic complications produced by the two nonequivalent positions of naphthalene were handled with a computer program which gave rate constants based on a least-squares fit to the experimental data. This program was written by Dr. C. Perrin and is based on the mathematical derivation presented in the Appendix; it is the analytical counterpart of the graphical integration procedure discussed in ref. 3. The program is designed for use when the solvent proton pool is not effectively infinite and when account must be taken of isotopic exchange from solvent to positions in the substrate other than that under study. For this, the program requires rate constants for exchange at the other positions but these need be only approximate since they enter as small corrections. The rate constant obtained is thus corrected for such return substitution and corresponds to the  $k_D$  and  $k_T$  and not the  $k_{\text{exptl}}$  of

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

our previous papers. These complications do not apply to benzene but the program was used in order to get the least-squares rate constants. Plots of  $\log(x - x_\infty)$  vs. time are linear and a sample run for benzene-*d* and benzene-*t* is shown in Figure 1. Furthermore, the program was designed to handle exchange reactions run on several compounds simultaneously; several of the runs with benzene-*t* contained other hydrocarbons whose rates are discussed in a subsequent paper.<sup>8</sup> In this way relative rates are obtained directly. Perrin's program also calculates standard deviations for each compound from the individual calculated and experimental measurements. Because the true system with mixtures is nonlinear, these standard deviations are approximate but they should be good approximations.

Results for runs discussed in this paper are summarized in Tables I and II.

Table I. Exchange of Naphthalene-*d* with LiCHA at 49.9°

Run no.	[ArD], mole/l.	[LiCHA], <sup>a</sup> mole/l.	10 <sup>3</sup> $k_1$ , sec.	10 <sup>4</sup> $k_2$ , <sup>b</sup> l./mole sec.
Naphthalene-1- <i>d</i>				
3	0.35	0.058	3.58 ± 0.10	7.3
4	0.10	0.060	3.24 ± 0.10	6.5
WRY-3 <sup>c</sup>	0.10	0.048 <sup>d</sup>	3.61 ± 0.07	7.7 <sup>d</sup>
Naphthalene-2- <i>d</i>				
12	0.097	(0.005) <sup>e</sup>	(0.32) <sup>f</sup>	(1.7)
10	0.097	(0.009) <sup>e</sup>	0.78 ± 0.05	(3.1)
5	0.097	0.056	2.14 ± 0.05	4.4
7	0.097	0.115	2.62 ± 0.06	4.4
6	0.097	0.213	3.06 ± 0.09	4.5
11 <sup>d</sup>	0.100	0.058	0.436 ± 0.09 <sup>g</sup>	0.89 <sup>g</sup>

<sup>a</sup> Formal concentration, *c*. <sup>b</sup> Model 2,  $K = 500$  l./mole <sup>c</sup> Run by W. R. Young in sealed tubes with naphthalene-1-*d*,*t* at 50.0°. Deuterium analyses were by low-voltage mass spectrometry. Tritium counting by liquid scintillation gave  $k_T = 2.12 \pm 0.04 \times 10^{-6}$  sec.<sup>-1</sup>;  $k_D/k_T = 1.70 \pm 0.05$ . <sup>d</sup> Assayed by bromobenzene method (ref. 9) which is thought to be more accurate than the base titrations used in the other runs. The resulting second-order rate constant is a few per cent high because of this comparison. <sup>e</sup> Base concentration probably in error. <sup>f</sup> A two-point kinetic run. <sup>g</sup> At 25.0°.

## Results and Discussion

**Kinetic Order.** In many experiments on the exchange reactions of toluene- $\alpha$ -*d* or - $\alpha$ -*t* with LiCHA the kinetic order in the basic catalyst was found to vary with the LiCHA concentration.<sup>7,9</sup> This effect was interpreted as aggregation of the catalytically active monomeric LiCHA to unreactive dimers, trimers, and higher polymers. Over the concentration range studied, the pseudo-first-order rate constants fitted well to second-order kinetics in monomeric LiCHA in which the concentration of monomer is related to the formal concentration, *c*, of LiCHA by eq. 1 which is derived from model 2<sup>9</sup> for the aggregation with  $K = 500$  l./mole.

$$c = [\text{monomer}]e^{K[\text{monomer}]} \quad (1)$$

The same phenomenon appears to apply to the exchange reactions of aryl hydrogens. A fourfold increase in LiCHA concentration increases the rate of exchange of naphthalene-2-*d* by less than 50% (Table

(8) Paper XX: A. Streitwieser, Jr., R. A. Caldwell, R. G. Lawler, and G. R. Ziegler, *ibid.*, **87**, 5399 (1965).

(9) A. Streitwieser, Jr., R. A. Caldwell, M. R. Granger, and P. M. Laughton, *J. Phys. Chem.*, **68**, 2916 (1964).

**Table II.** Exchange of Benzene with LiCHA at 49.9°

Run no.	[Benzene], mole/l.	[LiCHA], <sup>a</sup> mole/l.	10 <sup>6</sup> k <sub>D</sub> , sec. <sup>-1</sup>	10 <sup>4</sup> k <sub>2D</sub> , <sup>b</sup> l./mole sec.	10 <sup>6</sup> k <sub>T</sub> , sec. <sup>-1</sup>	10 <sup>4</sup> k <sub>2T</sub> , <sup>b</sup> sec. <sup>-1</sup>	k <sub>D</sub> /k <sub>T</sub>
19	0.25	0.058	0.56	1.1	0.34	0.69	1.67
25 <sup>c</sup>	0.24	(0.05) <sup>c</sup>	0.405 ± .015		0.274 ± 0.012		1.48
27 <sup>d</sup>	0.20	0.068			0.333 ± 0.09	0.65	
30 <sup>e</sup>	0.20	0.039			0.298 ± 0.20	0.69	
31 <sup>f</sup>	0.27	0.069			0.336 ± 0.015	0.65	
34 <sup>g</sup>	0.27	0.066			0.364 ± 0.007	0.71	
37 <sup>h</sup>	0.057	0.057			0.338 ± 0.013	0.69	

<sup>a</sup> Formal concentration, *c.* <sup>b</sup> Model 2, *K* = 500 l./mole. <sup>c</sup> Also contained 0.20 *M* toluene-2-*t*. Base concentration in this run is probably in error. <sup>d</sup> Also contained 0.20 *M* toluene-3-*t*. <sup>e</sup> Also contained 0.20 *M* toluene-4-*t*. <sup>f</sup> Also contained 0.28 *M* toluene-4-*d*(*t*). <sup>g</sup> Also contained 0.28 *M* toluene-2-*d*(*t*). <sup>h</sup> Also contained 0.080 *M* 2-phenylbutane-2-*d*(*t*).

I, runs 5, 6, 7). The second-order rate constants in monomeric LiCHA as calculated with eq. 1 are constant over this range. The base concentration was determined by acid titration rather than with our more recent technique of reaction with bromobenzene.<sup>9</sup> The resulting error is serious only for base concentrations below ~0.01 *M*. The deviations in runs 10 and 12 are attributed to incorrect base concentrations and are in the right direction; that is, traces of moisture in the system produce catalytically inactive lithium hydroxide which titrates as active base by the procedure used here.

The calculated *k*<sub>2</sub> values for benzene-*t* are constant over a base concentration range of almost a factor of 2. Several of these runs were at nearly the same base concentration and demonstrate excellent reproducibility.

We conclude that this procedure gives meaningful exchange rates and that the active catalyst is monomeric LiCHA in equilibrium with inactive aggregates as in the related exchange reactions at the α-position of toluene.

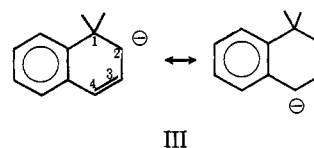
**Activation Parameters.** Other studies<sup>9</sup> have shown that the aggregation equilibrium is essentially independent of temperature at least in the 25–50° region; hence, an activation energy for the exchange reaction can be calculated from pseudo-first-order rate constants at the same base concentration, or *k*<sub>2</sub> values can be used in which eq. 1 is applied with the same value of *K* at different temperatures. The experiments with naphthalene-2-*d* at two temperatures, 49.9 and 25.0°, *k*<sub>2</sub> = 4.43 × 10<sup>-4</sup> and 0.89 × 10<sup>-4</sup> l. mole<sup>-1</sup> sec.<sup>-1</sup>, respectively, yield Δ*H*\* = 11.7 kcal./mole and Δ*S*\* = -38 e.u. The entropy depends on the model chosen for the aggregation equilibrium but the variation is only a few units and comparisons may be validly made with other compounds if the same model is used. For example, the exchange of toluene-α-*d* with LiCHA gives<sup>9</sup> Δ*H*\* = 8.8 kcal./mole and Δ*S*\* = -39 e.u., also for model 2. The 43-fold faster rate for toluene-α-*d* compared to naphthalene-2-*d* comes almost entirely from a lower activation enthalpy. It may be significant that the entropies of activation are so similar even though different types of C-H bonds are involved. The low entropy of activation has been interpreted as the additional solvation required by lithium cation at the transition state.

**Primary Isotope Effects.** For two runs in which benzene-*d* and -*t* are compared directly, *k*<sub>D</sub>/*k*<sub>T</sub> = 1.58 ± 0.1; one recent run on naphthalene-1-*d*,*t* gives the closely similar value *k*<sub>D</sub>/*k*<sub>T</sub> = 1.70 ± 0.05 (Table I).

These values are comparatively low for a primary isotope effect; application of the SSRS equation<sup>10,11</sup> (eq. 2) gives an equivalent *k*<sub>H</sub>/*k*<sub>D</sub> for benzene of 2.8 ± 0.4. This effect contrasts with that found for toluene-α-*d* and -α-*t*; *k*<sub>D</sub>/*k*<sub>T</sub> = 2.8 ± 0.2; *k*<sub>H</sub>/*k*<sub>D</sub> = 10 ± 2.<sup>9,11</sup>

$$k_H/k_D = (k_D/k_T)^{2.26} \quad (2)$$

**Mechanism.** The most straightforward mechanism is a direct exchange between some form of monomeric LiCHA ion pairs and the C-H bond to give an aryl-lithium and cyclohexylamine. The most important competing mechanism is that of addition-elimination in which the rate-determining step is nucleophilic addition to the aromatic ring followed by rapid exchange of the resulting allylic hydrogens as in Chart I. This mechanism shows important inconsistencies with the experimental results. One would expect no isotope effect with this mechanism and would also predict that the α- and β-positions of naphthalene would exchange at the same rate. A modified mechanism in which the elimination of LiCHA from the intermediate I is of comparable rate to the exchange equilibria fits the experimental results better. One could obtain a small primary isotope effect for this case as well as a faster exchange at the α-position of naphthalene; protonation of III is expected to be faster at the 4- than at the 2-position.<sup>12</sup>



Nevertheless, this mechanism may be rejected on the basis of results from parallel studies. Relative rates of different positions in other aromatic hydrocarbons are difficult to interpret with an addition-elimination mechanism—biphenyl is a particular example.<sup>13</sup> Exchange of aryl hydrogens with cesium cyclohexylamide (CsCHA) cannot go through an addition-elimination mechanism because the primary isotope effect in this case is high<sup>14</sup>; yet, relative rates with both reagents

(10) C. G. Swain, E. C. Stivers, J. F. Reuwer, Jr., and L. J. Schaad, *J. Am. Chem. Soc.*, **80**, 5885 (1958).

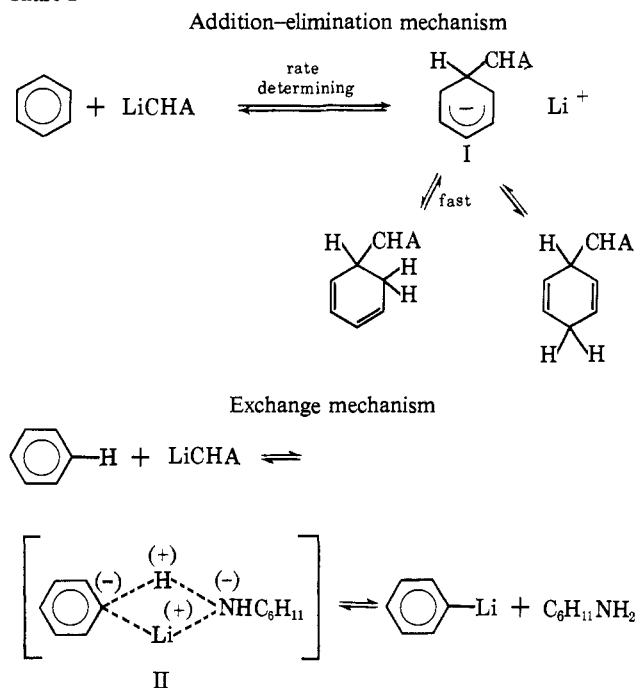
(11) A. Streitwieser, Jr., W. C. Langworthy, and D. E. Van Sickle, *ibid.*, **84**, 251 (1962).

(12) R. B. Bates, R. H. Carnighan, and C. E. Staples, *ibid.*, **85**, 3032 (1963).

(13) Paper XVIII: A. Streitwieser, Jr., and R. G. Lawler, *ibid.*, **87**, 5388 (1965).

(14) Paper XIX: A. Streitwieser, Jr., and R. A. Caldwell, *ibid.*, **87**, 5394 (1965).

Chart I



are similar for the ring positions of toluene,<sup>8,15</sup> a result not expected if two completely different mechanisms were operating. Naphthalene-1-*d,t*, pyrene-1-*d,t*, and anthracene-9-*d,t* give primary isotope effects of comparable magnitude to that for benzene-*d,t*.<sup>13</sup> Since the observation of a primary isotope effect in this mechanism depends on a balance in the rates of two competing reactions of an intermediate such a similarity is not expected when the structure is modified so dramatically.

Finally, at least one example, fluoranthene,<sup>13</sup> is known in which nucleophilic addition to the ring does occur. In this case, 3-(*N*-cyclohexylamino)fluoranthene was isolated and the nucleophilic addition appears to be associated with the formation of radical anions. Thus, the actual consequences of nucleophilic addition appear to differ from that postulated in the addition-elimination mechanism.

The alternative mechanism is a direct electrophilic exchange as shown in Chart I in analogy to the mechanism described earlier for exchange at the  $\alpha$ -position of toluene.<sup>16</sup> The postulate of substantial negative charge at the aryl carbon in the transition state, II, is in agreement with structural<sup>13</sup> and substituent<sup>8</sup> effects on relative rate, but the comparatively low isotope effect requires comment. One interpretation makes use of Cram's internal return mechanism.<sup>3,17</sup> Applied to our case, this hypothesis would mean that the diffusion away of cyclohexylamine is not rapid compared to the return reaction of amine and aryllithium and that, therefore, a significant fraction of such return proton exchanges occurs with the original isotope leading to no net reaction. Since the diffusion is expected to have a negligible isotope effect, such a blend would give an experimental isotope effect lower than that for the pro-

ton exchange step itself.<sup>8</sup> This type of mechanism appears to be rather general and must be considered whenever a proton exchange has a comparatively low primary isotope effect. Moreover, an experimental rate constant that is a composite of several reactions has obvious limitations as a measure of thermodynamic acidity.

One approach to determining the significance of internal return makes use of the SSRS equation or its equivalent (*vide supra*). If the return phenomenon is a significant part of an experimental rate constant, each individual step may follow the SSRS equation but the experimental composite isotope effects would not. Separate direct measurements of  $k_H$ ,  $k_D$ , and  $k_T$  would thus provide a potentially useful further criterion for the internal return phenomenon. We expect to report on our experiments in this direction in the near future.

At the present time the best evidence available that Cram's return mechanism is not important in the present case is that relative proton exchange rates of different aryl and arylalkyl positions are much the same for LiCHA and for CsCHA.<sup>8,15</sup> The latter catalyst gives a high isotope effect for benzene-*d,t*<sup>14</sup> and the internal return phenomenon therefore cannot be significant with CsCHA. Arylcesium derivatives are expected to be more reactive than the corresponding lithium compounds; if return cannot compete with solvent diffusion for the cesium case, such return should be even less significant for the lithium derivative. If this argument is sustained by subsequent work, Cram's internal return mechanism does not apply to the present system and the experimental rate constants are those of the simple forward step of proton removal. The low isotope effect for such a step could possibly be interpreted in terms of a highly unsymmetrical transition state with unequal N-H and C-H force constants,<sup>18</sup> but it then becomes difficult to rationalize the much higher isotope effect given by CsCHA. However, we are led to a more satisfactory interpretation on recognizing that those reactions with high isotope effects lead to organoalkali compounds that are highly ionic—benzyl lithium, cumylcesium, arylcesium, etc. Phenyllithium, on the other hand, undoubtedly has a predominantly covalent C-Li bond.<sup>19</sup> This covalent character is surely present in the transition state as well (in the microscopic reverse step of reaction of phenyllithium with cyclohexylamine the covalent character of the original C-Li bond is not likely to be lost completely at the transition state); the dotted line between the phenyl group and lithium in II represents a partially covalent bond. Consequently, the enforced proximity of the lithium and proton in II could well result in nonbonded interactions that would lead to substantial zero-point energy to partially compensate for the zero-point energy normally lost by the exchanging hydrogen; that is, an increase in the C-H-N bending frequency because of the proximity of the lithium partially compensates for the loss of the stretching frequency and leads to a lowered net isotope effect. In this mechanism the lithium in II is still highly cationic and the central carbon is still highly carbanionic suggesting that the exchange rates may well be valid measures of relative acidity. Further discussion of the observed relative deuterium exchange

(15) A. Streitwieser, Jr., R. A. Caldwell, and M. R. Granger, *J. Am. Chem. Soc.*, **86**, 3578 (1964).

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

(17) D. J. Cram, C. A. Kingsbury, and B. Rickborn, *ibid.*, **83**, 3688 (1961).

(18) F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961).

(19) G. E. Coates, "Organometallic Compounds," 2nd Ed., Methuen and Co., Ltd., London, 1960, p. 3.

rates of naphthalene positions relative to benzene ( $\alpha$ , 6.5;  $\beta$ , 4.1) is reserved for the following paper.

## Appendix

*A Generalized Treatment of Proton Exchange Kinetics.* The following treatment applies to the general case of hydrogen isotope exchange from different positions of several substrates in a solvent whose proton pool is not infinite relative to the substrates. For the reaction,  $A_i^* + S \xrightleftharpoons[k_i]{k_i} A_i + S^*$ , where  $S$  and  $A_i$  are normalities of hydrogen in solvent and the  $i$ th substrate, respectively,  $S^*$  and  $A_i^*$  are the normalities, in mole/l., of tritium in solvent and the  $i$ th substrate, and  $k_i$  is the second-order rate constant, assumed identical for forward and reverse reactions

$$\frac{dA_i^*}{dt} = k_i A_i S^* - k_i A_i^* S$$

By stoichiometry

$$A_i^* + A_i = A_{i0} \text{ (=the } na \text{ of ref. 3)}$$

$$S^* + S = S_0 \text{ (=the } 2b \text{ of ref. 3)}$$

$$S^* + \sum_j A_j^* = S_0^* + \sum_j A_{j0}^*$$

where the subscript 0 refers to initial conditions. Then, on substitution and simplification

$$\frac{dA_i^*}{dt} = -k_i A_i^* S_0 + k_i A_{i0} S_0^* + k_i A_{i0} \sum_j (A_{j0}^* - A_j^*)$$

Let  $y_i = A_i^*/A_{i0}^*$ , the activity relative to the initial activity,  $z_i = 1 - y_i$ , the fractional extent of reaction,  $\varphi_i = A_{i0}^*/A_{i0}$ , the initial specific activity of substrate  $i$  (corresponding to the  $x_0$  of ref. 3), and  $\sigma = S_0^*/S_0$ , the initial specific activity of the solvent, usually very small, unless there has been appreciable reaction prior to the removal of the first experimental point. These specific activities will always appear as ratios in the answer, so that only relative values are required. On rearranging

$$\frac{dz_i}{dt} + k_i S_0 z_i + k_i \sum_j A_{j0} \frac{\varphi_j}{\varphi_i} z_j = k_i S_0 - k_i S_0 \frac{\sigma}{\varphi_i}$$

Taking Laplace transforms

$$L[z_i(t)] = \bar{z}_i(s) = \int_0^\infty e^{-st} z_i(t) dt$$

rearranging, and using the relation

$$L\left[\frac{dz_i}{dt}\right] = s\bar{z}_i(s) - z_i(t=0)$$

$$(s + k_i S_0)\bar{z}_i + k_i \sum_j A_{j0} \frac{\varphi_j}{\varphi_i} \bar{z}_j = \frac{k_i S_0 (1 - \sigma \varphi_i)}{s}$$

These are  $n$  equations in  $n$  unknowns,  $\bar{z}_i$ , and may be solved by Cramer's rule. Let

$$\Delta(s) = \left| (s + k_i S_0)\delta_{ij} + k_i A_{j0} \frac{\varphi_j}{\varphi_i} \right|$$

an  $n \times n$  determinant, and therefore an  $n$ th order polynomial in  $s$ .

Let  $\Delta_j(s) = \Delta(s)$  in which column  $j$  has been replaced by  $k_i S_0 (1 - \sigma/\varphi_i)$ .

Let the  $n$  roots of  $\Delta(s)$  be  $\lambda_k$ ;  $\Delta(s) = \prod_{k=1}^n (s - \lambda_k)$ .

Then

$$\bar{z}_j(s) = \frac{1}{s} \frac{\Delta_j(s)}{\Delta(s)} = \frac{\Delta_j(s)}{s \prod_{k=1}^n (s - \lambda_k)}$$

Inverting the transforms requires finding the poles of  $\bar{z}_j(s)$ , i.e., the values of  $s$  such that  $\bar{z}_j(s) = \infty$ . Obviously,  $\bar{z}_j(0) = \infty$ , and  $\bar{z}_j(\lambda_k) = \infty$ . Then, on inverting the Laplace transform, there results

$$\bar{z}_j(t) = \frac{\Delta_j(0)}{\Delta(0)} + \sum_{i=1}^n \frac{1}{\lambda_i} \frac{\Delta_j(\lambda_i)}{\prod_{\substack{k=1 \\ k \neq i}}^n (\lambda_i - \lambda_k)} e^{\lambda_i t}$$

Also,  $y_j = 1 - z_j$ , the experimentally observed quantities.

Although this expression appears formidable, it is admirably suited to machine computation. The first term of  $y_j$ ,  $1 - \Delta_j(0)/\Delta(0)$ , is the relative activity at infinite time, and can be simplified to  $y_j(\infty) = (\sigma S_0 + \sum_i \varphi_i A_{i0})/\varphi_j (S_0 + \sum_i A_{i0})$ . Also, the roots,  $\lambda_k$ , of the equation,  $\Delta(s) = 0$ , may be shown to be equal to the eigenvalues of the Hermitian matrix

$$\left| -k_i S_0 \delta_{ij} - \sqrt{k_i k_j A_{i0} A_{j0}} \right|$$

Thus, the activities can be calculated as a function of time and a set of rate constants. The rate constants are fitted by the following iterative procedure.

The best values of the rate constants are those which minimize the sums of the squares of the deviations of experimental from calculated activities. Since, for a given compound, this sum is largely determined by the value of that compound's rate constant, and only slightly by other rate constants, the best rate constants are those for which

$$\frac{\partial \sum_i (y_j^{\text{exptl}} - y_j^{\text{calcd}})^2}{\partial \ln k_j} = 0$$

This derivative is evaluated by a finite differencing technique, and the next approximation for the rate constants is obtained by a modified Newton-Raphson procedure. Let the above derivatives equal  $f_j$ ;  $j = i, n$ . The next approximation to  $k_j$  is given by

$$\ln k_j^{\text{new}} = \ln k_j^{\text{old}} - \kappa k_j f_j / f_j'$$

Here,  $f_j' = \partial f_j / \partial k_i$ , and is approximated by the value of  $f_j'$  for the situation in which there is only a single substrate. This approximate value is readily calculated; the approximation does not affect the final result, but only the rate of convergence. Also,  $\kappa$  is an adjustable factor for optimizing the rate of convergence. It is initially set equal to 0.75, to avoid overshooting the correct rate constant. Every five iterations the behavior of the rate constant slowest to converge is inspected. If that rate constant is converging asymptotically ("overdamped"),  $\kappa$  is increased; if it is converging with oscillations ("underdamped"),  $\kappa$  is decreased.

There is an arbitrariness in referring the activities,  $y_j$ , to initial activities. The error in the initial activities is placed on an equal footing with those at other times

by treating the initial activities as intercepts to be fitted during each iteration, again by a Newton-Raphson procedure.

At each iteration, convergence is tested by inspecting whether all rate constants have changed by less than a fixed proportion (arbitrarily selected as 0.1%) during that iteration. Upon convergence, the second-order rate constants are converted to pseudo-first-order rate constants, at zero substrate concentration, for print-out.

One further pitfall should be mentioned. A rate constant of zero or infinity will also produce a zero value for  $f_j$ . This corresponds to *maximizing* the sum of the squares of the deviations, and divergence to such a value can occur if the initial guess at the rate constant is badly in error. However, in such a situation, it can be shown that  $f_j'$  must be negative. When this occurs, the rate constant must be increased or decreased (depending upon the sign of  $f_j$ ) by an order of magnitude, to force the convergence to a finite rate constant.

With this solution it is possible to take explicit ac-

count of other positions in a substrate molecule which acquire radioactivity as the reaction proceeds. Positions which exchange very rapidly may be considered to be a part of the solvent pool. The activity at a position which exchanges at a rate comparable to that of the position initially radioactive may be calculated for the parent position, since the counting method assumed does not distinguish among the various positions of a molecule. Finally, the resulting residuals between calculated and experimental activities are used to derive approximate standard deviations in the rate constants.

This program was written in IBM Fortran language. As an example of its versatility, a kinetic run consisting of benzene-*t*, toluene-2-*t*, and 2-phenylbutane-2-*t*, with three rate constants to be fitted, eight distinguishable hydrocarbon positions, and one set of benzylic hydrogens (assumed rapidly exchanging), was analyzed in less than 2 min. on the IBM 7090 computer. Analysis of this system by the previous, approximate technique would have required several hours of computation.

## Acidity of Hydrocarbons. XVIII. Exchange Reactions of Polycyclic Aromatic Protons with Lithium Cyclohexylamide<sup>1</sup>

A. Streitwieser, Jr., and R. G. Lawler<sup>2</sup>

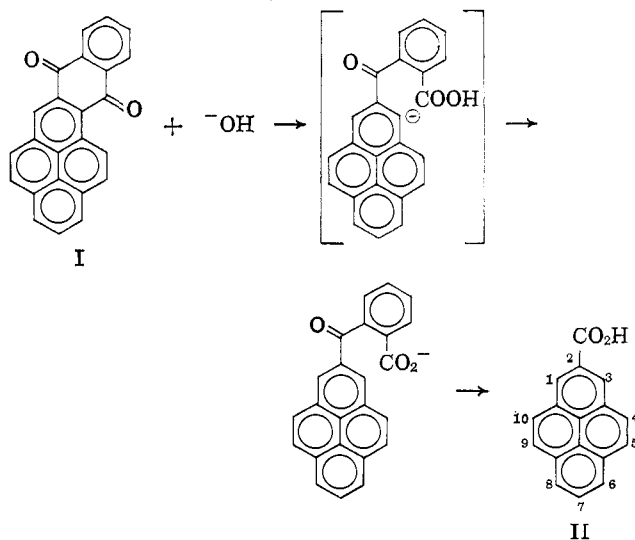
Contribution from the Department of Chemistry, University of California, Berkeley, California. Received July 19, 1965

*Relative rates of deuterium or tritium exchange with lithium cyclohexylamide were determined for various positions in benzene, naphthalene, phenanthrene, anthracene, and pyrene and have been found to span a relative rate range of almost 50-fold. The effect of structure on these rates is considered in terms of carbene resonance structures and molecular orbital polarizabilities, but the best correlation is with an inductive effect model based on a simple classical picture.*

The relative acidities of polycyclic aromatic hydrocarbons are of interest for several reasons. They provide a structural variation of  $\pi$ -electrons in a reaction in which conjugation may not be important. The possible applications of molecular orbital theory in such cases requires exploration. Such a series also provides a further test of a possible relationship between hydrocarbon acidities and amine basicities.

Indications of the relative acidities of different positions in polycyclic aromatic hydrocarbons have come from several sources. The cleavage of nonenolizable ketones with sodium amide to give an amide and a hydrocarbon<sup>3</sup> appears to go through carbanion inter-

mediates and provides useful inferences. Phenyl alkyl ketones give only benzene and the aliphatic amide; hence, phenyl anions are deduced to be more stable than alkyl anions. Unfortunately, this method has apparently not been applied to different polycyclic hydrocarbons. Isolated examples of KOH fusions are of value; for example, this reaction with 1,2-phthaloylpyrene (I) gives mostly pyrene-2-carboxylic acid<sup>4</sup> (II)



(1) (a) This work was supported in part by the Directorate of Chemical Sciences, Air Force Office of Scientific Research, Grants No. 62-175 and 64-554; (b) part XVII: A. Streitwieser, Jr., R. G. Lawler, and C. Perrin, *J. Am. Chem. Soc.*, **87**, 5383 (1965); (c) a preliminary communication was published in A. Streitwieser, Jr., and R. G. Lawler, *J. Am. Chem. Soc.*, **85**, 2854 (1963).

(2) National Science Foundation Predoctoral Fellow, 1960-1963; Eastman Kodak Science Award in Chemistry, 1962-1963.

(3) A. Haller and E. Bauer, *Compt. rend.*, **148**, 127 (1909); K. E. Hamlin and A. W. Weston, *Org. Reactions*, **9**, 1 (1957).

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