

Secondary α -Deuterium Isotope Effects and Relative Rates in the Halogen Exchange Reactions of Benzyl and Thenyl Chlorides¹

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The secondary deuterium isotope effects are found to be approximately the same for the isotopic halogen exchange reactions of $ArCD_2Cl$ where $Ar = \text{phenyl, 2-thienyl, or 3-thienyl}$. The reactivity of the compounds is found to be in the order 2-thienyl > phenyl > 3-thienyl. MO calculations with a pd^2 -hybridized thiophene model are shown to give acceptable agreement with the rate constant ratios found experimentally. Comparisons with the relative reactivities in the hydrogen exchange of benzene and thiophene are made.

In the last few years there have been a number of publications concerning SN2 reactions in solvents such as N,N-dimethylformamide (DMF)^{3a-c} and dimethyl sulfoxide.^{4a,b} Some of these investigations have dealt with halogen exchange reactions.^{3a,c,4a,b} It was therefore considered interesting to determine the secondary deuterium isotope effect in the (chemically) perfectly symmetric isotope exchange reaction using the radioactive Cl³⁶ isotope. It was also of some interest to see if the secondary isotope effect showed any dependence on different reactivities of the substrates. The substrates used in the present work were Cl³⁶-labeled benzyl chloride, 2-thenyl chloride, 3-thenyl chloride, and their α -deuterated counterparts; their exchange reactions with lithium chloride were studied at 40° in DMF solution. This work then gives, besides the secondary isotope effects, the reactivity relationships between the phenyl-, 2-thienyl-, and 3-thienyl groups which do not seem to have been determined before under controlled conditions for this fairly important type of reaction. The only information hitherto available in this respect seems to be a ratio of 2-thienyl:phenyl = 3.5 obtained from a product analysis in the competitive reaction between 2-thenyl chloride and benzyl chloride for sodium amoxide.⁵ The results of the present work are given in Table I.

Also included in this work is a molecular orbital calculation of some relevant properties of the thiophene system, the main purpose of which has been to stress the structural similarities between benzene and thiophene.

Results and Discussion

MO Calculations. In the present work the π -electron energies of some carbonium ions and their

uncharged thiophene and benzene counterparts have been calculated within the framework of MO theory utilizing the ω -technique. Overlap integrals between nearest neighbors have been included with the value $S_0 = 0.25$ for the carbon-carbon π -orbital overlap. The exchange integrals have been approximated as proportional to the overlap integrals. The computations have been carried out with an " ω -technique" program for the IBM 7094 digital computer.

In order to obtain a satisfactory choice for the sulfur coulomb integral, $\alpha_S = \alpha_0 + h_S\beta_0$, and for the carbon-sulfur π -overlap, kS_0 , the H_nX ionization potential fitting procedure suggested by Streitwieser⁶ was followed. Values employed for ω , α_0 , and β_0 were 1.25,⁷ -10.12, and -2.5 e.v., respectively. The α_0 - and β_0 -values were obtained by fitting the ionization potentials (electron impact) for ethylene (10.62 e.v.) and benzene (9.52 e.v.) to the calculated π -electron energy differences between the ions and neutral molecules. Then the ionization potential of H₂S (10.45 e.v.⁸) was used to obtain h_S .

The well-known Longuet-Higgins model for thiophene⁹ was used. This model utilizes the sulfur d-orbitals to form pd^2 hybrids that can conjugate with the carbon π -orbitals. From the ionization potentials of ethylene and H₂S Longuet-Higgins concluded that $h \sim 0$, and from the resonance energy of thiophene $k = 0.8$ was obtained. These parameter values have been confirmed in the present investigation, *i.e.*, with the use of the ω , α_0 - and β_0 -values given above, the ionization potential of H₂S (with "hybridized" sulfur¹⁰) gave $h = 0$, and the ionization potential of the thiophene (9.1 ± 0.2 e.v.¹¹) was then reproduced for $k \sim 0.8$ (a possible lower limit being $k = 0.6$). The h -value was obtained with the assumption that the overlap integral between the two sulfur hybrids has the value 0.25. As a matter of fact, if the overlap integral is assigned values from zero to unity, the h -value varies only slightly (from -0.2 to +0.3).

As pointed out by Longuet-Higgins, thiophene may be considered as a perturbed benzene system. Consequently the calculation of the *para*-localization index¹² for thiophene yields a value close to that of benzene. This index is a measure of the ease with which the

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(3) (a) P. Casapieri and E. R. Swart, *J. Chem. Soc.*, 4342 (1961); (b) W. M. Weaver and J. P. Hutchinson, *J. Am. Chem. Soc.*, 86, 261 (1964); (c) A. J. Parker, *J. Chem. Soc.*, 1328 (1961).

(4) (a) H. Elias and K. H. Lieser, *Chem. Ber.*, 94, 3128 (1961); (b) P. Casapieri and E. R. Swart, *J. Chem. Soc.*, 1254 (1963).

(5) T. L. Cairns and B. C. McKusick, *J. Org. Chem.*, 15, 790 (1950).

(6) A. Streitwieser, Jr., *J. Am. Chem. Soc.*, 82, 4123 (1960).

(7) N. Muller and R. S. Mulliken, *ibid.*, 80, 3489 (1958).

(8) D. C. Frost and C. A. McDowell, *Can. J. Chem.*, 36, 39 (1958).

(9) H. C. Longuet-Higgins, *Trans. Faraday Soc.*, 45, 173 (1949).

(10) It is realized that this treatment of H₂S, in which the molecule is treated as ethylene, may be artificial. The ionization potentials of ethylene and H₂S are, however, very close to each other. One could, of course, also have taken $h = 0$ directly, in agreement with the fact that carbon and sulfur are the same on the Pauling electronegativity scale.

(11) I. Omura, H. Baba, and K. Higashi, *J. Phys. Soc. Japan*, 10, 317 (1955).

(12) R. D. Brown, *J. Chem. Soc.*, 691 (1950).

Table I. Bimolecular Rate Constants at $40.10 \pm 0.05^\circ$

	Benzyl chloride	Benzyl chloride- α - d_2	3-Thenyl chloride	3-Thenyl chloride- α - d_2	2-Thenyl chloride	2-Thenyl chloride- α - d_2
$a \times 10^{2a}$	1.305	1.269	1.208	1.199	1.155	1.097
$b \times 10^{2a}$	0.785	0.785	0.964	0.964	0.943	0.943
α	0.808	0.808	0.788	0.788	0.795	0.795
$k_2 \times 10^{3b}$	7.08 ± 0.17	6.72 ± 0.15	5.96 ± 0.12	5.47 ± 0.16	20.91 ± 0.45	19.28 ± 0.51
k_H/k_D	1.05 ± 0.03			1.09 ± 0.03		1.08 ± 0.03
k_H/k_D per D	1.03			1.05		1.04
Relative rate	1.00		0.84 ± 0.03		2.95 ± 0.09	

^a mole l.⁻¹. ^b l. mole⁻¹ sec.⁻¹. Average of at least three runs. Errors are standard deviations.

particular molecule will undergo the Diels-Alder addition reaction. As is well known, neither benzene nor thiophene undergoes that kind of reaction under ordinary conditions.

The calculations of the π -electron energies of the thenyl and benzyl chlorides included a coulomb integral for the substituted ring carbon equal to $\alpha_0 + 0.1\beta_0$, to account for the electron-withdrawing effect of the CH_2Cl group by induction. The corresponding carbonium ions were treated simply as electron-deficient, conjugated systems with normal ($S_0 = 0.25$) overlap between the π -orbitals of the substituted ring carbon and the side chain sp^2 carbon. Thus the π -energy differences between the carbonium ion and the corresponding chlorides were computed and considered to reflect the activation energies for a bimolecular substitution of chlorine in the side chain, for the limiting case of complete bond breaking and no bond formation. The relative rates were then found to be (at 40°) $k_2/k_3 \sim 10^3$ and $k_3/k_{\text{benzyl}} \sim 0.6$ using the β_0 -value above corresponding to -58 kcal./mole. Comparison with the experimental values of Table I shows that the calculations predict the correct direction for these ratios. The magnitudes are also acceptable when the rather drastic assumption of the transition state is considered.¹³

The same calculations as discussed above were also carried out with a nonhybridized, furan-type, thiophene molecule. Here it is important to point out that, whereas the ionization potentials of thiophene and furan differ by only 0.07 e.v., the ionization potentials of H_2S and H_2O differ by 2.57 e.v. in the opposite direction. This circumstance is already an indication that the role played by oxygen and sulfur in compounds such as furan and thiophene is different. Thus with the parameters $h = 1.4$, $k \sim 0.2$ (obtained from the ionization potentials) the *para*-localization index indicated

(13) HMO calculations on the intermediates in aromatic hydrogen exchange in thiophene (i.e., σ -complexes) have been carried out by Melander, *Arkiv Kemi*, 8, 361 (1956), with the use of the Longuet-Higgins thiophene model. It was considered of some interest, though, to extend these calculations to include hyperconjugation and to treat the cases according to the ω -technique. The following parameters [S. Ehrenson, *J. Am. Chem. Soc.*, 83, 4493 (1961)] were then used for the hyperconjugatively stabilized intermediates: the coulomb integral for the hydrogenic quasi-group = $\alpha_0 - 0.3\beta_0$, $S_{\text{quasi}} = 0.63\beta_0$, and the coulomb integral for the quasi-group substituted ring carbon $\alpha_C = \alpha_0 - 0.075\beta_0$. Thus the following rate constant ratios were obtained (at 25°): $k_2/k_3 \sim 10^6$, $k_3/k_{\text{benzene}} \sim 0.2$. From Melander's work $k_2/k_3 \sim 10^4$, $k_3/k_{\text{benzene}} \sim 2$ (at 25° , $h = 0$, $k = 0.8$, $\beta_0 = -38$ kcal./mole) is obtained. The experimental value for k_2/k_3 is $\sim 10^3$ in the heterogeneous hydrogen exchange at 25° of thiophene: B. Östman and S. Olsson, *Arkiv Kemi*, 15, 275 (1960). Unfortunately the corresponding experimental rates relative to benzene can only be estimated since the benzene experiment, S. Olsson, *ibid.*, 16, 489 (1960), was carried out at a different acid strength (57 and 80% H_2SO_4 for thiophene and benzene, respectively). Estimates thus indicate $k_3/k_{\text{benzene}} > 1$. In protodesilylation of thiophene and benzene the rate constant ratios $k_2/k_3 = 43.5$, $k_3/k_{\text{benzene}} = 115$ are reported: F. B. Deans and C. Earborn, *J. Chem. Soc.*, 2303 (1959).

that thiophene should undergo the Diels-Alder reaction considerably faster than furan; the rate ratios discussed before were almost always in serious disagreement (in magnitudes and/or directions) with the experimental results. The more reasonable choice of $h = 0$, $k = 0.8$ did not change the pattern; for instance the calculated ionization potential of thiophene became 8.3 e.v. (moreover the experimental value was not reproduced at all for $h = 0$, $k = 0.1-1.1$).

Isotope Effects. From a recent compilation^{14a} of secondary α -isotope effects, k_H/k_D (per D, corrected to 40°) for the solvolyses of benzyl tosylate and isopropyl brosylate are found to be 1.12 and 1.13, respectively. In the SN_2 displacement of bromine by EtO^- in isopropyl bromide, $k_H/k_D = 1.00$ is reported.¹⁵ Leffek¹⁶ has recently reported k_H/k_D values for the SN_2 displacement of bromine by thiosulfate ion in methyl, ethyl, and *n*-propyl bromide which are found to be 1.01, 1.03, and 1.03 (per D, corrected to 40°), respectively. The present values for k_H/k_D in the SN_2 displacements of chlorine in the benzyl and thenyl chlorides (per D; see Table I) fit in this pattern insofar as empirically an isotopic rate constant ratio close to unity is obtained for an SN_2 transition state while ratios significantly larger than unity are produced in transition states of essentially complete carbonium ion character. Thus the transition state in the halogen exchange case may be said to look very much the same as in the (chemically) asymmetric cases. This, then, would also hold for the case of iodide exchange of methyl iodide in methanol where $k_H/k_D = 1.02$ (per D, corrected to 40°) is found.¹⁷ The interpretation clearly considers the zero-point energy as the decisive factor for secondary isotope effects of the present kind due to changes in the out-of-plane bending vibrations of the C-H bonds.¹⁸ The extensive model calculations by Wolfsberg and Stern¹⁹ show, however, that such reasoning, based only on deuterium effects, must be used with care. For example, for the transition state $[\text{X}_1 \cdots \text{CD}_3 \cdots \text{X}_2]^*$ they show that by changing only one of the stretching force constants f^*_{CX} , from being equal to the other, to zero the isotopic rate constant ratio changes about 8%. This change, however, will affect the zero-point energy factor to a lesser degree than the other factors involved in the isotopic

(14) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962: (a) p. 173; (b) p. 178.

(15) V. J. Shiner, Jr., *J. Am. Chem. Soc.*, 74, 5285 (1952).

(16) K. T. Leffek, *Can. J. Chem.*, 42, 851 (1964).

(17) A. A. Zavitsas and S. Seltzer, Brookhaven National Laboratory Annual Report, July 1, 1963, p. 56 (BNL 806(AS-17)).

(18) A. Streitwieser, Jr., R. H. Jagow, R. C. Fahey, and S. Suzuki, *J. Am. Chem. Soc.*, 80, 2326 (1958).

(19) M. Wolfsberg and M. J. Stern, *Pure Appl. Chem.*, 8, 325 (1964).

rate constant ratio expression. Willi and Wolfsberg²⁰ show for the same type of transition state (with a different choice of some of the force constants) that a 4% change in the f^*_{HCX} bending-force constant alone will change the isotopic rate constant ratio about 3%. It must be pointed out, however, that the models may be far from realistic, and that the conclusions as to the source of the secondary isotope effects must therefore still be open to question.

From the $k_{\text{H}}/k_{\text{D}}$ values in the present work it is seen that there is no difference (outside the errors) for the three different groups, *i.e.*, to this approximation we may conclude that the change in bonding in going from reactant to transition state is similar for the benzene and the thiophene system.

Rate Constant Ratios. The isotope effects discussed above may be given the interpretation that the central carbon of the side chain is positively charged in the transition state. That this carbon atom should carry a positive charge is also implied by the fact that, from a recent compilation^{14b} of Finkelstein substitutions of arylmethyl chlorides (in acetone), the carbonium ion character in these cases is actually greater than in the corresponding solvolytic reactions. Thus the relative rates of Table I indicate the following sequence: $+M_2 > +M_\phi \geq +M_3$. The inductive effects of the groups concerned suggested by the $\text{p}K_{\text{a}}$ values of the corresponding carboxylic acids²¹ are in the following order: $-I_2 > -I_3 > -I_\phi$. From the inductive effects alone one would predict that the 2-thienyl group should retard the reaction compared to the other groups. Thus one concludes that the positive charge is dispersed mainly by conjugation and only to a minor extent by induction. Since the MO treatment mainly takes into account the conjugative properties of the systems one would expect serious disagreements with the experiments if the inductive properties were important.²² It is interesting that the Finkelstein substitution of α -naphthylmethyl chloride^{14b} gives the ratio $k_{\alpha}/k_{\text{phenyl}} = 3.55$, which is fairly close to the corresponding ratio for the 2-thenyl compound in the present case. In the naphthyl case there is certainly stabilization of the positive charge by conjugation. It is also noteworthy that in a plot²³ of $\log k$ for Finkelstein reactions of ArCH_2Cl in acetone *vs.* the polarographic reduction potentials for ArCHO , the reduction potential of 2-thenaldehyde

will give a value of $\log k$ very close to that of α -naphthylmethyl chloride. The significance of the correspondence between direct displacement rates and the reduction potentials of the aldehydes has been pointed out by Streitwieser.²³ Similarities between naphthalene and thiophene have been pointed out by de Heer.²⁴

Conclusions

It is realized that the models chosen for the MO calculations are grossly oversimplified. In the SN_2 case it was not considered advisable at this point to include the incoming and leaving groups in the calculations, since this would introduce an additional set of vaguely known parameters.²³ In the protonation case¹³ the σ -complexes were assumed to represent the actual transition states, which is, of course, a very crude approximation.

In the SN_2 reactions the position of the transition states along the reaction coordinate will probably be the same for the three cases under consideration, *i.e.*, only the differences in dispersing the charge determine the activation energies. Hill and Fry²⁵ arrive at the same conclusion (based on chlorine isotope effects) for nucleophilic substitutions of different *para*-substituted benzyl chlorides.

In the protonation case the definite trend of decrease of the primary isotope effect ($k_{\text{ArT}}/k_{\text{ArD}}$) with decreasing reactivity has been observed and discussed.²⁶ The differences in the isotope effects undoubtedly must be due to different positions along the reaction coordinate for the three transition states under consideration. It is therefore probably less safe here than in the SN_2 case to attribute the different rates merely to the different charge dispersing capacities of the π -systems.

With regard to the model for thiophene itself it is concluded that the Longuet-Higgins model is able to explain satisfactorily the behavior of the compound for the cases discussed above, whereas the furan-type model gives very poor agreement with the experimental results. There has recently been some criticism²⁷ of the Longuet-Higgins model based on the fact that the promotional energies involved in the hybridization process should be very large. However, in any such process energy is also gained because of the favorable directional properties of the hybrids. To abandon the model at present because of the uncertainty involved in the estimates (based on the isolated sulfur atom) of these energy requirements seems, in view of the results arrived at above, to grossly underestimate the value of those predictions. It is important to realize, however, that there may well be derivatives of thiophene for which a nonhybridized model would describe the situation better. The hybridized model emphasizes the similarity with benzene but there are cases when the behavior of thiophene derivatives are quite different; for instance, in the nitration of 2-nitrothiophene²⁸ about equal amounts of 2,4-dinitrothiophene and 2,5-dinitrothiophene are formed, which for nitrobenzene should correspond to formation of equal amounts of *m*- and *p*-dinitrobenzene.

(20) A. V. Willi and M. Wolfsberg, paper submitted to the 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964.

(21) S. Gronowitz in "Advances in Heterocyclic Chemistry," Vol. I, A. R. Katritzky, Ed., Academic Press Inc., New York, N. Y., 1963, p. 82.

(22) In the case of hydrogen exchange with aromatic hydrogens, positive charge has to be dispersed as well. The hyperconjugatively stabilized σ -complexes then bear some resemblance to a (limiting) SN_2 transition state. Comparison in this case between thiophene and benzene must be exercised with care. If protonation on the sulfur is negligible the main difficulty is due to the difference in the acid strengths for the experiments under consideration. Thus, estimate of the k_3/k_{benzene} ratio based on the H_0 scale (or the H_R scale) yields the value 10^2 (or 10^3), differences in the solubility for benzene and thiophene being taken into account. The relative rates would then indicate the sequence $+M_2 > +M_3 > +M_\phi$. The MO treatment, however, indicates $+M_2 > +M_\phi > +M_3$. It is possible, therefore, that in this case inductive effects may be important in distributing the positive charge. It should be obvious from the foregoing, however, that the combined differences between experiments and ignorance of the nature of the transition states render any conclusions such as the latter extremely hypothetical.

(23) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," John Wiley and Sons, Inc., New York, N. Y., 1961, p. 368.

(24) J. de Heer, *J. Am. Chem. Soc.*, **76**, 4802 (1954).

(25) J. W. Hill and A. Fry, *ibid.*, **84**, 2763 (1962).

(26) L. Melander, *Arkiv Kemi*, **18**, 195 (1961).

(27) A. Mangini and C. Zauli, *J. Chem. Soc.*, 2210 (1960).

(28) B. Östman, *Arkiv Kemi*, **19**, 527 (1962).

Experimental

Preparation of the Benzyl and Thenyl Chlorides. Benzoic acid (Fisher certified reagent), 2-thenoic acid, and 3-thenoic acid (K & K Chemicals) were reduced with lithium aluminum hydride and lithium aluminum deuteride (Metal Hydrides) essentially according to Clovis and Hammond.²⁹ The yields of the alcohols thus obtained were about 80%. The thenyl alcohols were found to be isomerically pure by g.l.c. analysis. The alcohols were then converted to the corresponding benzyl and thenyl chlorides with thionyl chloride.²⁹ The yields were about 70%. The purity of the chlorides was checked with g.l.c. and n.m.r. For the deuterated compounds mass spectral analyses of the deuterium contents were made according to usual techniques^{30,31} and checked with n.m.r., yielding in all three cases 98 ± 2 mole % deuterium for the side chain.

Preparation of Cl³⁶-Labeled Compounds. Lithium chloride-36 was obtained by potentiometric titration^{32a} of lithium carbonate (Baker and Adamson) with ca. 1 N HCl³⁶ (Oak Ridge National Laboratory). The radioactive lithium chloride was recovered by lyophilization of the water solution. An approximately 0.02 M DMF solution of the labeled lithium chloride was then prepared and used to prepare the labeled benzyl and thenyl chlorides by exchange. An amount of the organic chloride was then added so that its concentration was about 0.2 M. The solutions were kept at 50° for about 60 hr. in the benzyl and 3-thenyl cases, and at 40° for 50 hr. in the 2-thenyl cases. The organic chloride was then recovered in the following manner. The DMF solution (100 ml.) was poured into 1000 ml. of water and 100 ml. of benzene. The benzene layer was washed twice with 250 ml. of water and then dried over potassium carbonate. The solvent was distilled away and the organic chloride was distilled *in vacuo*. The recoveries were about 60%. The purity of the chlorides was checked by comparing the n.m.r. spectra and the refractive indices with those of the starting materials. These properties of the compounds were unchanged.

Exchange Experiments. The exchange reactions were carried out at $40.10 \pm 0.05^\circ$ with solutions of the labeled organic chlorides in DMF (Matheson Coleman and Bell, spectroscopic) and with solutions of lithium chloride (Baker Analyzed reagent, dried to constant weight at 120°) in DMF. These stock solutions were kept for at least 1 hr. in the constant temperature bath before the start of the experiment. An equal volume (15.00 ml.) of each stock solution was then pipetted into a 50-ml. volumetric flask. The actual concentrations of organic chloride (*a*) and lithium chloride (*b*) are given in Table I. Ten aliquots (2.00 ml.) were then taken with pipets at suitable intervals and transferred to a quenching mixture of water (20 ml. of water in the benzyl and the 3-thenyl cases, 5 ml. of water in the 2-thenyl cases) and 2.00 ml. of xylene. The mixture was then shaken and placed in a centrifuge. The water layer was removed with a syringe and

the xylene layer was treated twice with 5 ml. of water (in the benzyl and 3-thenyl cases) and dried over potassium carbonate. In the 2-thenyl cases the washings with water were excluded; the xylene layer was dried over potassium carbonate after the initial treatment with water. These procedures were repeated with DMF solutions containing (i) labeled lithium chloride but no organic chloride and (ii) labeled organic chloride but no lithium chloride. By comparing the specific activities of the DMF solutions with those of the xylene solutions case i gave information on the amount of lithium chloride that possibly could dissolve in xylene and case ii gave a determination of the correction factor $y_{\text{xylene}}/y_{\text{DMF}}$ due to the solubility of the organic chloride in water and to the difference in sensitivity of the counter for xylene and DMF. Thus it was found that no lithium chloride was dissolved in xylene in any of the cases. By g.l.c. it was also found that only traces of DMF were left in the xylene layer. The following values of $y_{\text{xylene}}/y_{\text{DMF}}$ were obtained from at least three determinations for each compound (see Table II). The average deviations from the mean in these figures is about 0.5%.

Table II

Compd.	$y_{\text{xylene}}/y_{\text{DMF}}$	
	Protium	Deuterium
Benzyl chloride	1.066	1.060
3-Thenyl chloride	1.038	1.037
2-Thenyl chloride	0.926	0.928

The specific activity of the reaction solution multiplied by the corresponding $y_{\text{xylene}}/y_{\text{DMF}}$ value then gives for each case the initial activity (y_0) with which the specific activity (y) of the xylene layers is to be compared.

The counter used for the radioactive measurements was a five-wire glass counter containing Q-gas (butane and helium, Matheson) at 1 atm. The liquid sample was contained in a glass finger inserted into the center of the five anode wires. It was of glass drawn out as thin as possible and having a diameter of ~ 4 mm., the effective volume being ~ 1 ml. The finger and the glass walls of the counter were coated with conducting material forming the cathode. The efficiency was 10–15% and the background was ~ 100 c.p.m. The specific activity is simply the activity of the solution in the effective region. The readings were made at 1600–1700 v. (determined by a plateau). The precision was slightly better than $\pm 1\%$. Corrections for background ($\sim 5\%$ of the initial activity) and dead time ($\sim 300 \mu\text{sec.}$) were made. No corrections for the radioactive decay of Cl³⁶ (half-life 3×10^5 years) were necessary.

Kinetics. The rate constant *R* for the isotopic exchange is obtained from the expression³²

$$\ln \frac{y/y_0 - a/(a+b)}{b/(a+b)} = -\frac{a+b}{ab} R t$$

where *a* and *b* are the actual concentrations of "aryl" methyl chloride and lithium chloride, respectively;

(32) H. A. C. McKay, *Nature*, 142, 997 (1938).

(29) J. S. Clovis and G. S. Hammond, *J. Org. Chem.*, 27, 2285 (1962).

(30) J. Bigeleisen, M. Perlman, and H. Prosser, *Anal. Chem.*, 24, 1356 (1952).

(31) D. R. Christman, N. E. Day, P. R. Hansell, and R. C. Anderson, *ibid.*, 27, 1935 (1955).

y/y_0 is the relative specific activity of "aryl" methylchloride at time t (y_0 is the corrected initial specific activity; see above). In each run $((a + b)/ab)R$ was obtained by a least-squares fit of the data to a straight line using the IBM 7094 digital computer. The standard deviation for the slope then was about 3% in each run. Since the quantity $b/(a + b)$ was also computed by the program, the value of y/y_0 at time zero was obtained for each experiment. These values deviated by less than 1% from the theoretical value which is unity. The points were taken during the first 2 half-lives of the reactions. By allowing the exchange to proceed for about 10 half-lives the value for radioactive equilibrium, y_∞/y_0 , was obtained. These values deviated by about 2% from the theoretical value $a/(a + b)$.

The importance of allowing for the incomplete dissociation of lithium chloride in DMF has been pointed out by Weaver and Hutchinson^{3b} and by Casapieri and Swart.^{3a} The former authors find, in DMF at 0°, the relative rates of reaction of the lithium halides with methyl tosylate to be in the order $\text{Cl}^- > \text{Br}^- > \text{I}^-$, when the degree of dissociation is taken into account. This order for the halides is the reverse of that normally found (e.g., in acetone). When water was added to the DMF solvent the normal order of reactivity of chloride and iodide was obtained. The results were rationalized as being due to the higher charge density of chloride as compared to iodide; the higher charge density causes the rate retardation by water solvation and by ion pairing to be more effective for chloride than for iodide. The kinetic activity of ion pairs in the bromide exchange of *p*-nitrobenzyl bromide in liquid SO_2 has been considered by Lichtin and Rao.³³ They arrive, however, at the conclusion that, in their work, it was not necessary to include ion pairs in the rate expression.

The possible contribution of a first-order term (i.e., SN1) to the rate was eliminated by control experiments where the lithium chloride concentration was decreased by a factor of two, which caused no change in the bimolecular rate constant in any of the cases. This was also found in the benzyl chloride case by Casapieri and Swart^{3a} and in other cases of nucleophilic sub-

stitution in DMF by other authors (for references see ref. 3b).

Therefore, in the present work, the bimolecular rate constant, k_2 , can be expressed as

$$R = k_2\alpha b$$

where α is the degree of dissociation of lithium chloride. Thus by using the data of ref. 3a for the dissociation constant, the degree of dissociation, and the concentration of lithium chloride at 40°, the values of α applicable to the present case were obtained (Table I). For each pair, natural and deuterated compound, the same stock solution of lithium chloride was used, however, in order to eliminate differences in the isotope effects due to possible errors in the determination of α . The present value for k_2 in the benzyl chloride case agrees well (about 3% higher) with the previously reported^{3a} value at the same conditions.

The possible contribution to the observed rate by side reactions was not specifically investigated, but it is felt that the good agreement between the y_∞/y_0 values and the quantity $a/(a + b)$ mentioned above indeed indicates that such contributions may safely be neglected. However, it is to be noted that benzyl chloride reacts³⁴ with DMF at 150° to give N,N-dimethylbenzamide (97% yield after 4 hr.) and methyl chloride. If this reaction occurred to any appreciable extent, the specific activity (as defined here, see above) for a sample taken after 10 half-lives (y_∞) should be considerably affected since radioactive methyl chloride must necessarily disappear from the system during the reaction and the quenching procedure. The agreement, however, between the calculated and the experimentally found values of y_∞/y_0 seems to eliminate this possibility.

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