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HALIDE EXCHANGE IN ALKYL HALIDES:
SUBSTITUENT EFFECTS ON THE RATES OF HALIDE EXCHANGES

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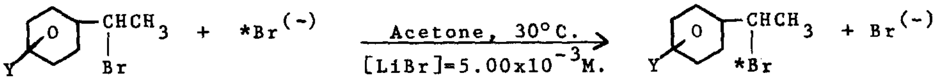
As part of a study of some aspects of the bimolecular nucleophilic substitution at saturated carbon, an examination of some halide exchanges has been undertaken. To minimize the factors involved, a system with both nucleophile and leaving group the same was desirable. Since the bromide-_radio_-bromide exchange on α-phenylethyl bromide[1] was one of the studies that led Gleave, Hughes and Ingold to propose the S_N2 mechanism for such substitutions[2] it seemed appropriate to study that system. Using lithium bromide as the inorganic bromide in anhydrous acetone, the bromide-_radio_-bromide ($^{82}Br^-$) exchanges for variously substituted α-phenylethyl bromides were followed by the electro-deposition method of Beronius[3]. Some data for the unsubstituted and the _para_-nitro, bromo, methyl and methoxy compounds are summarized in the accompanying Table. Both electron withdrawing and electron donating substituents greatly accelerate the bromide exchange reaction. A Hammett σρ plot[4] gives a deep U or V-shaped curve. Indeed, these results represent, to the author's knowledge, the greatest curvature yet reported in a Hammett correlation.

Linear free energy correlations, of which the Hammett Equation[4] is but one, are perhaps surprisingly frequently observed when one considers their simplicity and the multitudinous factors involved especially in the entropy contribution to the change in free energy. For rate as opposed to equilibrium processes, TABLE



Y	No. of runs	k$^{(a)}$ l/m.min.	$\log\left(k_y/k_h\right)$	$\sigma^{(b)}$	$\sigma^{+(c)}$
p-CH$_3$O	3	3.75±0.53	1.37	-0.27	-0.778
p-CH$_3$	3	0.360±0.020	0.349	-0.17	-0.311
p-H	4	0.161±0.008	0.00	0.00	0.00
p-Br	4	0.332±0.016	0.314	0.23	--
p-NO$_2$	1	0.683	0.628	0.78	--

(a) Bimolecular rate constant not corrected for bromide ion activity.

(b) "Normal" substituent constant, see for example, L.P. Hammett "Physical Organic Chemistry" Second Edition, McGraw-Hill, New York, 1970, pp.355-358.

(c) Substituent constant defined by H.C. Brown and Y. Okamoto [J. Amer. Chem. Soc., 80, 4979 (1958)] for cases with transition states greatly stablized by resonance electron donation.

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at the transition state solvation, charge separation, etc. further complicates the situation. Curvature in Hammett plots thus is not uncommon[6] and is usually assigned to a change in mechanism. While few substituents have thus far been examined in these halide exchange studies, the Hammett ρ-value or reaction constant for the electron donating *para*-methoxy and methyl substituents can be estimated to be about -9 with σ or about -2.2 with σ^+. Similarly, the unsubstituted and *para*-bromo and nitro substituents lead to a ρ-value of about +1. Mechanistically, this radical change in response to the electronic effect of the substituent means that as the *para*-substituent is changed from methoxy to methyl and hydrogen through bromo to nitro, there is a change from a large positive to a moderately large negative charge at the transition state for a reaction that is apparently bimolecular throughout[7,8].

In the ion pair mechanism for nucleophilic substitution at saturated carbon[9], it is proposed that the initial step of the reaction is formation of a contact or intimate ion pair by the substrate and its leaving group. The reaction could show the characteristics of S_N2, "mixed" or S_N1 mechanisms depending upon where in the series of solvation equilibria from the intimate ion pair to the free, independently solvated ions nucleophilic attack occurs. With the *para*-electron donating substituents in the α-phenylethyl bromide series, the large positive charge developing at the transition state for bromide exchange is clearly consistent with an ion pair mechanism. This is logical since the carbonium ion species of the ion pair should be stablized and more easily formed in these cases. With the electron withdrawing substituents, however, the developement of a negative charge at the transition state of the reaction suggests nucleophilic attack is now leading bond breakage, consistent with traditional S_N2 displacement in these cases.

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(4) L.P. Hammett, "Physical Organic Chemistry", Second Edition, McGraw-Hill, New York (1970), pp. 355-8.

(5) See for example, J.E. Leffler and E. Grunwald "Rates and Equilibria of Organic Reactions" Wiley, New York (1963), pp. 315-402.

(6) See for example, ref. 3, pp. 187-191 and A. Streitwiesser, Jr., "Solvolytic Displacement Reactions", McGraw-Hill, New York (1962),pp.18-20.

(7) The data at each concentration of lithium bromide show a linear *pseudo*-first order loss of ionic *radio*-bromide with a rate constant independent of alkyl halide concentration except in the case of the methoxy-substituent where the slower competing hydrogen bromide elimination leads to an accelerating apparent exchange rate as the reaction progresses. For the other substituents, the elimination reaction is 10^{-4} - 10^{-7} times the exchange rate and linearity is obtained for as many as six half-lives. The exchange rate increases but not linearly with increasing lithium bromide concentration due to ion pairing reducing the activity coefficient of the bromide ion as the concentration of the salt increases [cf. A.R. Stein, *J. Org. Chem.*, *38*, 4022 (1973)]. See also footnote 8.

(8) While the Beronius method for following halide-*radio*-halide exchanges is very clean and convenient, the inert electrolytes that could be used to maintain the reaction media at constant ionic strength (e.g. $LiNO_3$, $LiClO_3$, $LiClO_4$, Li picrate....) were either not sufficiently soluble in acetone or interfered with the electro-deposition of silver bromide. Consequently, it is not easily acertained whether the reaction remained bimolecular or if, for the methoxy substituent, mixed uni- and bimolecular kinetics were shown [cf. A. Ceccon, I. Papa and A. Fara, *J. Amer.Chem. Soc.*, *88*, 4643 (1966)]. However, when the concentration of lithium bromide is decreased by a factor of five, the apparent rate constant increases by a factor of approximately two for substituents other than methoxy. With methoxy, the increase was about 2.7 suggesting a unimolecular component in the observed rate.

(9) a) R.A. Sneen and J.W. Larsen, *J. Amer. Chem. Soc.*, *91*, 362, 6041 (1969).
b) R.A. Sneen, G.A. Felt and W.C. Dickason, *ibid*, *95*, 638 (1973).