

define partitioning factors P^+ and P^0 for TH_2^+ and TH , respectively; pK' is the pH where product transition takes place (see Table V). Using the equilibrium constraints (eq 8 of ref 4), the equation for the pH dependence of aminolysis (eq 7 of ref 4) becomes eq 7 (this paper). As in section A, the shape of the pH profile is

$$\frac{k_{\text{obsd}}}{[\text{free amine}]} = \frac{k_1((1 - P^+)[\text{H}^+] + K'(1 - P^0))([\text{H}^+] + K'P^0/P^+)}{[\text{H}^+] + K'} \quad (7)$$

uniquely a function of the three parameters P^+ , P^0 , and K' . Two examples of calculated pH dependences are given in Figure 6, where P^+ is varied while P^0 and K' remain constant. We draw attention to the shape of curve B, calculated using a partitioning ratio for TH_2^+ similar to that known for 2-methylthiazoline, which gives about 50% amine yield in acid solution.^{2,5} It is precisely the fact that the rate-pH profile for the intramolecular aminolysis of S-acetylcysteamine *did not* possess the predicted appearance which led Barnett and Jencks to postulate a novel mechanism.⁵

C. Imidate Hydrolysis and Ester Aminolysis Proceed through Three Intermediates. This is the situation described by Scheme I of the present paper. We define partitioning factors P^+ , P^0 , and P^- , and transition pH values pK' and pK'' , as in Table V. The steady-state

$$\frac{k_{\text{obsd}}}{[\text{free amine}]} = \frac{k_1([\text{H}^+]^2(1 - P^+) + K'[\text{H}^+](1 - P^0) + K'K''(1 - P^-))([\text{H}^+] + K'P^0/P^+ + K'K''P^-/P^+[\text{H}^+])}{[\text{H}^+]^2 + K'[\text{H}^+] + K'K''} \quad (10)$$

treatment leads to eq 3 for the dependence of amine yield on pH. The second-order rate constant for ester aminolysis (in terms of free amine) obeys eq 8; use of

$$\frac{k_{\text{obsd}}}{[\text{free amine}]} = \frac{\left[\left(\frac{k_3}{k_2 + k_3} \right) [\text{H}^+]^2 + \left(\frac{k_3'}{k_2' + k_3'} \right) K' [\text{H}^+] + \left(\frac{k_3''}{k_2'' + k_3''} \right) K'K'' \right] [k_1[\text{H}^+] + k_1' + k_1'[\text{OH}^-]]}{[\text{H}^+]^2 + K'[\text{H}^+] + K'K''} \quad (8)$$

the equilibrium condition (eq 9) and the definitions of

$$k_1[\text{H}^+]/k_2 = k_1'[\text{H}^+]/k_2'K_1 = k_1''K_w[\text{H}^+]/k_2''K_1K_2 \quad (9)$$

P^+ , P^0 , P^- , K' , and K'' converts eq 8 to 10. As before, the shape of the aminolysis pH profile is completely determined by the five parameters which describe the pH dependence of the products of imidate ester hydrolysis; the rate constant k_1 is a scale factor. Assumption of appropriate values for the partitioning factors and for K' and K'' allows the generation of families of product-pH curves and of the corresponding rate-pH profiles (see, for example, Figures 2 and 4). Detailed discussion of such curves is profitably deferred until relevant experimental situations are encountered.

Communications to the Editor

Chemically Induced Dynamic Nuclear Polarization Evidence for One-Electron Transfers during Some Halogen-Metal Exchange Reactions

Sir:

We offer evidence for the formation of free radicals during the exchange reaction between alkyllithium compounds and both alkyl and aromatic iodides. Our approach to the problem has been the search for, and the observation of, chemically induced dynamic nuclear polarization (CIDNP) in the protons of the organohalide formed during the exchange.¹ CIDNP has been shown to result when protons in reacting molecules become dynamically coupled to an unpaired electron while traversing the path from reactants to products.² Specifically, if an intermediate free radical is formed and then reacts rapidly in a sample whose nmr spectrum is being taken, polarization of proton

spins in the diamagnetic products can often be observed. Since both positive and negative polarization can occur, both nmr emission and enhanced absorption are possible. We propose that the simultaneous observation of both effects in an nmr spectrum under normal high-resolution operating conditions indicates that the protons giving rise to these signals spend some time in residence on an intermediate free radical.³

A spectrum⁴ taken of a reacting solution of ethyllithium and ethyl iodide in benzene at 40° is shown in Figure 1. The anomalous intensities exhibited by these lines are characteristic of CIDNP. The related ex-

(3) Intermolecular interactions between free radicals and nonreacting molecules also may give rise to polarization effects (see, for example, K. H. Hauser and D. Stehlik, *Advan. Magnetic Resonance*, **3**, 79 (1968)). However, strong positive polarization of protons is without precedent in such electromagnetically pumped dynamic nuclear polarization experiments on solutions of neutral free radicals. Furthermore, signal enhancement or deenhancement from protons in molecules other than those known to be reactants or products has not been observed in the present system; e.g., ethers which would be expected to be complexed strongly by the alkyllithium and held in the vicinity of the reaction site do not show polarization.

(4) Spectra were taken on a Varian A-60A spectrometer, which was purchased with funds supplied by the National Science Foundation.

(1) Similar results have been obtained by A. R. Lepley and R. L. Landau, *J. Amer. Chem. Soc.*, **91**, 748, 749 (1969).

(2) (a) H. R. Ward and R. G. Lawler, *ibid.*, **89**, 5518 (1967); (b) R. G. Lawler, *ibid.*, **89**, 5519 (1967); (c) J. Bargon and H. Fischer, *Z. Naturforsch.*, **22a**, 1551, 1556 (1967); (d) A. R. Lepley, *J. Amer. Chem. Soc.*, **90**, 2710 (1968).



Figure 1. Reaction of ethyllithium with ethyl iodide in benzene. (a) Spectrum taken during the reaction, showing the methylene (δ 3.2) and methyl protons (δ 1.85) of ethyl iodide and butane (δ 1.0-1.6) (3.5-2.5-ppm region scanned with a spectrum amplitude twice that of the remainder of spectrum). (b) Reference spectrum of ethyl iodide.

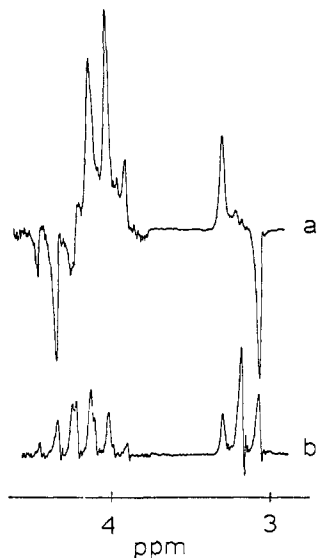


Figure 2. Reaction of *n*-butyllithium and *sec*-butyl iodide in benzene. (a) Spectrum taken during the reaction showing the α protons for *sec*-butyl iodide (δ 4.2) and *n*-butyl iodide (δ 3.2) (4.5-3.8-ppm region scanned with a spectrum amplitude four times that of remainder of spectrum). (b) Reference spectrum of *sec*-butyl iodide and *n*-butyl iodide.

change between *n*-butyllithium and *sec*-butyl iodide, under the same conditions, shows polarization of the methylene and methyne protons of both *n*-butyl iodide and *sec*-butyl iodide, respectively (Figure 2). Since polarization of approximately the same relative intensity is present in both iodides throughout most of the reaction (7 min), the *sec*-butyl iodide is believed to

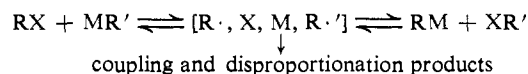
be polarized in the primary reaction, and not in a secondary reaction between *sec*-butyllithium and another iodide molecule. (Because of the polarization phenomenon, the relative intensities do not necessarily reflect relative concentrations.)

The reverse exchange, *sec*-butyllithium and *n*-butyl iodide, proceeds more rapidly, as expected, and gives a polarized spectrum similar to, but weaker than, that shown in Figure 2. In this reaction it is also possible to monitor the simultaneous disappearance of the methyne protons of *sec*-butyllithium and appearance of methylene absorption in *n*-butyllithium, demonstrating that a true halogen-metal exchange occurs.⁵

The reaction between ethyllithium and iodobenzene is more rapid than the other examples and is complete in less than 1 min, giving ethyl iodide (80%) and *n*-butane (20%, based on iodobenzene consumed). Polarization is observed for the methylene protons of the ethyl iodide which is similar in type but opposite in phase to that shown in Figure 1 (*i.e.*, the low-field lines show emission, the high-field lines enhanced absorption). Both the phase of the polarized spectrum and the rapidity of the reaction make it seem likely that the ethyl iodide polarization occurs in the primary reaction rather than in secondary reactions between ethyl iodide and ethyllithium.

In the hetero- and homoexchange reactions of alkyl halides and alkylolithiums reported here the reagents are eventually consumed by coupling and elimination reactions. Ethyllithium and ethyl iodide, for example, give ethane, ethylene, and *n*-butane.⁶ We have shown previously^{2a} that the similar reaction between *n*-butyllithium and *n*-butyl bromide proceeds by a radical path,⁷ and indeed the protons in the butane formed in the above case also show strong polarization.

These data are all consistent with a mechanism in which a one-electron transfer gives a caged radical pair (in which polarization occurs) which can react further in a variety of ways. Transfer of a second



electron gives halogen-metal exchange and a new halide with protons polarized.⁸ Reversal of the initial one-electron transfer returns the reagents with protons in the halide polarized. The coupling and dispro-

(5) Polarization is not observed in the protons of the organolithium compounds for reasons that are not yet clear. An intriguing possibility is the intermediacy of an alkyl radical-lithium iodide complex [L. Y. Tan and G. C. Pimentel, *J. Chem. Phys.*, **48**, 5202 (1968)] formed specifically from the alkylolithium compound. Such a complex might have a much shorter electron spin relaxation time than a free alkyl radical with corresponding decrease in nuclear polarization.

(6) In fact the observation of polarization of iodide molecules in a homoexchange reaction requires concurrent secondary reactions. In the absence of such secondary reactions the system rapidly reaches thermal equilibrium and enhanced absorption and emission cannot occur.

(7) Halogen-metal exchange is not expected to be important in this system, and polarization of the reactant bromide is neither expected nor observed.

(8) (a) We have not investigated the stereochemistry of the exchange, but the proposed mechanism is in reasonable accord with the observation that 2-iodooctane exchanges with *sec*-butyllithium with 20% retention and 80% racemization (R. L. Letsinger, *J. Amer. Chem. Soc.*, **72**, 4842 (1950)). (b) A similar mechanism for halogen-metal exchange has been proposed by C. G. Screttas (Ph.D. Dissertation, University of Tennessee, 1966).

portionation products most probably proceed from such a caged radical pair.⁹

This system provides one more example of what we believe to be a number of reactions in which a formal two-electron transfer can be more accurately described as two one-electron steps.¹⁰

(9) (a) In the case where R and R' are different groups the situation is actually more complicated than pictured above. During the course of reaction the system contains two organolithiums and two organohalides which may therefore undergo a total of four different sets of reactions of the above type. Since these will in general proceed at different rates, the over-all kinetic behavior of the system is very complex and is poorly understood at present. (b) Other reactions of the radicals are also possible, for example, an iodine transfer to give a polarized alkyl iodide and a new free radical.¹¹

(10) A similar suggestion has been offered by K. A. Bilevitch, N. N. Bubnov, and O. Yu. Okhlobystin, *Tetrahedron Letters*, 3465 (1968).

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Free Radical Iodide-Lithium Interchange¹

Sir:

The recent method for detecting unpaired electron precursors of reaction products through emission in the proton magnetic resonance spectra (pmr)^{2,3} has allowed us to show that interchange reactions between iodoalkanes and alkyllithium reagents involve an unpaired electron intermediate.

The systems considered include *n*-butyllithium reactions with 1-iodobutane (Figure 1e) or 2-iodopropane (Figure 1b-d) in the presence, or absence, of a Lewis base.⁴ Figure 1a shows the locations of the normal halide chemical shifts⁵ for a mixture of 2-iodopropane, δ 4.26 (septet, 1) and 1.83 (d, 6), and 1-iodobutane, 3.17 (t, 2), 1.5 (m, 4), and 0.8 (m, 3). In addition, *n*-butyllithium (Foote Mineral Co.) contributes a triplet at δ -0.83 ppm⁶ and the solvent, hexane, strongly absorbs in the region δ 1.7-0.7 ppm. Although *n*-butyllithium and 1-iodobutane react slowly without a Lewis base, no negative peak, only a distorted (slight upfield decrease and downfield increase) iodomethylene signal, was observed in the absence of the tertiary amine.

Signal combinations differ in upfield or downfield location of the negative portion of multiplets; the

(1) Presented in part before the Division of Organic Chemistry, 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept. 1968, Abstract ORGN 130.

(2) H. R. Ward and R. G. Lawler, *J. Amer. Chem. Soc.*, **89**, 5518 (1967); *Chem. Eng. News*, **46**, 40 (Jan 15, 1968).

(3) A. R. Lepley, *J. Amer. Chem. Soc.*, **90**, 2710 (1968).

(4) Alkyllithium depolymerization reagents: C. G. Screttas and J. F. Eastham, *ibid.*, **87**, 3276 (1965), and references cited therein. Amounts of tetramethylethylenediamine larger than 9 μ l result in uncontrollable 1-iodobutane reactions. Similar results can be obtained with 15-20 μ l of dry triethylamine or anhydrous ethyl ether as catalysts. N,N-Dimethylaniline (0.25 ml) did not significantly enhance the reaction. Very limited amounts of the former reagents have also been used with 2-iodopropane reactions.

(5) Measured with a Varian A-60A. Coupling constants were $J = 7-9$ cps.

(6) The location of this band shifts in the presence of Lewis bases: cf. T. L. Brown, *Advan. Organometallic Chem.*, **3**, 365 (1965).

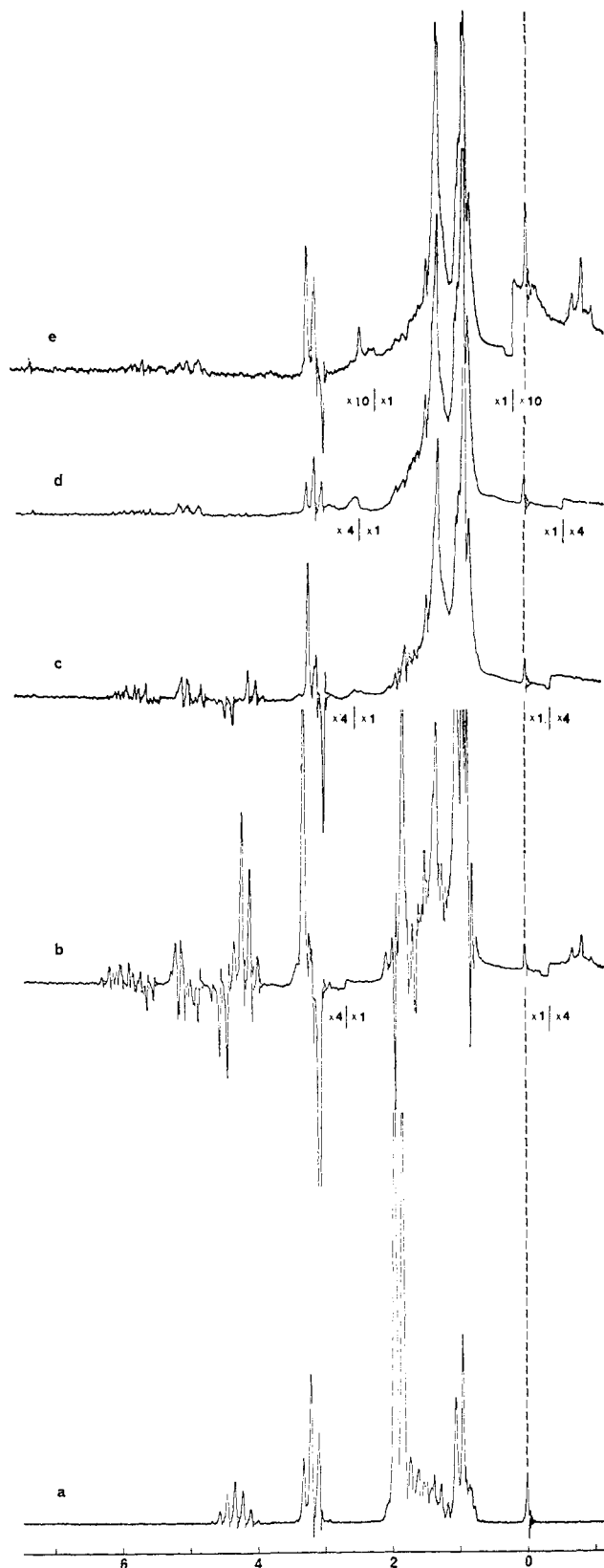


Figure 1. Proton magnetic resonance spectra in the range δ 7.5 to -1 ppm for (a) equimolar quantities of 1-iodobutane and 2-iodopropane in CCl_4 , (b-d) 2.4-min scans started at 2.5, 5.3, and 10 min, respectively, after the addition of 150 μ l of 2-iodopropane to 0.6 ml of 1.5 M *n*-butyllithium in hexane, and (e) 2.4-min scan started at 4.0 min after the addition of 90 μ l of 1-iodobutane to a solution of 7 μ l of tetramethylethylenediamine and 0.6 ml of 1.5 M *n*-butyllithium in hexane. TMS was used as an internal standard; relative amplifications are as shown.