The Reaction of Methyl Radicals with Isobutyryl and α-Deuteroisobutyryl Chlorides
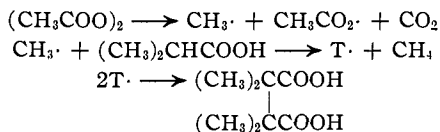
BY CHARLES C. PRICE AND HIROKAZU MORITA[1,2]

The methane formed from reaction of acetyl peroxide with an eightfold excess of isobutyryl chloride containing 60.27 mole % of α-deuterium was 35.9 mole % deuteromethane while that from 24.88 mole % α-deuteroisobutyryl chloride was 14.16 mole % deuteromethane. Analysis of these data indicates that at 100° an α-hydrogen of isobutyryl chloride reacts 1.22 ± 0.2 times as fast as an α-deuterium and 12.4 ± 0.2 times as fast as a β-hydrogen. The methyl free radical thus shows a far greater selectivity in attacking an α-hydrogen than does a chlorine atom, which removes an α- or a β-hydrogen atom of isobutyryl chloride at very nearly the same rate.[3]

Kharasch and Brown[3] have reported that the chlorination of isobutyryl chloride with sulfuryl chloride with benzoyl peroxide catalysis produces 85% of β-chloro- and 15% of α-chloroisobutyric acids. They presented convincing arguments for the following course for this reaction.

$$(ArCO_2)_2 \longrightarrow Ar\cdot$$
$$Ar\cdot + SO_2Cl_2 \longrightarrow ArCl + SO_2 + Cl\cdot$$

$$Cl\cdot + (CH_3)_2CHCOOH \xrightarrow{k\alpha} HCl + (CH_3)_2\overset{|}{\underset{COOH}{C}}\cdot(T\cdot)$$

$$Cl\cdot + (CH_3)_2CHCOOH \xrightarrow{k\beta} HCl + \cdot CH_2\overset{|}{\underset{COOH}{C}HCH_3}(P\cdot)$$

$$T\cdot + SO_2Cl_2 \longrightarrow (CH_3)_2CClCOOH + SO_2 + Cl\cdot$$
$$P\cdot + SO_2Cl_2 \longrightarrow ClCH_2\overset{|}{\underset{COOH}{C}HCH_3} + SO_2 + Cl\cdot$$
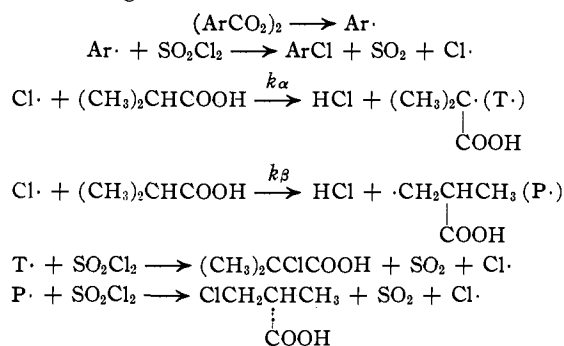
The observed ratio of chlorination products indicates that the six β-hydrogen atoms each react with a chlorine atom at very nearly the same rate as the one α-hydrogen. This is in contrast to the observations of Hass[4] that the tertiary hydrogen atoms in hydrocarbons react with chlorine atoms nearly four times as fast as the primary hydrogens.

Kharasch and Gladstone[5] have reported that the thermal decomposition of acetyl peroxide in isobutyric acid produces an 80% conversion to tetramethylsuccinic acid, based on the scheme

$$(CH_3COO)_2 \longrightarrow CH_3\cdot + CH_3CO_2\cdot + CO_2$$
$$CH_3\cdot + (CH_3)_2CHCOOH \longrightarrow T\cdot + CH_4$$
$$2T\cdot \longrightarrow (CH_3)_2\overset{|}{\underset{(CH_3)_2CCOOH}{C}COOH}$$

To account for the excellent yield of tetramethylsuccinic acid one must presume either that the methyl radical has a much greater selectivity than a chlorine atom in attacking the α-hydrogen, or else, as proposed by Ash and Brown,[6] that the primary radical (P·) is produced but that, in the absence of a material with which it can react readily (as, e.g., sulfuryl chloride), it reacts with isobu-

tyric acid, ultimately abstracting an α-hydrogen to produce the more stable tertiary radical (T·) and regenerating an isobutyric acid molecule.

$$CH_3\cdot + (CH_3)_2CHCOOH \longrightarrow P\cdot + CH_4$$
$$P\cdot + (CH_3)_2CHCOOH \longrightarrow T\cdot + (CH_3)_2CHCOOH$$
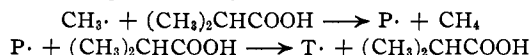
The present investigation of the reaction of acetyl peroxide with isobutyryl chloride isotopically labeled with deuterium in the α-position was undertaken in order to make a choice between these alternative explanations.

Experimental[7]

α-Deuteroisobutyryl Chloride.—Dimethylketene was prepared essentially by the procedure of Staudinger and Klever[8] as modified by vanAlphen.[9] This procedure proved more satisfactory than the preparation and pyrolysis of dimethyl ketene dimer[10] or the pyrolysis of isobutyryl phthalimide.[11]

A 1.5-l. three-necked flask was fitted with a 1-l. dropping funnel, a water-cooled Allihn condenser provided with a receiver immersed in ice, and a nitrogen inlet. Clean 20-mesh zinc (65 g., 1.0 g.-atom) was placed in the flask and the entire apparatus swept with dry nitrogen. Through the dropping funnel a solution of 115 g. (0.5 mole) of α-bromoisobutyryl bromide in 550 ml. of dry ether was added drop by drop onto the zinc. In many instances it was found that the reaction could be initiated more readily by adding a drop of water to the zinc before the addition of the ether solution. The reaction began with the vigorous boiling of ether and the distillate in the ice-cooled receiver consisted of a yellowish green solution of dimethylketene in ether. By occasional mild heating the reaction was continually kept in progress.

When the reaction was completed the colored solution was redistilled into a cooled receiver in order to remove traces of hydrogen bromide and isobutyryl bromide. It was then treated with 5 ml. of water, dried over anhydrous sodium sulfate and fractionally distilled in a flask provided with a Vigreux side arm. The yield of isobutyric acid (b.p. 150–152°) was 9.1 g. (21%).

When 4 ml. of heavy water (90% deuterium, d^{25}_4 1.0968) was used for the hydrolysis of the dimethylketene, the final fractional distillation was carried out in a slow stream of dry nitrogen. The yield of the acid (b.p. 151–153°) was 8.9 g. (20%), n^{25}D 1.3884. Over 100 g. of α-deuteroisobutyric acid was prepared in this way.

Conversion to the acid chloride was accomplished by the action of thionyl chloride on the acid.[12] From 100 g. of the deuterated acid (n^{25}D 1.3878, b.p. 150° (743.5 mm.)) and 165 g. of freshly redistilled thionyl chloride, 84.1 g. of the acid chloride (b.p. 90–91°) was obtained. For use in subsequent work the acid chloride was fractionally distilled twice through a 40-cm. glass-helices packed column provided with a partial take-off condensation head. For density determinations three successive 5-ml. samples of the

(1) Abstracted from the Ph.D. dissertation of Hirokazu Morita, June, 1952.

(2) Contribution from the Radiation Project of the University of Notre Dame, supported in part under Atomic Energy Commission Contract No. At(11-1)38.

(3) M. S. Kharasch and H. C. Brown, THIS JOURNAL, 61, 2142 (1939).

(4) See H. B. Hass in "The Science of Petroleum," 1st Ed., Oxford Univ. Press, New York, N. Y., 1938, pp. 2787-2794.

(5) M. S. Kharasch and M. T. Gladstone, THIS JOURNAL, 65, 15 (1943).

(6) A. B. Ash and H. C. Brown, Record Chem. Prog., 9, 81 (1948),

(7) We are deeply indebted to Dr. W. H. Urry and Frank W. Stacey of the University of Chicago for all the deuterium analyses by combustion and flotation density determination of the resulting water.

(8) H. Staudinger and H. W. Klever, Ber., 39, 968 (1906).

(9) J. vanAlphen, Rec. trav. chim., 43, 823 (1924).

(10) L. L. Miller and J. R. Johnson, J. Org. Chem., 1, 135 (1936).

(11) C. D. Hurd and M. F. Dull, THIS JOURNAL, 54, 2432 (1932).

(12) Org. Syntheses, 25, 58 (1945).

middle fraction (b.p. 90.3° (743.5 mm.), n^{25}D 1.4042) were taken.

Density determinations were performed by the use of a 5-ml. calibrated Lipkin pycnometer.[13] The density of isobutyryl chloride was found to be 1.0084 ± 0.0004 at 25.0° and that of the α-deuteroisobutyryl chloride was 1.0139 ± 0.0004. The formula of McLean and Adams,[14] where N_D

$$d_D = d_H \left[\frac{1 - N_D (1.006)}{M} \right]$$

is the number of deuterium atoms, M is the molecular weight of the hydrogen compound, and d_D and d_H the densities of the deuterated and hydrogen compounds, respectively, gave the deuterium content of the acid chloride as 60.44 mole %.[15] A sample, diluted threefold with redistilled isobutyryl chloride, was analyzed by combustion[7] and indicated the deuterium content to be 60.27 mole %.

Acetyl Peroxide.—In a clean dry 300-ml. erlenmeyer flask, immersed in a salt-ice cooling mixture, were placed 20 g. (0.2 mole) of acetic anhydride, then 100 ml. of sodium-dried ether followed by 10 g. (0.13 mole) of C.P. sodium peroxide. With occasional shaking, 35 g. of ice was added at such a rate that the temperature was kept well below 5°. When the addition was completed (15 minutes), the mixture was stirred for a few minutes, the ether solution carefully decanted off (behind a safety glass) and dried over anhydrous calcium chloride. When the dried solution was immersed in Dry Ice–acetone freezing mixture overnight, colorless crystals precipitated.

The crystalline acetyl peroxide was separated by decantation from most of the ether and the residue evacuated *at 1 mm. pressure or lower* by means of a high vacuum pump. When all traces of the ether had been removed, 25.0 g. of cold isobutyryl chloride was added and the resulting solution set aside in the cold. This solution of acetyl peroxide was kept in the cold until ready for use.

The peroxide content of the solution was determined iodimetrically according to the procedure of Kokatnur and Jelling[16] using 0.10 N standard sodium thiosulfate. An aliquot portion of the peroxide solution (1 ml.) was added to 30 ml. of 99% isopropyl alcohol followed by 1 ml. of saturated potassium iodide and 1 ml. of glacial acetic acid. This mixture was boiled for several minutes and the warm solution titrated directly with standardized thiosulfate solution to the disappearance of the yellow color. The yield of the peroxide on the basis of this titration amounted to 6.2 g. or 31% of the theoretical.

An alternative method for the preparation of the peroxide was employed in which barium peroxide was used as the reagent. A suspension of 23 g. of barium peroxide in 30 ml. of ice-cold water was shaken for a few minutes. In a 300-ml. erlenmeyer flask, 20 g. (0.2 mole) of acetic anhydride was added to 100 ml. of ether and the flask cooled in a salt-ice mixture. The cold suspension of barium peroxide was then gradually added with gentle shaking over a period of 10 minutes. The mixture was kept below 5° and shaken for about 10 minutes when most of the barium peroxide appeared to have reacted. The ether layer was carefully decanted, dried over anhydrous calcium chloride and the resulting dry ether solution treated as in the sodium peroxide procedure. Titration with 0.10 N thiosulfate solution indicated the yield of the peroxide to be 7.1 g. (61% of the theoretical).
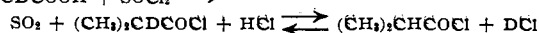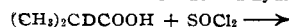
Decomposition of Acetyl Peroxide in Isobutyryl Chloride. —The decomposition was carried out in an apparatus similar to that used by Jensen.[17] It consisted of a 250-ml. three-necked flask provided with a 60-ml. dropping funnel, a mercury-sealed stirrer and an outlet for the gaseous products. The latter were led through a short water-cooled con-

denser to return any unreacted isobutyryl chloride to the reaction vessel, then to a trap kept at 0°, followed by a Dry Ice–acetone trap. The uncondensed gases were then passed through a tube containing Michler ketone in order to remove hydrogen chloride and next through several tubes of soda lime to absorb carbon dioxide, and finally through a calcium chloride drying tube so as to collect dry methane for analysis or alternatively the methane was bubbled through a saturated brine solution into an eudiometer.

Isobutyryl chloride (25 g.) was placed in the reaction flask and the entire apparatus swept with dry nitrogen for a few minutes. The flask was then heated by means of a hot water-bath kept at 100° and, with the stirrer in motion, a solution of 7.5 g. (0.064 mole) of acetyl peroxide in 25 g. of isobutyryl chloride was added drop by drop by means of the dropping funnel. The addition required about 40 minutes. When this addition was completed the reaction was allowed to proceed for another 20 minutes. From time to time the evolved methane was bubbled through a 5% solution of silver nitrate in order to detect any hydrogen chloride present. Negative tests were obtained. The volume of water displaced in the eudiometer tube was 1315 ml. (temperature of brine solution, 23.5°, barometric pressure 746 mm.) or 0.059 mole of methane.

The final liquid reaction mixture was distilled through a 45-cm. glass-helices packed column to remove isobutyryl chloride, first at atmospheric pressure, then at 150 mm. The pressure was slowly reduced to 20 mm., when a dark brown tarry residue remained. This residue was subjected to vacuum distillation at 3 mm. pressure to produce a white wax-like solid; yield 2.7 g., m.p. 138–142°. This was shown to be tetramethylsuccinic anhydride since hydrolysis with hot water gave tetramethylsuccinic acid, m.p. 188–189°. Thus from 0.064 mole of acetyl peroxide and 0.47 mole of isobutyryl chloride, 0.0173 mole (27% yield based on the peroxide, 59% based on methane formed) of tetramethylsuccinic anhydride was obtained.

No quantitative determinations of carbon dioxide or acetyl chloride and methyl acetate were attempted as these have been reported elsewhere.[17] However the liquid in the Dry Ice trap (b.p. 52–56°) presumably was a mixture of ester and acid chloride.

Decomposition of Acetyl Peroxide in 60.27 Mole % α-Deuteroisobutyryl Chloride.—The decomposition of 7.2 g. (0.062 mole) of the peroxide in 50 g. (0.47 mole) of α-deuteroisobutyryl chloride (d^{25}_4 1.0139, n^{25}D 1.4042, 60.27 mole % α-deuteroisobutyryl chloride) was carried out as described above. When the reaction was completed the entire apparatus was swept with dry nitrogen. The first 100 ml. of the gas was rejected and the ensuing gases were collected for analysis in the following order: two 25-ml. dry samples for mass spectrographic analysis and three 500-ml. samples for combustion analysis. From the residue, 1.94 g. of tetramethylsuccinic anhydride (m.p. 138–141°) was isolated.

The deuterium content of the acid chloride as well as the deuteromethane was made by the combustion and flotation temperature analysis at Prof. W. H. Urry's laboratory.[7] The sample of the deuteroacid chloride submitted for analysis was made up from 2 ml. of the deuteroacid chloride and 4 ml. of freshly redistilled isobutyryl chloride, the volumes being measured with a 2-ml. capacity standardized Fisher pipet. Analysis of this diluted sample gave 2.87 mole % of deuterium oxide which is equivalent to 20.09 mole % of the deuteroacid chloride. Since the dilution was threefold, the original stock solution contained 60.27 mole % α-deuteroisobutyryl chloride.

Analysis of the deuteromethane obtained from the peroxide decomposition in this 60.27 mole % α-deuteroisobutyryl chloride gave 8.80 mole % D₂O or 35.2 mole % deuteromethane. A mass spectrographic analysis of the same methane sample gave 36.5 mole %. This latter analysis was by the Consolidated Engineering Corporation, Pasadena, Cal.

Decomposition of Acetyl Peroxide in 24.88 Mole % α-Deuteroisobutyryl Chloride.—The 24.88 mole % deutero compound was prepared by dilution of the 60.27 mole % stock solution. After dilution, the acid chloride was redistilled immediately before use. The exact deuterium content was determined from a sample made up by pipetting 3 ml. of this redistilled deuteroacid chloride into 1 ml. of freshly distilled isobutyryl chloride. Analysis of this diluted α-deuteroisobutyryl chloride gave 18.87 mole % deutero compound. Therefore the original sample contained 24.88 mole % α-deuteroisobutyryl chloride.

(13) M. R. Lipkin, J. A. Davison, W. T. Harvey and S. S. Kurtz, Jr., *Ind. Eng. Chem., Anal. Ed.*, **17**, 55 (1944).

(14) A. McLean and R. Adams, THIS JOURNAL, **58**, 864 (1936).

(15) The fact that the value is so much lower than the deuterium content of the heavy water used may be due to some exchange between the acid chloride and hydrogen chloride.

(CH₃)₂CDCOOH + SOCl₂ ⟶

SO₂ + (CH₃)₂CDCOCl + HCl ⇌ (CH₃)₂CHCOCl + DCl

(16) V. R. Kokatnur and M. Jelling, THIS JOURNAL, **63**, 1432 (1941).

(17) E. V. Jensen, Ph.D. Thesis, Univ. of Chicago (1944); M. S. Kharasch, E. V. Jensen and W. H. Urry, *J. Org. Chem.*, **10**, 386 (1945).

When 7.4 g. (0.063 mole) of acetyl peroxide was decomposed in 50 g. (0.47 mole) of 24.88 mole % α-deuteroisobutyryl chloride (n^{25}D 1.4050), the analysis of three samples of the deuteromethane by the combustion-flotation-temperature technique[7] gave 14.25 mole %, 14.20 mole %, and 14.04 mole % deuteromethane, or an average of 14.16% deuteromethane.

Discussion

If we represent the rate of methyl radical attack on the α-deuterium as k_α^d, that on the α-hydrogen as k_α and that on the β-hydrogen as k_β, then the rates of formation of methane and deuteromethane may be expressed as

$$d[CH_4]/dt = k_\alpha[H_\alpha][CH_3\cdot] + k_\beta[H_\beta][CH_3\cdot] \quad (1)$$

$$d[CH_3D]/dt = k_\alpha^d[D_\alpha][CH_3\cdot] \quad (2)$$

The ratio of deuteromethane to methane formed then becomes

$$d[CH_3D]/d[CH_4] = k_\alpha^d[D_\alpha]/(k_\alpha[H_\alpha] + k_\beta[H_\beta]) \quad (3)$$

Since the extent of reaction in the work reported here never exceeded 12%, and since the relative concentrations of α-deuterium, and of α- and β-hydrogen therefore do not vary appreciably during the course of the reaction, the equation (3) will actually closely approximate the observed composition of the methane formed. Expressed as mole fraction of deuteromethane, this may then be written as
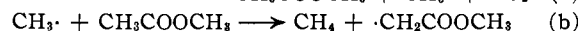
$$[CH_3D] = k_\alpha^d[D_\alpha]/(k_\alpha[H_\alpha] + k_\beta[H_\beta] + k_\alpha^d[D_\alpha])$$
$$= [D_\alpha]/\{(k_\alpha/k_\alpha^d)[H_\alpha] + (k_\beta/k_\alpha^d)[H_\beta] + [D_\alpha]\} \quad (4)$$

Substitution of the experimental data in equation (4) ([CH$_3$D] = 0.359, [D$_\alpha$] = 0.603, [H$_\alpha$] = 0.397, [H$_\beta$] = 6 and [CH$_3$D] = 0.1416, [D$_\alpha$] = 0.249, [H$_\alpha$] = 0.751, [H$_\beta$] = 6) and solution of the two simultaneous equations thus obtained gives values for $k_\beta/k_\alpha^d = 0.098 \pm 0.01$ and $k_\alpha/k_\alpha^d = 1.22 \pm 0.2$, from which $k_\alpha/k_\beta = 12.4 \pm 0.2$. The magnitude of experimental error indicated was estimated by inserting in equation (4) the high and low limits of deuteromethane observed in the two different experiments, [CH$_3$D] = 0.365 and 0.1404, respectively.[18]

It is of interest to note that the ratio of reactivity of α-hydrogen to α-deuterium is very much less than that reported by Urry[19] for isobutyric acid (4.3). Urry, however, assumed he could neglect methyl radical attack on the β-hydrogen atoms. If we treat our data on the basis of the same assumption, we get a ratio of 2.7 from the 60.27 mole % experiment.

Our data indicating that the α-hydrogen in isobutyryl chloride is twelve times as reactive as a β-

(18) The precision indicated does not include systematic errors, for example, the possibility of reaction of acetate formed from peroxide decomposition with methyl radicals.

$$CH_3\cdot + (CH_3COO)_2 \longrightarrow$$
$$CH_3COOCH_3 + CH_3\cdot + CO_2 \quad (a)$$
$$CH_3\cdot + CH_3COOCH_3 \longrightarrow CH_4 + \cdot CH_2COOCH_3 \quad (b)$$

If we assume (a) that methyl radicals do not react with acetyl peroxide to generate methane but by induced decomposition (reaction a), (b) that all the peroxide fragments which do not become methane become acetate in our reaction mixture and (c) that the reactivity of each primary α-hydrogen in reaction b is approximately one-fourth that of the tertiary α-hydrogen in isobutyryl chloride we can correct equation (4) for the generation of methane by reaction b. The values of the three rate ratios then become $k_\beta/k_\alpha^d = 0.086$, $k_\alpha/k_\alpha^d = 1.25$ and $k_\alpha/k_\beta = 14.6$.

(19) W. H. Urry, 12th Org. Chem. Symp., Denver, June, 1951.

hydrogen is in reasonable accord with data obtained by Colton[20] from studies on β-deuteropropionic acid, indicating attack by a methyl radical at the α-hydrogen in propionic acid is favored by a factor of 7.8. By the same technique on β-deuteroethylbenzene, Colton[20] found that the α-hydrogen in ethylbenzene was eleven times more reactive than the β.

The data on isobutyryl chloride reported herein indicate that at least the major part of the tertiary isobutyryl radicals (T$\cdot$) which dimerize to form tetramethylsuccinic acid was produced by favored attack of the methyl radical on the α-hydrogen atoms. Since the reactivity ratio reported here indicates that the direct methyl radical attack will produce 67% T$\cdot$ and 33% P$\cdot$, and since we have obtained a 59% yield of tetramethylsuccinic acid (based on methane formed), while Kharasch, Jensen and Urry[17] report a 60% yield on the same basis, it is not possible to state whether the exchange involving isomerization of P$\cdot$ to T$\cdot$, as proposed by Ash and Brown,[6] does in fact occur.

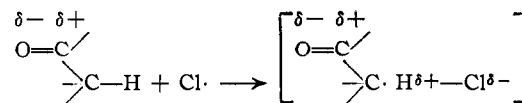In work on the chlorination of 2-methylpropane-2-d and α-d_1-toluene, reported since the completion of our experiments, Brown and Russell[21] have found that no exchange between radicals occurs in the chlorine atom attack on these compounds. From the relative reactivity toward a chlorine atom of primary hydrogen to tertiary (1 to 4.5) and of primary hydrogen to deuterium (1 to 2.55) the relative reactivity of tertiary hydrogen to tertiary deuterium in their system is 1.8 to 1.

It is of some interest to speculate on the origin of the selective factors involved in radical and atom attack on hydrogen atoms. Certainly in the process

$$\text{>C—H} + X\cdot \longrightarrow \text{>C}\cdot + H—X$$
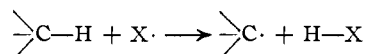
one of the important factors will be the relative stability of the new carbon radical formed. Since in isobutyryl chloride the tertiary hydrogen is also located in such a position that the resulting radical can be stabilized by resonance, it is not too surprising that the factor of fourfold for tertiary hydrogen vs. primary in isobutane is increased to 17.2 in isobutyryl chloride when X is a methyl radical.

The reason for the decrease of the factor to unity in isobutyryl chloride when X is a chlorine atom must involve an electrical effect in the transition complex.

$$\begin{array}{cc} \delta- \quad \delta+ \\ O=C \\ \text{>C—H} + Cl\cdot \end{array} \longrightarrow \left[\begin{array}{c} \delta- \quad \delta+ \\ O=C \\ \text{>C}\cdot \ H^{\delta+}—Cl^{\delta-} \end{array} \right]$$

Contributions of the bracketed structure to the transition state would involve unfavorable orientation of the strong carbonyl and incipient hydrogen chloride dipoles, a factor which would decrease the ease of attack on the α-position by chlorine relative to methyl.[22]

NOTRE DAME, INDIANA

(20) F. C. Colton, Ph.D. Thesis, Univ. of Chicago, June, 1950.

(21) H. C. Brown and G. A. Russell, THIS JOURNAL, 74, 3995 (1952).

(22) F. R. Mayo and C. Walling (Chem. Revs., 46, 269 (1950)) have suggested that such electrical factors may have important influences on radical displacement reactions.