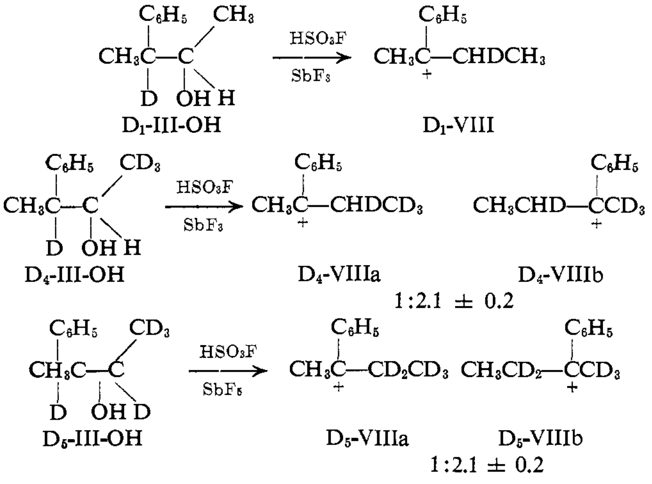
and a sharp singlet for H_3O^+ appears at δ 9.96. The benzylic ion with an identical spectrum was also generated independently in this medium from phenylethylmethylcarbinol.

When *threo*-III-OH in FSO_3H-SbF_5 at −60°, at different stages of conversion to benzylic ion, was quenched[8] by addition of this solution through a Dry Ice jacketed syringe to a rapidly stirring solution of SO_2–6 *N* aqueous KOH (9:1, v/v) at −78°, only mixtures of *threo*-III-OH and phenylmethylethylcarbinol (IX) with *ca.* 30% recovery were obtained with <1% of the recovered alcohols being *erythro*-III-OH (vpc). When *erythro*-III-OH solutions were quenched in the same way, only mixtures of *erythro*-III-OH and benzylic alcohol IX were obtained with <1% *threo*-III-OH (vpc).

Detailed information on the mechanism of formation of the benzylic ion from 3-phenyl-2-butanol was obtained with deuterated alcohol specimens prepared by conventional methods. The FSO_3H-SbF_5 solution of *erythro*-D_1-III-OH decomposes at −50° to give D_1-VIII with the β-methyl signal appearing as a clear doublet. When *threo*-D_4-III-OH is extracted into FSO_3H-SbF_5 from CH_2Cl_2 at −78° it decomposes at −50° to a mixture of D_4-VIIIa and D_4-VIIIb in which the ratio of phenyl-shifted D_4-VIIIb to phenyl-unshifted D_4-VIIIa is *ca.* 2.1 ± 0.2. *threo*-D_5-III-OH under the same conditions decomposes to a mixture of D_5-VIIIa and D_5-VIIIb in which the ratio of phenyl-shifted D_5-VIIIb to phenyl-unshifted D_5-VIIIa is again *ca.* 2.1 ± 0.2. A methylene proton signal is absent, and the β-methyl signal appears as a clear singlet at δ 1.60. The appearance of the proton signals for the α- and β-methyl groups and the methylene group in the case of the labeled systems, especially the D_5-III-OH, as well as the observed integrations, indicate very little or no extraneous proton exchange or scrambling.



$$CH_3C(C_6H_5)(D)-C(CH_3)(OH)H \xrightarrow[SbF_5]{HSO_3F} CH_3\overset{+}{C}(C_6H_5)-CHDCH_3$$

D_1-III-OH D_1-VIII

$$CH_3C(C_6H_5)(D)-C(CD_3)(OH)H \xrightarrow[SbF_5]{HSO_3F} CH_3\overset{+}{C}(C_6H_5)-CHDCD_3 \quad CH_3CHD-\overset{+}{C}(C_6H_5)CD_3$$

D_4-III-OH D_4-VIIIa D_4-VIIIb

1:2.1 ± 0.2

$$CH_3C(C_6H_5)(D)-C(CD_3)(OH)D \xrightarrow[SbF_5]{HSO_3F} CH_3\overset{+}{C}(C_6H_5)-CD_2CD_3 \quad CH_3CD_2-\overset{+}{C}(C_6H_5)CD_3$$

D_5-III-OH D_5-VIIIa D_5-VIIIb

1:2.1 ± 0.2

The high degree of phenyl scrambling indicates predominant phenyl participation (k_Δ) in the ionization step to give phenonium ion VI. Hydrogen-assisted ionization (k_H) leading directly to benzylic ion VIII would leave the phenyl group unshifted. Simple ionization (k_s) to give open secondary carbonium ion as a predominant process predicts competing hydrogen and phenyl migration to secondary carbon[2] and therefore diminished phenyl scrambling. Since phenonium ion accumulation is too small to allow direct nmr observation, ionization must be slower than conversion of phenonium ion VI to benzylic ion VIII. The rate-determining step must be initial heterolysis of the C–O bond, probably of ROH_2^+ species IV, present in low concentration in equilibrium with the unreactive diprotonated species V.

In order to give benzylic ion VIII, the phenonium ion must open, presumably reversibly, and rotate, presumably also reversibly, to a conformation favorable to hydride shift. A rather complex blend of deuterium isotope effects produces the VIIIb:VIIIa ratio of benzylic ions from D_5-III-OH and D_4-III-OH. With D_5-III-OH there are secondary deuterium isotope effects due to the CD_3 group on the direction of phenonium ion opening and on the deuteride shift in each of the classical ions. If the over-all β-deuterium isotope effect is as large as 1.28 per deuterium, then $(1.28)^3$ = 2.1 and the observed VIIIb:VIIIa ratio is accounted for. With D_4-III-OH there is a secondary β-deuterium isotope effect from the CD_3 group and a secondary α-deuterium isotope effect due to the D atom on the direction of opening. For the hydride shift, besides the secondary isotope effects from a CD_3 group and an α-D, there is a primary isotope effect due to the fact that H migrates in one open ion and D shifts in the other. The additional effects in D_4-III-OH compared to D_5-III-OH tend to cancel, and this cancelation seems to be quite complete, since nearly the same ratio of VIIIb:VIIIa is formed from D_4-III-OH and D_5-III-OH.

In both solvolysis[2a] of 3-phenyl-2-butyl toluenesulfonate and ionization of the system at hand, k_Δ appears to dominate over k_H and k_s. The solvolyses involve media of considerable nucleophilicity, and the rate constant for conversion to covalent product is too high to permit significant leakage from bridged to open classical ion. In nonnucleophilic FSO_3H-SbF_5 medium no stable covalent product can be formed, and therefore such leakage does occur and prevents accumulation of enough phenonium ion for direct observation. We presently are investigating ways of generating phenonium ions rapidly at much lower temperatures in the hope that ionization may be sufficiently fast relative to phenonium ion decay to permit direct observation of the bridged ions.

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(8) This quenching procedure was suggested to us by Dr. G. A. Olah.

(9) National Institutes of Health Predoctoral Fellow, 1965–1967.

Radical Anions as Intermediates in Substitution Reactions

Sir:

Evidence for the view that radical anions are intermediates in the carbon alkylation of nitroparaffin salts has recently been presented.[1] We now deal with the alkylation of a β-keto ester anion (I), a reaction which, as will become apparent, is also capable of proceeding as a radical-anion process.

Table I describes the variation in yields of carbon and oxygen alkylation products when the sodium salt of

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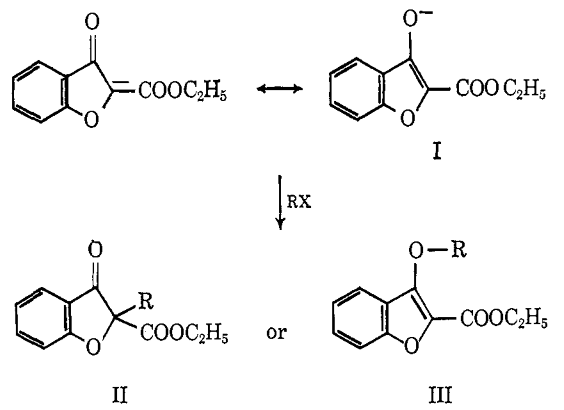
(1) R. C. Kerber, G. W. Urry, and N. Kornblum, *J. Am. Chem. Soc.*, **86**, 3904 (1964); **87**, 4520 (1965).



I is treated with benzyl, *m*-nitrobenzyl, and *p*-nitrobenzyl halides. It will be seen that all three iodides give identical yields of products (73% C and 18% O) and all three bromides give 65% C and 27% O. However, while benzyl chloride and *m*-nitrobenzyl chloride both yield 40% C and 51% O, *p*-nitrobenzyl chloride gives 90% C and 2% O. Here, just as in the alkylation of nitroparaffin salts,[1] the conjunction of a *p*-nitro group and a difficultly displaced leaving group (chloride) produces a dramatic increase in the amount of carbon alkylation.[2]

Table I. Yields of Products on Alkylating I[a]

Halide	Benzyl % C	Benzyl % O	*m*-Nitrobenzyl % C	*m*-Nitrobenzyl % O	*p*-Nitrobenzyl % C	*p*-Nitrobenzyl % O
Cl	40	50	40	52	90	2
Br	64	29	65	28	66	24
I	72	18	73	18	74	19

[a] In DMF at 0°; 0.1 M in sodium salt of I and in halide; all values the average of at least two runs.

Table II. Rates of Reaction of the Sodium Salt of 2-Carbethoxycoumaran-3-one (I)[a]

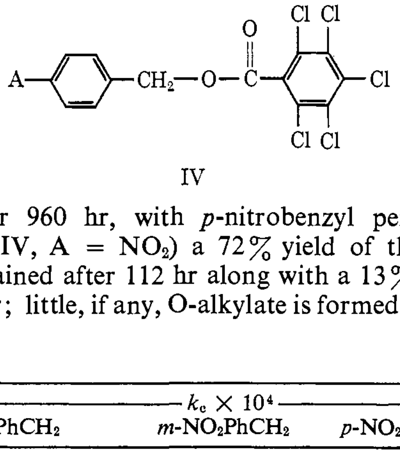
Halide	$k \times 10^4$ Benzyl	$k \times 10^4$ *m*-Nitrobenzyl	$k \times 10^4$ *p*-Nitrobenzyl
Cl	0.08	0.19	30
Br	13	49	53
I	200	440	440

[a] In DMF at 0°; 0.10 M both in salt and halide; k in units of M^{-1} sec.$^{-1}$

This increase in carbon alkylation when *p*-nitrobenzyl chloride is employed is accompanied by an equally unambiguous upsurge in rate. The three benzylic iodides react with I at rates which differ by a factor of only 2; for the three bromides the rates differ by a factor of 4. However, while benzyl chloride and *m*-nitrobenzyl chloride differ in rate by a factor of only 2, *p*-nitrobenzyl chloride reacts some 375 times faster than benzyl chloride (Table II).

The uniqueness of the reaction with *p*-nitrobenzyl chloride becomes especially clear when the total rates of Table II are broken down into their carbon and oxygen components by use of the product data in Table I. It then becomes apparent that the large increase in the rate of reaction observed when I is treated with *p*-nitrobenzyl chloride, as compared to that found with benzyl chloride and *m*-nitrobenzyl chloride, derives from a marked increase in the rate of carbon alkylation: the relative rates of carbon alkylation for benzyl, *m*-nitrobenzyl, and *p*-nitrobenzyl iodides are 1:2:2, and for the three bromides the relative rates are 1:4:4. However, with benzyl, *m*-nitrobenzyl, and *p*-nitrobenzyl chlorides the relative rates of carbon alkylation are 1:3:900 (Table III). In contrast, the relative rates of oxygen alkylation exhibit a trivial increase as one goes from benzyl to *m*-nitrobenzyl to *p*-nitrobenzyl.

The abnormal behavior of *p*-nitrobenzyl chloride becomes intelligible on the basis that alkylation of I is an SN2 process except in the case of *p*-nitrobenzyl chloride; here, with a comparatively difficultly displaced leaving group and a nitro group in the *para* position, a new reaction path involving radical anions becomes dominant.[1] Consistent with this view we find that the difference in the behavior of the benzyl and *p*-nitrobenzyl systems is even more striking when a leaving group still more difficult to displace than chloride, the pentachlorobenzoate, is involved. Whereas benzyl pentachlorobenzoate (IV, A = H) is recovered quantitatively after exposure to I in DMF at 25° for 960 hr, with *p*-nitrobenzyl pentachlorobenzoate (IV, A = NO_2) a 72% yield of the C-alkylate is obtained after 112 hr along with a 13% recovery of the ester; little, if any, O-alkylate is formed.



IV

Table III. Rates of Carbon and Oxygen Alkylation of I[a]

Halide	$k_o \times 10^4$ $PhCH_2$	$k_o \times 10^4$ *m*-NO_2PhCH_2	$k_o \times 10^4$ *p*-NO_2PhCH_2	$k_c \times 10^4$ $PhCH_2$	$k_c \times 10^4$ *m*-NO_2PhCH_2	$k_c \times 10^4$ *p*-NO_2PhCH_2
Cl	0.04	0.10	0.6	0.03	0.08	27
Br	4	14	13	8	32	35
I	36	79	75	144	320	325

[a] $k_c = k_{total}$(%C isolated)/100; $k_o = k_{total}$(%O isolated)/100; k values are given as M^{-1} sec^{-1}; in DMF at 0°.

Strong evidence supporting a radical-anion mechanism is provided by experiments in which the sodium salt of I is alkylated with *p*-nitrobenzyl chloride in the presence of electron acceptors.[1] As can be seen from Table IV, electron acceptors suppress carbon alkylation and, significantly, their effectiveness coincides with their ease of reduction: *p*-dinitrobenzene > *m*-dinitrobenzene > nitrobenzene.[3] It is a striking fact that with the most effective suppressor of carbon alkylation, *p*-dinitrobenzene (*p*-DNB), the yield of carbon

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(2) This is especially impressive when it is recognized that a well-defined leaving group effect is operative in these reactions—iodides give the most C-alkylate and chlorides the least [*cf.* also G. Brieger and W. M. Pelletier, *Tetrahedron Letters*, 3555 (1965); W. J. le Noble and J. E. Puerta, *ibid.*, 1087 (1966)]. Whatever its origin, it is important to note that this leaving group effect is completely reversed in the reaction employing *p*-nitrobenzyl chloride.

(3) A. H. Maki and D. H. Geske, *J. Am. Chem. Soc.*, **83**, 1852 (1961).

Table IV. Influence of Electron Acceptors on the Reaction of the Sodium Salt of I with *p*-Nitrobenzyl Chloride[a]

Acceptor (moles/mole of I)	% yield C-Alkylate	% yield O-Alkylate	$t_{1/2}$,[b] hr
None	90	2	0.5
C_6Cl_6 (2)	67	24	2
$C_6H_5NO_2$ (2)	67	26	3
m-DNB (2)	58	36	3
p-DNB (0.1)	47	42	4
p-DNB (1)	46	49	6
p-DNB (2)	44	46	7

[a] At room temperature; 0.1 *M* in sodium salt of I and in halide. [b] Time required for the reaction to go 50% to completion.

alkylate falls to 44% and that of the oxygen alkylate rises to 46%; this is essentially the product distribution obtained with benzyl and *m*-nitrobenzyl chlorides (Table I). Thus, by intercepting the radical-anion intermediate, *p*-DNB blocks the radical-anion reaction of I with *p*-nitrobenzyl chloride while allowing the S_N2 process to continue unchecked. In other words, *p*-DNB increases the proportion of oxygen alkylate by retarding carbon alkylation rather than by facilitating oxygen alkylation. As would be predicted from this view, the rate of reaction of I with *p*-nitrobenzyl chloride is reduced when electron acceptors are present, and the decrease is greatest with *p*-DNB (*cf.* Table IV).

Finally, in contrast to the effect which *p*-DNB has on the reaction of I with *p*-nitrobenzyl chloride, the addition of *p*-DNB to reactions employing benzyl chloride, *m*-nitrobenzyl chloride and bromide, and *p*-nitrobenzyl bromide and iodide is without effect on the product distribution or the rate of these reactions. All these facts are consonant with the proposal that alkylation of I by the various benzylic halides listed in Table I is an S_N2 process, except in the case of *p*-nitrobenzyl chloride.

Acknowledgment. We thank The Petroleum Research Fund, the Explosives Department of Du Pont, and the National Institutes of Health for generous support.

[4] National Institutes of Health Predoctoral Fellow, 1963–1965.

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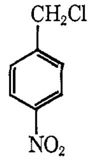
Chain Reactions in Substitution Processes Which Proceed *via* Radical-Anion Intermediates

Sir:

Good grounds exist for considering the alkylation of various anions by *o*- and *p*-nitrobenzylic chlorides, (*e.g.*, II and III) to be radical-anion processes.[1] In this communication we present evidence for the view that these radical-anion substitutions are chain reactions.[2]


II

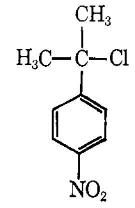

III

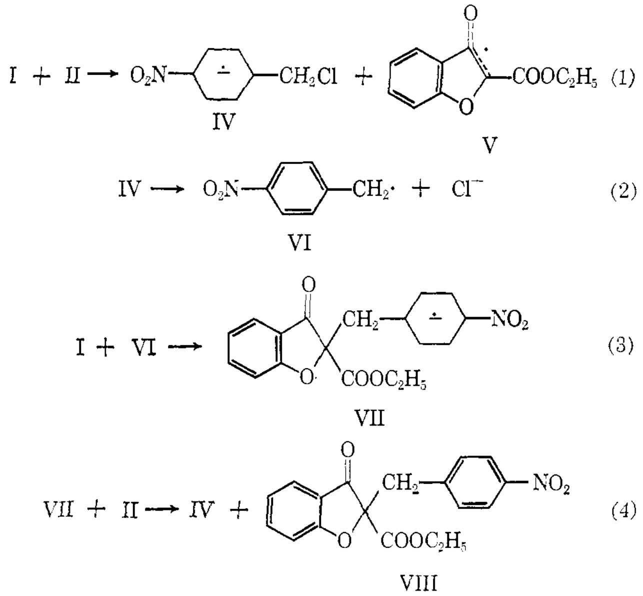
Table I summarizes the effect of cupric salts on the reaction between the sodium salt of 2-carbethoxycoumaran-3-one (I)[1c] and *p*-nitrobenzyl chloride. The consequences of adding 6 × 10^{-6} mole of cupric chloride/mole of I are particularly striking; the product distribution is changed from 90% C- and 2% O-alkylate to 45% C- and 48% O-alkylate and the second-order rate constant falls from 3 × 10^{-3} to 5 × 10^{-5}. Significantly, the product distribution and the rate constant in the presence of this amount of cupric chloride are not very different from that obtained on treating *m*-nitrobenzyl chloride with I; 40% C-, 52% O-, k = 1.9 × 10^{-5} M^{-1} sec^{-1}.[1c] Thus, cupric chloride, although present in only $^1/_{160,000}$ the concentration of *p*-nitrobenzyl chloride and I, is able to suppress the radical-anion reaction while allowing the S_N2 displacement process[1c] to proceed unchecked. It seems probable then that the reaction of *p*-nitrobenzyl chloride with I is a chain process, and the mechanism in Scheme I is proposed.

Table I. The Effect of Cupric Salts on the Product Distribution and Rate of Reaction of the Sodium Salt of 2-Carbethoxycoumaran-3-one (I) with *p*-Nitrobenzyl Chloride[a]

Added salt	Moles of salt/mole of I	% yield C-Alkylate	% yield O-Alkylate	$k \times 10^5$, M^{-1} sec^{-1}
None		90	2	300
$CuCl_2$	6 × 10^{-4}	44	50	
$CuCl_2$	3 × 10^{-4}	38	53	6
$CuCl_2$	6 × 10^{-6}	40[b]	60[b]	2
$CuCl_2$	6 × 10^{-6}	45[c]	48[c]	5[c]
$CuSO_4$	6 × 10^{-6}	88[b]	12[b]	
$CuSO_4$	6 × 10^{-6}	76[c]	15[c]	

[a] At 0° in DMF; both I and the *p*-nitrobenzyl chloride are 0.10 *M*. [b] By nmr. [c] In a Teflon bottle; the rate and product distribution of the uninhibited reaction was the same in glass and in Teflon.

Scheme I



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[1] (a) R. C. Kerber, G. W. Urry, and N. Kornblum, *J. Am. Chem. Soc.*, 87, 4520 (1965); (b) N. Kornblum, T. M. Davies, G. W. Earl, N. L. Holy, R. C. Kerber, M. T. Musser, and D. H. Snow, unpublished work; (c) N. Kornblum, R. E. Michel, and R. C. Kerber, *J. Am. Chem. Soc.*, 88, 5660 (1966).

[2] Dr. Russell has independently reached the same conclusion on different grounds regarding the 2-nitro-2-propyl anion; *cf.* G. A. Russell and W. C. Danen, *ibid.*, 88, 5663 (1966).