The conversion of some of these compounds into other derivatives of biological interest is the subject of the accompanying communication.[14]

[14] G. H. Jones, H. P. Albrecht, N. P. Damodaran, and J. G. Moffatt, *J. Amer. Chem. Soc.*, **92**, 5510 (1970).

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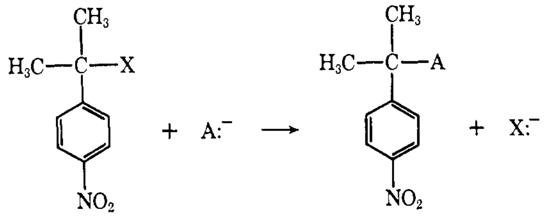
New and Facile Substitution Reactions at Tertiary Carbon. Entrainment

Sir:

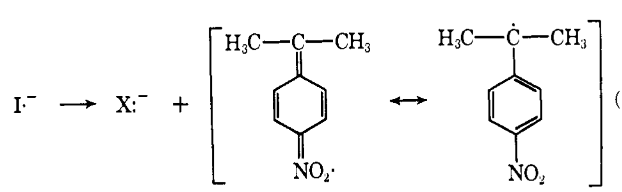
A number of examples of a new type of substitution at a tertiary carbon are now known.[1] Many of these reactions involve *p*-nitrocumyl chloride (Ia) and α,*p*-dinitrocumene (Ib) which undergo substitution by a variety of anions and amines according to eq 1;[1] a chain mechanism, described by eq 2–5 has been proposed.[1]


(1)

Ia, X = Cl
Ib, X = NO₂

II

$$\mathrm{I} + \mathrm{A}:^- \longrightarrow \mathrm{I}\cdot^- + \mathrm{A}\cdot \qquad (2)$$



III

$$\mathrm{III} + \mathrm{A}:^- \longrightarrow \mathrm{II}\cdot^- \qquad (4)$$

$$\mathrm{II}\cdot^- + \mathrm{I} \longrightarrow \mathrm{II} + \mathrm{I}\cdot^- \qquad (5)$$

If these reactions are, indeed, chain processes, then the anions which react most rapidly may well do so because they enter into the initiation step (eq 2) with the greatest facility. In other words, the anions which react most readily with Ia, and with Ib, are those which find it easiest to transfer one electron to the *p*-nitrocumyl system and, thereby, produce the chain carrying *p*-nitrocumyl radicals (eq 2 and 3). Conversely, according to this hypothesis, those anions which react slowly are the ones which have difficulty entering into the initiation step (eq 2).

The mechanism of eq 2–5 assigns not one, but two, roles to the anion. In the chain-propagating sequence (eq 4) the anion adds to the *p*-nitrocumyl radical in a manner reminiscent of the first stage of the Michael reaction;[2] since this is part of a chain-propagating sequence it should be a rapid process.

This point of view leads to the prediction that *p*-nitrocumyl radicals (III) can be intercepted not only by the anions used to produce them but, also, by other anions; that is to say, even those anions which react slowly with *p*-nitrocumyl chloride are able to compete for the *p*-nitrocumyl radicals (eq 4). It follows, then, that a catalytic amount of a reactive nucleophile should be capable of inducing the reaction of a less reactive (or nonreactive) nucleophile with *p*-nitrocumyl chloride (Ia) or α,*p*-dinitrocumene (Ib). As will be seen from the sequel, this prediction is amply fulfilled.

One of our more dramatic examples of entrainment involves α,*p*-dinitrocumene and sodium azide which, in the dark, do not react at all after 48 hr. In contrast, the lithium salt of 2-nitropropane reacts readily with α,*p*-dinitrocumene, the reaction being 87% complete in 3 hr. When α,*p*-dinitrocumene (1 mol) is treated with sodium azide (2 mol) in the presence of the lithium salt of 2-nitropropane (0.1 mol) all the α,*p*-dinitrocumene is consumed after 3 hr and a 97% yield of pure *p*-nitrocumyl azide is obtained. Thus, the 2-nitropropane anion transforms sodium azide from a reagent which does not react to one which reacts completely.

The reaction of α,*p*-dinitrocumene with sodium benzenesulfinate provides another clear example of entrainment. In the dark the reaction proceeds only

Table I. Reactions of α,*p*-Dinitrocumene Entrained by the Lithium Salt of 2-Nitropropane[a]

Anion	Mol % $(CH_3)_2CNO_2^-$ [b]	Time, hr	% reaction	R anion;[c] % yield
$(CH_3)_2CNO_2^-$		3	87	$RC(CH_3)_2NO_2$; 71
N_3^-		48	0	RN_3; 0
N_3^-	5	3	100	RN_3; 97
$C_6H_5SO_2^-$		96	8	$RSO_2C_6H_5$; 8
$C_6H_5SO_2^-$	5	4	100	$RSO_2C_6H_5$; 95[d]
$C_6H_5SO_2^-$	0.8	4	77	$RSO_2C_6H_5$; 75
$^-CH(CO_2C_2H_5)_2$		12	26	$RCH(CO_2C_2H_5)_2$; 26[e]
$^-CH(CO_2C_2H_5)_2$	5	12	53	$RCH(CO_2C_2H_5)_2$; 51[e,f]

[a] In the dark in hexamethylphosphoramide (HMPA). [b] Relative to anion. [c] R = *p*-nitrocumyl. [d] $RC(CH_3)_2NO_2$ also formed; 1% yield. [e] By nmr. [f] $RC(CH_3)_2NO_2$ also formed; 2% yield.

Table II. Reactions of *p*-Nitrocumyl Chloride Entrained by the Lithium Salt of 2-Nitropropane[a]

Anion	Mol % $(CH_3)_2CNO_2^-$ [b]	Time, min	% reaction	R anion;[c] % yield
$(CH_3)_2CNO_2^-$		90	85	$RC(CH_3)_2NO_2$; 53
NO_2^-		90	0	RNO_2; 0
NO_2^-	5	90	100	RNO_2; 93[d]
$C_6H_5SO_2^-$		15	18	$RSO_2C_6H_5$; 18[e]
$C_6H_5SO_2^-$	5	15	100	$RSO_2C_6H_5$; 96[e,f]
Quinuclidine[g]		36[h]	0[i]	[R quinuclidine]+; 0
Quinuclidine[g]	7	36[h]	79	[R quinuclidine]+; 63[j]

[a] In the dark in HMPA. [b] Relative to anion. [c] R = *p*-nitrocumyl. [d] $RC(CH_3)_2NO_2$ also formed; 3% yield. [e] By nmr. [f] $RC(CH_3)_2NO_2$ also formed; 4% yield. [g] In DMSO. [h] Hours. [i] *Cf.* ref 4. [j] $RC(CH_3)_2NO_2$ also formed; 8% yield.

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[1] N. Kornblum and F. W. Stuchal, *J. Amer. Chem. Soc.*, **92**, 1804 (1970).

[2] N. Kornblum, R. E. Michel, and R. C. Kerber, *ibid.*, **88**, 5663 (1966).

Table III. Entrainment in the Reactions of Sodium Benzenesulfinate with α,p-Dinitrocumene[a]

Anion	Entraining anion; mol %[b]	Time, hr	% reaction	R anion;[c] % yield
$^{-}CH(CO_2C_2H_5)_2$[d]		96	64	$RCH(CO_2C_2H_5)_2$; 57
$C_6H_5SO_2^-$[d]		96	8	$RSO_2C_6H_5$; 8
$C_6H_5SO_2^-$[d]	$^{-}CH(CO_2C_2H_5)_2$; 5	48	49	$RSO_2C_6H_5$; 48
$^{-}CH(CO_2C_2H_5)_2$		72	69	$RCH(CO_2C_2H_5)_2$; 65
$C_6H_5SO_2^-$		96	2	$RSO_2C_6H_5$; 1
$C_6H_5SO_2^-$	$^{-}CH(CO_2C_2H_5)_2$; 5	72	35	$RSO_2C_6H_5$; 35
N_3^-[e]		5	99	RN_3; 95[f]
$C_6H_5SO_2^-$[e]		6	32	$RSO_2C_6H_5$; 29
$C_6H_5SO_2^-$[e]	N_3^-; 5	6	67	$RSO_2C_6H_5$; 60[g]

[a] In the dark in DMSO except as otherwise noted. [b] Relative to $C_6H_5SO_2^-$. [c] R = p-nitrocumyl. [d] In HMPA. [e] Exposed to an ordinary fluorescent light. [f] J. W. Manthey, Ph.D. Thesis, Purdue University, 1969. [g] RN_3 also formed; 7% yield.

8% in 96 hr. However, when 5 mol % of the lithium salt of 2-nitropropane is present it goes to completion in 4 hr and gives a 95% yield of p-nitrocumyl phenyl sulfone; indeed, even as little as 0.8 mol % of the lithium salt of 2-nitropropane results in a 75% yield of the sulfone after 4 hr (Table I).

Entrainment is not restricted to reactions employing α,p-dinitrocumene. Thus, although p-nitrocumyl chloride (Ia) and sodium nitrite fail to react after 90 min in the dark, when 5 mol % of the lithium salt of 2-nitropropane is added the reaction goes to completion in 90 min and a 93% yield of α,p-dinitrocumene (Ib) is isolated. And while the reaction of p-nitrocumyl chloride with quinuclidine[3] is exceedingly slow in the dark (after 36 hr[4] none of the alkylated amine is isolated) with 7 mol % of the lithium salt of 2-nitropropane present a 63% yield of the pure alkylated quinuclidine is obtained after 36 hr. Entrainment is also observed in the reaction of sodium benzenesulfinate with p-nitrocumyl chloride (Table II).

While the 2-nitropropane anion is the most effective entraining agent, it is not unique; malonate and azide ions are also able to induce the reactions of other anions (Table III). Nor, as the result with azide ion shows, is entrainment restricted to reactions conducted in the dark.

Entrainment provides powerful support for the radical anion chain mechanism of eq 2–5. The entraining anion initiates chains and the entrained anion carries them along. We have, then, a simple explanation for what would otherwise be an inexplicable phenomenon.

Entrainment is also of interest as regards synthetic organic chemistry for it suggests how the range of these substitution reactions may be extended. Nucleophiles which, on their own, react too slowly to be useful—or which do not react at all—may be caused to react merely by adding a catalytic amount of a reactive nucleophile.

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(3) N. Kornblum and F. W. Stuchal, *J. Amer. Chem. Soc.*, **92**, 1804 (1970).

(4) At this time 6% of the theoretical amount of chloride ion has been liberated but it is virtually all due to dehydrohalogenation.

Synthetic Studies of Amino Acids by the Use of the Copper Complex. I. Syntheses of β-Hydroxy DL-Amino Acids by the Use of the Complex of Copper(II) with the Schiff Base Derived from Glycine and Pyruvic Acid

Sir:

Although the reaction of bis(glycinato)copper(II) (**1**) with aliphatic or aromatic aldehydes under basic conditions, which was first reported by Sato, Okawa, and Akabori,[1] is known to be important for the synthesis of β-hydroxy amino acids,[1-3] the amino acids are produced by the reaction only when the conditions are strongly basic, and hence such conditions are inadequate for the reactions involving aldehydes which easily isomerize or polymerize under basic conditions. The mechanism of this reaction, on the other hand, has generally been assumed to involve the carbanion (**2**) which was produced by the dissociation of the α-hydrogen of **1** attacking the carbonyl group of an aldehyde to give the complex of the resultant amino acid (**3**),[4] as shown in Scheme I. William and Busch[5] clarified by nuclear magnetic resonance study that the proton on the nitrogen atom as well as that on the α carbon of such a complex dissociates even under slightly alkaline conditions. Imado, *et al.*,[6] isolated bis(N-ethylidene-DL-threoninato)copper(II) (**4**) and confirmed its structure by X-ray crystal-structure analysis. However, no regard has been paid to the dissociation of the hydrogens

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(2) K. Okawa and S. Akabori, British Patent 814063 (1959).

(3) Y. Ikutani, T. Okuda, and S. Akabori, *Bull. Chem. Soc. Jap.*, 33, 582 (1962).

(4) A. Nakahara, *Yuki Gosei Kagaku Kyokai Shi*, 27, 951 (1969).

(5) D. H. William and D. H. Busch, *J. Amer. Chem. Soc.*, **87**, 4644 (1965).

(6) (a) Y. Sato, T. Takahashi, S. Imado, and N. Sugimoto, *Yakugaku Zasshi*, **81**, 819 (1961); (b) Y. Sato, K. Kodera, S. Imado, and N. Sugimoto, *ibid.*, **81**, 824 (1961); (c) S. Imado, *ibid.*, **81**, 828, 832, 837 (1961).