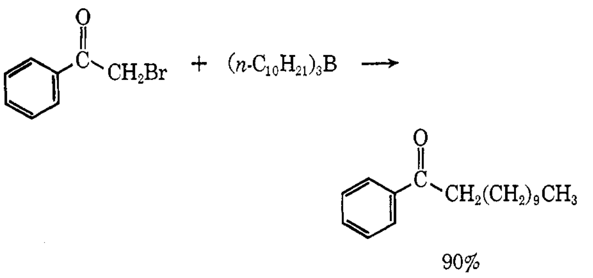

(5)

means of circumventing this difficulty.[11] This solution is currently under study and will be reported shortly.

Representative results are summarized in Table I.

Table I. Reaction of Representative α-Bromo Ketones with Organoboranes under the Influence of Potassium *t*-Butoxide

Bromo ketone[a,b]	Organoborane	R_3B, mmol	Temp, °C	Time, hr	Yield,[c] %
Phenacyl bromide	Triethyl	10	0	0.1	93
	Triethyl	20	0	0.1	100
α-Bromocyclohexanone	Triethyl	10	0	5.0	50
		20	0	0.25	24
				2.0	35
				5.0	50
				12	68
				48	68
α-Bromocyclohexanone	Triethyl	20	25	1.0	55
				d	71
Phenacyl bromide	Tri-*n*-butyl	10	0	0.1	61
		10	0	0.1	75[e]
		20	0	0.1	93
	Tri-*sec*-butyl	20	0	0.1	0
	Triisobutyl	20	0	0.1	0
	Tri-*n*-decyl	20	0	0.1	90

[a] 10.0 mmoles. [b] 10.0 mmoles of potassium *t*-butoxide was used, except where otherwise indicated. [c] Glpc analysis. The yield is based on the bromo ketone. [d] After 24 hr, the analysis revealed a yield of 58% with 10% of residual α-bromo ketone. Addition of 2.0 mmoles of potassium *t*-butoxide raised the product to 71%. [e] Simultaneous addition of the phenacyl bromide and the base to the organoborane.

The synthesis of α-bromocyclohexanone is illustrated by the following procedure. A 1-l. round-bottom flask was equipped with a mechanical stirrer and water condenser. Cupric bromide (223 g, 1.0 mol) was placed in the flask together with 500 ml of a 1:1 mixture of ethyl acetate and chloroform containing 49 g (0.5 mol) of cyclohexanone. The system was attached to a water aspirator, and a pressure sufficient to achieve gentle refluxing of the solvent was maintained. Stirring was then started and the evolution of hydrogen bromide began immediately. After 1 hr, the disappearance of the black cupric bromide was almost complete. The solution was filtered to remove the white precipitate of cuprous bromide and extracted with three 100-ml portions of a saturated solution of sodium bicarbonate. Removal of the solvent and distillation under reduced pressure gave 53 g (60%) of α-bromocyclohexanone, bp 66° (2 mm). A slight red color in the product could be removed by crystallization from pentane at −72°.

The following procedure for the conversion of α-bromocyclohexanone into 2-ethylcyclohexanone is representative. A 50-ml round-bottom flask equipped with septum inlet and magnetic stirring bar was flushed with nitrogen and maintained under a static pressure of the gas. Twenty milliliters of a 1 *M* solution of triethylborane in tetrahydrofuran was injected into the flask followed by 1.78 g (10 mmoles) of α-bromocyclohexanone. The flask was placed in an ice bath and stirring was initiated. Ten milliliters of a 1 *M* solution of potassium *t*-butoxide in tetrahydrofuran was then added dropwise over a period of 5 min. The solution was analyzed periodically for 2-ethylcyclohexanone by glpc, and a yield of 68% after 12 hr of reaction was established.

The same procedure was followed for the experiments with phenacyl bromide. In this case analysis of the reaction mixture immediately following completion of the addition of the potassium *t*-butoxide indicated the reaction was already complete.

Considerable study has been devoted to the halogenation of ketones.[12] In cases where the α-bromo ketone is readily accessible, the present procedure promises to provide a simple means for introducing alkyl substituents without the concurrent formation of polyalkylated materials and, in addition, promises to make it possible to introduce substituents of structural types that cannot now be introduced by the older alkylation procedures. We are currently exploring these possibilities.

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(11) E. F. Knights and H. C. Brown, *J. Am. Chem. Soc.*, **90**, 5280, 5281, 5283 (1968).

(12) H. O. House, ref 1, pp 144–156.

(13) National Science Foundation Postdoctorate Fellow at Purdue University, 1967–1968.

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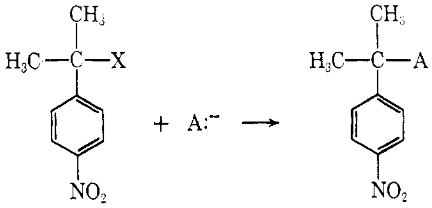
Received August 30, 1968

New and Facile Substitution Reactions at Tertiary Carbon. The *m*-Nitrocumyl System

Sir:

A new type of substitution at a tertiary carbon in which the chlorine of *p*-nitrocumyl chloride (Ia) undergoes replacement by a variety of anions (eq 1) was described in 1967.[1] More recently, a striking set of



(1)

Ia, X = Cl
b, X = NO_2

reactions in which the aliphatic nitro group of α,*p*-dinitrocumene (Ib) is smoothly displaced by a number of anions (eq 1, X = NO_2) was reported.[2] The facility with which Ia and Ib react (eq 1) is in sharp contrast to the lack of reactivity exhibited by cumyl chloride (IIa) and α-nitrocumene (IIb) toward the various anions.[1,2] Similarly, *p*-nitrobenzyl chloride, when treated with the lithium salt of 2-nitropropane,

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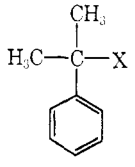
(1) N. Kornblum, T. M. Davies, G. W. Earl, N. L. Holy, R. C. Kerber, M. T. Musser, and D. H. Snow, *J. Am. Chem. Soc.*, **89**, 725 (1967).

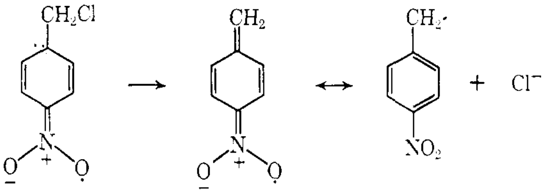
(2) N. Kornblum, T. M. Davies, G. W. Earl, G. S. Greene, N. L. Holy, R. C. Kerber, J. W. Manthey, M. T. Musser, and D. H. Snow, *ibid.*, **89**, 5714 (1967).



IIa, X = Cl
b, X = NO_2

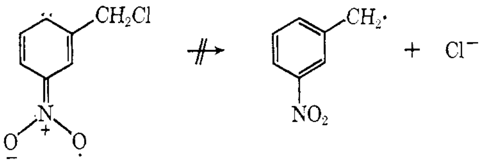
gives the carbon alkylate in 92% yield, whereas benzyl chloride, in common with most halides, gives only the oxygen alkylate (the normal SN2 product).[3] This ability of a *p*-nitro group to foster substitution in the cumyl system and carbon alkylation in the benzyl system is believed to have a common origin, the facility with which radical anions are formed in nitroaromatic systems.[1,2,3c,4]

m-Nitrobenzyl chloride, which would be expected to form radical anions as readily as *p*-nitrobenzyl chloride,[5] does not give any carbon alkylate on treatment with nitroparaffin salts; instead, oxygen alkylation is observed.[3] Here, although radical-anion formation is relatively facile, the next step in the carbon alkylation sequence is not; the radical anion derived from *m*-nitrobenzyl chloride (IV) has no contributing structures corresponding to III and, therefore, elimination of chloride ion by a process analogous to that of eq 2 is not available to radical anion IV (eq 3). The outcome is that SN2 displacement by the nitroparaffin anion (which gives oxygen alkylation) competes successfully with the radical-anion sequence in the case of *m*-nitrobenzyl chloride.[3c,4b,6]



(2)

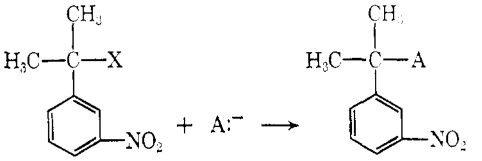
III



(3)

IV

m-Nitrocumyl chloride (Va), being a tertiary chloride, would not be expected to undergo SN2 displacements,[1] and since the radical anion derived from *m*-nitrocumyl chloride is analogous to IV, elimination of chloride ion should be relatively difficult. Nonetheless, when *m*-nitrocumyl chloride (Va) is treated with a solution of sodium thiophenoxide in DMF, a 96% yield of the pure tertiary sulfide VI, A = SC_6H_5, is obtained after 9 hr at 0° (eq 4). At room temperature the sodium salt of diethyl malonate also reacts cleanly with *m*-nitrocumyl chloride in DMF (or in DMSO), giving the tertiary alkylate VI, A = $CH(COOC_2H_5)_2$, in 90–94% yields (eq 4); in the same way, the sodium salt of diethyl *n*-butylmalonate is converted to the tertiary alkylate VI, A = $CH_3CH_2CH_2CH_2C(COOC_2H_5)_2$, in 87% yield (eq 4). Finally, treatment of *m*-nitrocumyl chloride with a solution of sodium azide in hexamethylphosphoramide (HMPA) gives the tertiary azide VI, A = N_3, in 87% yield.



(4)

Va, X = Cl
b, X = NO_2

VI

It is especially impressive that at 25° the aliphatic nitro group of α,*m*-dinitrocumene (Vb) is displaced by anions at easily measurable rates. Thus, Vb, in DMSO, reacts with sodiomalonic ester according to eq 4 to give, in 45 hr, a 96% yield of the alkylated malonic ester VI, A = $CH(COOC_2H_5)_2$; treatment with the sodium salt of *n*-butylmalonate provides the alkylate VI, A = $CH_3CH_2CH_2CH_2C(COOC_2H_5)_2$, in 85% yield. At 45° for 22 hr sodium thiophenoxide in DMF converts Vb into the tertiary sulfide VI, A = SC_6H_5, in 94% yield.

m- and *p*-nitrocumyl compounds differ in their behavior toward ambident anions. Thus, treatment of *m*-nitrocumyl chloride (Va) with sodium nitrite affords a 52% yield of the dinitro compound, *m*-$O_2NC_6H_4$-$C(CH_3)_2NO_2$, along with a 27% yield of *m*-nitrocumyl alcohol[7] (VI, A = OH); this is to be contrasted with the 92–95% yields of dinitro compound, *p*-$O_2NC_6H_4$-$C(CH_3)_2NO_2$, obtained from *p*-nitrocumyl chloride.[1] In HMPA the reaction of the lithium salt of 2-nitropropane with *m*-nitrocumyl chloride gives the carbon alkylate VI, A = $C(CH_3)_2NO_2$, in 33% yield, *m*-nitrocumyl alcohol[7] in 35% yield, and *m*-nitro-α-methylstyrene in 15% yield; in the *p*-nitrocumyl system, reactions employing the lithium salt of 2-nitropropane produce the carbon alkylate in 85–90% yields along with 5–10% yields of *p*-nitrocumyl alcohol.[7] While sodium benzenesulfinate reacts with *m*-nitrocumyl chloride in HMPA to give the sulfone VI, A = $SO_2C_6H_5$ (59% yield), and *m*-nitrocumyl alcohol[7] (11% yield),[8] either *p*-nitrocumyl chloride or α,*p*-dinitrocumene gives the pure sulfone, *p*-$O_2NC_6H_4C(CH_3)_2SO_2C_6H_5$, in 97% yield.[9]

The fact that *m*-nitrocumyl compounds give tertiary substitution products can be rationalized on the following basis: although radical anions derived from Va and Vb are stabilized by delocalization into the *m*-nitro group (*i.e.*, by structures analogous to IV), they are able to supply enough electron density to the carbon holding the side chain to permit elimination of chloride or nitrite ions (eq 5). It is important to recognize that the *m*-nitrocumyl radical produced in eq 5, even though devoid of resonance stabilization by

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[3] (a) L. Weisler and R. W. Helmkamp, *J. Am. Chem. Soc.*, **67**, 1167 (1945); (b) H. B. Hass and M. L. Bender, *ibid.*, **71**, 1767, 3482 (1949); (c) R. C. Kerber, G. W. Urry, and N. Kornblum, *ibid.*, **87**, 4520 (1965).

[4] (a) N. Kornblum, R. E. Michel, and R. C. Kerber, *ibid.*, **88**, 5660 (1966); (b) G. A. Russell and W. C. Danen, *ibid.*, **88**, 5663 (1966).

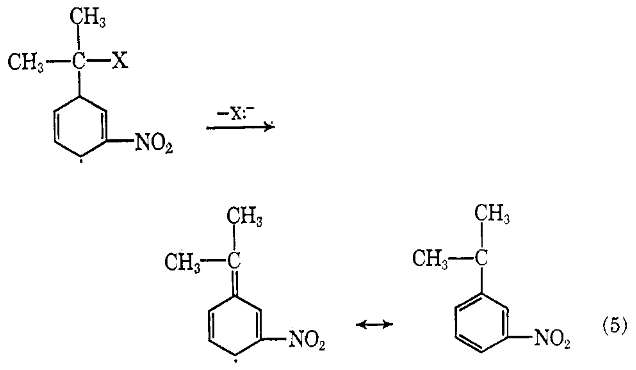
[5] D. H. Geske, J. L. Ragle, M. A. Bambanek, and A. L. Balch, *ibid.*, **86**, 987 (1964).

[6] Similarly, *m*-nitrobenzyl chloride does not undergo radical anion substitution on exposure to the sodium salt of β-hydroxycoumarilic acid ethyl ester.[4a]

[7] Presumably, the alcohol derives from the oxygen alkylate, but this has not been established.

[8] In addition, *m*-nitro-α-methylstyrene is isolated in 12% yield.

[9] These and other differences are discussed briefly in the accompanying communication: N. Kornblum, G. W. Earl, N. L. Holy, J. W. Manthey, M. T. Musser, D. H. Snow, and R. T. Swiger, *J. Am. Chem. Soc.*, **90**, 6221 (1968).



(5)

the *m*-nitro group, is a tertiary cumyl radical and, thus, is distinctly more stable than the benzylic radical of eq 3. Furthermore, in the *m*-nitrocumyl system, in contrast to the *m*-nitrobenzyl system,[3c] the S_N2 displacement does not compete; consequently, the radical-anion sequence can proceed without interference.

Since the reactions of eq 4 do not occur when the *m*-nitro group is replaced by hydrogen,[1,2] it is clear that the *m*-nitro group plays a vital role in bringing about substitution at the tertiary carbon atom, and since the presence of a nitro group is also crucial in the *p*-nitrocumyl system (where considerable evidence has already been gathered supporting the intermediacy of radical anions[1,2]), it is reasonable to assume that the reactions of the *m*-nitrocumyl system also proceed *via* radical anions.[3c]

Acknowledgment. We thank the Petroleum Research Fund and the Explosives Department of Du Pont for generous support.

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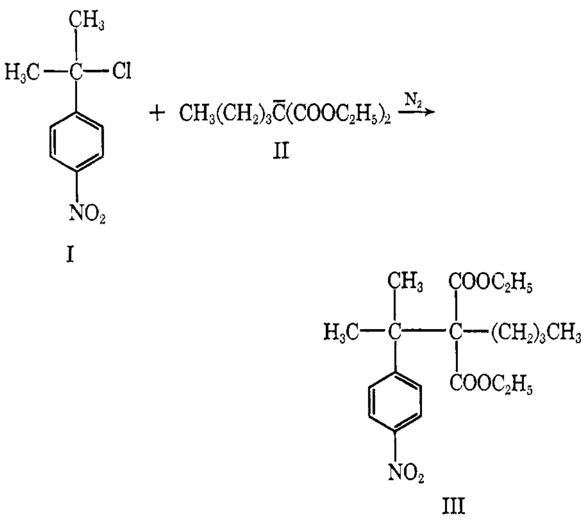
New and Facile Substitution Reactions at Tertiary Carbon. The Use of Oxygen as a Mechanistic Probe

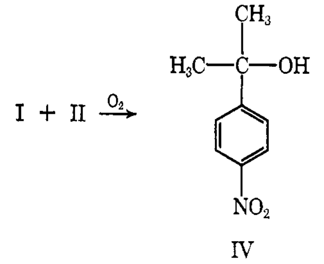
Sir:

In 1967 we reported that the chlorine of *p*-nitrocumyl chloride (I) is readily replaced by a variety of anions.[1] For example, treatment of I with the anion derived from *n*-butylmalonic ester (II) at 25° under nitrogen gives the alkylate III in 89% yield (eq 1). It has now been found that, when the reaction is conducted in the presence of oxygen, alkylation is completely suppressed. Not only is the alkylate III not formed, but, instead, *p*-nitrocumyl alcohol (IV) is isolated in 88% yield (eq 2). It is noteworthy that oxygen does not convert *p*-nitrocumyl chloride (I) to the alcohol IV in the absence of *n*-butylmalonate anion (II).

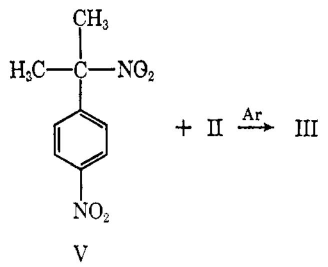
The results obtained with α,p-dinitrocumene (V) are also dramatic: treatment of V with the sodium salt of *n*-butylmalonic ester (II) results in a 98% yield of the alkylate III provided the reaction is carried out under argon (eq 3), but, under oxygen, *p*-nitrocumyl alcohol (IV) is the main product (80% yield) and the alkylate



(1)



(2)



(3)

III is obtained in a mere 6% yield. α,p-Dinitrocumene is, of course, completely stable to oxygen when the *n*-butylmalonate anion (II) is absent.

Suppression of substitution at the tertiary carbon of *p*-nitrocumyl chloride[1] and α,p-dinitrocumene[2] by oxygen is not restricted to reactions which employ the anion of *n*-butylmalonic ester; it is clear from the data of Tables I and II that this is a general phenomenon. It is also evident from Tables I and II that the anion of *n*-butylmalonic ester is not unique in promoting the conversion of *p*-nitrocumyl chloride (I) and α,p-dinitrocumene (V) to *p*-nitrocumyl alcohol (IV).[3]

These facts are easily understood on the basis of the chain mechanism proposed for substitution at the tertiary carbon of the *p*-nitrocumyl system (eq 4–7).[1,2] Oxygen, a very efficient scavenger of carbon free radicals, intercepts the *p*-nitrocumyl radicals (VI) before they undergo reaction 6 and converts them into peroxy radicals (eq 8); substitution is thereby prevented. The peroxy radicals VIII are then usually converted into *p*-nitrocumyl alcohol.[4] However, with sodium azide in

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(1) N. Kornblum, T. M. Davies, G. W. Earl, N. L. Holy, R. C. Kerber, M. T. Musser, and D. H. Snow, *J. Am. Chem. Soc.*, **89**, 725 (1967).

(2) N. Kornblum, T. M. Davies, G. W. Earl, G. S. Greene, N. L. Holy, R. C. Kerber, J. W. Manthey, M. T. Musser, and D. H. Snow, *ibid.*, **89**, 5714 (1967).

(3) The use of oxygen as a diagnostic was suggested to us by the work of G. A. Russell and W. C. Danen [*ibid.*, **88**, 5663 (1966)] who found that the 2-nitropropane anion is oxidized by molecular oxygen when *p*-nitrobenzyl chloride is present; they report, however, that the *p*-nitrobenzyl chloride is not consumed.

(4) G. A. Russell and A. G. Bemis [*ibid.*, **88**, 5492 (1966)] have shown that DMSO + $ROO^- \rightarrow$ $DMSO_2$ + RO^-. Since most of the reactions