of silica gel, the solids were washed with dichloromethane (2 × 10 mL), and the combined filtrate was evaporated to provide crude iodide **15**.

A solution of **15** dissolved in 10 mL of toluene was degassed and then brought under a nitrogen atmosphere, after which 0.5 mL (17 mmol) of tributyltin hydride and a catalytic amount (10 mg) of 2,2'-azobis(2-methylpropionitrile) was added as a radical initiator. The mixture was heated at 80 °C for 3 h, after which the solvent was evaporated, and the crude mixture was chromatographed (silica gel, 5% ether in hexane) to provide 0.16 g of **16** (68% yield overall from **13**).

To a solution of 0.15 g (0.32 mmol) of **16** in 3 mL of THF was added 1 mL of 1 M tetrabutylammonium fluoride in THF. The mixture was stirred, for 16 h under a nitrogen atmosphere, after which the solution was directly chromatographed (silica gel, 50% ether in hexane) to provide 0.065 g of **17** (88% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) 1.2–1.6 (4 H, m), 1.71 (2 H, q, J = 6 Hz), 2.03 (2 H, m), 2.85 (1 H, d, J = 3 Hz, OH), 3.57–3.73 (2 H, m), 3.78 (1 H, m, CHOH), 4.48, 4.50 (2 H, ABq, J = 10 Hz, $CH_2C_6H_5$), 4.89–5.00 (2 H, m, $=CH_2$), 5.77 (1 H, m, CH=), 7.20–7.35 (5 H, m, C_6H_5); ^{13}C NMR ($CDCl_3$, 75 MHz) 24.86 (CH_2), 33.70 (CH_2), 36.42 (CH_2), 36.85 (CH_2), 69.26 (CH_2O), 71.31 (CHOH), 73.33 (CH_2O), 114.48 ($=CH_2$), 127.64 (2 CH), 127.72 (CH=), 128.43 (2 CH), 137.92 (C), 138.76 (CH); MS, M^+ 234; $[\alpha]_D$ -3.2° (*c* 3, CH_3OH). Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.51; H, 9.62.

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Electron-Transfer Substitution Reactions: The *p*-Nitrocumyl System[1]

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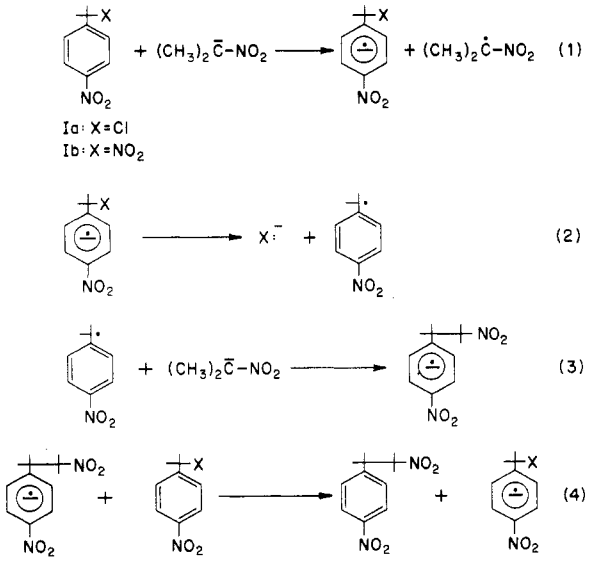
Facile substitution reactions at the tertiary carbon of *p*-nitrocumyl chloride and α,*p*-dinitrocumene are described. These reactions occur with a wide range of organic and inorganic nucleophiles and are noteworthy for providing novel and powerful means of synthesis; they occur readily under mild conditions, give excellent yields of pure products, and, in contrast to S_N2 displacements, are rather insensitive to steric hindrance. They are, therefore, especially valuable for the preparation of highly branched compounds. The view that these are electron-transfer chain processes derives from inhibition studies and, also, from the fact that these reactions are induced by one-electron-transfer agents.

The salts of nitroparaffins are capable of covalency formation at either carbon or oxygen.[2] In 1961 a detailed study of the alkylation reactions of nitroparaffin salts led to the conclusion that oxygen alkylation is a consequence of an S_N2 displacement by the nitroparaffin anion on the alkyl halide.[3] In 1964 it was shown that carbon alkylation derives from an electron-transfer process involving radical anions and free radicals as intermediates.[4a,b] Further evidence for the view that carbon alkylation is an electron-transfer process was reported in 1966, and by this time it had become clear that the carbon alkylation of nitroparaffin salts is a chain reaction. Consequently, the original nonchain mechanism was amended;[4c,d] the resulting chain sequence is illustrated by eq 1–4.

This type of substitution at a saturated carbon atom would constitute an interesting but thoroughly parochial phenomenon were it restricted to reactions of *p*-nitrobenzyl and *p*-nitrocumyl halides with nitroparaffin salts. In actuality electron-transfer chain processes prove to be much more widespread than originally envisaged[5,6] and, in this



(1) Substitution Reactions Which Proceed via Radical Anion Intermediates. 29. Part 28: Kornblum, N.; Kelly, W. J.; Kestner, M. M. *J. Org. Chem.* **1985**, *50*, 4720. This paper is based on the doctoral dissertations of the 12 junior authors. Reference to these theses is made by employing the initials of the author and the date of the thesis. Preliminary communications have appeared in: *J. Am. Chem. Soc.* **1967**, *89*, 725, 5714; **1970**, *92*, 1804, 5513.

(2) (a) Weisler, L.; Helmkamp, R. W. *J. Am. Chem. Soc.* **1945**, *67*, 1167. (b) Hass, H. B.; Bender, M. L. *Ibid.* **1949**, *71*, 1767. (c) Kornblum, N.; Pink, P. *Tetrahedron Suppl. 1* **1963**, *19*, 17.

(3) Kornblum, N.; Pink, P.; Yorka, K. V. *J. Am. Chem. Soc.* **1961**, *83*, 2779.

(4) (a) Kerber, R. C.; Urry, G. W.; Kornblum, N. *J. Am. Chem. Soc.* **1964**, *86*, 3904. (b) Kerber, R. C.; Urry, G. W.; Kornblum, N. *Ibid.* **1965**, *87*, 4520. (c) Kornblum, N.; Michel, R. E.; Kerber, R. C. *Ibid.* **1966**, *88*, 5660, 5662. (d) Russell, G. A.; Danen, W. C. *Ibid.* **1966**, *88*, 5663.

(5) (a) Kornblum, N. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 734. (b) Kornblum, N. In *The Chemistry of Functional Groups, Supplement F: The Chemistry of Amino, Nitroso and Nitro Compounds and Their Derivatives*; Patai, S., Ed.; Wiley: New York, 1982; p 361.

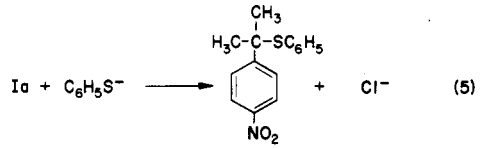
0022-3263/87/1952-0196$01.50/0

paper, we describe numerous examples of electron-transfer chain substitution at a saturated carbon atom.

With most primary and secondary halides the radical-anion pathway and the S_N2 displacement process are in competition, and it requires a difficultly displaced leaving group to provide an opportunity for the radical anion mechanism to predominate. With tertiary halides radical-anion substitution is observed free of competition from the S_N2 process;[7] it will be seen that a wide variety of facile substitution reactions take place at the tertiary carbon of *p*-nitrocumyl chloride (Ia) and α,*p*-dinitrocumene (Ib). The reactions of Ib are novel not only because they occur at a tertiary carbon but also because they involve a process without precedent—the displacement of a nitro group from a saturated carbon atom.

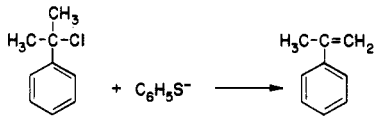
As regards the matter of mechanism, inhibition and entrainment studies (vide infra) provide powerful support for the view that these new substitution reactions of *p*-nitrocumyl chloride (Ia) and α,*p*-dinitrocumene (Ib) proceed via the chain sequence of eq 1–4.

Sodium thiophenoxide was the first reagent with which *p*-nitrocumyl chloride (Ia) was treated; the result was gratifying. At 0 °C, in dimethylformamide (DMF) solution, displacement of chloride occurred rapidly (half-life ca. 2 min) and a 95% yield of the pure tertiary sulfide (II) was isolated (eq 5).[8] In sharp contrast, cumyl chloride



Ia + $C_6H_5S^-$ → II + Cl^- (5)

reacted slowly with sodium thiophenoxide (half-life ca. 25 h) and a different path was followed; the product was almost entirely α-methylstyrene (eq 6.[9,10]



+ $C_6H_5S^-$ (6)

(6) We are here concerned with electron-transfer substitution at a saturated carbon. But it should be noted that since 1970 J. F. Bunnett and his associates have discovered a number of instances of electron-transfer substitution in aromatic systems: *Acc. Chem. Res.* **1978**, *11*, 413. Furthermore, electron-transfer substitution reactions in the quinoline and isoquinoline series have been found by J. F. Wolfe and by J. A. Zoltewicz, respectively: Wolfe, J. F.; Greene, J. C.; Hudlicky, T. *J. Org. Chem.* **1972**, *37*, 3199; *J. Am. Chem. Soc.* **1975**, *97*, 374. Zoltewicz, J. A.; Oestreich, T. M. *J. Am. Chem. Soc.* **1973**, *95*, 6863.

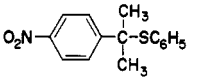
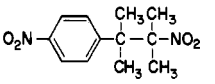
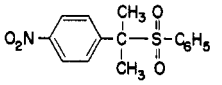
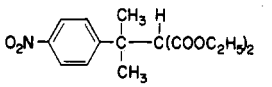
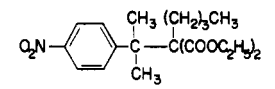
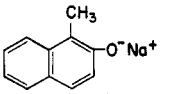
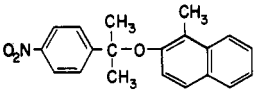
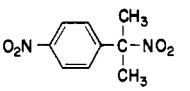
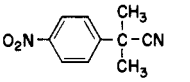
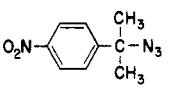
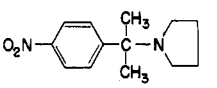
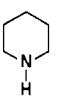
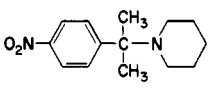
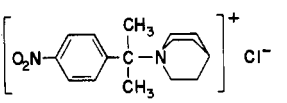
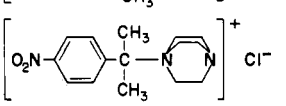
(7) The use of tertiary halides also makes it possible to avoid experimental complications and mechanistic ambiguities that arise as a consequence of the relatively high acidity of the methylene hydrogens of some of the benzyl halides. For example, the reaction of the sodium salt of 1-methyl-2-naphthoxide with *p*-nitrobenzyl chloride gives, in addition to the O and C alkylates, a 40% yield of *p*,*p*′-dinitrostilbene: D.H.S., 1970.

(8) The unlikely possibility that this result derives from elimination followed by addition of thiophenoxide (or thiophenol) to the olefin was ruled out by the fact that the isomeric sulfide was produced on treating the olefin with a mixture of sodium thiophenoxide and thiophenol: N. L.H., 1968.

(9) About 4% of the tertiary sulfide, $C_6H_5C(CH_3)_2SC_6H_5$, is also found. This result differs from that reported by us in our preliminary communication where it was stated that none of the tertiary sulfide could be detected and that, instead, the primary sulfide, $C_6H_5CH(CH_3)CH_2SC_6H_5$, was obtained in 56% yield along with a 6% yield of α-methylstyrene: *J. Am. Chem. Soc.* **1967**, *89*, 725. Apparently minor variations in experimental conditions determine whether or not thiophenol will add to the α-methylstyrene and, thereby, produce the primary sulfide.

(10) These differences, of course, argue against the idea that the reaction of *p*-nitrocumyl chloride with sodium thiophenoxide (eq 5) is a carbonium ion process.

Table I. Reaction of *p*-Nitrocumyl Chloride (Ia) and α,*p*-Dinitrocumene (Ib) with Nucleophiles

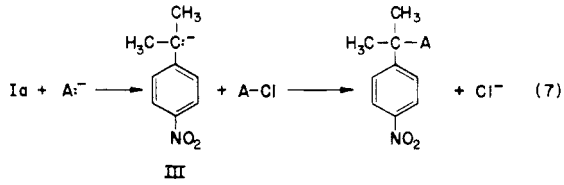
nucleophile	product	yield,[a] % from Ia	yield,[a] % from Ib
$C_6H_5S^-$ Na^+		95[b]	96
$(CH_3)_2\bar{C}$-NO_2 Li^+		90	90
$C_6H_5SO_2^-$ Na^+		95	94
$\bar{C}H(COOC_2H_5)_2$ Na^+		90	90
$CH_3(CH_2)_3\bar{C}(COOC_2H_5)_2$ Na^+		81	87
		92[b,c]	69[c]
$NaNO_2$		91	
NaCN		81	
NaN_3		95	94
		90	
		91	77[d]
		90	
		80	

[a] Pure, isolated product. [b] At 0 °C; all other reactions at room temperature. [c] Ca. 20% yield of α-methyl-*p*-nitrostyrene is also isolated. [d] Yield by VPC.

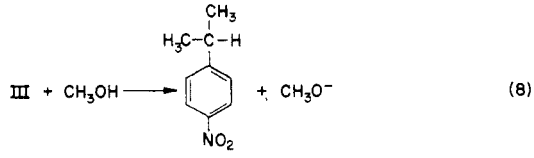
Table I presents the results of the reaction of *p*-nitrocumyl chloride (Ia) with a number of nucleophiles. These transformations occur at room temperature and proceed to completion in minutes or hours; yields refer to pure products. There is no precedent for such facile substitution at a tertiary carbon atom. It is also noteworthy that none of the reactions recorded in Table I occur with cumyl chloride; instead, the principal product is α-methylstyrene.[11] Clearly, the *p*-nitro group facilitates substitution at the tertiary carbon atom of *p*-nitrocumyl chloride.

(11) Cumyl chloride slowly solvolyzes in the solvents employed (DMF, Me_2SO, HMPA), and in some instances very small amounts of the substitution product are obtained, e.g. the 4% yield of cumyl phenyl sulfide reported in ref 9. Presumably, such products derive from the reaction of the cumyl carbonium ion with the nucleophile.

Since the reactions of Table I depend on the *p*-nitro group, the possibility that nucleophiles displace on chlorine to give a carbanion (III) and that this carbanion then gives rise to the observed product by displacing chloride ion from the chlorinated nucleophiles (eq 7) was considered. If this



were the case, one would anticipate that on conducting these reactions in protic solvents interception of the carbanion III to give *p*-nitrocumene would occur (eq 8). But

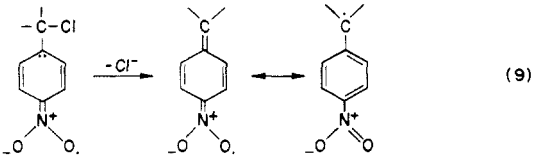


this is not what happens. When *p*-nitrocumyl chloride is treated with sodium thiophenoxide in methanol, or with the sodium salt of diethyl malonate in ethanol, the reactions are much slower than in DMF or Me_2SO—but the reaction course remains unchanged.

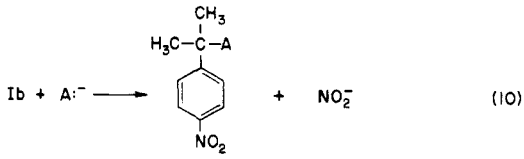
Powerful evidence against the carbanion mechanism is also provided by the fact that quinuclidine and DABCO[12] react with *p*-nitrocumyl chloride to give the quaternary ammonium chlorides (Table I). With these nucleophiles the second step of the two-step process of eq 7, rearward displacement of chloride ion from A–Cl, is clearly out of the question.

The ease with which substitution occurs at a tertiary carbon under mild conditions demonstrates that electron-transfer chain substitution, in contrast to S_N2 displacements, is rather insensitive to steric hindrance. This insensitivity is even more dramatic when it is realized that with the 2-nitropropane anion, the benzenesulfinate ion, and the nitrite ion covalency is established at the more hindered of two available positions—even though substitution occurs at a highly hindered carbon atom (Table I). The electron-transfer chain mechanism of eq 1–4 provides a simple basis for explaining this lack of sensitivity to steric hindrance.[13]

The displacement of a nitro group from a saturated carbon atom was unknown when this investigation was begun. That such a process might be observed was suggested by the second step of the chain mechanism of eq 1–4, i.e. the step in which expulsion of chloride ion from the radical anion occurs. This can be looked upon as an intramolecular elimination that produces an olefin—an olefin that also happens to be a free radical (eq 9).[14] If



this loss of chloride ion is indeed an intramolecular elimination, then an analogous elimination reaction may be anticipated for many atoms and groups that do not behave as leaving groups in S_N2 displacements. As a test of this possibility, a study of the chemistry of α,*p*-dinitrocumene Ib was undertaken. It transpires that nitrite ion is readily displaced (eq 10) and that the nucleophiles that work so

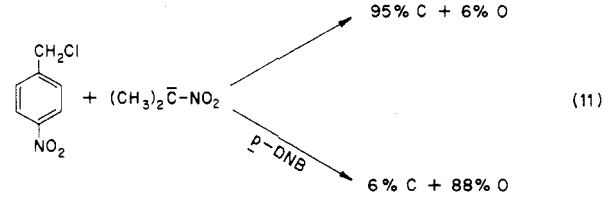


well with *p*-nitrocumyl chloride are equally effective with α,*p*-dinitrocumene. As with the chloride, these reactions proceed at room temperature, are complete in a matter of hours, and give excellent yields of pure products (Table I). And, here too, the *p*-nitro group is essential; in no instance does α-nitrocumene react with nucleophiles under conditions that result in complete reaction when α,*p*-dinitrocumene is employed.[15,16]

Assignment of the electron-transfer chain pathway of eq 1–4 to the reactions of Table I is predicated not only on the fact that good grounds exist for ruling out a carbonium ion[10] or a carbanion[16] mechanism but, more importantly, on inhibition studies and on the ability of one-electron-transfer agents to induce these reactions. We now describe some of these experiments.

The use of inhibitors is based on the fact that the chain sequence of eq 1–4 postulates radical anions and free radicals as intermediates. If this assumption is correct, powerful one-electron acceptors should be capable of intercepting the radical anions and, by depriving them of an electron, should inhibit or, at minimum, retard the overall reaction. Furthermore, free-radical scavengers by trapping the *p*-nitrocumyl radicals should also slow, or stop, substitution at the tertiary carbon atom. Finally, if these reactions are indeed chain processes, then much less than stoichiometric amounts of inhibitor should be effective. As can be seen from the sequel, the results obtained with a variety of inhibitors provide compelling support for the electron-transfer chain mechanism of eq 1–4.

Effect of *p*-Dinitrobenzene and *m*-Dinitrobenzene. Earlier,[4a,b] a study of the reaction of *p*-nitrobenzyl chloride with the lithium salt of 2-nitropropane showed that *p*-dinitrobenzene (*p*-DNB) inhibits the electron-transfer process, in which carbon alkylation occurs, but does not interfere with the S_N2 process, in which oxygen alkylation occurs (eq 11). Since *p*-nitrocumyl chloride is a tertiary



halide, competition from an S_N2 displacement process is virtually nonexistent. If, then, the radical anions of the chain sequence (eq 1–4) were intercepted by a powerful one-electron acceptor, e.g. *p*-DNB, the radical anion pro-

(12) 1,4-Diazabicyclo[2.2.2]octane.
(13) Kornblum, N.; Ackermann, P.; Swiger, R. T. *J. Org. Chem.* **1980**, *45*, 5294.
(14) Kerber, R. C.; Urry, G. W.; Kornblum, N. *J. Am. Chem. Soc.* **1965**, *87*, 4522.
(15) In this connection the paper by Kornblum et al. (Kornblum, N.; Carlson, S. C.; Widmer, J.; Fifolt, M. J.; Newton, B. N.; Smith, R. G. *J. Org. Chem.* **1978**, *43*, 1394) is of interest.
(16) The possibility that the reactions of α,*p*-dinitrocumene proceed via a carbanion mechanism analogous to that of eq 7 was considered. But the fact that α,*p*-dinitrocumene reacts with sodium thiophenoxide in absolute ethanol to give a 94% yield of pure *p*-nitrocumyl phenyl sulfide (II) provides a compelling argument against the carbanion mechanism: G.W.E., 1969.

cess would be inhibited and, thus, no reaction whatsoever should be observed. This proves to be the case. For example, the reaction of sodium nitrite with p-nitrocumyl chloride in HMPA (eq 12) proceeds 93% to completion in

(12)

20 min, but in the presence of 10 mol % of p-DNB no reaction occurs. In the same way the transformation of eq 13 is 65% complete in 75 s, but when 5 mol % of p-DNB is present, there is no reaction in this time.

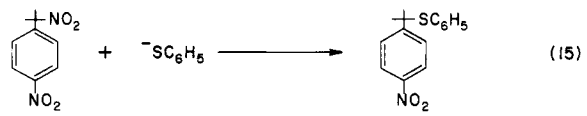
(13)

The reaction of sodium benzenesulfinate with p-nitrocumyl chloride (eq 14) is also inhibited by p-DNB. In the

(14)

absence of p-DNB an 80% yield of the pure sulfone is isolated after 10 min; in contrast, if 5 mol % of p-DNB is present, the yield of sulfone is only 2% and 86% of the p-nitrocumyl chloride is recovered. When the transformation of eq 14 is conducted in the presence of m-dinitrobenzene (m-DNB) at the 5 mol % level for 10 min, a 20% yield of the sulfone is obtained and 71% of the starting chloride is recovered. Here, as elsewhere,[4b,c] m-DNB is a less effective inhibitor than p-DNB; this is consistent with the fact that m-DNB undergoes one-electron reduction less readily than p-DNB.

Sodium thiophenoxide rapidly attacks p-DNB, forming nitrite ion and p-nitrophenyl phenyl sulfide.[17] However, the reaction of sodium thiophenoxide with m-DNB is so much slower that one is able to study the influence of m-DNB on the reaction of thiophenoxide with α,p-dinitrocumene (eq 15). In the absence of inhibitors a 96%



(15)

yield of the pure sulfide is isolated after less than 10 min. However, in the presence of 100 mol % of m-DNB (i.e., 1 mol of m-DNB for each mole of α,p-dinitrocumene), only 29% reaction occurs in 10 min and the time needed for the reaction to go to completion is about 45 min; here again the yield of pure p-nitrophenyl phenyl sulfide is 96%. Thus, even though the reaction of eq 15 is very fast, unmistakable retardation results from the presence of a good electron acceptor.

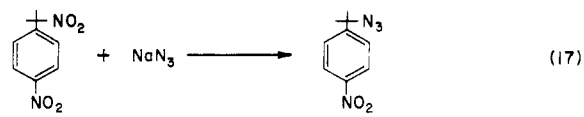
These and numerous other experiments employing p-DNB and m-DNB provide strong support for the view that radical anions are intermediates in substitution reactions of the p-nitrocumyl system.[18] They provide unambiguous evidence for the chain character of these processes.

Effect of Di-*tert*-Butyl Nitroxide. The mechanism of eq 1–4 invokes the p-nitrocumyl radical as part of a chain-carrying sequence. Since di-*tert*-butyl nitroxide is known to be a free-radical scavenger,[19] inhibition ought to be observed when reactions of p-nitrocumyl chloride (Ia) or α,p-dinitrocumene (Ib) are conducted in its presence. This is precisely what happens.

For example, the reaction of the lithium salt of 2-nitropropane with p-nitrocumyl chloride (eq 16) proceeds 67% to completion in 30 min. In contrast, when 5 mol % of di-*tert*-butyl nitroxide is present, only 1% reaction occurs.

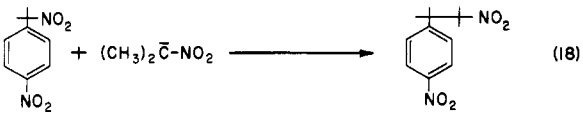
(16)

The reaction of α,p-dinitrocumene with sodium azide (eq 17) gives a 93% yield of p-nitrocumyl azide in 15 min. But if di-*tert*-butyl nitroxide is present at the 5 mol % level, only 3% of the azide is obtained and 92% of the starting α,p-dinitrocumene is recovered.



(17)

A study of the reaction of eq 18 revealed that in the absence of di-*tert*-butyl nitroxide, a 56% yield of 2,3-dimethyl-2-nitro-3-(p-nitrophenyl)butane is produced after a 40-min reaction time and 29% of the α,p-dinitrocumene is recovered. But when 5 mol % of the nitroxide is present, none of the product is obtained, and 97% of the starting α,p-dinitrocumene is recovered.



(18)

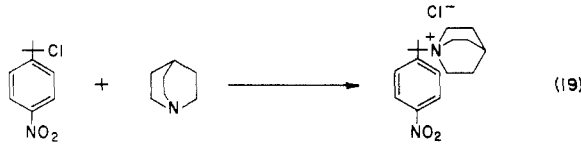
In the absence of di-*tert*-butyl nitroxide the reaction of eq 19 gave, after 5 h, 61% of the theoretical amount of chloride ion, and the quaternary ammonium salt was isolated in 54% yield. In contrast, an experiment in which nitroxide was present at the 5 mol % level produced 4% chloride ion and none of the quaternary ammonium salt; ca. 90% of the p-nitrocumyl chloride was recovered.

Effect of Oxygen. Since the chain sequence of eq 1–4 invokes the intermediacy of the p-nitrocumyl radical, and since oxygen is a scavenger of carbon free radicals, it ap-

(17) The use of p-DNB as a diagnostic in reactions employing the lithium salt of 2-nitropropane is also precluded by the fact that the anion of 2-nitropropane replaces one of the nitro groups of p-DNB at a rate comparable to that of its reaction with p-nitrocumyl chloride or α,p-dinitrocumene: Kornblum, N.; Cheng, L.; Kerber, R. C.; Kestner, M. M.; Newton, B. N.; Pinnick, H. W.; Smith, R. G.; Wade, P. A.; *J. Org. Chem.* **1976**, *41*, 1560. Also, see: Manthey, J. W. Ph.D. Thesis, Purdue University, Aug 1969, pp 134–135.

(18) The view that p-DNB and m-DNB function as inhibitors by removing an electron from the chain-carrying radical anions of eq 1–4 is in accord with the fact that p-DNB, the more effective of the two, undergoes one-electron reduction more readily than m-DNB. And nitrobenzene, which is even less effective than m-DNB, is the most difficulty reduced of the three nitro aromatics: Maki, A. H.; Geske, D. H. *J. Am. Chem. Soc.* **1961**, *83*, 1852. The possibility that nitro aromatics inhibit by trapping free radicals is considered unlikely because with some relatively slow electron-transfer chain reactions, e.g. the reaction of 2,2-dinitropropane with sodium benzene sulfinate, the presence of m-DNB, or nitrobenzene, speeds up the reaction. These effects, while small, appear to be real: Hall, A. L., unpublished work, Purdue University. Catalysis apparently derives from the reaction of the nucleophile, A:⁻, with m-DNB (or $C_6H_5NO_2$) to form m-DNB$^{\cdot-}$ (or $C_6H_5NO_2^{\cdot-}$) plus A$^{\cdot}$, and the radical anion is able to serve as a one-electron donor to an aliphatic nitro group, thereby initiating chains. With rapidly reacting nucleophiles the reverse effect—stripping one electron from a chain-carrying radical anion, i.e. inhibition, masks the relatively weak catalysis.

(19) Hoffmann, A. K.; Feldman, A. M.; Gelblum, E.; Hodgson, W. G. *J. Am. Chem. Soc.* **1964**, *86*, 642. Forrester, A. R.; Hay, J. M.; Thomson, R. H. *Organic Chemistry of Stable Free Radicals*; Academic: London, 1968; p 224.



(19)

peared that oxygen also ought to have an effect on the rate of these substitution reactions.[20] This proves to be the case.

After 6 h the reaction of quinuclidine with *p*-nitrocumyl chloride (eq 19) is 90% complete when conducted under nitrogen. However, a parallel experiment in which 1 mol % of oxygen is present goes only 12% to completion in 6 h.

Treatment of *p*-nitrocumyl chloride with sodium benzenesulfinate under argon gives a quantitative yield of the sulfone in 2 h (eq 14). In contrast, a duplicate experiment in which 1 mol % of oxygen is present undergoes less than 1% reaction in the 2-h period.

Effect of Galvinoxyl. Galvinoxyl, a stable free radical, is an efficient scavenger of free radicals.[21] Therefore, it too should function as an inhibitor for these reactions; and, indeed, it does. In the absence of galvinoxyl the reaction of α,p-dinitrocumene (Ib) with sodium benzenesulfinate gives a 56% yield of *p*-nitrocumyl phenyl sulfone in 30 min. But a duplicate experiment in which 5 mol % of galvinoxyl is present gives none of the *p*-nitrocumyl phenyl sulfone; instead the starting α,p-dinitrocumene is quantitatively recovered.

The reaction of *p*-nitrocumyl chloride with quinuclidine (eq 19) is also affected by galvinoxyl; without galvinoxyl, it is 94% complete in 4 h, but in the presence of 5 mol % of galvinoxyl it proceeds only 17% to completion.

Effect of Elemental Sulfur. Elemental sulfur is an excellent scavenger of free radicals,[22] and, as a consequence, one would expect it to inhibit these substitution processes; this prediction is realized. Thus, the reaction of α,p-dinitrocumene with sodium azide gives an 80–87% yield of *p*-nitrocumyl azide in 10 min; however, in the presence of 2 atom % of sulfur, only a 12% yield of *p*-nitrocumyl azide is obtained. And when 14 atom % of sulfur is employed, no reaction whatsoever occurs. Finally, the reaction of sodium nitrite with *p*-nitrocumyl chloride gives a 69% yield of α,p-dinitrocumene in 35 min; but if 10 atom % of sulfur is present, essentially no reaction occurs in this time.

Induced Reactions

In 1950, the reduction of diazonium salts by hypophosphorous acid, the method of choice for replacing a diazonium group by hydrogen, was shown to be an electron-transfer chain process in which free radicals are intermediates.[23] One of the compelling pieces of evidence for this mechanism is the fact that a catalytic amount of a rapidly reduced diazonium salt induces the reaction of a sluggishly reduced diazonium salt. The electron-transfer chain mechanism of eq 1–4 suggests that, in the same way, a small amount of a rapidly reacting nucleophile ought to induce the reaction of a nonreactive nucleophile with *p*-nitrocumyl chloride, and with α,p-dinitrocumene. This prediction is handsomely fulfilled.

Thus, α,p-dinitrocumene and sodium azide, in the dark, do not react at all after 48 h. In contrast, the lithium salt of 2-nitropropane reacts readily with α,p-dinitrocumene in the dark; after 3 h the reaction is 87% complete. If, however, 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 h in the dark and a 97% yield of pure *p*-nitrocumyl azide is obtained.

Although *p*-nitrocumyl chloride and sodium nitrite do not react in the dark for at least 90 min, a duplicate reaction in which 5 mol % of the lithium salt of 2-nitropropane is present proceeds to completion and gives a 93% yield of α,p-dinitrocumene. The chain mechanism of eq 1–4 provides a simple explanation of these, and numerous similar observations—the entraining anion initiates chains and the entrained anion carries them along.

If entrainment derives from facile one-electron transfer by the entraining anion, then other one-electron-transfer agents should also possess the capability of inducing these substitution reactions. This is precisely what is observed.

Thus, as already noted, α,p-dinitrocumene and sodium azide do not react in the dark. But if 5 mol % of sodium naphthalene, which is a one-electron-transfer agent,[24] is present, they react completely in less than 1 h to give a 97% yield of *p*-nitrocumyl azide. Even as little as 3 mol % of sodium trimesitylborane, which is also a one-electron-transfer agent,[25] results in a 92% yield of *p*-nitrocumyl azide in 30 min. Of special interest is the fact that a solution of sodium metal in hexamethylphosphoramide (HMPA), which is thought to contain solvated electrons,[26,25] produces *p*-nitrocumyl azide in 87% yield within 30 min when present at the 4 mol % level. Similarly, sodium nitrite and *p*-nitrocumyl chloride are caused to react in the dark by catalytic amounts of these electron-transfer agents.[32]

The fact that various one-electron-transfer agents induce substitution reactions in the *p*-nitrocumyl system is consonant with the view that these reactions are initiated by one-electron transfer. This, in turn, provides significant support for the electron-transfer chain mechanism of eq 1–4.

Experimental Section

Solvents. The reactions of Table I proceed most readily in dipolar aprotic solvents. In the early phases of this work *N,N*-dimethylformamide (DMF) was used. Later on it was recognized that dimethyl sulfoxide (Me_2SO) is often a more useful solvent than DMF. Virtually all these reactions proceed even more expeditiously in hexamethylphosphoramide (HMPA), the only possible exception being reactions employing amines.

Caution! HMPA should be handled with great care since it has been found to cause cancer in laboratory animals.[27]

The DMF (Du Pont) was purified as described by Kerber et al.[4b] Reagent-grade Me_2SO was distilled from calcium hydride under reduced pressure as was the HMPA. These solvents were stored in the dark under nitrogen and were deoxygenated by a stream of high-purity nitrogen or argon before use.

Reaction Conditions. Because of our interest in the matter of mechanism, most of the reactions were carried out under carefully deoxygenated conditions (freeze–pump–thaw procedure).[15] But such rigorous exclusion of oxygen is not necessary for synthetic work. All that is required is sweeping the system

(20) In the initial phases of these studies massive amounts of oxygen were employed. This prevented substitution, and instead, *p*-nitrocumyl alcohol was formed. These early experiments have been adequately summarized[5a] and, therefore, are not described here.

(21) Bartlett, P. D.; Funahashi, T. *J. Am. Chem. Soc.* **1962**, *84*, 2600.

(22) Bartlett, P. D.; Kwart, H. *J. Am. Chem. Soc.* **1950**, *72*, 1051. Bartlett, P. D.; Trifan, D. S. *J. Polym. Sci.* **1956**, *20*, 457.

(23) Kornblum, N.; Cooper, G. D.; Taylor, J. E. *J. Am. Chem. Soc.* **1950**, *72*, 3013.

(24) Garst, J. F. *Acc. Chem. Res.* **1971**, *4*, 400.

(25) Darling, S. D.; Devgan, O. N.; Cosgrove, R. E. *J. Am. Chem. Soc.* **1970**, *92*, 696.

(26) Fraenkel, G.; Ellis, S. H.; Dix, D. T. *J. Am. Chem. Soc.* **1965**, *87*, 1406.

(27) *Chem. Eng. News* **1975**, *54*(39), 17.

with high-purity nitrogen or argon long enough to ensure that most of the oxygen is removed—15–30 min generally suffices.

While many of the reactions proceed in the absence of light, they usually take place more rapidly in the light. Unless otherwise noted, reactions were conducted under ordinary laboratory illumination. Those that were carried out in the "light apparatus" were run under a light source that consisted of two 110-V, 20-W white fluorescent lights mounted horizontally about 12 cm apart.

Unless otherwise specified, reactions were carried out at room temperature. The temperature attained by reactions conducted in the light apparatus was ca. 5–10 °C higher than for reactions run in the dark, or with ordinary room illumination.

Reactions of Sodium Thiophenoxide. (a) With *p*-Nitrocumyl Chloride. In the dark, under argon a stirred solution of 1.32 g (10 mmol) of sodium thiophenoxide[28] in 100 mL of DMF was cooled in an ice bath for 2 h and then 1.99 g (10 mmol) of *p*-nitrocumyl chloride[13] (n^{20}_D 1.5561) was added; by chloride titration the half-life was ca. 2 min. After 2.5 h the product was poured into a mixture of ice and ethyl ether; the aqueous phase was further extracted with ethyl ether, and then the combined ether extracts were washed with water and dried ($MgSO_4$). Removal of the ether yielded 2.75 g of residue, mp 51–52 °C, which, on recrystallization from hexane, gave 2.49 g of *p*-nitrocumyl phenyl sulfide, mp 52–53 °C. The hexane mother liquors were evaporated to dryness, and the residue was chromatographed on Florisil with benzene–hexane (1:4); this gave an additional 0.09 g of the tertiary sulfide, mp 52–53 °C, bringing the total to 2.58 g (95% yield): NMR (CCl_4) δ 1.7 (s, 6 H), 7.1 (m, 5 H), 7.8 (AB q, 4 H).

Anal. Calcd for $C_{15}H_{15}NO_2S$: C, 65.94; H, 5.54; N, 5.14; S, 11.75; mol wt 273. Found: C, 66.14; H, 5.46; N, 5.16; S, 11.87; mol wt 275.

(b) With α,*p*-Dinitrocumene (Ib). A stirred solution of 1.314 g (10 mmol) of sodium thiophenoxide[28] in 20 mL of DMF was treated with 1.051 g (5 mmol) of α,*p*-dinitrocumene[28] in 5 mL of DMF. The reaction flask was placed under the light apparatus, and the course of reaction was followed by NMR analysis; it was complete in ca. 10 min. After 2 h, the product was poured into a mixture of ice–water and benzene and the aqueous phase was extracted with ether and chloroform. The extracts were washed with water and evaporated to dryness. The residue was chromatographed on silica gel with hexane–benzene mixtures. This gave 0.153 g of diphenyl disulfide, mp 60–61 °C. This was followed by 1.203 g (96% yield) of pure *p*-nitrocumyl phenyl sulfide (II); mp and mixed mp with the product obtained in part (a) 52–53 °C. The NMR spectrum of this product was identical with that obtained in part (a).

That the aliphatic nitro group is quantitatively displaced as nitrite ion was demonstrated by determining nitrite according to the procedure of Norman.[29]

Reactions of the Lithium Salt of 2-Nitropropane. (a) With *p*-Nitrocumyl Chloride.[13] *p*-Nitrocumyl chloride (2.00 g, 10 mmol), the lithium salt of 2-nitropropane[30] (1.90 g, 20 mmol), and 100 mL of HMPA were allowed to react for 2 h in the light apparatus. The crude product obtained on workup was digested with ethyl ether for 90 min after which the mixture was allowed to cool to room temperature. Filtration gave 1.926 g of white 2,3-dimethyl-2-nitro-3-(*p*-nitrophenyl)butane, mp 206–208 °C. Evaporation of the ethyl ether filtrate left a yellow solid that was chromatographed on acid-washed alumina with benzene. This gave another 0.114 g of the carbon alkylate: mp 206–208 °C; total yield 2.040 g (81%). Recrystallization from benzene-hexane did not change the melting point: NMR ($CDCl_3$) δ 1.55 (s, 12 H), 7.81 (q, 4 H). Anal. Calcd for $C_{12}H_{16}N_2O_4$: C, 57.13; H, 6.39; N, 11.10; mol wt 252. Found: C, 57.31; H, 6.54; N, 10.81; mol wt 257.[31]

In addition to the carbon alkylate, 0.148 g (8% yield) of *p*-nitrocumyl alcohol was isolated. When the mole ratio of nitroparaffin salt to *p*-nitrocumyl chloride was 5:1, the yield of pure carbon alkylate rose to 90%. In Me_2SO it takes about 5 times as long for the reaction to go to completion, the yields of carbon alkylate are lower (ca. 60%), and the amount of *p*-nitrocumyl alcohol formed is greater (ca. 20% yield).

(b) With α,*p*-Dinitrocumene. This reaction was carried out and worked up exactly as in part (a) with 2.102 g (10 mmol) of α,*p*-dinitrocumene,[28] 4.75 g (50 mmol) of the lithium salt of 2-nitropropane, and 100 mL of HMPA. There was isolated 2.281 g (90% yield) of pure 2,3-dimethyl-2-nitro-3-(*p*-nitrophenyl)butane, mp 206–208 °C, further identified by its NMR.

Reactions of Sodium Benzenesulfinate. (a) With *p*-Nitrocumyl Chloride. In HMPA, under the light apparatus, this reaction is complete in 10 min and gives a 95% yield of the pure sulfone, mp 130–131 °C.[13] In the dark, 3 h is required and the yield of sulfone is 92%. In Me_2SO under the light apparatus, 3 h is required for complete reaction and a 94% yield of sulfone is obtained.

(b) With α,*p*-Dinitrocumene. A mixture of sodium benzenesulfinate (1.64 g, 10 mmol), α,*p*-dinitrocumene (1.05 g, 5 mmol), and 25 mL of HMPA was allowed to react for 6 h in the light apparatus. The usual workup[13] gave 1.50 g of solid which, after chromatography on acid-washed alumina using hexane–benzene–ethyl ether, yielded 1.44 g (94% yield) of pure *p*-nitrocumyl phenyl sulfone, mp and mixed mp 130–131 °C, whose NMR was identical with that of the analytical sample.[13] The reaction exhibits a large light effect. In the dark, after 96 h, workup gave only an 8% yield of sulfone and a 90% recovery of the α,*p*-dinitrocumene. When Me_2SO is employed instead of HMPA, the reaction in the light apparatus takes 48 h to go to completion; nonetheless, it gives a 93% yield of the pure sulfone. In the dark, the reaction in Me_2SO goes only 2% after 96 h.

Reactions of the Sodium Salt of Diethyl Malonate. (a) With *p*-Nitrocumyl Chloride.[13] The sodium salt of diethyl malonate[32] (1.951 g, 10.7 mmol) and 1.001 g (5 mmol) of *p*-nitrocumyl chloride were allowed to react in 50 mL of Me_2SO under the light apparatus; in 25 h the reaction was 95% complete. After 72 h the product was poured into water and extracted with diethyl ether. The 0.013 g of solid that did not dissolve in either phase had a melting point 264–266 °C dec and was *p,p'*-dinitrobicumyl, 2% yield. After recrystallization from acetone, it melted 265–267 °C dec (lit.[33] mp 265 °C dec). Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.83; H, 6.14; N, 8.47. Found: C, 65.72; H, 5.99; N, 8.40.

The diethyl ether solution was cooled to 0 °C and stirred with ice-cold 2% aqueous sodium hydroxide at 0 °C for 30 min. The ether phase was washed with water and dried ($MgSO_4$), and then the ether was removed. The resulting yellow oil was chromatographed on silica gel with benzene–hexane and benzene–ether. This gave 1.529 g of (*p*-nitrocumyl)malonic acid diethyl ester, which on distillation at 1 mm yielded 1.46 g (90% yield) of a pale yellow oil: bp 158–160 °C; n^{20}_D 1.5154; NMR ($CDCl_3$) δ 1.14 (t, 6 H), 1.60 (s, 6 H), 3.81 (s, 1 H), 4.04 (q, 4 H), 7.54 (d, 2 H), 8.08 (d, 2 H). Anal. Calcd for $C_{16}H_{21}NO_6$: C, 59.43; H, 6.55; N, 4.33; mol wt 323. Found: C, 59.25; H, 6.35; N, 4.54; mol wt 330.

In the dark the rate and yields of products are very nearly the same.

(b) With α,*p*-Dinitrocumene. The sodium salt of diethyl malonate[32] (2.027 g, 11.1 mmol) was allowed to react with 1.050 g (5 mmol) of α,*p*-dinitrocumene[28] in 50 mL of Me_2SO under the light apparatus. After 20 h the reaction was 96% complete; it was worked up after 44 h as described in part (a). The yield of pure (*p*-nitrocumyl)malonic acid diethyl ester was 1.45 g (90%) and that of *p,p'*-dinitrobicumyl was 0.029 g (4%). A duplicate experiment in the dark was slightly slower. In DMF an 86% yield of pure (*p*-nitrocumyl)malonic acid diethyl ester was obtained after 44 h in the light apparatus.

Reactions of the Sodium Salt of *n*-Butylmalonic Acid Diethyl Ester. (a) With *p*-Nitrocumyl Chloride. A stirred solution of 2.001 g (10 mmol) of *p*-nitrocumyl chloride in 26 mL of Me_2SO was treated with 24.1 mL of a 0.82 M Me_2SO solution of the sodium salt of *n*-butylmalonic acid diethyl ester (20 mmol) under the light apparatus. After 2.5 h the reaction was worked

(28) Kornblum, N.; Cheng, L.; Kerber, R. C.; Kestner, M. M.; Newton, B. N.; Pinnick, H. W.; Smith, R. G.; Wade, P. A. *J. Org. Chem.* **1976**, *41*, 1560.

(29) Norman, G. M. *J. Chem. Soc.* **1912**, *102*, 1918. See: G.W.E., 1969.

(30) Kornblum, N.; Boyd, S. D.; Ono, N. *J. Am. Chem. Soc.* **1974**, *96*, 2583.

(31) The structure of the carbon alkylate was confirmed by converting it to 2,3-dimethyl-2-nitro-3-phenylbutane: J.W.M., 1969.

(32) M.M.K., 1973.

(33) Huang, R. L.; Marsingh, F. *J. Chem. Soc.* **1953**, 160.

up in the usual manner. Excess diethyl *n*-butylmalonate was removed from the crude product by distillation at 1 mm, and the residue was chromatographed on acid-washed alumina. This gave 3.16 g of *n*-butyl(*p*-nitrocumyl)malonic acid diethyl ester which, when recrystallized from hexane, gave long colorless needles: mp 41.5–42 °C; yield 3.07 g (81%); NMR ($CDCl_3$) δ 0.70–2.00 (complex m with superimposed s at 1.60 and t at 1.17, 21 H), 4.02 (q, 4 H), 7.55 (d, 2 H), 8.05 (d, 2 H); IR (KBr pellet) 1725 (C=O), 1525, 1350 cm^{-1} (NO_2). Anal. Calcd for $C_{20}H_{29}NO_6$: C, 63.30; H, 7.70; N, 3.69; mol wt 379. Found: C, 63.31; H, 7.89; N, 3.93; mol wt 372.

(b) With α,*p*-Dinitrocumene. To a solution of 2.10 g (10 mmol) of α,*p*-dinitrocumene in 26 mL of Me_2SO was added 24 mL of a Me_2SO solution containing 4.76 g (20 mmol) of sodio diethyl *n*-butylmalonate; the reaction was conducted under the light apparatus for 42 h and then worked up. Excess diethyl *n*-butylmalonate was removed by distillation at 1 mm (bp 80–81 °C), and the residue was dissolved in benzene. Chromatography on acid-washed alumina yielded 3.52 g of diethyl *n*-butyl(*p*-nitrocumyl)malonate which, when recrystallized from hexane, gave 2.98 g (87% yield) of colorless needles: mp 41.5–42 °C; IR and NMR identical with the spectra of the analytical sample of part (a).

Reactions of Sodium 1-Methyl-2-naphthoxide. (a) With *p*-Nitrocumyl Chloride.[13] At 0 °C a solution of sodium 1-methyl-2-naphthoxide[34] (3.49 g, 19.4 mmol) in 90 mL of DMF was treated with 3.53 g (17.6 mmol) of *p*-nitrocumyl chloride under the light apparatus. The reaction was 56% complete at the end of 4 h after which the rate leveled off sharply. The latter stages of the reaction proceeded very slowly.[35] Indeed, it was only 85% complete after 38 h at which time the reaction mixture was poured into water, benzene was added, and the mixture was acidified with carbon dioxide. The benzene extract was separated and the aqueous phase extracted with ethyl ether. The combined extracts were dried ($MgSO_4$), the solvents were removed, and the residual material was chromatographed on an alumina (Merck) column with benzene–ether mixtures to separate the neutral products from 1-methyl-2-naphthol. Further chromatography of the neutral fraction on alumina using hexane–benzene mixtures gave 0.42 g (17% yield) of α-methyl-*p*-nitrostyrene: mp 51–53 °C (lit.[36] mp 51–52.5 °C); confirmed by IR. This was followed by 3.11 g of *p*-nitrocumyl 1-methyl-2-naphthyl ether, mp 108–110 °C. Recrystallization from ethanol gave the pure ether: mp 110–111 °C; 2.96 g (62% yield); NMR ($CDCl_3$) δ 1.68 (s, 6 H), 2.59 (s, 3 H), 6.60 (d, 1 H), 7.28–8.25 (complex m, 9 H). Anal. Calcd for $C_{20}H_{19}NO_3$: C, 74.74; H, 5.96; N, 4.36; mol wt 321. Found: C, 74.86; H, 5.86; N, 4.37; mol wt 312.

Light has little, if any, effect on the rate of this reaction. In Me_2SO the reaction is faster than in DMF.

(b) With α,*p*-Dinitrocumene. To a solution of 1.819 g (10 mmol) of sodium 1-methyl-2-naphthoxide in 15 mL of Me_2SO was added a solution of 1.050 g (5 mmol) of α,*p*-dinitrocumene in 10 mL of Me_2SO. After 5 h in the light apparatus the product was worked up by pouring into a mixture of water and benzene. In this way 0.022 g (1% yield) of *p,p'*-dinitrobicumyl, mp 265–267 °C dec, was isolated. The benzene layer was washed with 5% aqueous sodium hydroxide and then with water and dried ($MgSO_4$). After removal of the benzene the residue was chromatographed on alumina with hexane–benzene mixtures. In this way 0.172 g (1.05 mmol) of α-methyl-*p*-nitrostyrene, mp 50–51 °C, was isolated; its IR and NMR spectra were identical with those of authentic material. The *p*-nitrocumyl 1-methyl-2-naphthyl ether that followed was recrystallized from carbon tetrachloride; mp and mixed mp with the analytically pure sample 110–111 °C; 1.11 g (69% yield); NMR identical with that of the analytically pure ether isolated in part (a).[37]

Reaction of Sodium Nitrite with *p*-Nitrocumyl Chloride.[13] A solution of 3.44 g (0.05 mmol) of sodium nitrite (which had been dried at 120 °C) in 100 mL of Me_2SO was added to 2.0 g (0.01 mmol) of *p*-nitrocumyl chloride. Under the light apparatus the half-life was 12 h. After 120 h the usual workup gave a crude product that was purified by chromatographing on acid-washed alumina and then recrystallizing from benzene–hexane. This gave 1.91 g (91% yield) of α,*p*-dinitrocumene: white crystals; mp 69–70 °C. Anal. Calcd for $C_9H_{10}N_2O_4$: C, 51.43; H, 4.80; N, 13.33; mol wt 210. Found: C, 51.53; H, 4.63; N, 13.47; mol wt 212.

A duplicate experiment in the dark typically had a half-life of 300 h.

Reaction of Sodium Cyanide with *p*-Nitrocumyl Chloride. Sodium cyanide [Baker's analyzed reagent dried at 100 °C (0.5 mm)] was employed. *p*-Nitrocumyl chloride (2.00 g, 10 mmol) was added to a solution of 1.00 g (20.4 mmol) of sodium cyanide in 100 mL of HMPA, and after 9 min under the light apparatus the reaction mixture was worked up as usual. The solid left on removing solvents was treated with 20 mL of benzene; the benzene-insoluble material (0.064 g) melted at 254 °C dec and presumably is *p,p'*-dinitrobicumyl. The benzene soluble material was chromatographed on acid-washed alumina using hexane–benzene mixtures. The first material to elute was a mixture of *p*-nitro-α-methylstyrene and *p*-nitrocumene. This was followed by 1.539 g (81% yield) of *p*-nitrocumyl cyanide: mp 80–81.5 °C; NMR ($CDCl_3$) δ 1.80 (s, 6 H), 7.97 (AB q, 4 H); IR (CCl_4) 4.47 very weak (CN), 6.58, 7.48 cm^{-1} (NO_2). Anal. Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.39; H, 5.42; N, 14.88.

The remaining work with sodium cyanide was exploratory in nature. If the reaction of sodium cyanide with *p*-nitrocumyl chloride is allowed to proceed for 24 h, a complex mixture is produced. The reaction of α,*p*-dinitrocumene with sodium cyanide in HMPA is somewhat slower than the reaction employing *p*-nitrocumyl chloride.

Reactions of Sodium Azide. (a) With *p*-Nitrocumyl Chloride. A solution of sodium azide in hot distilled water was decolorized with Darco activated carbon after which 2 vol of 95% ethanol was added. The mixture was cooled and filtered, and the azide was washed with ethanol and ethyl ether. It was then dried overnight on a rotary evaporator at room temperature (ca. 2 mm).

A solution of *p*-nitrocumyl chloride (1.50 g, 7.50 mmol) and sodium azide (0.975 g, 15 mmol) in 75 mL of HMPA was allowed to react for 15 min and was then worked up. Removal of the solvent gave a pale yellow oil weighing 1.55 g; n^{20}_D 1.5574. VPC analysis showed only one peak. Distillation at 0.6 mm and a bath temperature of 65–90 °C gave 1.47 g (95% yield) of *p*-nitrocumyl azide: n^{20}_D 1.5572; IR (neat) 2100 cm^{-1} (N_3); NMR (CCl_4) δ 7.85 (m, 4 H), 1.65 (s, 6 H). Anal. Calcd for $C_9H_{10}N_4O_2$: C, 52.42; H, 4.89; N, 27.17. Found: C, 52.31; H, 4.89; N, 27.01.

Light substantially affects the rate. Nonetheless, after 18 h in the dark a 95% yield of pure *p*-nitrocumyl azide was isolated.

(b) With α,*p*-Dinitrocumene.[28] A solution of 1.05 g (5.0 mmol) of α,*p*-dinitrocumene and 0.65 g (10 mmol) of sodium azide in 50 mL of HMPA was exposed to normal room light for 2 h. The usual workup gave a 94% yield of *p*-nitrocumyl azide, n^{20}_D 1.5572, which had the same VPC, NMR, and IR as the analytically pure sample isolated in part (a). When conducted in the light apparatus, the reaction was complete in less than 10 min. The reaction is less rapid in Me_2SO; a duplicate of the above reaction in Me_2SO required 5 h in the light apparatus. The effect of light is dramatic; even in HMPA, after 14 days in the dark the reaction is only ca. 20% complete.

Reaction of Pyrrolidine with *p*-Nitrocumyl Chloride. Pyrrolidine was dried over potassium hydroxide and distilled; the colorless liquid, bp 87 °C, had n^{20}_D 1.4425.

A solution of *p*-nitrocumyl chloride (1.62 g, 8.10 mmol) and pyrrolidine (1.18 g, 16.6 mmol) in 40 mL of Me_2SO was allowed to react for 18 h under the light apparatus. The solution was then poured into a mixture of ice-cold 5% aqueous sodium hydroxide and benzene. After separation, the aqueous alkaline solution was repeatedly extracted with benzene, and then the combined extracts were washed with water and dried ($MgSO_4$). The residue obtained

(34) D.H.S., 1970.

(35) Here, as in other reactions employing phenolic salts, the rate of reaction falls sharply in the later stages. Presumably, this is due to the fact that olefin formation gives rise to 1-methyl-2-naphthol, which, by hydrogen bonding to 1-methyl-2-naphthoxide ions, strongly reduces their reactivity. Since only a slight excess of the naphthoxide salt is employed, such inactivation becomes especially important in the later stages of the reaction. This problem is eliminated by using an extra 1 mol of the naphthoxide salt (cf. the reaction with α,*p*-dinitrocumene).

(36) Brubacher, G.; Suter, E. *Helv. Chim. Acta* **1950**, *33*, 256.

(37) Sodium phenoxide and sodium 2-naphthoxide react with Ia and Ib to give the ethers in 50–65% yield: T.M.D., 1968. D.H.S., 1970.

on removal of the benzene was chromatographed on alumina (Merck) with hexane–benzene for elution. In this way 1.69 g (90% yield) of pure *N*-(*p*-nitrocumyl)pyrrolidine was obtained as a yellow liquid: n^{20}_D 1.5557; NMR (CCl_4) δ 8.07 (d, 2 H), 7.65 (d, 2 H), 2.55 (m, 4 H), 1.75 (m, 4 H), 1.38 (s, 6 H). Anal. Calcd for $C_{13}H_{18}N_2O_2$: C, 66.64; H, 7.74; N, 11.96; mol wt 234. Found: C, 66.46; H, 7.67; N, 11.92; mol wt 234.

Reactions of Piperidine. (a) With *p*-Nitrocumyl Chloride. Piperidine was dried over potassium hydroxide and distilled; the colorless liquid, bp 106 °C, had n^{20}_D 1.4528.

A solution of *p*-nitrocumyl chloride (0.80 g, 4 mmol) and piperidine (0.68 g, 8.1 mmol) in 20 mL of Me_2SO was allowed to react for 20 h under the light apparatus. Workup as described for the pyrrolidine experiment gave a crude product that was chromatographed on silica gel with hexane–benzene and then benzene for elution. In this way 13 mg (2% yield) of α-methyl-*p*-nitrostyrene was obtained. This was followed by 4 mg of a white solid, mp 268 dec (very likely *p,p'*-dinitrobicumyl). Further elution with ether–benzene mixtures gave 0.910 g of *N*-(*p*-nitrocumyl)piperidine, which was treated with Darco in hot hexane. After removal of the solvent, 0.903 g (91% yield) of an oil that solidified to yellow crystals, mp 47–48 °C, was produced: NMR (CCl_4) δ 8.08 (d, 2 H), 7.67 (d, 2 H), 2.42 (m, 4 H), 1.2–1.8 (br m), 1.33 (s, 12 H). Anal. Calcd for $C_{14}H_{20}N_2O_2$: C, 67.72; H, 8.12; N, 11.28; mol wt 248. Found: C, 67.90; H, 8.24; N, 11.38; mol wt 245.

A duplicate experiment in the dark proceeded only 30% to completion.

(b) With α,*p*-Dinitrocumene. A solution of 1.60 g (7.62 mmol) of α,*p*-dinitrocumene[28] in 40 mL of Me_2SO was treated with 1.40 g (16.5 mmol) of piperidine. The reaction was allowed to proceed under the light apparatus. After 227 h the mixture was poured into 375 mL of ice-cold 5% aqueous sodium hydroxide and extracted with benzene. After washing with water and drying ($MgSO_4$), removal of the benzene gave 1.362 g of an orange oil that by VPC analysis consisted of *N*-(*p*-nitrocumyl)piperidine (77%), α,*p*-dinitrocumene (9%), *p*-nitrocumyl alcohol (4%), and an unknown (ca. 6%).

Chromatography on acid-washed alumina gave 0.936 g of *N*-(*p*-nitrocumyl)piperidine contaminated by ca. 5% of an unknown. This material was dissolved in pentane, cooled to −80 °C, and then warmed to 0 °C, and the small amount of red-orange solid was removed by filtration. The filtrate was cooled to −80 °C, and the yellow crystals that formed were isolated and recrystallized from fresh pentane at −80 °C. In this way pure *N*-(*p*-nitrocumyl)piperidine was isolated: mp 47–48 °C; IR and NMR identical with that of the analytical sample obtained in part (a).

Reaction of Quinuclidine with *p*-Nitrocumyl Chloride. Quinuclidine (Mallinckrodt) was purified by a modification of the procedure of Halpern and Weiss.[38] A solution of the amine in petroleum ether (bp 35–37 °C) was dried over sodium metal. After solvent removal under reduced pressure, the amine was sublimed through a U-tube coated with a sodium mirror into a flask also coated with a sodium mirror. The amine was then resublimed, giving white crystals, mp 161–163 °C (sealed tube) [lit.[39] mp 158–159 °C (sealed tube)].

A solution of *p*-nitrocumyl chloride (1.61 g, 8.05 mmol) and quinuclidine (1.78 g, 16.0 mmole in 40 mL of Me_2SO was allowed to react for 10 h under the light apparatus. The reaction product was poured into 350 mL of benzene. Ether (150 mL) was then added, and the resulting turbid solution was cooled at 5 °C for 2 h. The pale yellow solid that resulted was isolated, washed with benzene and with ether, and then dissolved in anhydrous ethanol. This solution was treated with decolorizing carbon (Darco), heated to boiling, and filtered. The ethanol solution was concentrated on a rotary evaporator to incipient precipitation, and then ether was added. The resulting white solid was isolated by filtration, washed with ether, and dried over phosphorus pentoxide at 100 °C (1 mm) for 24 h and at 25 °C for 48 h. In this way 2.2 g (90% yield) of (*p*-nitrocumyl)quinuclidinium chloride was obtained as a fluffy white powder. These crystals are soluble in water and in ethanol but are insoluble in hot acetone, benzene, ether, carbon tetrachloride, and chloroform: NMR (D_2O, relative to H_2O at δ 4.50) δ 8.00 (d, 2 H), 7.75 (d, 2 H), 3.34 (t, 6 H), 1.86 (s) and 1.6–2.17 (br m) with a combined area of 13 H. Anal. Calcd for $C_{16}H_{23}ClN_2O_2$: C, 61.83; H, 7.46; Cl, 11.41; N, 9.01. Found: C, 61.69; H, 7.46; Cl, 11.60; N, 9.14. The effect of light on this reaction is dramatic; in the dark little, if any, alkylation of quinuclidine took place in 12 h.

Reaction of 1,4-Diazabicyclo[2.2.2]octane (DABCO) with *p*-Nitrocumyl Chloride. DABCO was purified as described for quinuclidine; mp 155–157 °C (sealed tube) [lit.[40] mp 156–157 °C (sealed tube)]. A solution of *p*-nitrocumyl chloride (1.61 g, 8.05 mmol) and DABCO (1.79 g, 16 mmol) in 40 mL of Me_2SO was allowed to react for 36 h under the light apparatus. The orange solution was poured into 150 mL of benzene, 300 mL of ether was added, and the turbid solution was held at 5 °C for 12 h. The resulting yellow solid was isolated, treated with ethanol, and filtered. The ethanol solution was stirred with decolorizing carbon (Darco) at room temperature and filtered. The pale yellow filtrate was concentrated to incipient precipitation, and ether was added; the resulting off-white solid was washed with ether and dried at 25 °C (1 mm) over phosphorus pentoxide for 1 week. This gave a pale yellow solid that was placed in a water-saturated atmosphere overnight and then washed with 100-mL portions of acetone, benzene, and then acetone. The white solid was placed in a vacuum desiccator at 1 mm for 30 min to remove organic solvents. The resulting monohydrate 1.96 g (80% yield) was exposed to the atmosphere for 5 h and then placed in a desiccator over Drierite for 12 h. By NMR there were 1.03 mol of water/mol of alkylated DABCO. NMR (D_2O, relative to H_2O at δ 4.50) δ 8.00 (d, 2 H), 7.76 (d, 2 H), 4.50 (s, 2 H), 2.8–3.7 (2 complex m, symmetrical to each other, 12 H), 1.95 (s, 6 H). Anal. Calcd for $C_{15}H_{22}ClN_3O_2 \cdot H_2O$: C, 54.62; H, 7.33. Found: C, 53.91; H, 7.31.

The molecular weight was determined by titrating for chloride ion (assuming one chloride per molecule): theoretical 330, found 334.

Inhibition Studies

Although only one example of the use of each inhibitor is described, it should be emphasized that for each of the substitution reactions summarized in Table I inhibition has been demonstrated—often with a number of different inhibitors. These experiments are described in the doctoral dissertations of the junior authors.

***p*-DNB.** A solution of *p*-nitrocumyl chloride (1.0 g, 5 mmol) and sodium nitrite (0.69 g, 10 mmol) in 100 mL of HMPA was allowed to react in the light apparatus for 20 min. It was then poured into water and extracted with benzene; the extracts were washed with water and dried ($MgSO_4$), and the benzene was removed. The residue was chromatographed on acid-washed alumina (Merck) with benzene-hexane (40:60). This gave 0.04 g of a mixture of the starting chloride and *p*-nitro-α-methylstyrene.[41] Continued elution with benzene gave 0.960 g (88% yield) of α,*p*-dinitrocumene, mp 65–67 °C; its ^1H NMR spectrum duplicated that of an authentic sample. Chloride ion titration of the aqueous HMPA phase indicated 93% reaction.

A duplicate experiment in the presence of 85 mg (10 mol %) of *p*-DNB gave 0.721 g of a liquid whose ^1H NMR showed it to be a mixture of *p*-nitrocumyl chloride and *p*-nitro-α-methylstyrene;[41] there was no evidence of α,*p*-dinitrocumene. Chloride ion titration showed 3% reaction.

Di-*tert*-Butyl Nitroxide. A solution of 0.840 g (4.00 mmol) of α,*p*-dinitrocumene and 0.52 g (8.00 mmol) of sodium azide in 20 mL of HMPA was allowed to react for 15 min in the light apparatus. The crude product obtained

(38) Halpern, A. M.; Weiss, K. *J. Am. Chem. Soc.* **1968**, *90*, 6297.
(39) Wawzonek, S.; Wilkinson, T. C. *J. Org. Chem.* **1966**, *31*, 1732.
(40) Mann, F. G.; Baker, F. C. *J. Chem. Soc.* **1957**, 1881.
(41) On acid-washed alumina, *p*-nitrocumyl chloride undergoes significant elimination and the *p*-nitro-α-methylstyrene elutes with its parent chloride. Hence, *p*-nitrocumyl chloride is never recovered pure, but rather as a mixture with the olefin.

on the usual workup was chromatographed on acid-washed alumina using hexane–benzene mixtures. This gave 0.770 g (93% yield) of a very pale yellow liquid whose ^{1}H NMR spectrum is identical with that of authentic *p*-nitrocumyl azide.

Repetition of this experiment in the presence of 0.0282 g (0.194 mmol) of di-*tert*-butyl nitroxide resulted in the recovery of 0.746 g of pure α,*p*-dinitrocumene, mp and mixed mp 67–68 °C. In addition, 0.046 g of a mixture of *p*-nitrocumyl azide and α,*p*-dinitrocumene (whose ^{1}H NMR indicated equal amounts) was isolated.

Oxygen. A solution of *p*-nitrocumyl chloride (0.20 g, 1.0 mmol) and sodium benzenesulfinate (0.33 g, 2 mmol) in 20 mL of HMPA was allowed to react in the dark for 2 h under argon. It was worked up by pouring into water and extracting with benzene. Titration of the aqueous–HMPA phase showed that the theoretical amount of chloride ion had been produced and the pale yellow solid obtained on removal of benzene had the ^{1}H NMR spectrum of pure *p*-nitrocumyl phenyl sulfone.[13]

A duplicate reaction run in the presence of 0.246 mL (0.011 mmol) of oxygen gave less than 1% chloride ion, and the liquid obtained on removal of benzene had no detectable amount of the sulfone.

Galvinoxyl. A solution containing 0.210 g (1 mmol) of α,*p*-dinitrocumene, 0.32 g (2 mmol) of sodium benzenesulfinate, and 20 mL of HMPA was worked up after 30 min under the light apparatus. The crude product, a white solid, by ^{1}H NMR was composed of *p*-nitrocumyl phenyl sulfone (56%) and unreacted α,*p*-dinitrocumene (44%). A duplicate of this experiment conducted in the presence of 20 mg (0.05 mmol) of galvinoxyl gave, on workup, a dark yellow solid that, by ^{1}H NMR consisted of α,*p*-dinitrocumene and products from the galvinoxyl; it was devoid of *p*-nitrocumyl phenyl sulfone.

Sulfur. *p*-Nitrocumyl chloride (0.80 g, 4 mmol), and sodium nitrite (0.56 g, 8 mmol) in 20 mL of HMPA were allowed to react for 35 min under the light apparatus. On workup 0.579 g (69% yield) of pure α,*p*-dinitrocumene was obtained and 75% of the theoretical amount of chloride ion had been liberated. A duplicate experiment in which 0.0128 g of sulfur (10 atom %) was present gave 2% chloride ion and no α,*p*-dinitrocumene.

Induced Reactions

Use of the Lithium Salt of 2-Nitropropane. A solution of α,*p*-dinitrocumene (1.05 g, 5 mmol) and sodium azide (0.65 g, 10 mmol) in 50 mL of HMPA was allowed to react for 48 h in the dark. On workup 1.03 g (98% recovery) of pure α,*p*-dinitrocumene was obtained. A duplicate experiment in which 47 mg (0.50 mmol) of the lithium salt of 2-nitropropane was present was worked up after 3 h in the dark. A yellow oil (1.03 g) was obtained, and this on chromatography through alumina gave 1.00 g (97% yield) of *p*-nitrocumyl azide; n^{20}_D 1.5571–1.5575; ^{1}H NMR and IR identical with those of the pure azide.

Use of Sodium Naphthalene. Sodium (ca. 46 mg, 2 mmol) was added to a solution of naphthalene (0.704 g, 5.5 mmol) in dry, thoroughly degassed, HMPA (50 mL). The stirred mixture was maintained under argon for several hours by which time all the sodium had dissolved.

In the dark, to a stirred solution of α,*p*-dinitrocumene (2.10 g, 10 mmol) and sodium azide (1.30 g, 20 mmol) in 100 mL of HMPA was added 25 mL of a ca. 0.02 M solution of sodium naphthalene (0.5 mmol) over the course of 30 min. After an additional 30 min the reaction mixture was worked up to give 2.106 g of an oil that was chromatographed on acid-washed alumina. In this way 2.002 g (97% yield) of *p*-nitrocumyl azide, n^{20}_D 1.5570, was isolated; its ^{1}H NMR was identical with that of the pure azide.

Use of Sodium in HMPA. The preceding experiment was repeated with the exception that, instead of sodium naphthalene, 20 mL of a ca. 0.02 M solution of sodium in HMPA (0.4 mmol) was introduced in the course of 45 min. After an additional 15 min the reaction mixture was worked up to give 2.008 g (97% yield) of *p*-nitrocumyl azide, which had ^{1}H NMR and IR spectra identical with those of the pure azide.

Use of Sodium Trimesitylborane. This was prepared in the same way as sodium naphthalene. Here, however, 0.405 g (1.1 mmol) of trimesitylborane,[42] 0.023 g (1 mmol) of sodium, and 50 mL of HMPA were used; the solution was ca. 0.02 M in sodium trimesitylborane.

This reaction was conducted in the dark, under argon, with the same precautions as the sodium naphthalene experiment. A solution containing 0.210 g (1 mmol) of α,*p*-dinitrocumene and 0.13 g (2 mmol) of sodium azide in 10 mL of HMPA was prepared. To this solution was added 1.5 mL of the 0.02 M solution of sodium trimesitylborane (0.03 mmol) in 15 min, and then the reaction was allowed to continue for an additional 15 min and then worked up. This gave 211 mg of a yellow liquid whose ^{1}H NMR showed that it was 92% *p*-nitrocumyl azide and 8% α,*p*-dinitrocumene.

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Registry No. **Ia**, 14500-58-4; **Ib**, 3276-35-5; **I** (X = $C(CH_3)_2NO_2$), 14851-03-7; **I** (X = OH), 22357-57-9; **I** (X = $SO_2C_6H_5$), 70951-74-5; **I** (X = $C(CH_3)_2C_6H_4NO_2$-4), 30034-76-5; **I** (X = $CH(CO_2CH_2CH_3)_2$), 14851-05-9; **I** (X = $C(CO_2CH_2CH_3)_2(CH_2)_3CH_3$), 14851-06-0; **I** (X = H), 1817-47-6; **I** (X = CN), 71825-51-9; **I** (X = N_3), 105639-48-3; **II**, 15013-24-8; DABCO, 280-57-9; $NaSC_6H_5$, 930-69-8; $(H_2C)_2NO_2C^-Li^+$, 3958-63-2; $C_6H_5SSC_6H_5$, 882-33-7; $C_6H_5SO_3Na$, 515-42-4; $(H_3CCH_2O_2C)_2CH_2$·Na, 996-82-7; $H_3C(CH_2)_3CH(CO_2CH_2CH_3)_2$·Na, 22600-93-7; 4-$O_2NC_6H_4C(CH_3)$=$CH_2$, 1830-68-8; sodium 1-methyl-2-naphthoxide, 14851-07-1; 1-methyl-2-naphthyl ether, 14851-08-2; pyrrolidine, 123-75-1; *N*-(*p*-nitrocumyl)pyrrolidine, 105639-49-4; piperidine, 110-89-4; *N*-(*p*-nitrocumyl)piperidine, 105639-50-7; quinuclidine, 100-76-5; (*p*-nitrocumyl)quinuclidinium chloride, 105639-51-8; 1-(*p*-nitrocumyl)-1,4-diazabicyclo[2.2.2]octyl chloride, 105639-52-9; sodium naphthalene, 3481-12-7; sodium trimesitylborane, 34527-99-6.

(42) Brown, H. C.; Dodson, V. H. *J. Am. Chem. Soc.* **1957**, *79*, 2302.