Formation of Isocyanates by Deoxygenation of *C*-Nitrosocarbonyl Compounds

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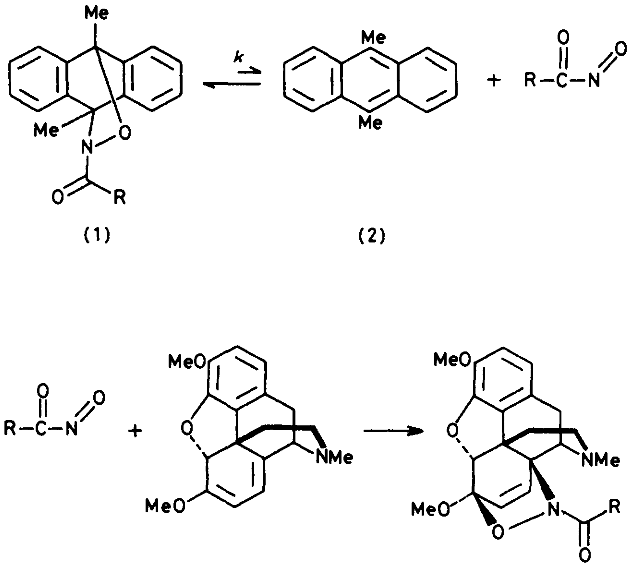
The cycloadduct (1a) of 9,10-dimethylanthracene (2) (hereinafter referred to as DMA) and nitrosocarbonylbenzene decomposed in benzene at 80 °C in the presence of triphenylphosphine to give DMA, triphenylphosphine oxide, and phenyl isocyanate in high yield. The corresponding adducts of 4-chloro-(1b), 4-methoxy-(1c), and 4-nitro-nitrosocarbonylbenzene (1d) behaved likewise. The cycloadduct of DMA and 4-methoxybenzylnitrosocarbonylmethane (1e) and of DMA and 1-(4-methoxyphenyl)-2-nitrosocarbonylethane (1f) gave lower (20—30%) yields of isocyanates. The rates of decomposition of the adduct (1a) in the presence of either the conjugated diene thebaine (3) or various phosphorus(III) derivatives were the same within experimental error. A similar observation was made for compound (1d). The formation of isocyanates is believed to involve slow dissociation of the cycloadducts followed by rapid deoxygenation of the transient nitrosocarbonyl compounds by triphenylphosphine. Stable complexes (8) of triphenylphosphine oxide with *N*-(4-nitrophenyl)-*N'*-propylurea and *N*-(4-nitrophenyl)-*N'*-phenylurea are described.

OXIDATION of hydroxamic acids, RC(:O)NHOH, is believed to generate transient nitrosocarbonyl compounds, RC(:O)N=O, which may be trapped as cycloadducts (dihydro-2*H*-1,2-oxazines) by conjugated dienes.[1] Further, adducts [*e.g.* (1)] of nitrosocarbonyl compounds and DMA, when heated in the presence of reactive dienes, *e.g.* thebaine (3), give DMA and the complementary adducts (4). These reactions are thought to involve an initial, slow dissociation of the adducts (1) to give DMA and RC(:O)NO (Scheme 1). It appeared, therefore, that thermal dissociation of these adducts should allow exploration of the reactions of nitrosocarbonyl compounds with co-reactants sensitive to oxidation. We record here deoxygenation reactions using triphenylphosphine.[2]

RESULTS AND DISCUSSION

C-Nitroso-compounds are known to react rapidly with phosphines to give the corresponding phosphine oxides and various nitrogenous products.[3] We expected that nitrosocarbonyl compounds would behave similarly, and this proved to be so. Thus, the nitrosocarbonylbenzene adduct (1a) and triphenylphosphine (2.3 mol equiv.) were heated in benzene under reflux for 2 h to give DMA, triphenylphosphine oxide, and phenyl isocyanate. The last product was characterised as *N*-(4-chlorophenyl)-*N'*-phenylurea and its yield (98%) was determined by g.l.c. Similarly, the adducts (1b) and (1c) gave 4-chlorophenyl isocyanate (92%) and 4-methoxyphenyl isocyanate (88%), respectively. Efficient aryl migration was observed even when the phenyl group carried a strongly electron-withdrawing substituent. Thus, the adduct (1d) with triphenylphosphine (1 mol equiv.) yielded 4-nitrophenyl isocyanate, which was converted *in situ* with ethanol into the corresponding urethane for analysis by g.l.c. (89% yield). The formation of isocyanates is believed to follow the pathway shown in Scheme 2. The nitrosocarbonylarene, released slowly by unimolecular dissociation of the DMA adduct (1) (Scheme 1), is captured by triphenylphosphine to give the dipolar intermediate (5) or the related species (6) and (7). It is likely that collapse of the intermediate (5) to give the observed products then proceeds, as shown, with concerted migration of the aryl residue. An alternative process involving fragmentation of the intermediate (5) to give an acylnitrene, RC(:O)–N:, cannot be completely excluded. However, high yields of isocyanates were observed in a solvent (benzene) susceptible to attack by nitrenes, and in the presence of an excess of triphenylphosphine which is able, in principle, to trap a free



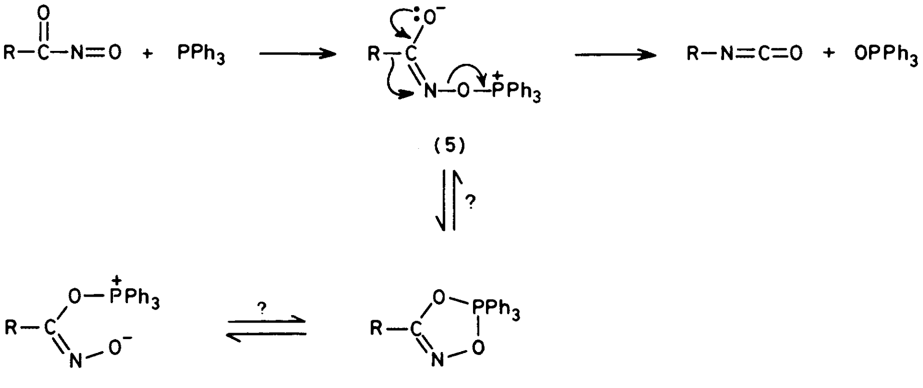
(1) (2)

(3) (4)

a; R = Ph
b; R = 4-ClC_6H_4
c; R = 4-$MeOC_6H_4$
d; R = 4-$O_2NC_6H_4$
e; R = 4-$MeOC_6H_4CH_2$
f; R = 4-$MeOC_6H_4CH_2CH_2$

SCHEME 1

nitrene as the phosphine imide, $RC(:O)N=PPh_3$.[4] The two adducts (1e) and (1f) were studied to test whether groups other than aryl would migrate readily from carbon to nitrogen. The corresponding isocyanates were formed in both cases but in low yield (20—30%). The yields were determined by conversion of the isocyanates *in situ* with aniline into the corresponding *N*-aralkyl-*N'*-phenylureas, which were purified chromatographically and then weighed. Some loss must have occurred in this process, but it appeared that the slower migration of the aralkyl groups had allowed some alternative, and so far undefined, reaction to intervene.



SCHEME 2

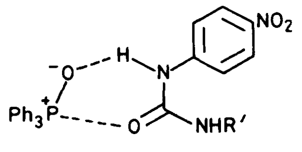
In the foregoing discussion we have assumed that the reactions with thebaine (Scheme 1) and triphenylphosphine (Scheme 2) involve nitrosocarbonyl compounds as common intermediates. Two consequences follow from this assumption: (i) an adduct (1) should react with thebaine (3) and with triphenylphosphine at the same rate, namely the rate of dissociation of the adduct (rate constant *k* in Scheme 1), and (ii) the reaction with triphenylphosphine, like that with thebaine,[1] should be kinetically first-order. The second consequence is especially important since bimolecular mechanisms for deoxygenation are conceivable. For example, attack by triphenylphosphine on the carbonyl oxygen of adducts (1) could lead to DMA and the dipolar species (7), which might then decompose to the observed products *via* the intermediates (6) and (5) (Scheme 2). Kinetic studies on the reactions of the new *N*-aroyl adducts (1b—d) (4 mM solutions) with thebaine (3) (4 mM) were carried out, as described before for compound (1a),[1] in benzene at 60 °C, the release of DMA being monitored spectrometrically [absorption at 385 nm or at 399 nm with adduct (1d)]. First-order kinetics were observed and higher initial concentrations of thebaine (8 mM) did not significantly affect the rates (see Table). Deoxygenation reactions of the adducts (1a) and (1d—f) (all 4 mM solutions in benzene) were also studied using two initial concentrations (4 and 8 mM) of triphenylphosphine. The first-order rate constants for the reaction of adducts (1a) and (1d) with triphenylphosphine were similar to those with thebaine and, again, the rates were insensitive to the initial concentration of triphenylphosphine. Moreover, the reactions of adduct (1a) with triethyl phosphite and tris(dimethylamino)phosphine proceeded at essentially the same rate as with triphenylphosphine. We conclude, therefore, that both types of reaction (Schemes 1 and 2) involve a common intermediate, very probably a nitrosocarbonyl compound, formed in a unimolecular, rate-determining step from the adduct (1). The rate constants varied little with the nature of the *N*-acyl group in the adduct (1); in particular, the *N*-benzoyl (1a) and *N*-4-chlorobenzoyl (1b) adducts reacted with thebaine at the same rate, within experimental error. These two adducts were therefore used to test for consistency between the kinetic data obtained with thebaine and the yields of isocyanates produced competitively with a deficiency of triphenylphosphine as follows. The adducts (1a) and (1b) (1 mol equiv. of each) were heated together in benzene under reflux for 2.5 h with triphenylphosphine (1 mol equiv.). Analysis (g.l.c.) of the products revealed phenyl- and 4-chlorophenyl-isocyanates in the ratio 46 : 54 (44 : 56 in a duplicate experiment). This is the result expected if the adducts dissociate at near-equal rates to give an intermediate which is trapped rapidly and irreversibly by the phosphine.

Dissociation rates ($10^5k/s^{-1}$) (Schemes 1 and 2) for the adducts (1) in benzene (4 mM) at 60 °C

Co-reactant		Adduct					
		(1a)	(1b)	(1c)	(1d)	(1e)	(1f)
Thebaine	4 mM	5.4	5.2	9.1	4.0		
	8 mM	4.7	5.1	8.2	4.3		
Ph_3P	4 mM	6.2			4.0	5.7	6.2
	8 mM	6.1			3.5	4.8	6.5
$(EtO)_3P$	4 mM	6.4					
	8 mM	7.0					
$(Me_2N)_3P$	4 mM	6.7					
	8 mM	6.6					

The conversion of hydroxamic acids into isocyanates *via* the adducts (1) constitutes, formally, a variant on the classical Lossen rearrangement. A related conversion has been described by Bittner *et al.*[5] who treated benzohydroxamic acids with triphenylphosphine and diethyl azodicarboxylate. The major products, *O*-carbamoyl hydroxamates, were believed to arise by reaction of the starting material with the derived aryl isocyanate. The species (5) (or its *N*-protonated form) was proposed as an intermediate but there was no evidence for the involvement of nitrosocarbonyl compounds.

As described above, the isocyanates formed according to Scheme 2 were characterised as the corresponding crystalline ureas after treatment with amines. This procedure worked smoothly for all the adducts (1) apart from (1d) which, initially, gave puzzling results. Addition of propylamine to the reaction mixture, believed to contain 4-nitrophenyl isocyanate, gave a sharp-melting substance which differed in solubility, melting point, and spectroscopic properties from the expected product, *N*-(4-nitrophenyl)-*N*′-propylurea. A similarly unexpected result was obtained with aniline in place of propylamine. Microanalytical data showed these products to be 1 : 1 complexes of the expected ureas and triphenylphosphine oxide which was present in the original reaction mixtures. Moreover, the complexes were formed in high yield by keeping equimolar amounts of 4-nitrophenyl isocyanate, triphenylphosphine oxide, and the appropriate amine in benzene at room temperature or by treating the preformed ureas with triphenylphosphine oxide. We consider that complex formation involves hydrogen bonding [*e.g.* structure (8)] rather than covalent bonding between phosphorus and the urea. The latter possibility may be discounted, at least for solutions ($CDCl_3$), since the complexes showed ^{31}P chemical shifts, δ 31.6 p.p.m. (downfield from H_3PO_4), characteristic of phosphine oxides and not of pentacovalent, phosphorane derivatives. A related phenomenon has been described by Allen *et al.*[6] who have proposed hydrogen-bonded structures for the 1 : 1 adducts of triarylphosphine oxides and toluene-4-sulphonamide.



(8)

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. N.m.r. spectra were recorded for deuteriochloroform solutions with tetramethylsilane as internal standard, and i.r. spectra for KBr discs. Light petroleum refers to the fraction boiling in the range 60—80 °C.

Cycloadducts (1b–d) *of DMA* (2) *and Nitrosocarbonylarenes*.—The adducts were prepared, as for the adduct (1a),[1] by oxidation of the appropriate benzohydroxamic acid with tetraethylammonium periodate in the presence of 9,10-dimethylanthracene (DMA) in dichloromethane. Thus prepared were N-(4-*chlorobenzoyl*)-9,10-*dihydro*-9,10-*dimethyl*-9,10-*epoxyiminoanthracene* (1b), as prisms, m.p. 124—126 °C (from benzene–light petroleum) (Found: C, 73.7; H, 5.0; N, 3.8. $C_{23}H_{18}ClNO_2$ requires C, 73.5; H, 4.9; N, 3.8%); $\nu_{max.}$ 1 660 cm^{-1}; δ 7.2—7.6 (m, ArH), 2.75 (s, 9-Me), and 2.04 (s, 10-Me); 9,10-*dihydro*-N-(4-*methoxybenzoyl*)-9,10-*dimethyl*-9,10-*epoxyiminoanthracene* (1c), as plates, m.p. 129—131 °C (decomp.) (from benzene–light petroleum) (Found: C, 77.4; H, 5.8; N, 3.8. $C_{24}H_{21}NO_3$ requires C, 77.6; H, 5.7; N, 3.8%); $\nu_{max.}$ 1 660 cm^{-1}; δ 7.15—7.65 (m, ArH), 6.71 (d, *J* 8 Hz, H *ortho* to MeO), 3.72 (s, OMe), 2.73 (s, 9-Me), and 2.09 (s, 10-Me); and 9,10-*dihydro*-9,10-*dimethyl*-N-(4-*nitrobenzoyl*)*epoxyiminoanthracene* (1d), as prisms, m.p. 126—128 °C (from benzene–light petroleum) (Found: C, 71.2; H, 4.7; N, 7.1. $C_{23}H_{18}N_2O_4$ requires C, 71.5; H, 4.7; N, 7.25%); $\nu_{max.}$ 1 670 cm^{-1}; δ 8.06 (d, *J* 8 Hz, H *ortho* to NO_2), 7.15—7.65 (m, ArH), 2.82 (s, 9-Me), and 2.06 (s, 10-Me).

Preparation of 4-*Methoxyphenylacetohydroxamic Acid and* 3-(4-*Methoxyphenyl*)*propanohydroxamic Acid*.—These hydroxamic acids were prepared from the corresponding carboxylic ethyl esters by treatment with ethanolic hydroxylamine using the standard procedure.[7] Thus prepared were 4-*methoxyphenylacetohydroxamic acid*, m.p. 154—156 °C (from ethyl acetate) (Found: C, 59.5; H, 5.8; N, 7.5. $C_9H_{11}NO_3$ requires C, 59.7; H, 6.1; N, 7.7%); $\nu_{max.}$ 3 200br and 1 630 cm^{-1} and 3-(4-*methoxyphenyl*)*propanohydroxamic acid*, m.p. 113—115 °C (from ethyl acetate–light petroleum) (Found: C, 61.2; H, 6.9; N, 7.5. $C_{10}H_{13}NO_3$ requires C, 61.5; H, 6.7; N, 7.2%); $\nu_{max.}$ 3 280 and 1 665 cm^{-1}.

Cycloadducts, (1e) *and* (1f), *of DMA and* (4-*Methoxyphenyl*)-*nitrosocarbonylmethane and* 1-(4-*Methoxyphenyl*)-2-*nitrosocarbonylethane respectively*.—The foregoing hydroxamic acids were each oxidised with tetraethylammonium periodate in the presence of DMA in dichloromethane as above to afford 9,10-*dihydro*-N-(4-*methoxyphenylacetyl*)-9,10-*dimethyl*-9,10-*epoxyiminoanthracene* (1e), m.p. 133—134 °C (from ethyl acetate–light petroleum) (Found: C, 77.7; H, 6.0; N, 3.5. $C_{25}H_{23}NO_3$ requires C, 77.9; H, 6.0; N, 3.6%); $\nu_{max.}$ 1 670 cm^{-1}; δ 7.5—7.12 (m, ArH), 6.70 and 6.58 (ABq, *J* 8 Hz, ArH), 4.70 (s, OMe), 3.42 (s, CH_2), 2.70 (s, 9-Me), and 2.08 (s, 10-Me) and 9,10-*dihydro*-N-[3-(4-*methoxyphenyl*)-*propanoyl*]-9,10-*dimethyl*-9,10-*epoxyiminoanthracene* (1f), m.p. 126.5—128.5 °C (from ethyl acetate–light petroleum) (Found: C, 78.0; H, 6.4; N, 3.4. $C_{26}H_{25}NO_3$ requires C, 78.2; H, 6.3; N, 3.5%); $\nu_{max.}$ 1 680 cm^{-1}; δ 7.5—7.1 (m, ArH), 6.83 and 6.78 (ABq, *J* 9 Hz, ArH), 3.70 (s, OMe), 2.74 (s, 9-Me), 2.50 [m, $(CH_2)_2$], and 2.18 (s, 10-Me).

Reactions of the Cycloadducts (1a—d) *with Triphenylphosphine*.—The adduct (1a) (50 mg, 0.15 mmol) and triphenylphosphine (87 mg, 0.33 mmol) were heated in dry benzene (1 ml) under reflux for 2 h. The mixture was diluted to 5 ml with dry benzene and analysed (g.l.c.; 7% F60–1%Z; 75 °C). Phenyl isocyanate (98% yield) was identified by comparison with authentic material. Treatment of the mixture with 4-chloroaniline gave *N*-(4-chlorophenyl)-*N*′-phenylurea, m.p. and mixed m.p. 234—236 °C. Similarly, adduct (1b) gave 4-chlorophenyl isocyanate (92% by g.l.c.) and thence, with aniline, *N*-(4-chlorophenyl)-*N*′-phenylurea, and adduct (1c) gave 4-methoxyphenyl isocyanate (88%) and thence *N*-(4-methoxyphenyl)-*N*′-phenylurea, m.p. and mixed m.p. 191—193 °C. The adduct (1d) (55 mg, 0.14 mmol) and triphenylphosphine (37 mg, 0.14 mmol) were heated in benzene (1.5 ml) under reflux for 2.5 h. Addition of propylamine or aniline to the reaction mixture gave the corresponding triphenylphosphine oxide–urea complexes (8) described below. Alternatively, addition of ethanol (5 ml) gave ethyl *N*-(4-nitrophenyl)carbamate which was identified by g.l.c. (1% OV1; 150 °C; 89% yield). In a preparative experiment, the adduct (1d) (101 mg) and triphenylphosphine (79 mg) were heated in benzene as before. The mixture was treated with ethanol (10 ml) to afford, after preparative t.l.c., ethyl *N*-(4-nitrophenyl)carbamate (49 mg, 77%), m.p. and mixed m.p. 128—129 °C.

Preparation of N-(4-*Methoxybenzyl*)-N'-*phenylurea and* N-(4-*Methoxyphenethyl*)-N'-*phenylurea.*—A solution of ethyl chloroformate (1.3 g) in acetone (5 ml) was added slowly with stirring to 4-methoxyphenylacetic acid (1.7 g) and triethylamine (1.5 g) in acetone (25 ml) and water (3 ml) at 0 °C. After 30 min, a solution of sodium azide (1 g) in water (5 ml) was added dropwise. After 1 h at 0 °C the mixture was poured into ice–water (*ca.* 100 ml) and extracted with ether. The extract was dried (Na_2SO_4) and evaporated to give a dark oil which was heated in dry benzene (15 ml) until evolution of nitrogen had ceased. The resulting mixture, containing 4-methoxybenzyl isocyanate, was treated with an excess of aniline at room temperature for 2 h. The mixture was diluted with chloroform (100 ml) and washed successively with dilute hydrochloric acid and water and then dried (Na_2SO_4) and evaporated. The residue crystallised from ethyl acetate–light petroleum to afford N-(4-*methoxybenzyl*)-N'-*phenylurea* (0.70 g), m.p. 160—162 °C (Found: C, 70.2; H, 6.4; N, 11.2. $C_{15}H_{16}N_2O_2$ requires C, 70.3; H, 6.25; N, 10.9%); $\nu_{max.}$ 3 325 and 1 635 cm^{-1}; *m/z* 256. Similarly, 3-(4-methoxyphenyl)propanoic acid (1.8 g) gave N-(4-*methoxyphenethyl*)-N'-*phenylurea* (1.0 g), m.p. 169—170 °C (from ethyl acetate–light petroleum) (Found: C, 71.2; H, 6.9; N, 10.7. $C_{16}H_{18}N_2O_2$ requires C, 71.1; H, 6.7; N, 10.4%); $\nu_{max.}$ 3 400, 3 260, and 1 160 cm^{-1}; *m/z* 270.

Reactions of the Cycloadducts (1e) *and* (1f) *with Triphenylphosphine.*—The adduct (1e) (97 mg, 0.25 mmol) and triphenylphosphine (67 mg, 0.25 mmol) were heated in dry benzene (5 ml) under reflux for 6 h under nitrogen. Aniline (*ca.* 3 ml) was added and the mixture was kept at room temperature for 2 h then diluted with chloroform (50 ml) and the solution was washed with dilute hydrochloric acid and then water. The products were separated by preparative t.l.c. [silica gel; ethyl acetate–light petroleum (2 : 1) as developer] to give *N*-(4-methoxybenzyl)-*N'*-phenylurea (18 mg, 29%), which was identical (mixed m.p., i.r.) with a sample prepared as described above. Essentially the same yields of the urea were obtained with an excess (2 mol equiv.) of triphenylphosphine and when aniline was added at the beginning, rather than the end, of the heating period. Similarly, the adduct (1f) gave *N*-(4-methoxyphenethyl)-*N'*-phenylurea (23%). The formation of isocyanates from both adducts (1e) and (1f) was also indicated by the presence of a strong band, $\nu_{max.}$ 2 260 cm^{-1}, in the i.r. spectra of the mixtures before addition of aniline.

Kinetic Studies.—These were conducted as before [1,8] for solutions in benzene at 60 °C. The initial concentrations of adducts and co-reactants and the measured rate constants for the formation of DMA [absorption at 385 nm or at 399 nm with adduct (1d)] are given in the Table. Generally, ' infinity ' readings agreed well with those calculated for quantitative release of DMA, but some unaccountable variations were noted; it is possible that DMA was not completely stable for the extended periods (24 h) of heating employed for these studies.

Complexes (8) *of* N-(4-*Nitrophenyl*)-N'-*propylurea and* N-(4-*Nitrophenyl*)-N'-*phenylurea with Triphenylphosphine Oxide.*—Equimolar amounts of 4-nitrophenyl isocyanate, propylamine, and triphenylphosphine oxide were kept in dry benzene at room temperature for 30 min to give, essentially quantitatively, the *complex* (8; R' = Pr), m.p. 108—110 °C (from ethyl acetate–light petroleum) (Found: C, 67.05; H, 5.7; N, 8.1. $C_{28}H_{28}N_3O_4P$ requires C, 67.1; H, 5.6; N, 8.4%); $\nu_{max.}$ 3 380, 3 280, 3 240, 3 145, 3 080, 1 710, and 1 618 cm^{-1}. Similarly, 4-nitrophenyl isocyanate, aniline, and triphenylphosphine oxide gave the *complex* (8; R' = Ph), m.p. 158—160 °C (from ethyl acetate–light petroleum) (Found: C, 69.8; H, 5.1; N, 7.9. $C_{31}H_{26}N_3O_4P$ requires C, 69.5; H, 4.85; N, 7.85%); $\nu_{max.}$ 3 350, 3 310, 3 260, 3 210, 3 145, 3 080, 1 720, and 1 600 cm^{-1}; $\nu_{max.}$ ($CHCl_3$) 3 300br, 1 715, and 1 600 cm^{-1}.

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REFERENCES

[1] G. W. Kirby and J. G. Sweeny, *J. Chem. Soc., Perkin Trans. 1*, 1981, 3250; see also G. W. Kirby, *Chem. Soc. Rev.*, 1977, **6**, 1.

[2] Preliminary communication: J. E. T. Corrie, G. W. Kirby, and R. P. Sharma, *J. Chem. Soc., Chem. Commun.*, 1975, 915.

[3] J. I. G. Cadogan, *Quart. Rev.*, 1968, **22**, 222; J. I. G. Cadogan and R. K. Mackie, *Chem. Soc. Rev.*, 1974, **3**, 87.

[4] See R. A. Abramovitch in ' Organic Reaction Intermediates,' ed. S. P. McManus, Academic Press, London, 1973.

[5] S. Bittner, S. Grindberg, and I. Kartoon, *Tetrahedron Lett.*, 1974, 1965.

[6] D. W. Allen, F. G. Mann, and J. C. Tebby, *J. Chem. Soc., Perkin Trans. 1*, 1972, 2793, and references cited therein.

[7] S. R. Sandler and W. Karo, ' Organic Functional Group Preparations,' Academic Press, New York, 1972, vol. III, p. 419.

[8] P. Horsewood, G. W. Kirby, R. P. Sharma, and J. G. Sweeny, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1802.