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RADICAL AND IONIC REACTIONS OF TETRABUTYLAMMONIUM *aci*-NITRONATES.[1]

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The use in synthesis of quaternary ammonium compounds has expanded enormously since the early investigations by Makosza and coworkers in 1965.[2] The reactions of a wide range of quaternary ammonium salts, often prepared *in situ* by phase transfer techniques, have been extensively studied.[3,4] To the best of our knowledge no study of the preparation and reaction of tetraalkylammonium salts of nitroalkanes has been made.

In connection with another project we required large quantities of the compound, p-$NO_2C_6H_4CH_2CMe_2NO_2$, whose preparation by reaction of the lithium salt of 2-nitropropane with *p*-nitrobenzyl chloride in dimethylformamide by the radical $S_{RN}1$ process has been described by Kornblum and coworkers.[5,6] Since larger scale reactions than those reported[5] required large volumes of dipolar aprotic solvents and prior preparation of the lithium salt of 2-nitropropane we decided to attempt this reaction using a phase transfer technique. Commercial 40% tetrabutylammonium hydroxide was found to readily dissolve 2-nitropropane, 2-nitrobutane and 3-methyl-2-nitrobutane.[7] When an aqueous solution of tetrabutylammonium 2-nitro-2-propanide so formed was stirred with *p*-nitrobenzyl chloride in chloroform, dichloromethane or benzene the required carbon alkylate was formed (see Table, expts 1, 2 and 3). Since the reactions in benzene and dichloromethane proceeded in good yield, reactions using aqueous solutions of the sodium salt of 2-nitropropane containing only catalytic quantities of the tetrabutylammonium *aci*-nitronate were attempted. When benzene was used as solvent quite good yields could be obtained (see Table, expt 5). The catalysed reaction in dichloromethane was considerably slower and proceeded in somewhat poorer yield (expt 4).

Table: Products from reaction of tetrabutylammonium *aci*-nitronates with various substrates

Expt.	Substrate[a]	Method[b]	Solvent	Time	Products[c]
1	Ar^1CH_2Cl	A	$CHCl_3$	2 h	$Ar^1CH_2CMe_2NO_2$(22)
2	Ar^1CH_2Cl	A	CH_2Cl_2	30 min	$Ar^1CH_2CMe_2NO_2$(60)[d]
3	Ar^1CH_2Cl	A	C_6H_6	1.5 h	$Ar^1CH_2CMe_2NO_2$(73)[d]
4	Ar^1CH_2Cl	B	CH_2Cl_2	10-30 h	$Ar^1CH_2CMe_2NO_2$(50-60)
5	Ar^1CH_2Cl	B	C_6H_6	3-5 h	$Ar^1CH_2CMe_2NO_2$(65-70)
6	Ar^2CH_2Cl	A	CH_2Cl_2	3 h	Ar^2CHO(63) $Ar^2CH_2CMe_2NO_2$(13)
7	Ar^3CH_2Cl	A	CH_2Cl_2	5 h	Ar^3CHO(63) Ar^3CH_2OH(4)
8	$PhCH_2Cl$	B	CH_2Cl_2	5 h	PhCHO(45)
9	$PhCH_2Cl$	B	CH_2Cl_2	4 d	PhCHO(80)
10	$PhCH_2Cl$	B	C_6H_6	6 d	PhCHO(65)
11	Ar^1CHCl_2	A	CH_2Cl_2	40 min	$Ar^1CH(Cl)CMe_2NO_2$(62)
12	Ar^1CHCl_2	A	C_6H_6	60 min	$Ar^1CH(Cl)CMe_2NO_2$(58)
13	Ar^1CHCl_2	A[e]	CH_2Cl_2	30 min	$Ar^1CH(Cl)CMe(Et)NO_2$(58)[f]
14	Ar^2CHCl_2	A	CH_2Cl_2	4 d	$Ar^2CH(Cl)CMe_2NO_2$(54)
15	Ar^1CBr_3	A[g]	CH_2Cl_2	<5 min	$Ar^1C{\equiv}CAr^1$(30) $Ar^1CH{=}CMe_2$(38)
16	Ar^1NO_2	C	Me_2CO	<5 min	$Ar^1CMe_2NO_2$(73)
17	Ar^1NO_2	C	C_6H_6	<5 min	$Ar^1CMe_2NO_2$(76)
18	Ar^1NO_2	C[h]	C_6H_6	<5 min	$Ar^1CMe(^iPr)NO_2$(40) Ar^1OH(16) (E)-$Me(^iPr)C{=}NOAr^1$(24) (Z)-$Me(^iPr)C{=}NOAr^1$(11)
19	Ar^1NO_2	C[h]	Me_2SO	<5 min	$Ar^1CMe(^iPr)NO_2$(37) Ar^1OH(20) *(E)*-$Me(^iPr)C{=}NOAr^1$(19) *(Z)*-$Me(^iPr)C{=}NOAr^1$(14)

Footnotes to Table.

a Ar^1 = *p*-$NO_2C_6H_4$; Ar^2 = *o*-$NO_2C_6H_4$; Ar^3 = *m*-$NO_2C_6H_4$

b Method A: The substrate (10.0 mmol) in the organic solvent (10 ml) was stirred under nitrogen with a solution prepared from the nitroalkane (15 mmol) and 40% tetrabutylammonium hydroxide (10 ml).

Method B: The substrate (0.1-0.3 mol) in the organic solvent (25-50 ml) was stirred under nitrogen with a solution prepared by dissolving the nitroalkane (0.15-0.45 mol) in 40% tetrabutylammonium hydroxide (4-5 ml) and the required volume of 6-10 M aqueous sodium hydroxide.

Method C: Powdered *p*-dinitrobenzene (10 mmol) was added to a solution of the anhydrous tetrabutylammonium *aci*-nitronate (12-20 mmol) in the organic solvent (10-20 ml). Unless otherwise stated the nitroalkane used was 2-nitropropane.

c Yields of pure compounds are given in parenthesis. New compounds (formulae in italics) gave the required elementary analysis and had the expected spectroscopic properties.

d Small amounts (2-5%) of *p*-nitrobenzyl alcohol, *p*-nitrobenzaldehyde and *p,p'*-dinitrostilbene oxide could also be isolated.

e Using 2-nitrobutane.

f Mixture of separable diastereomers in approximately equal amounts.

g The tribromo compound (1 mmol) in dichloromethane (10 ml) was stirred under nitrogen with a solution prepared from 40% tetrabutylammonium hydroxide (4 ml) and 2-nitropropane (6 mmol).

h Using tetrabutylammonium 3-methyl-2-nitro-2-butanide (20 mmol).

The mechanism of this reaction is undoubtedly of the radical anion, radical chain type ($S_{RN}1$) since *m*-nitrobenzyl chloride (expt 7) and benzyl chloride (expts 8, 9, 10) give only S_N2 *O*-alkylation reactions (leading ultimately to aldehydes), whereas *p*-nitrobenzyl (and to a lesser extent *o*-nitrobenzyl) chloride gives the *C*-alkylated product. This behaviour is completely analogous to the corresponding behaviour of benzyl chlorides in dipolar aprotic solvents.[5,6] The difference in rate of the reaction of *p*-nitrobenzyl chloride and benzyl chloride (compare expts 4 and 5 with 9 and 10) also indicates the radical nature of the reaction.

The two phase procedure was also found to be convenient for the conversion of *o*- and *p*-nitrobenzylidene dichlorides to the corresponding mono *C*-alkylated derivatives (see expts 11, 12, 13 and 14) *via* the $S_{RN}1$ process.[8] In contrast to the reaction of *o*-nitrobenzyl chloride, the reaction of *o*-nitrobenzylidene chloride appears to occur solely by *C*-alkylation. The subsequent elimination ($E_{RC}1$)[8] reaction which gives rise to styrenes did not take place as readily as in dimethyl sulphoxide allowing useful and readily obtainable yields of the mono *C*-alkylated products.[9] These results constitute the first report of $S_{RN}1$ reactions conducted in non-polar aprotic solvents.

The reaction of *p*-nitrobenzotribromide with the 2-nitro-2-propanide ion under phase transfer conditions gave 4,4'-dinitrotolan and *p*-nitro-β,β-dimethylstyrene (see expt 15). The details of the mechanism of this conversion are currently under investigation, however the first step is removal of bromine by the anion of 2-nitropropane to give 2-bromo-2-nitropropane and the anion, $p\text{-}NO_2C_6H_4\bar{C}Br_2$. Under more dilute conditions than those in expt 15, and using deuterium oxide, 2-bromo-2-nitropropane and 50-70% yields of *p*-nitrobenzylidene dibromide with >95% deuterium in the α-position can be isolated.

The tetrabutylammonium salts of the nitroalkanes could be obtained in anhydrous form by evaporation under vacuum of the aqueous solutions resulting from reaction of a slight excess of the appropriate nitroalkane with tetrabutylammonium hydroxide. The crystalline (very hygroscopic) salts so obtained were readily soluble in alcohols, dimethyl sulphoxide, acetone, benzene and dichloromethane. The anhydrous salts were far more reactive than the corresponding lithium salts. The reactions with *p*-dinitrobenzene in dimethyl sulphoxide, acetone and benzene were extremely rapid (see expts 16, 17, 18 and 19) whereas the reactions of the corresponding lithium salts which gave similar product proportions take from 3 to 30 hours in dimethyl sulphoxide.[10,11] The formation of the *p*-nitrophenyl ethers of methyl isopropyl ketoxime from *p*-dinitrobenzene and tetrabutylammonium 3-methyl-2-nitro-2-butanide is without precedent and presumably involves the *p*-nitrophenyl nitronate esters formed by sterically induced *O*-attack of the *aci*-nitronate ion on *p*-dinitrobenzene. The mechanism of this and other more sterically hindered reactions is under further study.

Footnotes and References

1) This investigation was supported by a grant from the Australian Research Grants Committee.
2) M. Makosza and B. Serafinowa, *Rocz. Chem.*, 39, 1223, 1401, 1595, 1799, 1805 (1965), also see M. Makosza, *Tetrahedron Letters*, 673, 677 (1969).
3) J. Dockx, *Synthesis*, 441 (1973).
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6) N. Kornblum, *Angew. Chem., Int. Ed. Engl.*, 14, 744 (1975).
7) This nitro compound instantaneously dissolves in 1.5 M $N\overset{+}{Bu_4}\ \overset{-}{OH}$ but is not appreciably dissolved by 5 M NaOH after 2 hours.
8) D.J. Freeman and R.K. Norris, *Aust. J. Chem.*, 30, 2631 (1976).
9) The nitroalkane dimers formed in the secondary $E_{RC}1$ process are difficult to separate from the primary mono-*C*-alkylated products.
10) R.K. Norris and D. Randles, unpublished results.
11) N. Kornblum, L. Cheng, R.C. Kerber, M.M. Kestner, B.N. Newton, H.W. Pinnick, R.G. Smith, and P.A. Wade, *J. Org. Chem.*, 41, 1560 (1976).