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CARBON-ALKYLATION OF SIMPLE NITRONATE ANIONS BY N-SUBSTITUTED PYRIDINIUMS

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Abstract—N-Primary and -secondary alkyl and N-(substituted benzyl) groups are transferred at ≤100° from N-substituted 2,4,6-triphenylpyridiniums to give carbon alkylation of the anions of nitro-methane and ethane and 2-nitropropane in preparatively useful yields (24 examples). Non-chain radical substitution processes are probably involved.

According to a recent review[1] there existed until recently only two examples of simple C-alkylation† of nitronate anions, both[2,3] intramolecular cyclisations. C-Alkylation by radical-chain processes described by Kornblum[4] had usually required additional activation in the form of a nitro or *p*-nitrophenyl group at the reaction centre.‡ After our preliminary communication[5] was submitted, a preliminary communication by Russell and co-workers[6] became available which reported that primary and secondary alkyl mercury halides participate with nitronate anions in $S_{RN}1$ processes when irradiated in nitrogen-purged dimethylformamide $RHgX + R'_2C{:}NO_2^- \rightarrow RR'_2CNO_2 + X^- + Hg^0$. Previously, Seebach and co-workers[7] had shown that dilithio derivatives of nitroalkanes are smoothly *C*-alkylated by primary alkyl and benzyl halides.

Despite these recent advances, and in view of the great potential of nitroaliphatics as synthetic intermediates,[1] the need clearly exists for a general C-alkylation technique of simple nitronate anions. We believe that the presently reported alkylation with 1-substituted-2,4,6-triphenylpyridiniums fills this gap in synthetic methodology.

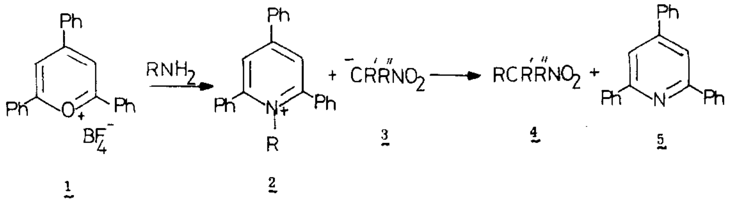
We have shown that 1-substituted pyridiniums (**2**) [themselves now available from primary amines and pyrylium **1** under very mild conditions[8] (Table 1)] transfer their N-substituent to a wide variety of nucleophiles.[9] We now report conditions under which they C-alkylate nitronate anions (**3**) to nitro compounds (**4**) in moderate to high yield.

N-Benzyl and N-(substituted benzyl) groups are transferred to nitronate anions in refluxing ethanol (Table 2): to optimise yields with respect to the alkylating agent it was found best to use 3 moles of the nitronate anion. Yields were 55–78% (average 65%) for reactions with the anion of nitromethane, somewhat lower (35–57%, average 51%) for the anion of nitroethane, and lowest for reactions with 2-nitropropane anions (41–44%, average 42%) (see later).

The reaction proceeds much faster in dimethyl sulphoxide: lower temperatures and shorter times being required than for comparable cases in ethanol. Heating at 100° was required for alkylation while 50° sufficed for benzylation (Table 3). However, we now find that yields are high for reactions with 2-nitropropane anion (44–75%, average 62%), moderate for nitroethane anion (33–52%, average 43%), and low for the nitromethane anion: we believe the reason for this to be the easy further reaction of the products for the last two anions with further alkylating agent, causing the formation of mixtures.

Noteworthy are the useful yields achieved using secondary alkyl (isopropyl, cyclohexyl) and 2- and 3-picolyl groups. Furthermore, benzyls other than *p*-nitrobenzyl may be used successfully in the reactions reported here (whereas the para nitro group is necessary in the Kornblum reaction[4a]).

The ^{1}H NMR spectra of the compounds prepared here are reported in Table 4. All have been satisfactorily analysed, and products were pure by glc



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†Carbon-acylations are somewhat more common, see e.g. the use of acylimidazoles [D. C. Baker and S. R. Putt, *Synthesis* 478 (1978)].

‡Kornblum has recently shown that a *p*-cyanophenyl group also facilitates $S_{RN}1$ processes: N. Kornblum and M. J. Fifolt, *J. Org. Chem.* 360 (1980).

Table 1. Preparation of 1-alkyl-2,4,6-triphenylpyridinium tetrafluoroborates[a]

1-Substituent	Yield (%)	M.p. (°C)	Lit. m.p. (°C)	Ref.
$PhCH_2$	81	193-195	196-197	b
$ClC_6H_4CH_2$(o)	76	197-199	200	c
$Cl_2C_6H_4CH_2$(o,p)	65	233-235	239	c
$ClC_6H_4CH_2$(p)	83	141-142	144	c
$MeC_6H_4CH_2$(p)	79	118-120[d]	134	e
$PhCH_2CH_2$	75	265-270	274	f
n-C_4H_9	69	196-198	201-202	b
n-C_6H_{13}	57	240-242	236-238	e
Cyclohexyl	52	180-182	180-182	f
Pr^i	51	168-170	171-173	e
2-Picolyl	68	215-216	218-219	f
3-Picolyl	63	159-163	166-168	f

Footnotes

[a] Reaction time· 2 hr. Crystal form: white needles. [b] U. Gruntz, A.R. Katritzky, D.H. Kenny, M.C. Rezende and H. Sheikh, J. Chem. Soc. Chem. Comm. 701 (1977). [c] A.R. Katritzky, U. Gruntz, A.A. Ikizler, D.H. Kenny and B.P. Leddy, J. Chem. Soc. Perkin I 436 (1979). [d] New polymorphic form· plates (Found. C, 74.3; H, 5.1; N, 2.7. requires C, 74.5; H, 5.2; N, 2.8%). [e] A.R. Katritzky, G. Liso, E. Lunt, R.C. Patel, S.S. Thind and A. Zia, J. Chem. Soc. Perkin I in the press, paper 9/820. [f] A.R. Katritzky, U. Gruntz, D.H. Kenny, M.C. Rezende and H. Sheikh, J. Chem. Soc. Perkin I 430 (1979).

(Carbowax 220m) (as reported in Tables 1 and 2). For further details see Ref. 10].

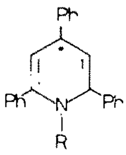
The mechanism of the reaction of nitronate anions with pyridinium

Previous nitroalkane syntheses involving the displacement of a leaving group by nitronate anion have been shown to involve a radical chain mechanism (eqns 1 and 2),[11] termed $S_{RN}1$ by Bunnett.[12] Many substrates are known to participate in $S_{RN}1$ reactions and interest in this area continues to be considerable: e.g. recent extension to primary or secondary alkyl mercury chlorides or bromides.[6]

$$RX \xrightarrow{e^-} RX^- \rightarrow R + X^- \qquad (1)$$

$$R^{\cdot} + Nu^- \rightarrow RNu^- \rightarrow RNu + e^-. \qquad (2)$$

Although we observed no light acceleration, dark inhibition, or rate retardation in the presence of *m*-dinitrobenzene [usual criteria for establishing electron transfer processes[4a]] of the reaction of 1-benzyl-2,4,6-triphenylpyridinium BF_4^- with sodium 2-nitropropanide, we nevertheless believe that the ease of reaction under mild conditions indicates a radical reaction mechanism. Typical S_N2 reactions of these pyridiniums with hundredfold excess of nucleophile require a reaction time of 1 hr at 100° in chlorobenzene.[13]



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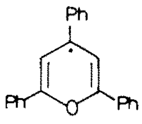

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We believe that our reactions involve charge transfer complexes between **2** and **3** and/or intermediates of type **6**; the latter is similar to stabilised cyano and carbethoxy substituted pyridinyls previously found.[14] Furthermore, (a) 2,4,6-triphenylpyrylium has itself been reduced to its radical (**7**) with Zn in acetonitrile[15] and (b) N-(*p*-nitrobenzyl)-pyridinium chloride[16] reacts with the anion of 2-nitropropane *via* an electron-transfer mechanism.

Quantitative kinetic measurements on this reaction are under way to define the precise mechanism, order of reaction, solvent dependence, *etc.*[17]

Table 2. Preparation of nitroalkanes in ethanol: $R^1R^2R^3CNO_2$

R^1	R^2	R^3	React. time (hr)	Yield (%)	b.p./mm	Lit. b.p./mm	Found C	Found H	Found N	Found Cl	Formula	Required C	Required H	Required N	Required Cl
$PhCH_2$	H	H	1	78[a]	120-130/15	125-135/1[b]	63.4	6.0	9.3	-	$C_8H_9NO_2$	63.6	6.0	9.3	-
$PhCH_2$	Me	H	2	53[a]	87-89/1	67-69/0.2[c]	65.9	6.9	8.4	-	$C_9H_{11}NO_2$	65.5	7.0	8.5	-
$PhCH_2$	Me	Me	6	41[a]	88-92/1	Oil[d]	66.8	7.3	8.2	-	$C_{10}H_{13}NO_2$	67.0	7.3	7.8	-
$ClC_6H_4CH_2$(o)	H	H	1	61	95-98/2	-	51.6	4.4	7.4	19.1	$C_8H_8ClNO_2$	51.8	4.3	7.6	19.1
$ClC_6H_4CH_2$(o)	Me	H	2	52	84-86/0.5	-	54.1	5.4	6.8	18.0	$C_9H_{10}ClNO_2$	54.1	5.0	7.0	17.8
$ClC_6H_4CH_2$(o)	Me	Me	6	44	91-92/1	-	56.4	5.7	6.3	16.6	$C_{10}H_{12}ClNO_2$	56.2	5.6	6.6	16.6
$Cl_2C_6H_3CH_2$(o,p)	H	H	1	55	85-87/2	-	43.5	3.5	6.2	32.5	$C_8H_7Cl_2NO_2$	43.6	3.2	6.4	32.3
$Cl_2C_6H_3CH_2$(o,p)	Me	H	2	35	61-63/0.5	-	46.3	4.0	5.9	30.1	$C_9H_9Cl_2NO_2$	46.2	3.9	6.0	30.3
$ClC_6H_4CH_2$ (p)	H	H	1	62	82-84/1	Oil[e]	52.0	4.0	7.7	19.4	$C_8H_8ClNO_2$	51.8	4.3	7.6	19.1
$ClC_6H_4CH_2$(p)	Me	H	2	57	106-109/2	Oil[f]	54.2	5.2	6.8	17.6	$C_9H_{10}ClNO_2$	54.1	5.0	7.0	17.8
$MeC_6H_4CH_2$(p)	H	H	1/2	68	63-64/1	-	65.7	7.1	8.6	-	$C_9H_{11}NO_2$	65.5	7.0	8.5	-
$MeC_6H_4CH_2$(p)	Me	H	1	54	65-67/0.5	Oil[f]	67.0	7.3	7.4	-	$C_{10}H_{13}NO_2$	67.0	7.3	7.8	-
$MeC_6H_4CH_2$(p)	Me	Me	1	42	88-90/0.5	-	68.0	7.8	7.4	-	$C_{11}H_{15}NO_2$	68.4	7.8	7.3	-

Footnotes

[a] Single pure compound by g.l.c. (Carbowax 220m, 200 °C). [b] J.W. Baker and I.S. Wilson, J. Chem. Soc. 842 (1927). [c] G.B. Bachmann and R.J. Maleski, J. Org. Chem. 37, 2810 (1972). [d] J.F. Brown, Jr. J. Am. Chem. Soc. 77, 6341 (1955). [e] R. Henning, F. Lehr and D. Seebach, Helv. Chim. Acta 59, 2213 (1976). [f] F.G. Bordwell, W.J. Boyle and K.C. Yee, J. Am. Chem. Soc. 92, 5926 (1970).

Table 3. Preparation of nitroalkanes in dimethyl sulphoxide: $R^1R^2CMeNO_2$

R^1	R^2	React. time (hr)	Yield (%)	B.p. (°C/mm)	Lit. b.p. (°C/mm)	Ref.	Found C	H	N	Cl	Formula	Required C	H	N	Cl
$PhCH_2$	Me	1	75	99-102/2	Oil	b	67.2	7.1	8.0	-	$C_{10}H_{13}NO_2$	67.0	7.3	7.8	-
$PhCH_2$	H	1	52	94-96/2	67-69/0.2	c	65.4	6.9	8.6	-	$C_9H_{11}NO_2$	65.5	7.0	8.5	-
$ClC_6H_4CH_2$(o)	Me	1	65	88-91/1			56.0	5.9	6.6	16.9	$C_{10}H_{12}ClNO_2$	56.2	5.6	6.6	16.6
$ClC_6H_4CH_2$(o)	H	1	47	93-97/1			53.9	4.8	7.2	17.5	$C_9H_{10}ClNO_2$	54.1	5.0	7.0	17.8
$MeC_6H_4CH_2$(p)	Me	1	69	97-100/1			68.1	8.1	7.1	-	$C_{11}H_{15}NO_2$	68.4	7.8	7.3	-
$MeC_6H_4CH_2$(p)	H	1	43	78-80/1	Oil	d	67.3	7.2	7.7	-	$C_{10}H_{13}NO_2$	67.0	7.3	7.8	-
n-C_4H_9	Me[a]	2	73	55-60/2	-	-	57.8	10.5	10.0	-	$C_7H_{15}NO_2$	57.9	10.3	9.7	-
n-C_4H_9	H[a]	2	46	64-66/20	176, 760	e	54.9	10.0	10.9	-	$C_6H_{13}NO_2$	55.0	9.9	10.7	
n-C_6H_{13}	Me[a]	2	62	95-98/0.5	-		62.0	10.9	8.0	-	$C_9H_{19}NO_2$	62.4	11.0	8.1	-
n-C_6H_{13}	H[a]	2	38	81-83/4	102-105/23	f	60.3	10.4	8.9	-	$C_8H_{17}NO_2$	60.4	10.7	8.8	-
$PhCH_2CH_2$	Me	2	68	104-106/0.5			68.6	7.8	7.4	-	$C_{11}H_{15}NO_2$	68.4	7.8	7.3	-
Cyclohexyl	Me	5	48	82-84/0.8			63.3	10.0	8.0	-	$C_9H_{17}NO_2$	63.2	9.9	8.2	-
Cyclohexyl	H	5	33	67-69/0.8			61.3	9.5	9.0		$C_8H_{15}NO2$	61.2	9.6	8.9	-
Pr^i	Me	4	52	42-43/5			54.8	9.5	10.6	-	$C_6H_{13}NO_2$	55.0	9.9	10.7	-
2-Picolyl	Me	1	61	109-110/2			59.9	6.7	15.6	-	$C_9H_{12}N_2O_2$	60.0	6.7	15.6	-
3-Picolyl	Me	1	44	122-126/2			60.1	6.7	15.6	-	$C_9H_{12}N_2O_2$	60.0	6.7	15.6	-

Footnotes

[a] Single pure compound by g.l.c. (Carbowax 220m, 200 °C). [b] J.F. Brown, Jr., J. Am. Chem. Soc. 77, 6341 (1955). [c] G.B. Bachmann and R.J. Maleski, J. Org. Chem. 37, 2810 (1972). [d] F.G. Bordwell, W.J. Boyle and K.C. Yee, J. Am. Chem. Soc. 92, 5926 (1970). [e] Dictionary of Organic Compounds', Eyre & Spottiswoode, London 1965, Vol. 4, 2457. [f] Footnote c, p. 2473.

Table 4. ^{1}H NMR spectra[a] of nitroalkanes $R^1R^2R^3CNO_2$

Substituents			δ (ppm)				
R^1	R^2	R^3	R^1			R^2	R^3
			CH_2	Ph	Alkyl		
$PhCH_2$	H	H	3.45(t)	7.50(s)	-	4.75(t)	4.75(t)
$PhCH_2$	Me	H	3.40(t)	7.45(s)	-	1.60(d)	4.95(m)
$PhCH_2$	Me	Me	3.25(s)	7.30(s)	-	1.60(s)	1.60(s)
$ClC_6H_4CH_2$(o)	H	H	3.35(t)	7.30(s)	-	4.65(t)	4.65(t)
$ClC_6H_4CH_2$(o)	Me	H	3.30(t)	7.20(m)	-	1.55(d)	4.90(m)
$ClC_6H_4CH_2$(o)	Me	Me	3.35(s)	7.1-7.4(m)	-	1.55(s)	1.55(s)
$Cl_2C_6H_3CH_2$(o, p)	H	H	3.30(t)	7.15(s, 2H) 7.30(s, 1H)	-	4.50(t)	4.50(t)
$Cl_2C_6H_3CH_2$(o, p)	Me	H	3.20(t)	7.15(s, 2H) 7.30(s, 1H)	-	1.50(d)	4.85(m)
$ClC_6H_4CH_2$(p)	H	H	3.25(t)	7.20(d)	-	4.55(t)	4.55(t)
$ClC_6H_4CH_2$(p)	Me	H	2.95(t)	7.15(d)	-	1.40(d)	4.50(m)
$MeC_6H_4CH_2$(p)	H	H	3.20(t)	7.10(s)	2.30(s)	4.50(t)	4.50(t)
	Me	H	3.10(t)	7.10(s)	2.30(s)	1.50(d)	4.75(m)
	Me	Me	3.10(s)	7.00(s)	2.30(s)	1.50(s)	1.50(s)
2-Picolyl	Me	Me	3.34(s)	7.15(t) 7.55(m) 8.5(d)		1.60(s)	1.60(s)
3-Picolyl	Me	Me	3.15(s)	7.1-7.6(m, 2H) 8.2-8.6(m, 2H)	-	1.56(s)	1.56(s)
n-C_4H_9	Me	H	-	-	0.7-2.0(m)	1.50(d)	4.45(m)
n-C_4H_9	Me	Me	0.8(t)	-	1.0-2.0(m)	1.45(s)	1.45(s)
n-C_6H_{13}	Me	H	-	-	0.55-2.2(m)	1.55(d)	4.65(m)
n-C_6H_{13}	Me	Me	-	-	0.8-2.0(m)	1.65(s)	1.65(s)
$PhCH_2CH_2$	Me	Me	-	7.2(s)	2.0-2.7(m)	1.60(s)	1.60(s)
Cyclohexyl	Me	H	-	-	1.0-2.5(m)	1.50(d)	4.30(m)
	Me	Me	-	-	1.6-2.1(m)	1.45(s)	1.45(s)
Pr^i	Me	Me	-	-	0.8-2.5(m)	1.45(s)	1.45(s)

Footnote. [a] $CDCl_3$ solutions: ca. 50 mg/0.5 ml.

EXPERIMENTAL

M.ps were obtained on a Kofler hot stage apparatus and are uncorrected. IR spectra were run using NaCl plates on a Perkin–Elmer 257 grating infrared spectrophotometer, neat in the case of the nitroalkanes and in Nujol mull elsewhere unless otherwise stated. ^{1}H NMR spectra were run on a Perkin–Elmer 60 MHz R12 permanent magnet spectrometer in deuteriochloroform, unless otherwise stated, with tetramethylsilane as the internal standard.

2,4,6-*Triphenylpyrylium tetrafluoroborate* was prepared by the method of Lombard and Stephan[18] (45%), m.p. 253° (lit.[18] 253–255°).

N-*Substituted* 2,4,6-*triphenylpyridinium tetrafluoroborates*. For a typical preparation, 2,4,6-triphenylpyrylium tetrafluoroborate (12 g, 0.03 mole) and benzylamine (2.8 g, 0.03 mole) were stirred in abs. EtOH (50 ml) with Et_3N (0.3 g, 0.003 mole) for 2 hr. The crude product was filtered off, washed with ether (25 ml) and recrystallised as white needles from abs. EtOH (15 ml). The same procedure was adopted for the other pyridinium salts, except isopropyl and cyclohexyl, which were instead stirred in ether.

Reaction of 1 *alkyl*-2,4,6-*triphenylpyridinium tetrafluoroborates with nitronate anions in ethanol* In a typical experiment, NaH (0.72 g, 0.03 mole) was dissolved in EtOH (30 ml). Nitromethane (1.83 g, 0.03 mole) was added with stirring, followed by 1-benzyl-2,4,6-triphenylpyridinium tetrafluoroborate (4.85 g, 0.01 mole). The soln was refluxed with stirring for 1 hr: the reaction was followed by tlc (silica; $CHCl_3$). When no further pyridinium remained, the soln was cooled; the resulting crystalline by-product 2,4,6-triphenylpyridine was filtered off. The filtrate was added to water (50 ml), extracted with ether (3 × 25 ml) and the extract dried over $MgSO_4$. Dry HCl was passed to remove residual 2,4,6-triphenylpyridine and the solution was evaporated under reduced pressure (25°/15 mmHg). The crude product was distilled *in vacuo* (1 mmHg) yielding 2-phenylnitroethane.

Reaction of 1-*alkyl*-2,4,6-*triphenylpyridinium tetrafluoroborates with nitronate anions in dimethylsulphoxide.* In a typical experiment, NaH (0.72 g, 0.03 mole) was dissolved in MeOH (10 ml), and 2-nitropropane (2.67 g, 0.03 mole) was added with stirring. After removal of the MeOH *in vacuo* (25°/0.5 mmHg), the resulting white product was mixed with 1-hexyl-2,4,6-triphenylpyridinium tetrafluoroborate (4.79 g, 0.01 mole) and dissolved in dimethylsulphoxide (30 ml). The soln was heated at 80° for 2 hr and again followed by tlc (silica; $CHCl_3$). An identical isolation procedure to the above was followed, yielding 2-methyl-2-nitrooctane.

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