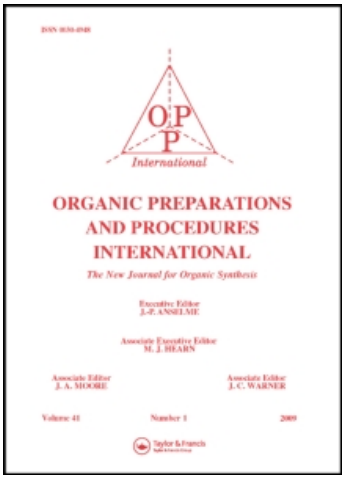

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DIRECT ALKYLATION OF NITROARENES *via* VICARIOUS NUCLEOPHILIC SUBSTITUTION OF HYDROGEN†

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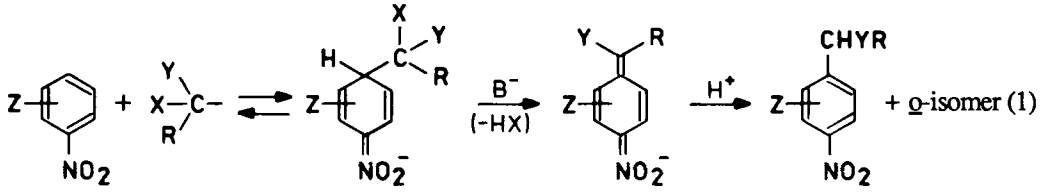
The vicarious nucleophilic substitution (VNS) provides an efficient method of introducing α-functionalized alkyl substituents into nitroaromatic rings according to Eq. 1.[1]



The few reports about alkylation of nitroarenes and some heterocycles by treatment with dimethylsulfoxide anion,[2] trimethylsulfoxonium ylides,[3,4] and triphenylphosphonium methylide[4] are limited to the introduction of methyl substituents. Alkyl substituents in general can be introduced into nitroaromatic rings via addition of alkylmagnesium halides followed by oxidation of the resulting σ-adducts.[5] Introduction of unsubstituted groups into nitroaromatic rings via VNS can be difficult because the reacting carbanions should have only one substituent acting simultaneously as carbanion stabilizing and leaving group. Moreover, the anions of the products formed according to the VNS scheme (Eq. 1) are stabilized only by the nitroaromatic substituent and hence susceptible to undesired transformations. The perfluoroalkylsulfonyl substituent provides very efficient stabilization of a carbanion and has simultaneously high leaving ability;[6] therefore reaction with the carbanion of alkyl perfluoromethyl sulfone seemed a promising process for nucleophilic alkylation of nitroarenes.

Indeed, nitroarenes reacted with butyltrifluoromethyl sulfone in the presence of strong base according to Eq. 2, yielding the alkylated products in moderate yields (Table). In all cases, the reaction produced substantial amounts of tars and thus resulted in poor material balance of the starting nitroarenes. In spite of the moderate yields of alkylated nitroarenes, the method can be of

$$\text{H-Ar-NO}_2 + \text{n-C}_4\text{H}_9\text{SO}_2\text{CF}_3 \xrightarrow[\text{DMF}]{\text{NaH}} \text{n-C}_4\text{H}_9\text{-Ar-NO}_2 + \text{CF}_3\text{SO}_2^- \qquad (2)$$

synthetic use in some cases.

TABLE. Butylation of Nitroarenes

Nitroarene	Position of C_4H_9	Yieldd(%)a
1,3-Dinitrobenzene	4-	23
2,4-Dichloronitrobenzene	6-	31
1-Nitronaphthalene	2-	19
	4-	18
2-Methoxy-5-nitropyridine	6-	47
6-Nitroquinoline	5-	24
8-Nitroquinoline	7-	46

a) Isolated pure products.

EXPERIMENTAL SECTION

Mps are uncorrected. ^1H NMR spectra were recorded on a Varian Aspect EM-360 (60 MHz) spectrometer in CCl_4 using TMS as an internal standard or on a Bruker AM-500 (500 MHz) instrument in $CDCl_3$ using the solvent signal as a reference. Coupling constants are given in Hz. IR spectra were taken on a Beckman IR 4240 spectrophotometer. ColuJmn chromatographies were performed on Kieselgel 60 (70-230 mesh; E. Merck). Sodium hydride was used as an oil dispersion (50%) without removal of the oil. Nitroaromatic compounds were commercially available.

n-Butyltrichloromethyl sulfide, bp. 92-94°/17 mm Hg, lit.[9] bp. 88-89°/12 mm Hg was prepared in 80% yield from n-butyl isothiocyanate[7] and chloroform in a catalytic two-phase system following a literature procedure.[8]

n-Butyltrifluoromethyl sulfide, bp. 92-94°/760 mm Hg, lit.[11] bp. 90-93°/760 mm Hg was obtained in 50% yield from n-butyltrichloromethyl sulfide and dry hydrogen fluoride in an autoclave at 100° according to a literature procedure.[10] It was oxidized in 70% yield to *n-butyltrifluoromethyl sulfone*, 82-84°/35 mm Hg by means of CrO_3 in AcOH;[12] ^1H NMR: δ 3.20 (CH_2); lit.[6] δ 3.24 (CH_2).

General Procedure for Alkylation.- n-Butyltrifluoromethyl sulfone (1.425 g, 7.5 mmol) in dry dimethylformamide (1 ml) was slowly added to a stirred suspension of sodium hydride (0.36 g, 7.5 mmol, 50% in oil) in dimethylformamide (2 ml) at room temperature under nitrogen. The mixture was stirred for 20-30 min. until NaH disappeared and gas evolution ceased. At this point, a solution of nitroarene (5 mmol) in DMF (3 ml) was added in one portion. The resulting colored mixture was stirred for 1 hr (with cooling if necessary to maintain the temperature ambient), poured into ice-cold 5% HCl (220 ml) and extracted with methylene chloride (3 x 20 ml). The organic extracts were combined, washed with 10% aqueous NaCl (2 x 20 ml) and dried. The solvent was removed and the residue was chromatographed.

4-Butyl-1,3-dinitrobenzene;[13] eluent: CCl_4; oil; IR (film): 1545, 1355 (NO_2) cm^{-1}; ^1H NMR (60 MHz, CCl_4): δ 0.84-1.65 (m, 7H, $CH_3CH_2CH_2$), 2.58-2.84 (m, 2H, benzylic CH_2),6.87 (d, $J_{5,6}$ = 8.2, 1H, H5), 7.47 (dd, $J_{5,6}$ = 8.2, 1H, H6), 7.71 (d, $J_{2,6}$ = 2.2, 1H, H2).

Anal. Calcd. for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.39; N, 12.49
Found: C, 53,61; H, 5.37; N, 12.34

6-Butyl-2,4-dichloronitrobenzene; eluent: hexane-ethyl acetate (30:1); oil; IR (film): 1545, 1375 (NO_2) cm^{-1}; ^1H NMR (60 MHz, CCl_4): δ 0.84-1.80 (m, 7H, $CH_3CH_2CH_2$), 2.25-2.46 (m, 2H, benzylic CH_2), 6.48-6.72 (m, 2H, H aromatic).

Anal. Calcd. for $C_{10}H_{11}C_{l2}NO_2$: C, 48.41; H, 4.47; N, 5.65; Cl, 28.58
Found: C, 48.73; H, 4.43; N, 5.29; Cl, 28.38

2-Butyl-1-nitronaphthalene;[14] eluent: hexane; oil; IR (film): 1535, 1365 (NO_2) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 0.92 (m, 3H, CH_3), 1.40 (m, 2H, CH_3CH_2), 1.68 (m, 2H, $CH_3CH_2CH_2$), 2.75 (m, 2H, benzylic CH_2), 7.39 (d, $J_{3,4}$ = 8.48, 1H, H3), 7.52-7.62 (m, 2H, H6 & H7), 7.68 (m, 1H, H5), 7.87 (m, 1H, H8), 8.89 (d, $J_{3,4}$ = 8.48, 1H, H4).

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.39; H, 6.74; N, 5.84

4-Butyl-1-nitronaphthalene;[14] eluent: hexane; oil; IR (film): 1520, 1340 (NO_2) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 0.98 (m, 3H, CH_3), 1.47 (m, 2H, CH_3CH_2), 1.75 (m, 2H, $CH_3CH_2CH_2$), 3.15 (m, 2H, benzylic CH_2), 7.39 (d, $J_{2,3}$ = 7.84, 1H, H3), 7.62-7.73 (m, 2H, H6 & H7), 8.14 (d, $J_{2,3}$ = 7.84, 1H, H2), 8.15 (m, 1H, H5), 8.60 (m, 1H, H8).

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.13; H, 6.88; N, 6.21

6-Butyl-2-methoxy-5-nitropyridine; eluent: CCl_4; crystals, mp. 29-30° (hexane); IR (KBr): 1595, 1330 (NO_2) cm^{-1}; ^1H NMR (60 MHz, CCl_4): δ 0.84-1.86 (m, 7H, $CH_3CH_2CH_2$), 2.61-2.88 (m, 2H, benzylic CH_2), 3.60 (s, 3H, OCH_3), 5.91 (d, $J_{3,4}$ = 8.2, 1H, H3), 7.38 (d, $J_{3,4}$ = 8.2, 1H, H4).

Anal. Calcd. for $C_{10}H_{14}N_2O_3$: C, 57.13; H, 6.71; N, 13.33
Found: C, 57.08; H, 6.87; N, 13.31

5-Butyl-6-nitroquinoline; eluent: $CHCl_3$-CCl_4 (1:1); oil; IR (film): 1545, 1365 (NO_2) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.02 (m, 3H, CH_3), 1.57 (m, 2H, CH_3CH_2), 1.78 (m, 2H, $CH_3CH_2CH_2$), 3.21 (m, 2H, benzylic CH_2), 7.59 (dd, $J_{2,3}$ = 4.16, $J_{3,4}$ = 8.68, 1H, H3), 8.02, 8.07 (AB, J = 9.16, 2H, H7 & H8), 8.53 (m, 1H, H4), 9.04 (dd, $J_{2,3}$ = 4.16, $J_{2,4}$ = 1.67, 1H, H2).

Anal. Calcd. for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17
Found : C, 67.69; H, 6.11; N. 10.50

7-Butyl-8-nitroquinoline; eluent: $CHCl_3$-CCl_4 (1:1), solidified oil; IR (KBr): 1535, 1360 (NO_2) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 0.94 (m, 3H, CH_3), 1.43 (m, 2H, CH_3CH_2), 1.70 (m, 2H, $CH_3CH_2CH_2$), 2.76 (m, 2H, benzylic CH_2), 7.48 (m, 2H, H3 & H6), 7.87 (d, $J_{5,6}$ = 8.52, 1H, H5), 8.19 (dd, $J_{3,4}$ = 8.32, $J_{2,4}$ = 1.67, 1H, H4), 8.96 (dd, $J_{2,3}$ = 4.26, $J_{2,4}$ = 1.67, 1H, H2).

Anal. Calcd. for $C_{13}H_{14}N_2O_3$: C, 67.81; H, 6.13; N, 12.17
Found: C, 67.54; H, 6.12; N, 12.09

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