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The First Conversion of Primary Alkyl Halides to Nitroalkanes under Aqueous Medium

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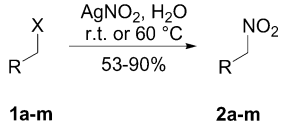
Abstract: Primary nitroalkanes and α,ω-dinitroalkanes can be easily obtained in aqueous medium by reaction of the corresponding halo derivatives with silver nitrite. The procedure works well with both alkyl bomide and alkyl iodide and proceeds in satisfactory to good yields even in the presence of other functionalities, minimizing the formation of the undesired alkyl nitrites.

Nitroalkanes are one of the fundamental classes of substances in organic chemistry.[1] Historically, they have been important as explosives and precursors for azo dyes.[2] Today, they play a key role as synthetic intermediates or targets in the preparation of dyes, plastics, perfumes, pharmaceuticals and many natural products.[3] This is primarily due to the fact that the nitroalkanes undergo a variety of carbon−carbon bond-forming processes, and the nitro group can be converted into several other functional groups.[4] Thus, an easy and convenient availability of the aliphatic nitro compounds is crucial. These molecules can be obtained (i) by direct nitration of aliphatic hydrocarbons under certain conditions, activated hydrocarbons via anionic intermediates, alkenes, and ketones (α-nitration),[4e,5] (ii) by conversion of other functionalities to the nitro group (carbonyls, oximes, azides, etc.),[3a,4c,6] and (iii) by nitration of the alkyl halides with metal nitrites. For the latter method, silver nitrite in diethyl ether (Victor−Meyer reaction), potassium nitrite, or sodium nitrite in *N*,*N*-dimethylformamide (DMF) or in dimethyl sulfoxide (DMSO) (Kornblum reaction) have been frequently used.[7,8] The conversion of alkyl halides to nitro compounds is one of the most used methods for the preparation of nitroalkanes; any way, long-reaction times, the use of toxic solvents, and tedious workup are demanded and/or low yields are obtained. Moreover, a further and serious drawback is that the obtained products are usually a mixture, difficult to purify, of the desired nitroalkanes together with the undesired alkyl nitrites.

SCHEME 1



Increasingly demanding environmental legislation, public and corporate pressure, and the resulting drive toward clean technology in the chemical industry, with emphasis on reduction of waste at the source, will require increasing attention on the use of less toxic and environmentally compatible materials in the design of new synthetic methods.[9] Recently, there has been increasing recognition that organic reactions carried out in water may offer advantages over those occurring in organic solvents because water is cheap and safe, it allows a precise control of the reactivity, and/or the selectivity of the reaction can be dramatically influenced when carried out in water.[10] With the aim to develop more efficient processes and in continuation with our studies devoted to the chemistry of aliphatic nitro compounds,[4c,11] we have now found the first methodology for the title conversion in aqueous medium. In fact, treatment of primary alkyl halides **1** with 4 equiv of silver nitrite at room temperature or 60 °C (Scheme 1) allows satisfactory to good yields (53−90%, Table 1) of a variety of primary nitroalkanes **2**, mainly in very short reaction times (0.5−1.25 h). The reason for using 4 equiv of silver nitrite is that in these conditions the reaction is fast enough to minimize the competitive formation of the corresponding alcohol.

Although our method works well with both alkyl bromides and alkyl iodides, the latter often show a higher reactivity (e.g., **1g** vs **1a**, **1g** vs **1c**, and **1j** vs **1d**). Furthermore, other functionalities such as carbon−carbon double bonds, ester, imide, and ketone are preserved under our mild reaction conditions. Of particular interest is the possibility to perform the one-pot trans-

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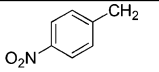
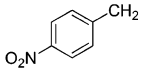
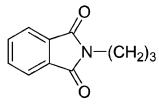
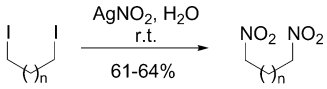
TABLE 1. Primary Nitroalkanes 2

Entry	Product	R	X	Reaction time (h)	Temp. (°C)	Yield (%)[a]
a[12]	2a		Br	24	60	53
b[13]	2b	Ph	Br	2	r.t.	55
c[14]	2c	$CH_3(CH_2)_8$	Br	2.5	r.t.	85
d[15]	2d	$H_2C{=}CH(CH_2)_8$	Br	5	60	64
e	2e		I	1	60	65
f	2f	Ph	I	0.5	r.t.	56
g	2g	$CH_3(CH_2)_8$	I	0.5	r.t.	93
h[16]	2h	$CH_3(CH_2)_6$	I	1	r.t.	83
i[17]	2i	$CH_3(CH_2)_9$	I	0.75	r.t.	84
j	2j	$H_2C{=}CH(CH_2)_8$	I	1.25	r.t.	83
k	2k		I	1	60	84
l[18]	2l	$AcOCH_2(CH_2)_2$	I	0.75	r.t.	90
m	2m	$PhCOCH_2$	I	0.75	60	80

[a] Yield of pure, isolated product.

SCHEME 2



3a-c **4a-c**

n(Yield %) = 3(62%), 6(64%), 8(61%).

formation of α,ω-diiodo structures **3** to the corresponding dinitroalkanes **4** (Scheme 2, 61−64%).

The NMR spectra and the GC analysis of the crude reaction mixtures show that by our conditions the formation of alkyl nitrites, as byproducts, is strongly depressed, since in most of the cases the nitrite could not be detected or, in a few cases, less than 4−5% of the above side products were observed. The reaction has also been tested in the presence of a catalytic amount of cetyltrimethylammonium bromide (CTABr) without any improvement. The method failed with secondary halo derivatives, probably because of the prevalent formation of side produts, as previously reported.[19]

Compared with the standard procedures, our method offers a series of important advantages such as (i) the minimization of the formation of the undesidered alkyl nitrites, (ii) better yields, (iii) easier workup, and (iv) shorter reaction times.

In conclusion, we have reported the first eco-friendly procedure for the conversion of primary alkyl halides to nitroalkanes under aqueous medium, and this result can be of great interest due to the large need of aliphatic nitro compounds as the key building blocks in organic synthesis.

Experimental Section

To a water solution (2 mL) of the iodoalkane (1 mmol) was added $AgNO_2$ (4 mmol) and the reaction flask was wrapped with silver paper to protect the reaction mixture from light. After being stirred at the appropriate temperature (see Table 1), the reaction mixture was filtered, extracted with EtOAc, and dried over Na_2SO_4 and the solved was evaporated under reduced pressure. The crude products were purified by column chromatography (hexane:EtOAc, 95:5). To verify the efficiency of the reaction in a larger scale, we tested, as a representative example, the conversion of **1h** (20 mmol) to **2h**, without significant changes of both the reaction time and yield. As a criterion of purity, ^{1}H NMR or ^{13}C NMR spectra of the compounds prepared are reported in the Supporting Information.

1-Nitroundecane (2i): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, J = 6.9 Hz, 2H), 1.28 (m, 16H), 1.99 (m, 2H), 4.38 ppm (t, J = 7.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 22.9, 26.4, 27.6, 29.0, 29.45, 29.48, 29.6, 29.7, 32.1, 75.9 ppm; GC-MS m/z 154 ($M^+ - HNO_2$), 138,124,110, 97, 83, 69, 55, 43; IR (neat) 2928, 2855, 1555, 1468, 1381 cm^{-1}.

2-(4-Nitrobutyl)-1*H*-isoindole-1,3(2*H*)-dione (2k): white solid, mp 69−72 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.79 (m, 2H), 2.05 (m, 2H), 3.74 (t, J = 7.0 Hz, 2H), 4.44 (t, J = 7.0 Hz, 2H), 7.72 (dd, J = 5.5, 3.4 Hz, 2H), 7.84 ppm (dd, J = 5.5, 3.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.7, 25.6, 36.9, 75.0, 123.5, 132.1, 134.3, 168.5 ppm; GC-MS m/z 213, 200, 160, 148, 130, 104, 76; IR (neat) 2940, 1772, 1713, 1548, 1438, 1377, 725, 714, 666 cm^{-1}.

3-Nitro-1-phenylpropan-1-one (2m): white solid, mp 72−74 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.69 (t, J = 6.2 Hz, 2H), 4.85 (t, J = 6.2 Hz, 2H), 7.52 (m, 2H), 7.65 (m, 1H), 8.00 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.7, 25.6, 36.9, 75.0, 123.5, 132.1, 134.3, 168.5 ppm; GC-MS m/z 179, 132, 120, 105, 77, 51; IR (neat) 2927, 1773, 1718, 1551, 1054, 726, 690, 666 cm^{-1}.

1,5-Dinitropentane (4a): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.50 (m, 2H), 2.06 (m, 4H), 4.40 ppm (t, J = 6.9 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4, 26.7, 75.1 ppm; GC-MS m/z 69, 41; IR (neat) 2927, 1560, 1546, 1432, 1375 cm^{-1}.

1,8-Dinitrooctane (4b): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.63 (m, 8H), 2.00 (m, 4H), 4.38 ppm (t, J = 7.0 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.3, 27.5, 28.7, 75.8 ppm; GC-MS m/z 158, 95, 81, 69, 55, 41; IR (neat) 2922, 2859, 1551, 1436, 1383 cm^{-1}.

1,10-Dinitrodecane (4c): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.67 (m, 12H), 1.99 (m, 4H), 4.37 ppm (t, J = 7.0 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.3, 27.5, 28.9, 29.2, 75.9 ppm; GC-MS m/z 152, 109, 95, 83, 69, 55, 41; IR (neat) 2926, 2855, 1541, 1448, 1385 cm^{-1}.

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Supporting Information Available: The ^{1}H NMR or ^{13}C NMR spectra of the compounds prepared are reported as a criterion of purity. This material is available free of charge via the Internet at http://pubs.acs.org.

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