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NEW SYNTHETIC 'TRICKS'. DIRECT CONVERSION OF NITRO COMPOUNDS TO NITRILES

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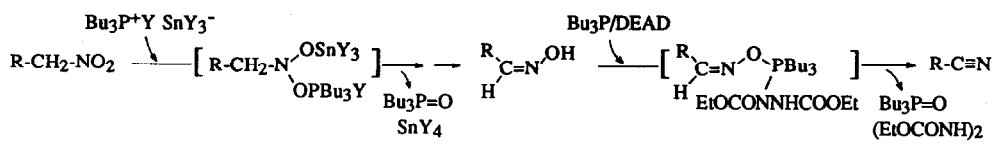
Summary.- *Treatment of primary nitro groups, in CH_2Cl_2 at 0 °C, with $Sn(SPh)_4$, R_3P, and DEAD affords quickly and almost quantitatively the corresponding nitriles, in a combined process of deoxygenation and dehydration. The same result can be obtained, although not so rapidly, using only R_3P (2 equiv.) and DEAD (1 equiv.).*

Nitro and cyano groups, owing to their effect on the acidity of α-CH_2 and α-CH, play an essential role in the current synthetic methodology regarding C-C bond formation reactions.[1] The transformation of a primary nitroalkane (**1**) into a nitrile (**2**), which permits the transfer of the nucleophilic character from C1 (see **1**$^-$) to C2 (see **2**$^-$), constitutes an 'umpolung' case similar to that involved in the conversion of nitro to carbonyl groups.

$\overset{2}{\text{R-CH}_2}\text{-}\overset{1}{\text{CH}_2}\text{-NO}_2$ (**1**) $\quad$ $\overset{2}{\text{R-CH}_2}\text{-}\overset{1}{\text{CH}^-}\text{-NO}_2$ (**1**$^-$) $\quad$ $\overset{2}{\text{R-CH}_2}\text{-}\overset{1}{\text{C}}\equiv\text{N}$ (**2**) $\quad$ $\overset{2}{\text{R-CH}^-}\text{-}\overset{1}{\text{C}}\equiv\text{N}$ (**2**$^-$)

There are a few methods for the direct transformation of **1** into **2**.[2,3] *We describe here two novel, improved procedures which we have developed in the light of the following reasonings:* (i) the first isolable intermediates arising from the reduction of primary nitro groups with appropriate reagents may be (and often are) the aldoximes, the stable tautomers of the nitrosoalkanes; (ii) in the presence of a dehydrating agent, the Z aldoxime (H and OH in anti),[4] usually the kinetically favoured isomer, may lose water rapidly before isomerising to its E isomer, much less prone to dehydration;[5] and (iii) heating and strong acids should be avoided otherwise rearrangement and cleavage byproducts (or other byproducts, depending on the reagents employed) could contaminate the desired nitrile.

Thus, in the first method (method A), we have taken advantage of the reducing power of $Sn(SPh)_3^-$,[6] a complex that for convenience we have generated in this work from $Sn(SPh)_4$ and Bu_3P [≡ Bu_3P^+SPh + $Sn(SPh)_3^-$],[7] and of the dehydrating properties of Bu_3P/DEAD [≡ $Bu_3P^+N(COOEt)N^-COOEt$].[8] When nitro compounds of type **1** and nitromethyl derivatives in general (see **3**-**9**, in the Table) were added to a 0.2:2:1:1 mixture of $Sn(SPh)_4$/Bu_3P/DEAD/DMAP[9] in CH_2Cl_2 at 0 °C, an instantaneous reaction took place, so that practically quantitative amounts of the corresponding nitriles were obtained *within 5 min!*, probably according to the following sequence of events (where Y means PhS):[10]



In the second method (method B) we have eliminated $Sn(SPh)_4$ (and DMAP[9]). The reaction is slower than in method A, but almost equally satisfactory (see the Table). It is worth noting that *the 2:1 molar ratio between R_3P and DEAD is essential for the performance of the method!* Thus, this reaction is a striking application of DEAD, since apparently 1 molecule of DEAD activates 2 of R_3P, the mixture showing both reducing and dehydrating ability. It might take place as follows (although a previous dehydration of RCH_2NO_2 to RCNO,[11] which would be reduced in situ by the second molecule of Bu_3P, is not ruled out):

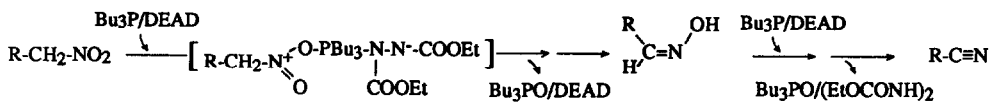
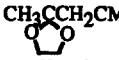
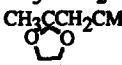
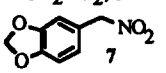
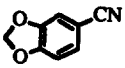
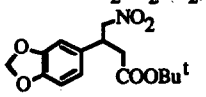
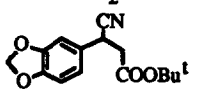


Table. Conversion of Nitro Compounds to Nitriles in CH_2Cl_2 at 0 °C

substrate	product	[Sn(SPh)4/Bu3P/DEAD/DMAP][a]		(Bu3P/DEAD)[b]	
		reaction time	yield	reaction time	yield
$CH_3(CH_2)_{11}NO_2$, 3	$CH_3(CH_2)_{10}C{\equiv}N$	10 min	98%	60 min	90%
$CH_3COCH_2CMe_2CH_2NO_2$, 4	$CH_3COCH_2CMe_2C{\equiv}N$	5 min	85%	60 min	92%
 5		5 min	98%	30 min	92%
$PhCH_2NO_2$, 6	$PhC{\equiv}N$	5 min	96%	30 min	90%
 7		5 min	99%	30 min	92%
4-MeOPh$CH_2CH_2NO_2$, 8	4-MeOPh$CH_2C{\equiv}N$	5 min	99%	90 min	90%
 9		5 min	95%	30 min	93%

[a] Method A. To a stirred solution of 0.2 mmol of Sn(SPh)4 [prepared from $SnCl_4$/4PhSH/4Et3N in C_6H_6], 2.2 mmol of Bu3P, 1.1 mmol of DEAD, and 1.1 mmol of DMAP in 5 ml of CH_2Cl_2 at 0 °C (under N_2), 1.0 mmol of nitro derivatives 3-9 were added. Usually, after few min TLC indicated a quantitative conversion. Straightforward separation by 'flash' chromatography on silica gel using CH_2Cl_2 afforded the nitriles in a pure condition (TLC and 200 MHz ^1H NMR). [b] Method B. To a stirred solution of 1.0 mmol of 3-9 and 1.1 mmol of DEAD in 5 ml of CH_2Cl_2 at 0 °C, under N_2, 2.2 mmol of Bu3P were added. Generally half an hour later on, most nitro compounds had disappeared (TLC). Separation of the pure nitrile was performed as in method A.

In summary, both methods are truly efficient and mild. Owing to the reducing power of $Sn(SPh)_3^-$ and the well-known reactivity of R_3P/DEAD, a few functional group incompatibilities are however to be expected (e.g., azides,[6] alcohols[8]). Work is planned to search new applications and limitations of these procedures.[12]

References and footnotes

1. For reviews see: Arseniyadis, S.; Kyler, K. S.; Watt, D. S. *Org. React.* **1984**, *31*, 1. Rosini, G.; Ballini, R. *Synthesis* **1988**, 833.
2. (a) Olah, G. A.; Narang, S. C.; Field, L. D.; Fung, A. P. *J. Org. Chem.* **1983**, *48*, 2766: Me_3SiI for 16 h (nitromethylarenes, 90-96% yields; 1-nitrohexane, 10% yield). (b) Denis, J. N.; Krief, A. *J. Chem. Soc., Chem. Comm.* **1980**, 544: 2 equiv. of PI_3 in the presence of Et3N (1 example, 82% yield). (c) Olah, G. A.; Vankar, Y. D.; Gupta, B. G. B. *Synthesis* **1979**, 36: SO_2/Et3N at 40 °C (58-86% yields) or $(Me_2N)_3P$ in hot 1,2-dichloroethane (50-85% yields). (d) Wehrli, P. A.; Schaer, B. *J. Org. Chem.* **1977**, *42*, 3956: PCl_3 in py (31-77% yields). (e) For earlier works, see refs. 3-6 in ref. 2c.
3. Nevertheless, there are in principle plenty of indirect, two-stage or multi-stage possibilities for the same conversion, mainly on the basis of the several methods available for the dehydration of aldoximes. For recent references, cf.: Konwar, D.; Boruah, R. C.; Sandhu, J. S. *Tetrahedron Lett.* **1990**, *31*, 1063 (AlI_3, 82 °C), and ref. 3-6 therein. Thomas, H. G.; Greyn, H. D. *Synthesis* **1990**, 129 (NC-COOR, Et3N).
4. In a very recent work on the reduction of nitroalkanes to oximes (Bartra, M.; Romea, P.; Urpí, F.; Vilarrasa, J. *Tetrahedron* **1990**, 46, 587), we assigned erroneously configuration E to two Z aldoximes, on the basis of ^1H NMR spectra (according to Kabalka, G. W.; Goudgaon, N. M. *Synth. Commun.* **1988**, *18*, 693). Indeed, these mistakes appear sometimes in the literature, probably due to the use/abuse of the old syn-anti and cis-trans nomenclature, in opposite senses. For leading references on the determination of the stereochemistry of oximes, see refs. 1-10 in the following excellent paper: Heinisch, G.; Holzer, W. *Tetrahedron Lett.* **1990**, *31*, 3109.
5. See, e.g.: Carotti, A.; Campagna, F. *Synthesis* **1979**, 56.
6. Bartra, M.; Urpí, F.; Vilarrasa, J. *Tetrahedron Lett.* **1987**, *28*, 5941.
7. No significant advantages have been found in this work in using Et3P instead of Bu3P (see Urpí, F.; Vilarrasa, J. *Tetrahedron Lett.* **1986**, *27*, 4623). Ph_3P cannot be recommended, since with this phosphine the reaction is extremely slow.
8. The common reagents used in the Mitsunobu reaction are Ph_3P and DEAD. Review: Mitsunobu, O. *Synthesis* **1981**, 1.
9. The use of 1 equiv. of Sn(SPh)4 is not necessary: rates and yields are the same with only 0.2±0.1 equiv. 4-Dimethylaminopyridine may be ruled out if desired: yields are only slightly lower if DMAP is lacking.
10. The method shows a resemblance to a very interesting one in which Bu3P/PhSSPh was utilised to convert secondary nitroalkanes to imines, and hence to ketones (Barton, D. H. R.; Motherwell, W. B.; Zard, S. Z. *Tetrahedron Lett.* **1984**, *25*, 3707). This mixture is however not active enough for our purposes: **8** plus 2 equiv. of Bu3P and PhSSPh under our concentration conditions (but at r.t. for 24 h), gave only 26% of nitrile and 27% of oxime (32% of **8** was recovered).
11. For the dehydration of primary nitro compounds to nitrile oxides, see: Shimizu, T.; Hayashi, Y.; Shibafuchi, H.; Teramura, K. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2827, and refs. therein.

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