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High-yield Synthesis of Nitriles by Oxidation of Aldehyde *N,N*-Dimethylhydrazones with Dimethyldioxirane†

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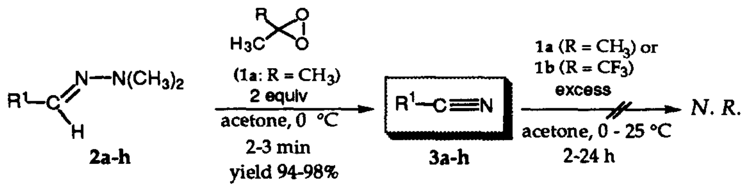
Abstract: Using dimethyldioxirane, the selective transformation of aldehyde *N,N*-dimethylhydrazones into the corresponding nitriles was achieved in high yield and under mild conditions. The detemination of the substituent effect on rates, along with an estimate of the primary kinetic isotope effect using $PhCH{=}NNMe_2$ and $PhCD{=}NNMe_2$ provided useful hints concerning the reaction mechanism. It was also observed that the nitrile products do not undergo further oxidation, even with excess dioxirane.

***Keywords**: Dioxiranes; Oxidation; N,N-dialkylhydrazones; Nitriles.*

Several procedures are available for carrying out the transformation of aldehydes into nitriles;[1] among these, particularly valuable is the oxidative conversion of aldehyde *N,N*-dialkylhydrazones using peracids, such as magnesium monoperoxyphtalate hexahydrate (MMPP).[1f]

Dioxiranes,[2] especially dimethyldioxirane (DMD) (**1a**)[3] and methyl(trifluoromethyl)dioxirane (TFD) (**1b**)[4] in the isolated form, have nowadays become well established as powerful oxidants. Indeed, these reagents can be employed to carry out a number of synthetically useful oxidative transformations,[5] including the easy regeneration of the carbonyl moiety from acetals and orthoesters.[6] In this context, we have shown that dioxiranes are excellent reagents for the selective regeneration of the C=O moiety from ketone hydrazones in neutral media and mild conditions.[7] We now report on the successful application of dimethyldioxirane (**1a**) for the clean, high-yield conversion of aldehyde *N,N*-dimethylhydrazones into nitriles (Scheme 1).



Scheme 1

Typical results in Table 1 show that representative hydrazones **2a-h** can be converted into the corresponding nitriles in almost quantitative yield and in a remarkably short reaction time.

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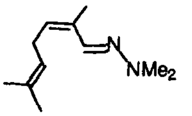
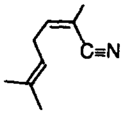
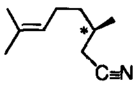
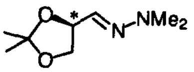
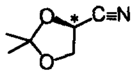
Table 1. Synthesis of nitriles by oxidation of *N,N*-dimethylhydrazones with dimethyldioxirane (**1a**) in acetone.[a]

entry	substrate(#)		relative rates [b]	product (#)		% yield [c]
1	*m*-$O_2NC_6H_4$-CH=N-N(Me)$_2$	(**2a**)	0.156	*m*-$O_2NC_6H_4$-C≡N	(**3a**)	97
2	*p*-ClC_6H_4-CH=N-N(Me)$_2$	(**2b**)	0.603	*p*-ClC_6H_4-C≡N	(**3b**)	98
3	C_6H_5-CH=N-N(Me)$_2$	(**2c**)	(1.000)	C_6H_5-C≡N	(**3c**)	97
3'	C_6H_5-CD=N-N(Me)$_2$	(**2c'**)	1.000[d]			
4	*p*-$MeOC_6H_4$-CH=N-N(Me)$_2$	(**2d**)	2.580	*p*-$MeOC_6H_4$-C≡N	(**3d**)	98
5	*(E)*-C_6H_5CH=CH-CH=N-N(Me)$_2$	(**2e**)	–	*(E)*-C_6H_5CH=CH-C≡N	(**3e**)	92
6		(**2f**)	–		(**3f**)	97
7		(**2g**) *(99%)*[e]	–		(**3g**) *(98%)*[f]	92
8		(**2h**) *(93.5%)*[e]	–		(**3h**) *(93%)*[f]	92

[a] All reactions routinely run at 0 °C, with dioxirane to substrate molar ratio ca. 2 to 1; in all cases, during 2-3 min a > 98% substrate conversion was achieved as determined (±2%) by GC (SPB-1, 0.25 µm film thickness, 30 m × 0.25 mm ID, capillary column). [b] From competition kinetic experiments (ref. 14). [c] Isolated yield. [d] Primary kinetic isotope effect (k_H/k_D) = 1.00, based on competition kinetic experiments (ref. 14). [e] Optical purity (o.p.) of the corresponding aldehyde starting material at 20 °C (Perkin-Elmer MC 241 spectropolarimeter). [f] O.p. from rotation of the given material at 20 °C.

Substrates **2a-h**[8,9] were obtained starting with the corresponding aldehyde and *N,N*-dimethylhydrazine. To these, dioxirane **1a** was applied in the isolated form as acetone solution;[3-7] the latter was obtained according to described protocols.[3] In the simple general procedure, an aliquot (10-15 mL) containing 2 equiv of a standardized cold solution of dimethyldioxirane (**1a**) (ca. 0.1 M in acetone) was added to a stirred solution of 1 equiv of the hydrazone (0.5-0.7 mmol) in acetone (5 mL), kept at 0 °C. The nitriles **3a-h**[10] (Table 1) could be obtained in practically pure form simply upon removal of the acetone solvent in vacuo; they were identified upon comparison of their physical constants and spectral characteristics (MS, FT IR, and/or ^1H NMR, ^{13}C NMR) with those of authentic samples and/or literature data.[10,11]

Application of the more powerful methyl(trifluoromethyl)dioxirane (**1b**) to carry out the transformation at hand was less satisfactory than **1a**, yielding inferior nitrile yields and lower substrate conversions; seemingly, the hydrazones are capable of triggering the competitive decomposition of **1b**.[7]