

Oxidative Conversion of *N,N*-Dimethylhydrazones Derived from Aliphatic and Heteroaromatic Aldehydes into Nitriles with Hydrogen Peroxide or 3-Chloroperoxybenzoic Acid

Jacek Młochowski, Krystian Kloc and Elżbieta Kubicz

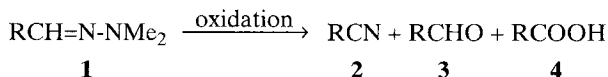
Wrocław (Poland), Institute of Organic Chemistry, Biochemistry and Biotechnology, Technical University

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Oxidation of compounds having azomethine C=N group is a useful way for synthesis of various important products such as oxaziridines, nitrones, amides, carboxylic esters and others [1–3]. Several works concerned with these reactions have been recently reported [4–11].

Four years ago, we reported that *N,N*-dimethylhydrazones derived from aromatic aldehydes, are oxidized with 3-chloroperbenzoic acid (MCPBA) or better with hydrogen peroxide activated with 2-nitrobenzeneseleninic acid (2-NBSA), to give aromatic nitriles in good to excellent yields [10]. In the same reaction, *N,N*-dimethylhydrazones derived from aliphatic aldehydes gave nitriles in unsatisfactory yields. They were accompanied with substantial amounts of parent aldehydes. Only recently, when our work was in progress, Fernandez, Lassaletta et al. reported successful oxidative conversion of dimethylhydrazones into nitriles with magnesium monoperoxyphthalate [11].

In this paper, we present a general method useful for the synthesis of aliphatic and heteroaromatic nitriles by simple oxidation of corresponding aldehyde *N,N*-dimethylhydrazones with MCPBA. Hydrogen peroxide in the presence of various oxygen-transfer catalysts was also tested. Although hydrogen peroxide was less effective than MCPBA it could be considered as a cheap, ecologically neutral oxidant for large-scale synthesis.



Dimethylhydrazones **1a–c** were oxidized, as model compounds with hydrogen peroxide in the presence of catalytic amounts of Na₂WO₄ · 2H₂O, Na₂MoO₄ · 2H₂O, NH₄VO₃,

V₂O₅, TeO₂, SeO₂, 2-NBSEA, [C₅H₅N⁺(CH₂)₁₅CH₃]₃[PMo₁₂O₄₀]³⁻ or H₃PO₄ · 12MoO₃ · 24H₂O (PMA). The best results were achieved when phosphomolybdic acid was used as the catalyst. Nitriles **2a–c** obtained in moderate to high yields were accompanied with small amounts of aldehydes **3a–c** and acids **4a–c** as shown in Table 1.

Better results in the nitrile synthesis were achieved when MCPBA was used as an oxidant. Saturated and unsaturated aliphatic, and π-excess and π-deficient heteroaromatic nitriles **2** were obtained in good to excellent yields (Table 2).

Taking into consideration former results [10, 11] and the data presented in this work, one can conclude that oxidation of easily available aldehyde *N,N*-dimethylhydrazones with peroxy compounds is a general way for simple synthesis of aliphatic, aromatic and heteroaromatic nitriles. For the preparation of aliphatic and heteroaromatic nitriles the common reagent – 3-chloroperbenzoic acid can be used as an effective oxidant.

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Experimental

Dimethylhydrazones **1** were prepared in 72–98 % yield from the corresponding aldehydes (freshly distilled or recrystallized before using) and dimethylhydrazine without solvent (**1a–k**, **m–o**) or in methanol (**1l**, **p–s**) according to the methods reported in refs. [2, 10, 12]. Usually the reaction was continued for 20 h. Exceptions were **1q** (3 days) and **1p** (10 days). In both these cases twice molar excess of hydrazine in the pres-

Table 1 Results of oxidation of dimethylhydrazones **1** with hydrogen peroxide in the presence of PMA

Dimethylhydrazone	R	Yield (%)	Oxidation products, yield %		
			Nitrile (2)	Aldehyde (3)	Acid (4)
1a	C ₇ H ₁₅	95	87	3	5
1b	C ₅ H ₁₁	94	50	3	11
1c	C ₃ H ₇ (CH ₃)CH	93	73	9	4

Table 2 Results of oxidation of dimethylhydrazones **1** to nitriles **2** with MCPBA

Nit-rile	R	Reac-tion time h	Yield %	Nit-rile	R	Reac-tion time h	Yield %
2a	C ₇ H ₁₅	2	94	2k	-CH ₂ CH ₂ CH ₂ -	4	94
2b	C ₅ H ₁₁	6	93	2l	HOCH ₂ (CH ₃) ₂ C	2	35
2c	C ₃ H ₇ (CH ₃)CH	2	90	2m	Thien-2-yl	2	88
2d	C ₂ H ₅	2	58	2n	Thien-3-yl	2	91
2e	C ₃ H ₇	4	71	2o	Fur-2-yl	2	82
2f	(CH ₃) ₂ CH	5	65	2p	(1-methyl)-pyrrol-2-yl	2	79
2g	C ₉ H ₁₉	2	90	2q	Indol-3-yl	2	73
2h	CH ₃ CH=CH	5	61	2r	Pyrid-3-yl	4	82
2i	C ₂ H ₅ CH=(CH ₃)C	2	80	2s	Pyrid-4-yl	240	78
2j	(CH ₃) ₂ C=CH(CH ₂) ₂ CH- CH ₃	2	94				

ence of molecular sieves was used. The crude products thus obtained checked by m.ps., IR and ¹H-NMR, were essentially pure to be used for experiments.

Oxidation of N,N-dimethylhydrazones **1** to nitriles **2** with hydrogen peroxide

To a mixture of PMA (0.452 g, 0.2 mmol), hydrogen peroxide (10.2 ml, 100 mmol) and methylene chloride (10 ml), cooled in an ice/salt bath and vigorously stirred, a solution of dimethylhydrazone (**1a**, **1b** or **1c**) (10 mmol) in methylene chloride (5 ml) was added dropwise during 30 min. The reaction was continued for additional 2.5 h and temperature of the reaction mixture was slowly increased to 20 °C. After this period, the organic layer was separated, and the aqueous layer was extracted with methylene chloride (3×10 ml). The organic solutions were combined, washed with aqueous sodium chloride, dried over anhydrous sodium sulfate, and methylene chloride was evaporated in vacuo. The liquid residue was analysed using GC Hewlett-Packard 5890 apparatus with capillary column HP-1, 25 m, 0.2 mm, 70 °C, 8°/min, 300 °C.

Oxidation of N,N-dimethylhydrazones **1** to nitriles **2** with MCPBA

To a solution of dimethylhydrazone **1** (10 mmol) in methylene chloride (20 ml) cooled in an ice/salt bath and vigorously stirred, a solution of 55 % MCPBA (3.77 g, 12 mmol) in methylene chloride (50 ml) (the aqueous layer was removed from this solution before using) was added dropwise during 30 min. The reaction was continued for an additional time (Table 2). After the reaction was finished, the solution was washed with saturated sodium carbonate (3×30 ml), dried over anhydrous potassium carbonate, and the methylene chloride was evaporated in vacuo. The crude nitriles **2i**, **j**, **m**, **r**, **s** were purified by column chromatography (silica gel, chloroform or ethyl acetate) and compound **2q** by recrystallization from chloroform. Other products were essentially pure nitriles.

Nitriles **2a**, **b**, **d-f**, **h**, **k**, **m**, **o-s** were identified by comparison of their MS spectra (Hewlett-Packard 5971A) with data reported in the library NBS 49K. Other nitriles mentioned earlier in the literature [13–17] gave satisfactory spectroscopic

I.R. (Perkin-Elmer 621 spectrometer) and ¹H-NMR (Tesla 80 MHz spectrometer, CDCl₃; TMS as an internal standard), data listed below.

2-Methylvaleronitrile (**2c**)

Oil [13]; ¹H-NMR: 0.96 (t, 3H, J = 7.3 Hz, CH₃CH₂); 1.31 (d, 3H, J = 8 Hz, CH₃CH); 1.54 (m, 4H, CH₂); 2.58–2.75 (m, 1H, CH). I.R. (film): $\tilde{\nu}_{\text{CN}} = 2240 \text{ cm}^{-1}$.

2-Methyl-2-pentenitrile (**2i**)

Oil [14]; ¹H-NMR: 1.04 (t, 3H, J = 9 Hz, CH₃); 1.87 (s, 3H, CH₃); 2.19 (quintet, 2H, J = 9 Hz, CH₂); 6.33 (t, 1H, J = 9 Hz, CH). I.R. (film): $\tilde{\nu}_{\text{CN}} = 2220 \text{ cm}^{-1}$.

2,6-Dimethyl-5-heptenitrile (**2j**)

Oil [15]; ¹H-NMR: 1.30 (d, 3H, J = 9 Hz, CH₃); 1.66 (m, 8H, (CH₃)₂C, CH₂); 2.08 (q, 2H, J = 9 Hz, CH₂); 2.59 (q, 1H, J = 9 Hz, CHCN); 5.03 (t, 1H, J = 8 Hz, CH). I.R. (film): $\tilde{\nu}_{\text{CN}} = 2242 \text{ cm}^{-1}$.

2,2-Dimethyl-3-hydroxypropionitrile (**2l**)

Oil [16]; ¹H-NMR: 1.35 (s, 6H, CH₃); 2.67 (s, 1H, OH); 3.57 (s, 2H, CH₂). I.R. (film) $\tilde{\nu}_{\text{CN}} = 2240 \text{ cm}^{-1}$, $\tilde{\nu}_{\text{OH}} = 3460 \text{ cm}^{-1}$.

3-Thiophencarbonitrile (**2n**)

Oil [17]; ¹H-NMR: 7.42 (m, 2H, 3-H and 4-H); 7.95 (dd, 1H, J = 1 Hz and 2 Hz, 2-H). I.R. (film): $\tilde{\nu}_{\text{CN}} = 2238 \text{ cm}^{-1}$.

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Address for correspondence:
Prof. Dr. Jacek Młochowski
Technical University of Wrocław
Institute of Organic Chemistry
Biochemistry and Biotechnology
Wybrzeże Wyspiańskiego 27
PL-50370 Wrocław, Poland