

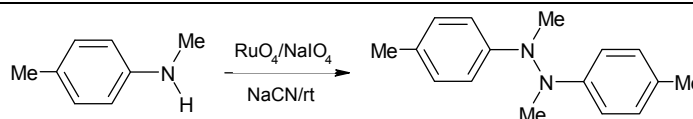
HOMOLYTIC PATHWAY FOR THE RuO₄-OXIDATION OF AMINES

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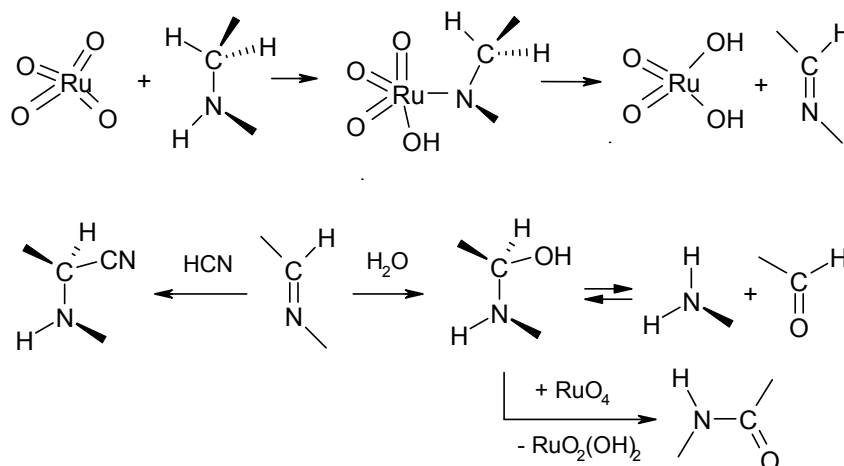
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Oxidation by RuO₄ of R-NH-Me (R = *p*-Me-C₆H₄) gave, in the presence of NaCN, the hydrazine derivative R-NMe-NMe-R as main reaction product. A homolytic mechanism is advanced.



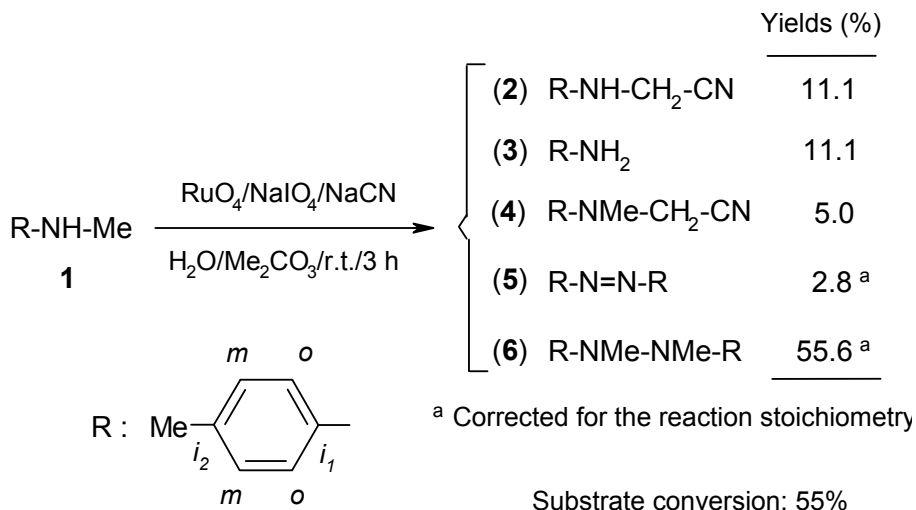
It is well known that secondary amines carrying C-H bonds in α to N atom (R-NH-CHR₂) undergo oxidation by ruthenium-based catalysts^{1,2} (including ruthenium tetroxide)³⁻⁵ to yield imines (R-N=CR₂), by a formal 1,2-dehydrogenation process. By analogy with the oxidation of secondary alcohols, the advanced mechanism³ involves two distinct hydrogen-transfer processes: the first for the N-H proton, the second for the C-H one (Scheme 1). RuO₄ acts as a two-electron

oxidant.³ At their turn, imines are reactive compounds. For instance, if the oxidation is performed in the presence of NaCN, α -aminonitriles are formed from imines and HCN (generated *in situ*). In the absence of cyanide, nucleophilic addition of water leads to a hemiaminal, which can be split into a mixture of primary amine and aldehyde and/or oxidized towards the corresponding amide.^{4,5}

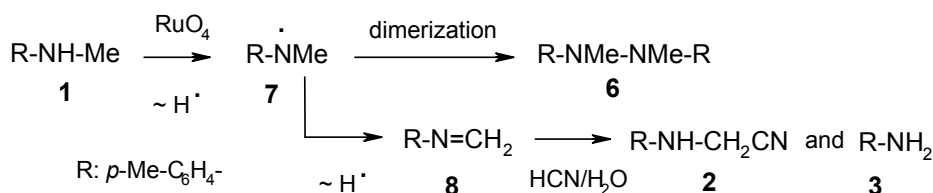


Scheme 1

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Scheme 2



Scheme 3

Recently, starting from *N*-methyl-*p*-toluidine (**1**), we identified the compounds **2-6** as oxidation products in the presence of sodium cyanide (Scheme 2). The use of RuO₄ (generated *in situ* from catalytic RuO₂ and excess NaIO₄) is essential: the substrate conversion dropped to about 10% in its absence.

As advanced before in Scheme 1, the nitrile **2** and *p*-toluidine (**3**) were the expected products. Quite surprisingly, the main reaction product was instead the hydrazine derivative **6**, which can be viewed as a stable, dimeric form of the free radical **7** (Scheme 3). Alternatively, this species might suffer also a homolytic abstraction of hydrogen from the methyl group to give the imine **8**, the aforementioned precursor of both **2** and **3**. These results seem indicate a homolytic mechanism for the RuO₄-catalyzed oxidation of the secondary amine **1**. Further work is needed to clarify the mechanism and to circumscribe its application area.

Compounds **1-5** are all commercial products. Derivative **6** was prepared as described in the literature.⁶⁻⁸ The oxidation reactions were performed as already presented,⁹ but using an environmental friendly co-solvent (dimethyl carbonate, DMC)¹⁰ instead of chloroform. To a NaCN solution [196 mg (4 mmol) in water (10 mL)] was added RuO₂.xH₂O

(10 mg), toluidine **1** (1 mmol in 10 mL of DMC), and the co-oxidant (NaIO₄) aqueous solution (0.4 M; 10 mL, 4 mmol), in this order. The heterogeneous reaction mixture was magnetically stirred at room temperature for 3h and then worked-up as described in a previous paper.¹¹ Identification of the various reaction products was made by comparison of the NMR spectra before and after the addition of small samples of the pure compounds into the analyzed samples. The amounts quoted in Scheme 2 were calculated from the NMR data obtained in the presence of 1,4-dimethoxybenzene, added as internal standard.¹¹

Pertinent NMR characteristics, obtained in CDCl₃ solutions, are presented below. Chemical shifts are expressed in ppm (δ scale) and interproton coupling constants in Hz. Aromatic protons and carbons are abbreviated as shown in Scheme 2. The ¹³C NMR data of **6** are reported for the first time.

***N*,4-Dimethylphenylamine (1)**. δ_H: 2.23 (s, 3H, 4-CH₃), 2.78 (s, 3H, N-CH₃), 3.2 (br. s, 1H, NH), 6.52 (d, *J*=8.5, 2H, *o*), 6.99 (d, *J*=8.5, 2H, *m*). δ_C: 20.4 (4-CH₃), 31.1 (N-CH₃), 112.7 (*o*), 126.5 (*i*₂), 129.8 (*m*), 147.2 (*i*₁).

***N*-(4-methylphenyl)aminoacetonitrile (2)**. δ_H: 2.26 (s, 3H, CH₃), 3.90 (s, 1H, NH), 4.01 (s, 2H, CH₂), 6.61 (d, *J*=8.5, 2H, *o*), 7.06 (d, *J*=8.5, 2H, *m*). δ_C:

20.5 (4-CH₃), 33.1 (CH₂), 113.9 (*o*), 117.3 (CN), 129.5 (*i*₂), 130.1 (*m*), 142.8 (*i*₁).

4-Methylphenylamine (3). δ_H: 2.22 (s, 3H, CH₃), 6.57 (d, *J*=8.5, 2H, *o*), 6.93 (d, *J*=8.5, 2H, *m*). δ_C: 20.4 (CH₃), 115.2 (*o*), 127.6 (*i*₂), 129.7 (*m*), 143.8 (*i*₁).

***N*-Methyl-*N*-(4-methylphenyl)aminoacetonitrile (4)**. δ_H: 2.27 (s, 3H, 4-CH₃), 2.92 (s, 3H, N-CH₃), 4.05 (s, 2H, CH₂), 6.76 (d, *J*=8.6, 2H, *o*), 7.09 (d, *J*=8.6, 2H, *m*). δ_C: 20.4 (C-CH₃), 39.4 (N-CH₃), 42.7 (CH₂), 115.4 (*o*), 115.5 (CN), 129.8 (*i*₂), 130.0 (*m*), 145.7 (*i*₁).

***Bis*-(4-methylphenyl)diazene (5)**. δ_H: 2.43 (s, 6H, CH₃), 7.30 (d, *J*=8.4, 4H, *o*), 7.81 (d, *J*=8.4, 4H, *m*). δ_C: 21.6 (CH₃), 122.9 (*o*), 129.8 (*m*), 141.3 (*i*₂), 151.0 (*i*₁).

***N,N'*-Dimethyl-*bis*-(4-methylphenyl)hydrazine (6)**. δ_H: 2.25 (s, 6H, C-CH₃), 2.90 (s, 6H, N-CH₃), 6.74 (d, *J*=8.5, 4H, *o*), 7.04 (d, *J*=8.5, 4H, *m*). δ_C: 20.4 (C-CH₃), 33.6 (N-CH₃), 112.8 (*o*), 127.7 (*i*₂), 129.9 (*m*), 147.0 (*i*₁).

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