

Aerobic Oxidation of Amines

An Unconventional Cobalt-Catalyzed Aerobic Oxidation of Tertiary Nitrogen Compounds to *N*-Oxides

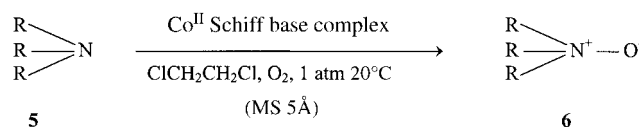
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The propensity of cobalt complexes to bind with molecular oxygen^[1] and the use of such dioxygen–cobalt complexes as catalysts for various oxidation reactions have been subjects of intensive research in recent years.^[2] The oxygenation of organic compounds catalyzed by such dioxygen–cobalt complexes and with aldehyde as a sacrificial agent^[3] has led to several important methodologies for the epoxidation of olefins,^[4] oxidation of sulfides to sulfones,^[5] and oxidation of imines to oxaziridines.^[6] However, the oxygenation of organic compounds, in which molecular oxygen serves as the oxidant and cobalt complexes as catalysts under ambient conditions without the sacrificial agent, although a desirable goal, has not been very successful. To the best of our knowledge there are only two relevant literature reports describing the oxygenation of trialkylphosphanes^[7] and olefins, and cyclic ethers.^[8]

The cobalt Schiff base complexes **1**,^[4b] **2**,^[9] **3**,^[10] and **4**^[11] are well known to bind with molecular oxygen^[4b,9,10] and show very high reactivity in oxygenation reactions with molecular oxygen as the oxidant along with an aldehyde as a sacrificial agent, but there are no reports on the oxygenation of organic compounds with these complexes as catalysts and molecular oxygen as the sole oxidant.

Oxidation of tertiary nitrogen compounds to *N*-oxides is an important synthetic transformation. In the search for environmentally friendly methods for this transformation the use of hydrogen peroxide with the catalysts methyltrioxorhenium(vii),^[12] manganese porphyrin,^[13] flavin,^[14] TS-1,^[15] molecular sieves,^[16] and tungstate-exchanged Mg/Al-layered double hydroxide^[17] has been reported. In continuation of our studies on oxidation with molecular oxygen as the primary oxidant^[18] we report here on the first successful oxidation of tertiary nitrogen compounds **5** to *N*-oxides **6** catalyzed by cobalt(II) Schiff base complexes (Scheme 1).

A wide variety of tertiary nitrogen compounds were oxidized to give their corresponding *N*-oxides in nearly quantitative yields by simply bubbling molecular oxygen into a solution of the tertiary nitrogen compound in 1,2-dichloroethane at room temperature in the presence of 5-Å molecular sieves and with the cobalt Schiff base complex **1** as the catalyst. These results are summarized in Table 1. Pyridines containing electron-donating groups (Table 1, entries 2, 3, and 6) were found to react faster than pyridines bearing electron-withdrawing groups (Table 1, entries 4 and



Scheme 1. Oxidation of tertiary nitrogen compounds **5** to *N*-oxides **6** catalyzed by a cobalt(II) Schiff base.

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Table 1: Oxidation of tertiary nitrogen compounds to *N*-oxides.^[a]

Entry	Substrate	<i>t</i> [h]	Yield [%]
1		8	80
2		8	85
3		10	75
4		14	55
5		12	50
6		10	65
7		12	50
8		6	92
9		6	90
10	(C ₂ H ₅) ₃ N	5	92

[a] All reactions were conducted with substrate (10 mmol) and Co^{II} Schiff base complex **1** (0.5 mol%) in 1,2-dichloroethane (10 mL) at room temperature under an oxygen atmosphere in the presence of 5-Å molecular sieves (see Experimental Section).

5). To evaluate the relative efficiency of various Co^{II} Schiff base complexes, we prepared complexes **2–4** and studied the oxidation of 4-picoline under similar conditions with 0.5 mol% of these catalysts. All of these complexes were found to be efficient catalysts for this transformation; however, compound **1**^[19] was found to be most efficient probably as a consequence of the effect of the ligands, which are known to affect the oxidation potential.^[20] In a control experiment in the absence of catalyst no oxidation was observed. Although these reactions could also be performed without 5-Å molecular sieves, their presence was found to enhance the reaction rate. We assume the molecular sieves remove the moisture in the reaction system and that added with the oxygen gas.

Although the mechanism of this reaction is not yet clear, it probably involves the coordination of the tertiary nitrogen compound and molecular

oxygen with the cobalt complex (\rightarrow **7**), formation of the binuclear μ -peroxocobalt complex **8**, homolytic cleavage of the O–O bond followed by the formation of reactive oxometal species **9**, and intramolecular transfer of oxygen to the nitrogen atom to yield the *N*-oxide (Scheme 2). The formation of superoxocobalt complexes such as **7** have been assumed earlier for cobalt Schiff base complexes in the presence of tertiary amines.^[21] The formation of the binuclear μ -peroxocobalt complex **8** and the oxometal species **9**, and intramolecular oxygen transfer to the tertiary amine are analogous to steps in the mechanistic pathway for the oxidation of tributylphosphane to tributylphosphane oxide with molecular oxygen catalyzed by bis(acetylacetonato)cobalt(II).^[7]

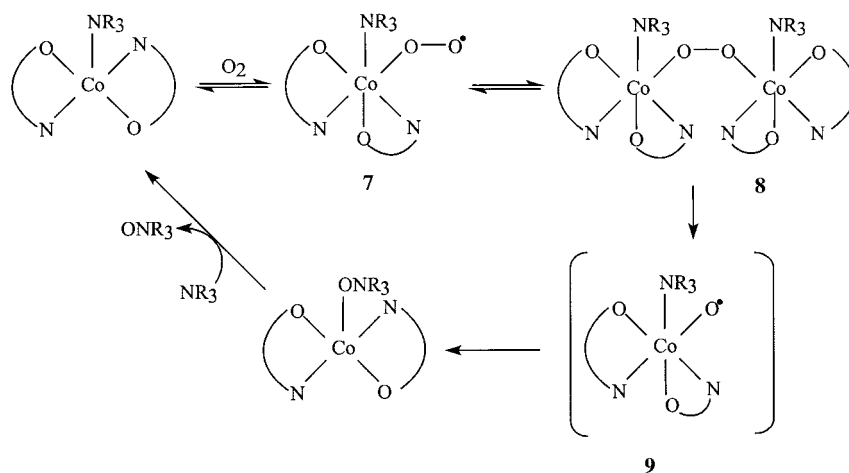
In summary, we have demonstrated for the first time that cobalt Schiff base complexes can catalyze the oxidation of tertiary nitrogen compounds with molecular oxygen as the sole oxidant to afford *N*-oxides in excellent yields under mild conditions. The simplicity of the system, simple workup, and excellent yields make this method an attractive, environmentally acceptable synthetic tool.

Experimental Section

All the reagents and solvents used were laboratory reagent grade and purified before use. Cobalt Schiff base complexes **1**,^[4b] **2**,^[9] **3**,^[10] and **4**^[11] were prepared according to literature procedures.

A typical procedure for the oxidation of tertiary nitrogen compounds to *N*-oxides: Molecular oxygen was bubbled at room temperature (20°C) into a stirred solution of 4-picoline (0.93 g, 10 mmol) and cobalt Schiff base complex **1** (25 mg, 0.5 mol%) in dichloroethane (10 mL), which contained 5-Å molecular sieves (1 g). The progress of reaction was monitored by TLC (SiO₂). At the end of reaction the molecular sieves were removed by filtration, and the reaction mixture was passed through a silica gel column with dichloromethane/MeOH (95:5) as the eluent. Removal of solvent and standard workup gave 4-picoline *N*-oxide (0.93 g, 85%). Other *N*-oxides were prepared by this procedure; their reaction times and yields are given in Table 1. The products were identified by comparing their physical and spectroscopic data with literature data.

For comparing the efficiency of various Co^{II} Schiff base complexes, experiments were carried out with 4-picoline under similar conditions, and the residue obtained after passage through the silica



Scheme 2. Proposed mechanism for the oxidation.

gel column was analyzed by HPLC for conversion of 4-picoline to 4-picoline *N*-oxide.

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