

On the Oxidation of Different Iminic Bonds by Excess of 3-Chloroperbenzoic Acid

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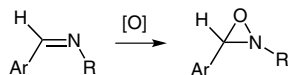
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Abstract: In the present work the behavior of different substituted iminic bonds toward the oxidative action of 3-chloroperbenzoic acid is reported. The C=N bond was or was not oxidized to oxaziridines, amides, oximes, nitroso-, nitro-, and azodioxy compounds depending on the substituents at the iminic group and on the imine/MCPBA stoichiometric ratio.

Key words: imines, oxidation, oxaziridines, C-nitroso compound, oximes

Although the reduction¹ and hydrolysis² of imines has been largely studied, only a few publications report its behavior toward oxidizing agents. It has been reported that benzylidene alkylamines lead to the corresponding oxaziridines by stoichiometric oxidation with peracids,³ urea hydrogen peroxide,⁴ and cobalt-mediated molecular oxygen⁵ (Scheme 1).



[O] = MCPBA, urea-hydrogen peroxide, Co/O₂

Scheme 1 Synthetic methodology for oxaziridine generation

A number of thermally stable oxaziridines, obtained by oxidation of benzylidene alkylamines,⁶ have been employed both as oxygenating and/or aminating agents of nucleophilic species⁷ and as reagents in cycloaddition reactions with heterocumulenes,⁸ alkenes,⁹ alkynes,¹⁰ and nitriles.¹¹ Reports of reactions of imines with excess MCPBA are scarce. Previously, we have reported that the oxidation of benzylidene alkylamines **1–3** by 1.1 mmol of MCPBA in CH₂Cl₂ solution led to oxaziridines **1a–3a** in good yields (>90%),¹² while nitroso compounds **1b–3b** rapidly dimerized to azodioxy compounds **1c–3c** and were obtained employing 2.2 mmol of MCPBA (Scheme 2). Furthermore compounds **2b**, **3b**, **2c**, and **3c**, having a hydrogen at the α position of R¹, undergo isomerization into oximes **2d** and **3d** by heating in toluene solution.

Moreover, the azodioxy dimer **3c** was obtained in quantitative yield by reaction of 1.1 mmol MCPBA with the isolated oxaziridine **3a**.

The same result was obtained on oxidizing the cyclic imine 3,4-dihydro-2*H*-pyrrole **4** with 1.1 mmol of MCPBA; the condensed oxaziridine **4a** (yield 98%) was obtained in this case. Product **4a** was subsequently oxidized into nitroso compound **4b** that rapidly dimerized to azoxydimer **4c** when a further 1.1 mmol of MCPBA were added. Furthermore, on heating **4c** in toluene (80 °C), **4d** was obtained (yield 80%, Scheme 3).¹²

Continuing our studies on the oxidation of imines with MCPBA we have discovered outcomes strongly dependent on the C=N bond substituents. Due to the lower basicity of the nitrogen in **5–7** with respect to compounds **1–4**, the second oxygen transfer on oxaziridines **5a–7a**, formed on initial oxidation, did not take place. Instead, *N,N*-diarylamides **8–10** were obtained both with 1.1 mmol or 2.2 mmol of peracid, after a carbon–nitrogen migration of the aryl group (Scheme 4). Amides were also obtained in reactions of imines with sodium perborate¹³ or with MCPBA and BF₃·OEt₂.¹⁴

A further decrease of basicity of the imine nitrogen as in oximes **11**, isoxazolines **12**, benzothiadiazines **13**, and osazones **14** (Figure 1), due to the presence of a heteroatom on the nitrogen atom, diminished the reactivity towards C=N oxidation, and starting materials were recovered even using 5.0 mmol of MCPBA. Instead the osa-

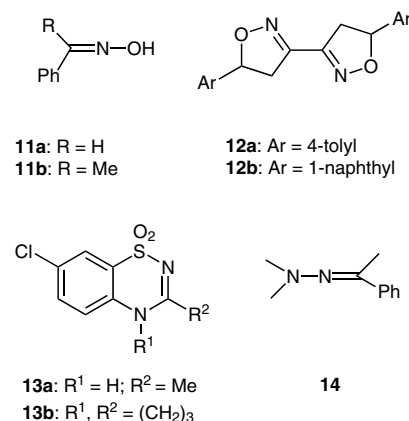


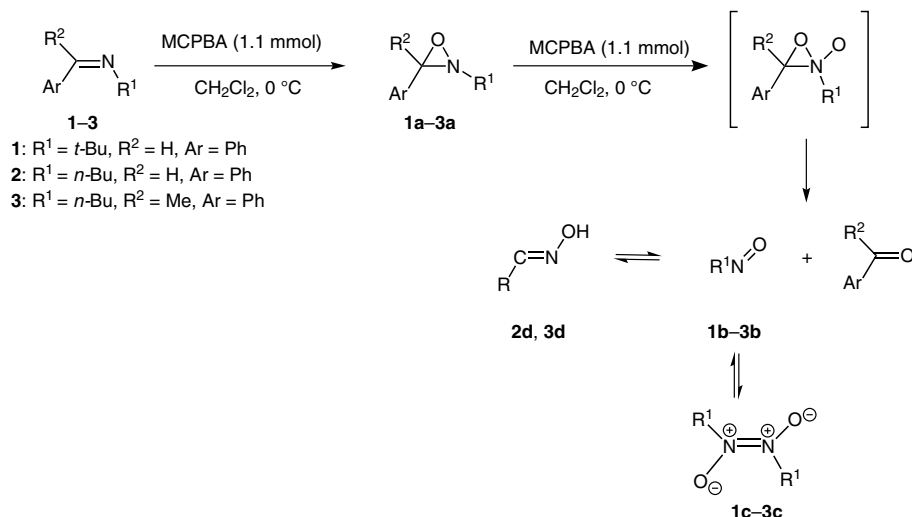
Figure 1

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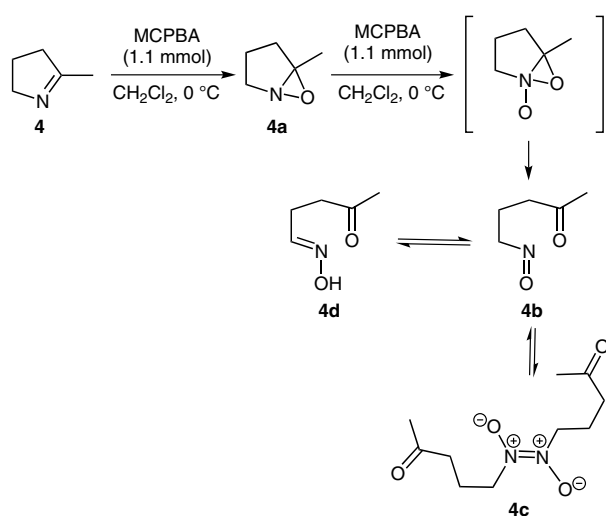
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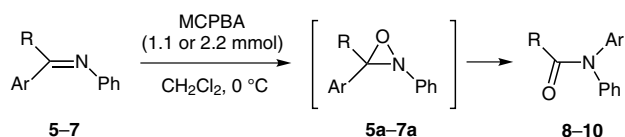
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Scheme 2 Oxidative action of the MCPBA toward *N*-alkyl imines



Scheme 3 Oxidative action of MCPBA toward cyclic imines



5, 8: R = H, Ar = Ph
6, 9: R = H, Ar = 4-ClC₆H₄
7, 10: R = Me, Ar = C₆H₅

Scheme 4 Oxidative action of MCPBA toward aryl imines

zone **14** was oxidized on the amine nitrogen, leading to a mixture of different products.¹⁵

On the contrary, imines containing a heteroatom at the imine carbon showed high reactivity towards oxidation. Oxazolines **15** reacted with 1.1 mmol of peracid leading to the stable oxaziridines **15** after five hours. Further addition of 1.1 mmol of peracid to **15a** led to an unstable *N*-oxide intermediate which converted into **15b** in equilibrium with the dimeric compound **15c** (yield 98%) and/or oxime **15d** (R = H, Scheme 5).¹²

Other heterocycles with similar structure exhibit the same behavior. When **16** was treated with 2.2 mmol of peracid, **16b** was formed, which converted into the azoxydimeric form **16c** (yield 98%,¹⁶ Scheme 6). These results indicate that the oxygen bound to the iminic carbon atom increases reactivity toward oxidation reaction.

Imidazoline **17**, which contains a nitrogen atom connected to the imine carbon was transformed (50%) into nitroso compound **17b** and subsequently into azoxydimer **17c** when treated with 1.1 mmol of MCPBA. It was not possible to isolate oxaziridine **17a** and the intermediate form of the second oxidation because of their high reactivity. Instead, **17** led to **17c** (yield 99%) when treated with 2.2 mmol of peracid (Scheme 7).

Only a 50% conversion of 2*H*-1,2,4-benzothiadiazine derivatives **18** and **19**,¹⁷ structurally similar to the imidazolines, into nitroso compounds **18b-19b** was observed on reacting with 1.1 mmol of MCPBA, with azoxydimers **18c** and **19c** being isolated as final products. On the other hand, when 2.2 mmol of peracid were employed the transformation to the azoxydimers was complete (99%, Scheme 8).

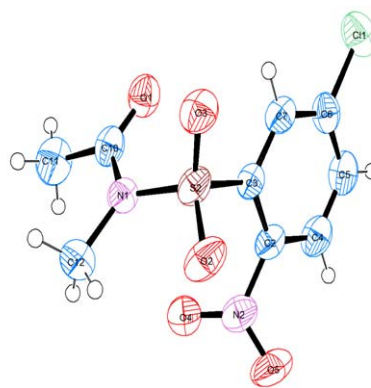
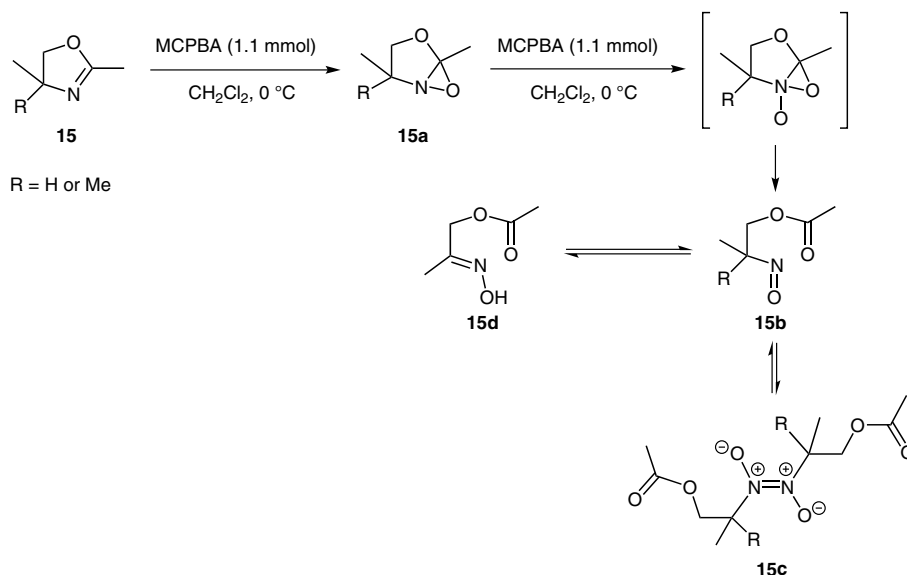
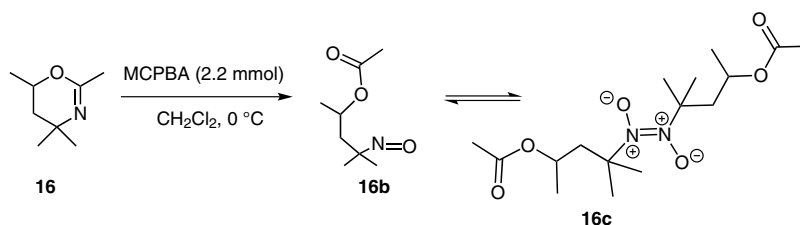


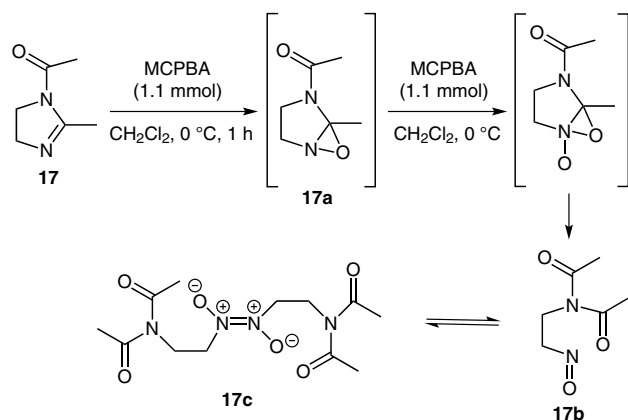
Figure 2 Projection of compound **18e** at 298 K



Scheme 5 Oxidative action of the MCPBA toward O-activated cyclic imines



Scheme 6 Oxidative action of the MCPBA toward O-activated cyclic imines



Scheme 7 Oxidative action of the MCPBA toward N-activated cyclic imines

Furthermore, nitro compound **18e** (90% yield) was isolated on treatment of **18** with 5.5 mmol of MCPBA. The structure of **18e** was characterized by X-ray crystallographic analysis (Figure 2).¹⁸

In summary, in this work we have examined the influence of substituents on the behavior of imines towards MCPBA. Oxygen, nitrogen, or sulfur, attached to the nitrogen, render the substrates resistant to oxidation of the π -bond. On the contrary, a heteroatom or carbon substitu-

ent on the imine carbon make the imine double bond more reactive; oxaziridines, amides, oximes, nitroso-, nitro-, and azoxy compounds can be synthesized depending on the imine/MCPBA stoichiometric ratio.

General Procedure

An excess of MCPBA (1.1 or 2.2 mmol) in CH_2Cl_2 (3 mL) was added to a solution of the requisite imine (1.0 mmol), dissolved in CH_2Cl_2 (5 mL), with stirring and cooling (0–5 °C). When reaction was complete (5–6 h), the excess of *m*-chloroperbenzoic acid, and the benzoic acid formed was removed by filtration. The filtrate was washed twice with a dilute solution of Na_2SO_3 (5%), then with a solution of Na_2CO_3 (5%), and finally with H_2O . After drying over anhydrous MgSO_4 , the mixture was concentrated in vacuo, and the crude product was purified by column chromatography (silica gel partly deactivated with Et_3N).

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