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

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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 azoxydimer 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-2H-pyrole 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 secondary 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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zone 14 was oxidized on the amine nitrogen, leading to a mixture of different products. 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 15 led to an unstable N-oxide intermediate which converted into 15 in equilibrium with the dimeric compound 15c (yield 98%) and/or oxime 15d (R = H, Scheme 5). 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 azoxydimers 16c (yield 98%, 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 2H-1,2,4-benzothiadiazine derivatives 18 and 19, 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
Furthermore, nitro compound (90% yield) was isolated on treatment of \(18\) with 5.5 mmol of MCPBA. The structure of \(18\) was characterized by X-ray crystallographic analysis (Figure 2).

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 \(\pi\)-bond. On the contrary, a heteroatom or carbon substituent 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 anhyd \(MgSO_4\), 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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**Supporting Information**

Supporting Information for this article is available online at [http://www.thieme-connect.com/ejournals/toc/synlett](http://www.thieme-connect.com/ejournals/toc/synlett).
Scheme 8 Oxidative action of the MCPBA toward S-activated cyclic imines

References and Notes


(16) Compound 16e: total yield 98%, 179.4 mg; E-Isomer: yield 89.7 mg, 49%, oil; Rf = 0.33 (PE–EtOAc = 9:1). 1H NMR (400.13 MHz, CDCl3): δ = 1.25 (3 H, d, J = 6.5 Hz, CHCH3), 1.57 (3 H, s, CCH3), 1.59 (3 H, s, CCH3), 1.96 (3 H, s, COCH3), 1.97–2.07 (1 H, m, CHCH3), 2.47–2.53 (1 H, m, CHCH3), 5.02–5.10 (1 H, m, CHCH3). 13C NMR (100.62 MHz, CDCl3): δ = 20.8, 24.5, 27.6, 45.7, 66.8, 86.1, 170.3. FTIR (CHCl3): 2948, 2845, 1730, (C=O), 1270, (NO), 1080 cm–1. ESI-HRMS: m/z calcd for C17H33N2O6[M + H]+: 361.2333; found: 361.2330.


(18) (a) Crystal Data for Compound 18e: C17H33N2O6, Fw = 292.69, T = 298 K, monoclinic, space group P21/n, a = 11.983(13) Å, b = 7.370(6) Å, c = 15.357(12) Å, β = 90, β = 112.89(5) (Mo Kα) = 0.491 mm–1; crystal dimensions 0.3 × 0.2 × 0.06 mm. The X-ray experiments were carried out at r.t. by a Bruker-Nomius KappaCCD diffractometer, using Mo Kα radiation (λ = 0.71073 Å). Data collection was performed by COLLECT (Nonius, 2002). COLLECT and EVAL. Nonius BV, Delft, The Netherlands), cell refinement by DIRAX® and data reduction by EVAL (Nonius, 2002). COLLECT and EVAL. Nonius BV, Delft, The Netherlands). Absorption effects were corrected by SADABS. The crystal structure was solved by SIR2011® and refined by SHELXL-97. The H atoms were placed at calculated positions and refined according to a riding model approximation. The software used for preparing the material for publication: WinGX®. The software used for molecular graphics: Ortep-3.18g