Iron and manganese (III) – porphyrins as new applicable catalysts for selective oxidation of imines with urea–hydrogen peroxide

Bahador Karami*, Morteza Montazerozohori, Majid Moghadam and Mahnaz Farahi

Department of Chemistry, Yasouj University, Yasouj 75918-74831 PO Box 353, Iran

A variety of imines were oxidised with urea–hydrogen peroxide using iron(III) and manganese (III)- tetraphenyl-porphyrins [Fe(TPP)Cl], [Mn(TPP)Cl] and manganese (III)-octabromotetraphenyl porphyrin [Mn(TPPBr_8)Cl] as catalysts. Experimental results showed the released urea from UHP acts as an axial ligand. These catalysts showed high selectivity in oxidation of imines to corresponding nitrones and oxaziridines at 0°C to room temperature.

Keywords: oxidation, imines, porphyrin, oxaziridines, nitrones

The development of an efficient model of systems mimicking the activity of cytochrome P-450 has been one of the areas of intense research activity.[1,2] Many metalloporphyrin complexes, mainly iron and manganese, proved to be able to catalyse oxidation reactions. Among the more biologically significant of these processes are *O*- and *N*-dealkylation,[3] olefin and arene epoxidation,[4,5] alkane hydroxylation,[6,7] oxidation of nitroso[8] and primary aromatic amines to nitro derivatives.[9] Various single oxygen-atom donors such as PhIO, ClO^-, H_2O_2 or IO_4^- have been used for these transformations.[10-17] High yields and rates have been obtained with these biomimetic systems making them useful for complete conversion of various substrates and potentially useful preparative oxidations in organic chemistry.

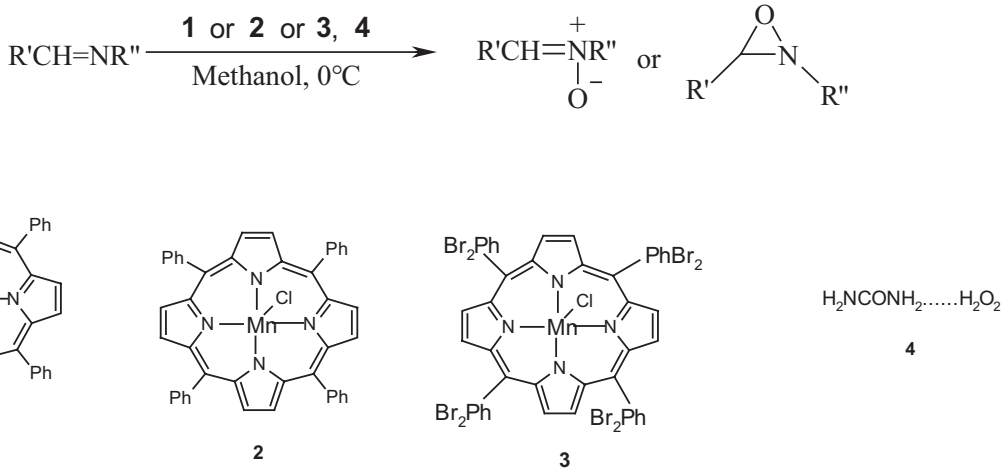
In the present work, we report iron(III)- and manganese(III)-porphyrins **1–3** as biomimetic catalysts for oxidation of imines to corresponding oxaziridines and nitrones using urea–hydrogen peroxide (UHP) **4** as single oxygen donating compound. We have chosen UHP adduct **4** because it has been used as an odourless, safe, non-toxic and easy-to-use white crystalline powder which releases hydrogen peroxide locally on application in many reports. Over the past few years, several papers have been published on the use of **4** in oxidation reactions such as Baeyer–Villiger oxidation of ketones,[18,19] oxidation of sulfides to sulfones,[20] oxidation of aromatic aldehyde,[21] and epoxidation of alkenes.[22,23] Recently we reported oxidation of imines to oxaziridines and nitrones using the **4**/maleic anhydride system.[24] In these application, **4** alone or in combination with carboxylic acid or anhydride as catalyst (rarely inorganic complex as co-catalyst) has been produced as a mild and efficient oxidant.[25]

Result and discussion

Urea hydrogen peroxide **4** as mentioned above has an active available oxygen content that can be used for different oxidation systems. Amongst organic compounds, carboxylic acid or anhydrides have been used as good mediators for transfer of the active oxygen in these systems.[25] Amongst inorganic catalysts, metal Schiff-base complexes have been used widely as efficient catalysts for oxidation of various substrates with hydrogen peroxide. For example, Ti-(salen) catalysed sulfoxidation reaction with **4** in methanol at 0°C[26] and cationic Co(III)-salen was used for Baeyer–Villiger oxidation in the presence of various hydrogen peroxide derivatives as oxidant in CH_2Cl_2 at room temperature.[27] Organic mediators such as maleic anhydride was found to be need as co-catalyst for efficient epoxidation of alkenes in the presence of [Fe(TPP)Cl] **1**/**4** systems.[25] During the search for a good mediator[24] or catalyst that can transfer active oxygen of **4** to imine oxidation systems, we found that [Fe(TPP)Cl] **1**, [Mn(TPP)Cl] **2** and [Mn(Br_8TPP)Cl] **3** suitably catalyse oxidation of imines to related oxaziridines and nitrones in the presence of **4** as oxidant (Scheme 1).

A wide variety of imines were oxidised with metalloporphyrins **1–3**/**4** systems in methanol. The oxidation reactions were performed under mild condition at 0°C in 10–15 minutes with good to excellent yields (Table 1, Scheme 1).

As indicated in Table 1, the *N*-aryl imines (entries 1–4) were oxidised to nitrones, while *N*-alkyl imines (entries 5–10) were converted to their corresponding oxaziridines. The remaining conjugation in aryl imines may be the main reason why nitrones are formed instead of oxaziridines. These results confirm our recent reports.[24]

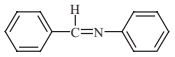
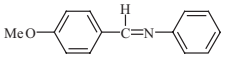
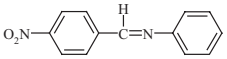
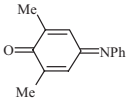
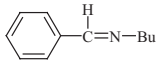
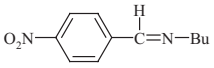
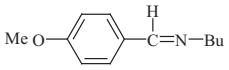
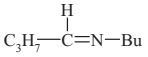
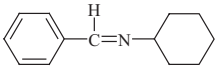
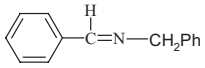
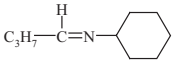


1 **2** **3** **4**

Scheme 1

* Correspondent. E-mail: karami@mail.yu.ac.ir; karamivk@yahoo.com

Table 1 Oxidation of imines with **4** catalysed by metalloporphyrins **1–3** in methanol at 0°C[a]

Entry	Substrate	Product[b]	Time/ min	Yield/ %[c]
1		Nitrone	10	85
2		Nitrone	15	90
3		Nitrone	10	90
4		Nitrone	10	95
5		Oxaziridine	15	90
6		Oxaziridine	15	95
7		Oxaziridine	15	90
8		Oxaziridine	15	80
9		Oxaziridine	15	85
10		Oxaziridine	15	90
11		Oxaziridine	15	85

[a]Reaction conditions: imines (1 mmol), UHP (1 mmol), catalyst (1 mol%), methanol (10 ml).
[b]Both IR and ^{1}H NMR spectra confirmed the resulted products.
[c]Isolated yields.

To study the effect of solvent, oxidation of *N*-butyl phenyl imine (entry 5, Table 1) was performed in different solvents. As shown in Table 2, methanol is the best solvent due to the relatively good solubility of catalyst and starting materials. Following the investigation of axial ligand effect on activity of catalyst, it was interesting that absence or presence of the axial ligand (imidazole or *N*-methylmorpholine-*N*-oxide) on **1, 2** or **3** catalysts did not have considerable effect in conversion of imines to related oxaziridines and nitrones. We suggest that the released urea during the progress of reaction acts as axial ligand (Scheme 2). This observation is in agreement with other literature reports for this type of systems.[28,29]

Table 2 Effects of solvent and temperature on oxidation of *N*-butyl phenyl imine with Fe (TPP) Cl/UHP

Solvent	Completion time of reaction [min] 0°C	RT
CH_2Cl_2	100[a]	140[a]
$CHCl_3$	100[a]	140[a]
CH_3OH	15[b]	30[a]
CH_3CN	60[b]	60[a]

[a]The reaction was not completed within time.
[b]The reaction was completed within time.

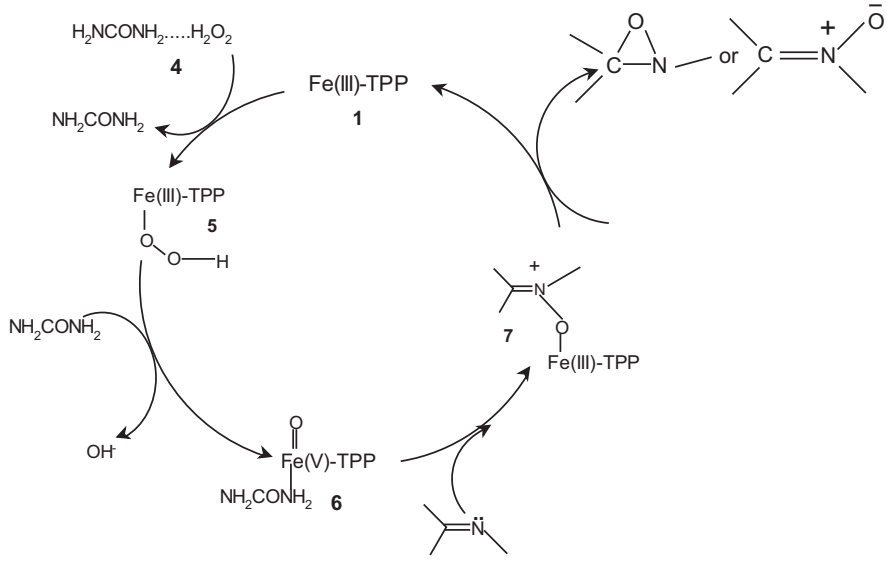
The effect of catalyst amount was investigated using 1/100, 1/50, 1/25 and 1/15 molar ratios of **1** on conversion of *N*-butyl phenyl imine (entry 5, Table 1). The results revealed that 1/100 molar ratio was optimum and higher amounts of catalyst did not have any effect on completion of reaction.

Based on published observations, oxidation reactions containing **4** as oxidant were done at 0°C, room temperature and rarely at reflux. Performance of our experiments in these conditions, showed relatively shorter reaction times at 0°C than others because of the higher efficiency of **4** at 0°C.

It is interesting that the performance of the above optimisation on metalloporphyrins **2** and **3** showed similar results, including the type of products, yields and reaction times, as for metalloporphyrin **1**. However, the reactions with metalloporphyrin **1** were clean and easy to work up and therefore we focused on metalloporphyrin **1** as catalyst in this report.

Generally in such systems an oxo-intermediate is considered as direct oxidant. Isolation and characterisation of such an oxo-intermediate is difficult but evidences, especially severe colour change of catalyst during the reaction[30,31] supports formation of [Fe^V(O)TPP] **6** or [Mn^V(O)TPP] as oxo intermediate in the presence of **4**. Following these evidences and other reported mechanisms,[25] the mechanism shown in Scheme 2 is proposed for oxidation of imines by **1**.

In Scheme 2, **1** is converted to hydroperoxy iron(III) porphyrin species **5** by released H_2O_2 from **4**, then with entrance of urea as axial ligand, [Fe^V(O)TPP] **6** is formed as direct oxidant. Although hydroperoxy iron (III) porphyrin **5** can be assumed as the active species without the presence



Scheme 2

of oxo-compound **6**. In the next stage, the imine approaches oxidant species **6** and an unstable intermediate **7** is formed that can release oxaziridines or nitrones and regenerated **1**.

Comparison of this method for the oxidation of imines with our previous report[24] in terms of amount of catalyst used, conditions, and yields, show advantages such as catalytic amount (1%mol for porphyrin compared to 100% for maleic anhydride system) and shorter reaction times, with retention of yields, in similar conditions.

In conclusion, the results show that the type of the used metalloporphyrins **1-3** had no important effects on completion of the reaction. In this paper, we have described a facile, mild and biomimetic synthesis of oxaziridines and nitrones using catalytic amounts of metalloporphyrins **1–3** as biological-model catalysts in the presence of **4** as stable, safe and non-toxic oxidant. Several advantages of this method including high yields of products, short reaction times, inexpensive (catalytic amount of metalloporphyrins **1–3** and non necessity of axial ligand) and ease of isolation of products, which make this reaction convenient and efficient.

Experimental

Chemicals were purchased from Aldrich, Fluka and Merck. UHP **4** was synthesised according to a previous report.[27] Metalloporphyrins **1–3** was prepared a previously described method.[32] The reactions were monitored by TLC. The products were isolated and identified by comparison of their physical and spectral data with authentic samples. IR spectra were recorded on an FT-IR Jasco-680 instrument and the ^{1}H NMR spectra were obtained on a Bruker instrument 300 MH_Z model.

Typical procedure: oxidation of imine (entry 10) to oxaziridine by metalloporphyrin 1

A suspension of *N*-benzyl phenyl imine (entry 10, Table 1) (0.39 g, 2 mmol), **4** (0.188 g, 2 mmol), **1** (0.0144 g, 0.02 mmol) in methanol (10 ml) was stirred at 0°C. The progress of the reaction was monitored by TLC (*n*-hexane-ethyl acetate: 80: 20). The reaction was completed after 15 min. The reaction mixture was filtered and the methanol was removed under reduced pressure. The residue was purified by a short pad of silica gel (silica gel 60). Highly pure oxaziridines (Table 1, entry 10) was obtained in 90% yield (0.38 g). IR and ^{1}H NMR spectra data confirmed the identity of the product. ^{1}H NMR ($CDCl_3$) δ: 4.12(d of d, J = 16, 4 Hz, 2H), 4.81(s, 1H), 7.45–7.60(m, 10 H). ^{13}C NMR ($CDCl_3$) δ: 135.8, 134.8, 130.3, 129.8–127.9(5 CH), 80.4, 65.9. IR (KBr): 3040(m), 2960(m), 1490(s), 1450(s), 1400(s), 760(s), 720(s), 690(s).

Typical procedure: oxidation of imine (entry 1) to nitrone by metalloporphyrin 1

A suspension of *N*-phenyl phenyl imine (entry 1, Table 1) (0.362 g, 2 mmol), **4** (0.188 g, 2 mmol), **1** (0.0144 g, 0.02 mmol) in methanol (10 ml) was stirred at 0°C. The progress of the reaction was monitored by TLC (*n*-hexane-ethyl acetate: 80 : 20). The reaction was completed after 10 min. The reaction mixture was filtered and the methanol was removed under reduced pressure. The residue was purified by a short pad of silica gel (silica gel 60). Highly pure nitrone (Table 1, entry 1) was obtained in 85% yield (0.33 g). IR and ^{1}H NMR spectra data confirmed the identities of the product. ^{1}H NMR ($CDCl_3$) δ: 7.27–7.97(m, 10H), 8.49(s, 1H). ^{13}C NMR ($CDCl_3$) δ: 160.4, 152.1, 136.3–128.2(6 CH), 120.9(CH). IR (KBr): 3040–2840(sh, s), 1640(s), 1600(s), 1480(s), 1440(s), 1200(s), 760(s), 640(s).

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