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Oxidation with Perhalogenated, Water-soluble Metalloporphyrins: Application to Oxidation of Substituted 2-Methylpyrroles

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Perchlorinated, sulfonated metalloporphyrin **1** cleanly oxidized substituted 2-methylpyrroles **2a–f** in the presence of iodosylbenzene to produce the corresponding allylic alcohols **3a–f**.

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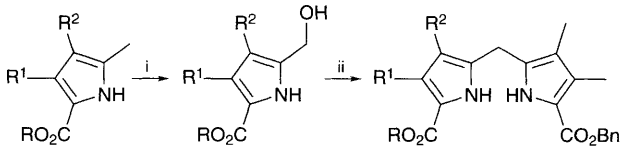
In 1979, Groves and coworkers first reported the cytochrome P-450 monooxygenase-like activity in iron *meso*-tetraphenylporphyrin (ClFeTPP).[1] This spurred wide interest in exploiting metalloporphyrins as oxidation catalysts. Much progress has been made since then on their synthetic applications as well as enhancement of efficacy of the catalysts. Alkene epoxidations[2] and hydrocarbon oxidations[3] are two areas that have been well studied. As for improvement of the catalysts, firstly, introduction of halogens on the *ortho*-phenyl groups of TPP was found to enhance their activity.[4] Halogenation imparts steric protection and electronic activation to the metalloporphyrin. Secondly, further halogenation of the β-porphyrin positions has achieved the full benefit of such a dual effect yielding more robust catalysts with additional resistance to oxidative catalyst destruction.[5] Such perhalogenated metalloporphyrins can be rendered water soluble by sulfonation of the *meta*-position of the phenyl rings.[6]

We report herein a straightforward and efficient oxidation of substituted 2-methylpyrroles using the perchlorinated, sulfonated catalyst iron(III) *meso*-tetra(2,6-dichloro-3-sulfonatophenyl)-β-octachloroporphyrin chloride ($ClFeTPPCl_8S_4\beta Cl_8$) **1** and iodosylbenzene as the oxygen atom donor. The allylic alcohol products (**3a–f**) were converted under mild conditions to the dipyrromethanes, **4a–f**. Compounds **2a–e** were also reacted with excess of furfurylamine to yield the (2-furylmethyl)-2-pyrrolylmethylamines, **5a–e**. This is the first example of an oxidation of allylic methyl groups in general and 2-methylpyrroles in particular, using a metalloporphyrin catalyst towards a synthetically useful end.

When a cold (0 °C) solution of the pyrrole **2a** (0.20 mmol) in 3 mol dm^{-3} HCl–MeCN (1 : 1, *v*/*v*) containing a catalytic amount (0.0009 mmol) of **1**, in the presence of iodosylbenzene (1 equiv.) was allowed to react for 10 min, the crude allylic alcohol **3a** was obtained (see Scheme 1). ^1H NMR of the crude alcohol **3a** indicated essentially clean oxidation without the presence of any starting material. We did not attempt further purification of **3a** due its known instability. Its IR spectrum exhibited an absorption at 3300 cm^{-1} while the mass spectrum gave a peak at *m*/*z* 225 ($M^+ - 18$). It was gratifying to find that compound **3a** underwent smooth coupling with 2-benzyl oxycarbonyl-3,4-dimethylpyrrole, under very mild conditions (CH_2Cl_2, room temp., 3 h) to provide the dipyrromethane **4a**† in 42% yield (from **2a**). In similar fashion, **2b–f** were oxidized and coupled, to furnish the unsymmetrical dipyrromethanes **4b–f** (38, 40, 32, 35 and 25%, in two steps from the corresponding 2-methylpyrroles). In a control experiment, pyrrole **2a** was treated with 1 equiv. of iodosylbenzene in the absence of catalyst **1**, and the resulting crude mixture was treated with 2-benzyloxycarbonyl-3,4-dimethylpyrrole. The yield of the dipyrromethane **4a** isolated in this case varied between 5 and 15%. Upon further examination of the effect of iodosylbenzene alone on several other 2-methylpyrroles, it became evident that the yields of the final dipyrromethanes obtained were substantially lower than in the presence of catalyst.

In contrast to $Pb(OAc)_4$ oxidation, which is the only other reliable oxidant of 2-methylpyrroles, the ease of oxidation with **1** stands out as a clear advantage. Furthermore, $Pb(OAc)_4$ oxidation (HOAc, Ac_2O, 80 °C, 24 h) leads to the corresponding acetoxymethylpyrroles which only under harsh conditions (conc. HCl, reflux) can be converted to symmetrical dipyrromethanes. When 2-acetoxymethyl-5-benzyloxycarbonyl-3-ethyl-4-methylpyrrole was treated overnight at room temperature with 2-benzyloxycarbonyl-3,4-dimethylpyrrole in CH_2Cl_2 (see above), the ^1H NMR of the crude reaction mixture indicated only a 15% conversion to the dipyrromethane **4a**. On the other hand, direct generation of allylic alcohols by our method allows ready manipulation of these synthetically and biosynthetically important compounds.

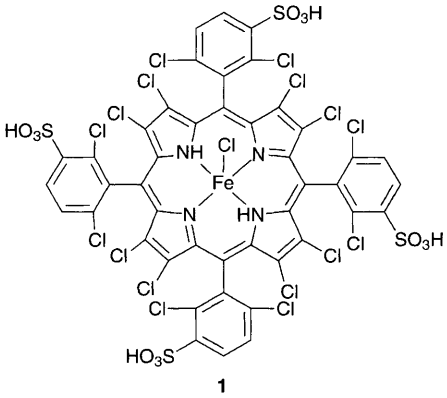
As an example we have examined the reaction of allylic alcohols **3a–f**, with furfurylamine. Thus, when a solution of compound **3a** in CH_2Cl_2 was allowed to react with an excess of furfurylamine, the novel (2-furylmethyl)-2-pyrrolylmethylamine **5a** was obtained in 36% yield (from **2a**). The secondary amine **5a** showed a peak at *m*/*z* 352 (M^+) in its mass spectrum. Similarly, the furan derivatives **5b–c** were prepared from their



2a–f **3a–f** **4a–f**

a; R = CH_2Ph, R^1 = Me, R^2 = Et
b; R = CH_2Ph, R^1 = Me, R^2 = $[CH_2]_2CO_2Me$
c; R = CH_2Ph, R^1 = Me, R^2 = $[CH_2]_7Me$
d; R = Et, R^1 = Me, R^2 = Et
e; R = Et, R^1 = Et, R^2 = Et
f; R = Et, R^1 = Me, R^2 = Me

Scheme 1 *Reagents and conditions*: i, $ClFeTPPCl_8S_4\beta Cl_8$ **1** (0.0009 mmol)–PhIO (1 equiv.), 3 mol dm^{-3} HCl–Me_3CN (1 : 1, *v*/*v*), 0 °C, 10 min; ii, 2-Benzyloxycarbonyl-3,4-dimethylpyrrole (1.5 equiv.), CH_2Cl_2, room temp., 3 h.



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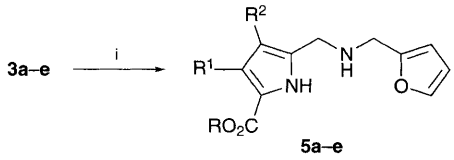

5a–e

Scheme 2 *Reagents and conditions*: i, Furfurylamine (3 equiv.), CH_2Cl_2, room temp., 3 h. Substituents **a–e** as in Scheme 1

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corresponding allylic alcohols (32, 30, 28 and 32%, in two steps from the corresponding 2-methylpyrroles).

It is evident from the preliminary results reported in this communication that the perhalogenated, water-soluble metalloporphyrin **1** is an efficient catalyst in the oxidation of 2-methylpyrroles.

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Footnote

† All compounds reported herein exhibited spectral data in full accord with structural assignments. In addition, new compounds gave satisfactory high-resolution mass spectrometric measurements.

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