ChemComm
RSC Publishing
COMMUNICATION
View Article Online
View Journal

Nitrous oxide reduction-coupled alkene–alkene coupling catalysed by metalloporphyrins†

Cite this: DOI: 10.1039/c3cc43912g

Received 24th May 2013,
Accepted 4th August 2013

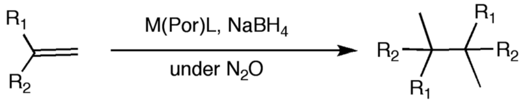
DOI: 10.1039/c3cc43912g

www.rsc.org/chemcomm

Shunsuke Saito,[a] Hiro Ohtake,[b] Naoki Umezawa,[a] Yuko Kobayashi,[a] Nobuki Kato,[a] Masaaki Hirobe[b] and Tsunehiko Higuchi*[a]

Porphyrin complexes of iron, manganese and cobalt catalysed reductive dimerization of alkenes with $NaBH_4$ under N_2O. The reaction system using Fe^{III} porphyrin generated an Fe^{I} porphyrin intermediate that reduced N_2O to regenerate Fe^{III} porphyrin.

Metalloporphyrins are versatile catalysts, *e.g.* for oxidation,[1a] cyclopropanation and aziridination.[1b] These catalysts have been extensively investigated, mainly as model compounds for the active sites of peroxidases and cytochrome P450, *i.e.*, natural oxidation catalysts. Molecular oxygen, peroxides and various other oxidants have been examined as oxidants.[2] We have shown that the oxidation of alkanes, alkenes, aromatics and *N*-carbonyl cyclic amines is efficiently catalysed by ruthenium porphyrins with heteroaromatic *N*-oxides as oxidants.[3] We therefore considered that other molecules having an N–O bond might also serve as oxidants for metalloporphyrin catalysts. Physico-chemically, nitrous oxide (N_2O) is a stable, CO_2-like molecule. Huge amounts of N_2O are generated as a by-product of industrial processes such as Nylon 6-6 and nitric acid production. However, there have been few reports on utilization of N_2O for organic synthesis, *e.g.* metalloporphyrin-catalysed oxidation utilizing N_2O.[4] At present, most industrially generated N_2O is simply decomposed catalytically to N_2 and O_2, since N_2O itself is a potent contributor to global-warming and an ozone-depleting substance. We and other groups previously reported alcohol formation from alkenes with $NaBH_4$ under O_2 catalysed by porphyrin complexes of Mn,[5] Rh,[6] Co[7] and Fe.[8] In some cases, small amounts of the dimerised alkene were also formed.[7,8] Here, we report a N_2O reduction-coupled alkene coupling reaction catalysed by metalloporphyrins (Scheme 1). Interestingly, the alkene was reductively dimerised at room temperature when N_2O was used instead of O_2 in the iron porphyrin-catalysed system, *i.e.*, the use of N_2O completely suppressed oxidation.



Scheme 1

α-Methylstyrene (**1a**) dimerised to afford mainly 2,3-dimethyl-2,3-diphenylbutane (**2a**) with $NaBH_4$ in the presence of iron *meso*-tetraphenylporphyrin chloride (Fe^{III}(TPP)Cl) (1 mol%) under N_2O[9] (Table 1). Addition of HO^- or MeO^- enhanced the reaction, resulting in complete consumption of **1a** (entries 1–3). Note that almost all added HO^- should be converted into MeO^- in the solvent (toluene–MeOH (1 : 1)) because the equilibrium of $^-OH + MeOH \rightleftarrows H_2O + MeO^-$ lies far to the right (there is a *ca.* 300-fold excess of MeOH over added HO^- and the pK_a values of MeOH and H_2O are almost the same). The catalytic activity of iron *meso*-tetrakis(pentafluorophenyl)porphyrin chloride (Fe(TPFPP)Cl) was higher than that of Fe(TPP)Cl (entries 4 and 5). Small amounts of inseparable oligomers of **1a** were also formed and no oxygenated products were found. The reaction did not proceed in the absence of Fe(TPP)Cl or N_2O.

Table 1 Reductive coupling of α-methylstyrene **1a** with $NaBH_4$ catalysed by iron porphyrins under N_2O

Entry	Catalyst	Base	Time (h)	Yield (%)
1	Fe(TPP)Cl	KOH	14	73
2	Fe(TPP)Cl	Me_4NOH	14	87
3[a]	Fe(TPP)Cl	—	14	41
4	Fe(TPFPP)Cl	KOH	4	69
5[a]	Fe(TPP)Cl	KOH	4	29
6[a]	Mn(TPP)Cl	KOH	14	25
7[a]	Co(TPP)Cl	KOH	14	33
8[a]	Rh(TMP)CH_3	KOH	16	1.5
9[a]	Cyanocobalamin	KOH	14	5
10[b]	Fe(TPP)Cl[b]	Me_4NOH	14	69

Catalyst: 1 mol% unless otherwise noted. Solvent: toluene–MeOH (1 : 1). TMP: *meso*-tetramesitylporphyrinato. [a] Starting material **1a** remained. [b] Catalyst: 0.05 mol%.

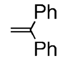
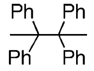
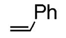
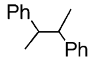
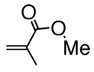
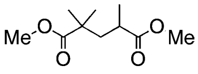
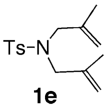
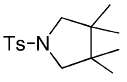
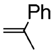
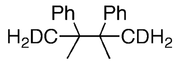
---

[a] *Graduate School of Pharmaceutical Sciences, Nagoya City University, 3-1 Tanabe-dori, Mizuho-ku, Nagoya 467-8603, Japan. E-mail: higuchi@phar.nagoya-cu.ac.jp; Fax: +81 52 836 3435; Tel: +81 52 836 3435*

[b] *Graduate School of Pharmaceutical Sciences, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan*

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c3cc43912g

Table 2 Reductive coupling of alkenes with the $NaBH_4$–Fe porphyrin–N_2O system

Entry	Substrate	Base	Product, isolated yield
1	 **1b**	Me_4NOH	 **2b**, 93 %
2	 **1c**	Me_4NOH	 **2c**[a)], 31 %
3[b]	 **1d**	NaOMe	 **2d**, 34 %
4[b]	 **1e**	KOH	 **2e**, 18%
5[c]	 **1a**	KOH	 **2a'**, 77 %

Reaction conditions: Fe(TPP)Cl (1 mol%), $NaBH_4$ (2.0 eq.), base (0.1 eq.) at r.t. for 14 h under N_2O. [a] 1 : 1 mixture of *meso*- and DL-form. [b] Fe(TPFPP)Cl (0.5 mol%) was used. [c] $NaBD_4$ was used instead of $NaBH_4$.

Mn(TPP)Cl, Co(TPP)Cl and Rh(TMP)CH_3 and cyanocobalamin showed lower catalytic activity than Fe(TPP)Cl (entries 6–9). The use of 0.05 mol% of Fe(TPP)Cl in the reaction of **1a** afforded **2a** in 69% yield, *i.e.*, the turnover number reached 1380 or more (entry 10).

As shown in Table 2, 1,1-diphenylethylene (**1b**) similarly gave the coupling product (**2b**). Coupling of styrene (**1c**) afforded **2c** as a 1 : 1 mixture of *meso*- and DL-form in low yield. Other types of alkenes were also examined as substrates of this reaction system. Cyclohexene did not react (data not shown). On the other hand, methyl methacrylate **1d** afforded an isolable head-to-tail coupling product **2d** and an inseparable mixture of oligomers, probably due to radical chain reaction. This reaction can be regarded as a kind of telomerization, and presumably involves a carbon radical intermediate.

Intramolecular coupling was examined by using (*N,N*-dimethallyl)-*p*-toluenesulfonamide **1e**, and the head-to-head ring-closed product **2e** was obtained in 18% yield.

The use of $NaBD_4$ instead of $NaBH_4$ gave deuterated product **2a′**, *i.e.*, the terminal position of the alkene was deuterated. This result suggests that an iron–hydride bond is formed and the reaction proceeds *via* insertion of the C–C double bond into the iron–hydride bond.

Consumption of N_2O was confirmed by measuring the FT-IR spectra of the gas phase (absorptions at 2212 and 2236 cm^{-1}) over the reaction solution in the sealed reaction vessel, in order to confirm the involvement and consumption of N_2O (Fig. 1). N_2O was completely consumed under the reaction conditions (**1a**, $NaBH_4$, Fe(TPP)Cl). On the other hand, consumption of N_2O was not observed in the absence of Fe(TPP)Cl, but began once Fe(TPP)Cl was added.

This result indicates that Fe^{II}(TPP) is unable to reduce N_2O and a more reductive species is formed, because $NaBH_4$ easily reduces iron(III)porphyrin to iron(II)porphyrin.

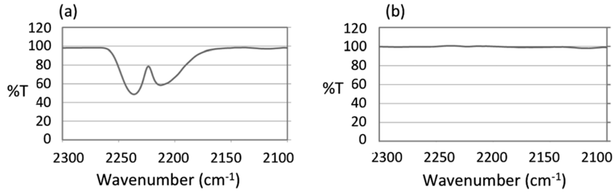


Fig. 1 FT-IR spectra of the gas phase in the sealed reaction vessel. (a) Gas phase three hours after mixing alkene **1a** and $NaBH_4$ in toluene–MeOH under N_2O. (b) Gas phase one hour after the addition of Fe(TPP)Cl (1 mol%) to the mixed solution.

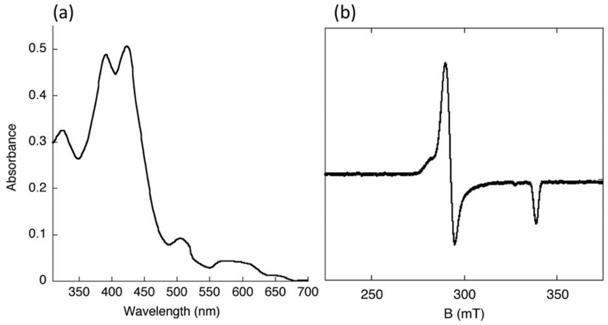
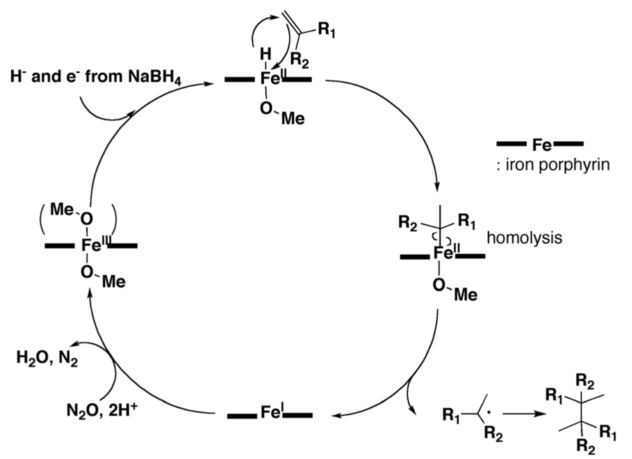


Fig. 2 UV-Vis spectra (a) and EPR spectra (b) of the reaction mixture of **1a**, Fe(TPP)Cl, $NaBH_4$ and Me_4NOH in toluene–MeOH (1 : 1) under Ar. (a) [Fe(TPP)Cl] 15 μM at 298 K. (b) [Fe(TPP)Cl] 100 μM at 77 K.

In order to confirm this speculation, we analysed the reaction spectroscopically. Fe(TPP) solution in the presence of $NaBH_4$ under Ar showed the spectrum of Fe^{II}(TPP) almost exclusively (Fig. S1(a), ESI†). The addition of **1a** to the mixture completely altered the UV-Vis spectrum, producing a split Soret band (λ_{max} 391 nm and 418 nm) (Fig. 2(a)). This spectrum indicates the formation of $[Fe^{I}(TPP)]^-$ since the spectral pattern is in good accordance with the reported spectrum of $[Fe^{I}(TPP)]^-$.[10] When N_2O was bubbled into the solution at 20 °C, the spectrum changed into that of Fe^{II}(TPP) (Fig. S1(b), ESI†).

Next, we observed the electron paramagnetic resonance (EPR) spectrum of a mixed solution of Fe(TPP)Cl, excess $NaBH_4$, and **1a** under Ar at 77 K. Before the addition of alkene, the solution showed no signal, probably because EPR-silent Fe^{II}(TPP) was formed by the reduction of Fe^{III}(TPP)Cl with $NaBH_4$. However, a distinct low-spin signal appeared after addition of **1a** (Fig. 2(b)). The *g* values (g = 2.23 and 1.94) and line shape unambiguously indicated the formation of $[Fe^{I}(TPP)]^-$ species.[11] Bubbling of N_2O into the solution at 20 °C caused the signal to disappear. These results indicate that $[Fe^{I}(TPP)]^-$ reduces N_2O to N_2 and O^{2-}, regenerating Fe^{III}(TPP). There has been one paper reporting N_2O reduction by $[Fe^{I}(TPP)]^-$ species,[12] based on the electrochemistry (reduction potential) of the Fe(TPP) complex, but without spectroscopic support. In the present study, we obtained direct spectroscopic evidence that $[Fe^{I}(TPP)]^-$ reacted with N_2O.

Previously our group found that the reaction of styrene and Fe(TPP)Cl in the presence of $NaBH_4$ affords the σ-alkyl-Fe porphyrin complex (Scheme 2).[8b] Therefore, **1a** may form a similar complex having an Fe–C bond. We propose the reaction mechanism shown in Scheme 2 in light of the above results.



Scheme 2 Proposed mechanism of the reductive coupling of alkenes with the N_2O–Fe(Por)–$NaBH_4$ system.

It is known that both Fe^{III}(Por)$(OMe)_2$ and Fe^{III}(Por)OMe are formed in the presence of a 10-fold excess of MeO^- over Fe^{III}(Por)Cl in toluene–MeOH.[13] Either Fe^{III}(Por)$(OMe)_2$ or Fe^{III}(Por)OMe would be reduced to Fe^{II}(Por) with $NaBH_4$ and a small amount of H–Fe^{II}(Por)$^-$ is presumably also formed because $NaBH_4$ can transfer both a hydride and one electron to Fe(Por). Formation of H–Fe^{II}(Por)$^-$ has also been proposed in electrochemical reduction of H_2O catalysed by Fe(TPP).[14] The alkenyl group is inserted into the Fe–H bond to afford the σ-alkyl-Fe(Por) complex initially. The Fe–C bond of *tert*-alkyl-Fe(Por) is homolytically cleaved to give the *tert*-alkyl radical and Fe^{I}(Por)$^-$ at room temperature due to the higher stability of the *tert*-alkyl radical as well as steric repulsion. The two radicals afford the homo-coupling product, and Fe^{I}(Por)$^-$ reduces N_2O to N_2 and H_2O, regenerating Fe^{III}(Por). Kojo *et al.* suggested that $NaBH_4$ and iron porphyrin form the hydrogen radical ($H^\bullet$).[15] $H^\bullet$, which is formed by homolysis of the H–Fe bond of the intermediate, attacks the alkene to afford the same radical as that formed in Scheme 2. However, this alternative pathway is considered unlikely because the UV-Vis spectrum of Fe(TPP)Cl with $NaBH_4$ in the absence of alkene under Ar showed only Fe^{II}(TPP) species, not Fe^{I}(TPP). The role of RO^- has not been clarified, but it may stabilise Fe^{I}(Por)$^-$ species against degradation through protonation of the basic pyrrole nitrogens and/or facilitate Fe–C bond cleavage by acting as an axial ligand.

We have found a novel N_2O reduction-coupled alkene dimerization catalysed by metalloporphyrins under mild conditions (at ordinary pressure and room temperature). We carefully examined the reaction intermediates spectroscopically and proposed a reaction mechanism. The porphyrin complex of iron, which is the most abundant transition metal, was the most effective among those tested. This reaction system forms a carbon radical under mild conditions (r.t., dark). Fe^{I}(Por)$^-$, a highly reduced form of iron porphyrin, was confirmed to be formed in this reaction. Thus, the reaction enables both N_2O consumption and synthesis of coupling products, some of which would be useful for organic synthesis. Since N_2O may become the dominant ozone-depleting substance emitted in the 21st century,[16] the reaction system described here might prove useful as a green process to decrease emissions of N_2O, perhaps in conjunction with large-scale synthetic applications.

This work was partly supported by Grants-in-Aid for Scientific Research on Priority Areas (No. 19028054, 20037056, ''Chemistry of Concerto Catalysis'') from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

Notes and references

1 For reviews: (*a*) M. Costas, *Coord. Chem. Rev.*, 2011, **255**, 2912–2932; (*b*) B. J. Anding and L. K. Woo, in *Handbook of Porphyrin Science*, ed. K. M. Kadish, K. M. Smith and R. Guilard, World Scientific, 2012, ch. 100, vol. 21, pp. 145–319.

2 (*a*) B. Meunier, A. Robert, G. Pratviel and J. Bernadou, in *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith and R. Guilard, Academic Press, San Diego, 2000, ch. 31, vol. 4, pp. 119–187; (*b*) J. T. Groves, K. Shalyaev and J. Lee, in *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith and R. Guilard, Academic Press, San Diego, 2000, ch. 27, vol. 4, pp. 17–40.

3 R. Ito, N. Umezawa and T. Higuchi, *J. Am. Chem. Soc.*, 2005, **127**, 834–835, and references therein.

4 (*a*) J. T. Groves and J. S. Roman, *J. Am. Chem. Soc.*, 1995, **117**, 5594–5595; (*b*) H. Tanaka, K. Hashimoto, K. Suzuki, Y. Kitaichi, M. Sato, T. Ikeno and T. Yamada, *Bull. Chem. Soc. Jpn.*, 2004, **77**, 1905–1914.

5 I. Tabushi and N. Koga, *J. Am. Chem. Soc.*, 1979, **101**, 6456–6458.

6 Y. Aoyama, T. Watanabe, H. Onda and H. Ogoshi, *Tetrahedron Lett.*, 1983, **24**, 1183–1186.

7 T. Okamoto and S. Oka, *J. Org. Chem.*, 1984, **49**, 1589–1594.

8 (*a*) T. Santa, T. Mori and M. Hirobe, *Chem. Pharm. Bull.*, 1985, **33**, 2175–2178; (*b*) T. Mori, T. Santa, T. Higuchi, T. Mashino and M. Hirobe, *Chem. Pharm. Bull.*, 1993, **41**, 292–295.

9 N_2O gas that we used had 99.999% warranted purity (Showa Denko K. K.).

10 D. Lexa, J. Mispelter and J.-M. Savéant, *J. Am. Chem. Soc.*, 1981, **103**, 6806–6812.

11 G. S. Srivatsa, D. T. Sawyer, N. J. Boldt and D. F. Bocian, *Inorg. Chem.*, 1985, **24**, 2123–2125.

12 M. Bayachou, L. Elkbir and P. J. Farmer, *Inorg. Chem.*, 2000, **39**, 289–293.

13 T. Otsuka, T. Ohya and M. Sato, *Inorg. Chem.*, 1984, **23**, 1777–1779.

14 I. Bhugun, D. Lexa and J.-M. Savéant, *J. Am. Chem. Soc.*, 1996, **118**, 3982–3983.

15 S. Kojo and S. Sano, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2864–2870.

16 A. R. Ravishandra, J. S. Daniel and R. W. Portmann, *Science*, 2009, **326**, 123–125.