

# Aerobic Palladium-catalysed 1,4-*cis*-Diacetoxylation and 1,4-*cis*-Chloroacetoxylation of Cyclohexa-1,3-diene using a Tetrakis(methoxyhydroquinone)porphyrin

Helena Grennberg and Jan-E. Bäckvall

Department of Organic Chemistry, University of Uppsala, Box 531, S-751 21 Uppsala, Sweden

The use of Co(tetraphenylporphyrins), carrying methoxy substituents in the *meso*-phenyl groups, in aerobic, quinone-free palladium-catalysed 1,4-oxidations of cyclohexa-1,3-diene provides an entry to *cis*-disubstituted products, until now inaccessible by aerobic procedures.

Palladium-quinone-catalysed 1,4-oxidations of 1,3-dienes [(eqn. (1))] are high-yielding, regio- and stereo-selective reactions that give access to synthetically useful substances.<sup>1</sup> By varying the chloride ion concentration (LiCl) both the product selectivity and the relative stereochemistry of the product are controlled.<sup>1a,b</sup> The 1,4-diacetoxylation was developed into an aerobic process by the use of a one-pot triple catalytic system,<sup>2</sup> the efficiency of which was recently improved by the use of a bifunctional cobalt[tetrakis(hydroquinone)porphyrin], Co(TQP), as oxygen activating agent and electron transfer mediator.<sup>3</sup> One limitation with the aerobic oxidations developed so far has been that chloride ions, even in catalytic amounts, deactivate the oxygen-activating metal-macrocycle.<sup>4</sup> Thus, the aerobic 1,4-diacetoxylation has been limited to chloride-free reaction conditions. This has reduced the scope of the aerobic reaction since under these conditions, only the *trans* addition products such as *trans*-1 were possible to obtain. During the course of the work with Co(TQP), it was discovered that the hydroquinone-protected Co[*meso*-tetra(2,5-dimethoxyphenyl)porphyrin] Co(TDMPP) was compatible with the presence of chloride ions in the aerobic 1,4-oxidation of cyclohexa-1,3-diene. Interestingly, the reaction proceeds in the absence of an electron transfer mediator (ETM) such as a quinone.<sup>2</sup> The mechanism therefore must involve a direct electron transfer from palladium to the oxidised metal-macrocycle.

Co(TDMPP) was prepared by a Lindsey condensation of 2,5-dimethoxybenzaldehyde and pyrrole to yield the porphyrin, followed by metallation using Co(OAc)<sub>2</sub>·4H<sub>2</sub>O.<sup>3,5</sup> The catalyst was examined in an aerobic 1,4-diacetoxylation of cyclohexa-1,3-diene in the absence of *p*-benzoquinone. The rate of oxygen consumption was measured and compared to

those of the corresponding reactions catalysed by Co(TQP) or Co(TPP).

Co(TQP) gives a fast oxygen consumption and a good isolated yield of 1,4-diacetoxycyclohex-2-ene **3** (Fig. 1 and Table 1), indicating an efficient electron transfer. In contrast, Co(TPP) gave no conversion of the diene under these conditions, whereas the hydroquinone-protected Co(TDMPP) somewhat surprisingly yielded a rapid oxygen consumption. After only 4 h all diene was converted to diacetate **3** and benzene. The isolated yield of **3** was only 35% but, more importantly, the relative stereochemistry of the product was completely reversed from the 70% *trans* observed using Co(TQP) to 75% *cis* with Co(TDMPP).<sup>†</sup> This is the first

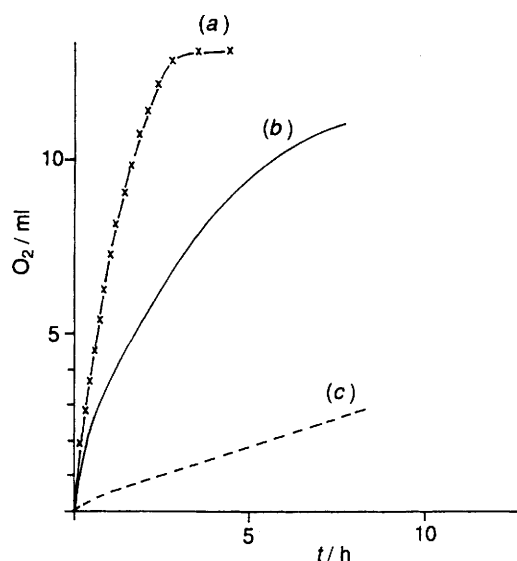
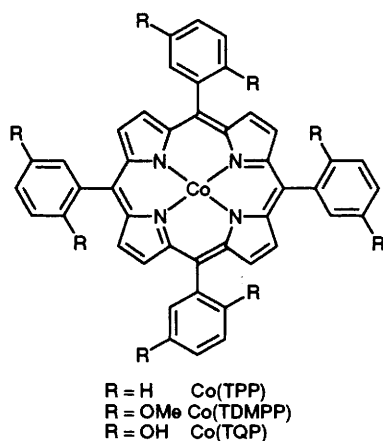
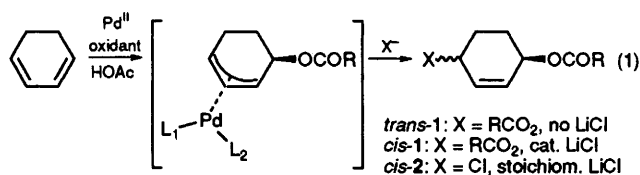


Fig. 1 Aerobic oxidation of 1 mmol of cyclohexa-1,3-diene: (a) Co(TDMPP), (b) Co(TQP) and (c) Co(TPP)

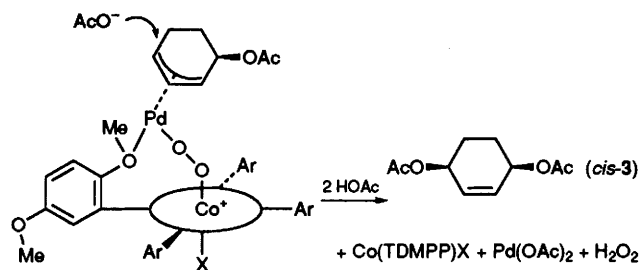
Table 1 Aerobic 1,4-oxidation of cyclohexa-1,3-diene<sup>a</sup>

Co(P)	Yield <sup>b</sup> (%) (t/h)	<i>cis</i> : <i>trans</i> <sup>c</sup>
TPP	0 (24 h)	—
TQP	70 <sup>d</sup> (10 h)	30 : 70
TDMPP	35 <sup>d</sup> (4 h)	75 : 25
2-TMMPP	18 <sup>d</sup> (5 h)	75 : 25
3-TMMPP	7 (10 h)	45 : 55
4-TMMPP	<5 (10 h)	55 : 45

<sup>a</sup> Conditions: 2.5 mol% Pd(OAc)<sub>2</sub>, 2.0–2.5 mol% Co(porphyrin), 2 ml HOAc, 1 mmol of cyclohexa-1,3-diene. 25 °C, 1 atm. of O<sub>2</sub>.

<sup>b</sup> Isolated yield. <sup>c</sup> The relative stereochemistry of the product was determined by <sup>1</sup>H NMR. <sup>d</sup> A complete conversion of the diene into diacetate and benzene was observed.

<sup>†</sup> The product distribution between diacetate and benzene was determined by capillary GC and GC-MS. The relative stereochemistry of the diacetate **3** was determined using <sup>1</sup>H NMR spectroscopy.



Scheme 1

example of a *cis*-selective aerobic diacetoxylation of cyclohexa-1,3-diene, and there are interesting mechanistic implications of the reaction.

To study the mechanism of this Co(TDMPP)-catalysed oxidation, the reaction was run in the presence of catalytic amounts of LiCl, which has been found to deactivate Co(TQP) as well as the other metal-macrocycles previously employed.<sup>4</sup> Co(TDMPP) was found to be equally active under these conditions both regarding rate of oxygen consumption and isolated yield, and the relative amount of *cis*-3 was increased to >80%.<sup>‡</sup> The observed results therefore indicate a direct electron transfer from Pd<sup>0</sup> to oxidized Co(TDMPP) via a mechanism different from that of the 1,4-diacetoxylation catalysed by palladium and quinone. One possible mechanism involves a bidentate coordination of palladium to the porphyrin via the cobalt-superoxide and a *meso*-methoxyphenyl unit (Scheme 1), which would activate the ( $\pi$ -allyl)palladium intermediate towards nucleophilic attack.

In order to gain further insight into the mechanism of this quinone-free *cis*-diacetoxylation, *meso*-tetra(monomethoxyphenyl)porphyrins (TMMPP) with the methoxy units in the 2-, 3- and 4-positions, respectively, were prepared and examined as described above. According to the mechanism proposed in Scheme 1, only the 2-methoxyphenylporphyrin (2-TMMPP) would be expected to give the bidentate complexation to

<sup>‡</sup> The porphyrins could be recovered after the reaction and <sup>1</sup>H NMR showed that the methoxy units were virtually untouched. In case of the 2- or 3-methoxy compounds, no transformation into *p*-quinones could be detected.

palladium required for electron transfer to occur. As seen from the results (Table 1), 2-TMMPP was the most efficient of the three isomers, yielding 18% of 3 in 5 h. 3-TMMPP required 10 h to give 7%, whereas 4-TMMPP yielded less than 5% in 10 h.<sup>‡</sup> Also, Co(2-TMMPP) was active in the presence of a catalytic amount of LiCl. These results support the mechanism suggested in Scheme 1.

We were pleased to find that Co(TDMPP) was also active in the presence of stoichiometric amounts of LiCl. Under these conditions, chloride acts as a nucleophile<sup>1b</sup> [eqn. (1)] resulting in a 30% isolated yield of *cis*-1,4-chloroacetate 2 (>98% *cis*), a product previously inaccessible *via* the aerobic procedure.

It can thus be concluded that Co(TDMPP) acts as an electron transfer mediator as well as an oxygen activating agent in aerobic palladium-catalysed 1,4-oxidations of cyclohexa-1,3-diene. Under chloride- and quinone-free conditions the *cis*-diacetate is formed, a product previously impossible to obtain under aerobic conditions. Moreover, this catalyst was found to be active in the presence of LiCl, in contrast to the metal-macrocycles previously used, a property which provides new opportunities for selective aerobic oxidations.

Financial support from the Swedish Natural Science Research Council and the Swedish Research Council for Engineering Science is gratefully acknowledged.

Received, 28th April 1993; Com. 3/02451B

## References

- (a) J. E. Bäckvall, S. E. Byström and R. E. Nordberg, *J. Org. Chem.*, 1984, **49**, 4619; (b) J. E. Bäckvall, J. E. Nyström and R. E. Nordberg, *J. Am. Chem. Soc.*, 1985, **107**, 3676; (c) J. E. Bäckvall and J. O. Vågberg, *J. Org. Chem.*, 1988, **53**, 5695; (d) J. E. Bäckvall, *Pure Appl. Chem.*, 1992, **64**, 429.
- J. E. Bäckvall, A. K. Awasthi and Z. D. Renko, *J. Am. Chem. Soc.*, 1987, **109**, 4750; J. E. Bäckvall, R. B. Hopkins, H. Grennberg, M. M. Mader and A. K. Awasthi, *J. Am. Chem. Soc.*, 1990, **112**, 5161.
- H. Grennberg, S. Faizon and J. E. Bäckvall, *Angew. Chem.*, 1993, **105**, 269; *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 263.
- H. Grennberg, *Comprehensive Summaries from the Faculty of Science*, 392. Doctoral Dissertation, Uppsala University 1992.
- J. S. Lindsey, I. C. Schreiman, H. Hsu, P. C. Kearney and A. M. Marguerettaz, *J. Org. Chem.*, 1987, **52**, 827; A. D. Adler, F. R. Longo, R. Kampas and J. Kim, *J. Inorg. Nucl. Chem.*, 1970, **32**, 2443.