Stereoselective Dioxygenation of a Racemic Tryptophan Derivative catalysed by Chiral Manganese Porphyrins

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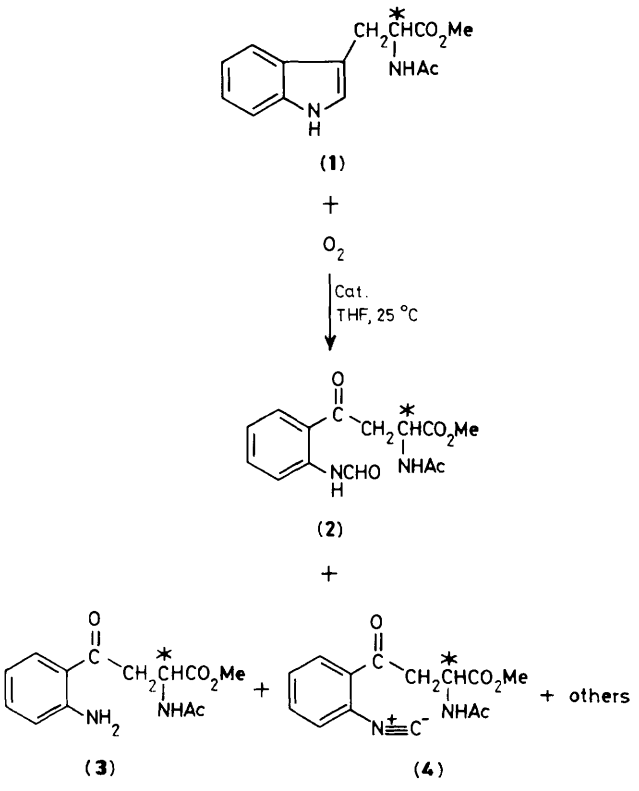
The first asymmetric dioxygenation reactions of the racemic tryptophan derivatives, *N*-acetyl-L-(+)- [and D-(−)]-tryptophan methyl ester, are reported, in which predominant generation of methyl 2-D-acetoamido-3-(2-formamidobenzoyl)propionate has been achieved in 23.3% enantiomeric excess in the catalytic system using the manganese complex of α,α,α,α-tetrakis[*o*-L(−)-camphanoylamido)phenyl]porphyrin.

Asymmetric reactions in catalytic systems are of wide interest in connection with enzymatic reactions. Recently, many mono-[1] and di-oxygenase models[2] using transition metal complexes have been investigated, and asymmetric mono-oxygenation reactions have already been reported.[3] However, there is no report on an asymmetric reaction as a dioxygenase model. We report here the first stereoselective dioxygenation of the racemic tryptophan derivatives, *N*-acetyl-L-(+)- [and D-(−)]-tryptophan methyl esters (**1**) to give a total dioxygen inserted ring-opening product having an asymmetric centre:

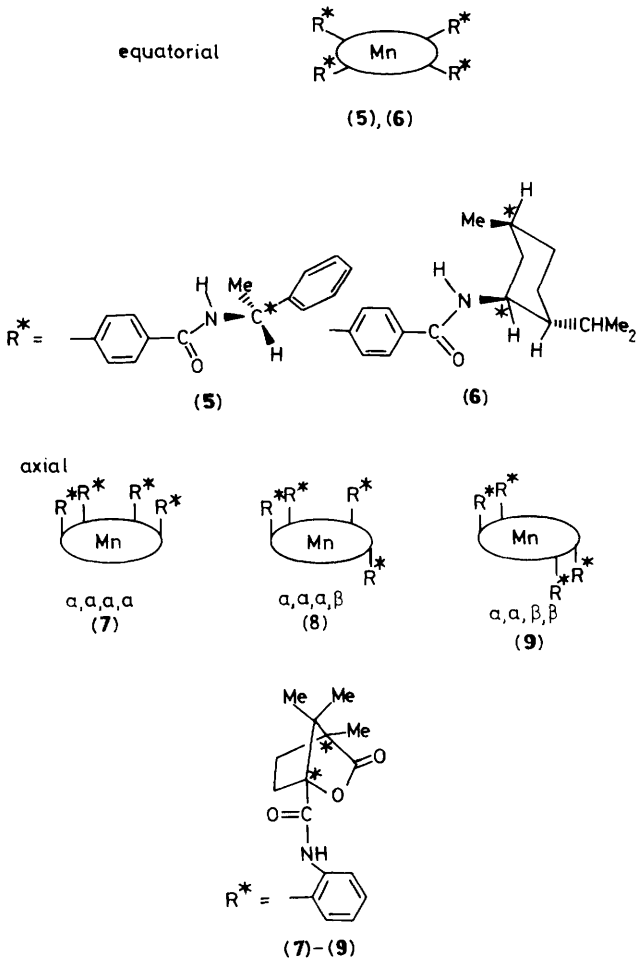
methyl 2-D-(−) or L-(+)-acetoamido-3-(2-formamidobenzoyl)propionate (**2**), catalysed by chiral manganese porphyrin complexes (Scheme 1).†

The substrate (**1**) was prepared by a literature method.[4] The chiral porphyrins used as catalysts are shown in Scheme 2. The porphyrins (**5**) and (**6**) were prepared for the first time by the amide linkage reaction of 5,10,15,20-tetrakis(*p*-carboxyphenyl)porphyrin with D-(+)-α-methylbenzylamine and L-(−)-menthylamine, respectively. The 5α,10α,15α,20α substituted porphyrin (**7**) and the 5α,10α,15α,20β (**8**) and 5α,10α,15β,20β-isomers (**9**) were prepared according to the literature.[5] The oxygenolyses of the racemates (**1**) (1.0×10^{-4} mol) by the manganese porphyrin complex (1.0×10^{-5} mol) under an atmosphere of dioxygen was carried out at room temperature in tetrahydrofuran (5 cm^3) for 3 days.‡ The product (**2**) was identified with an authentic sample by ^1H n.m.r., i.r., mass, and electronic spectroscopy. The amounts of unchanged (**1**) and the product (**2**) were determined spectrophotometrically after separating them from the reaction mixtures by t.l.c. on silica gel [Merck F254; R_f 0.41 for (**1**) and 0.23 for (**2**) in ethyl acetate]; $\lambda_{max.}$ (ε) 290 (5230) and 281 nm (6140) for (**1**), and 320 (3620) and 258 nm (9460) for (**2**) in methanol. The selectivity was estimated from c.d. spectra [$\lambda_{max.}$ 220 nm for (**1**), 250 nm for (**2**) in methanol].

The variations in c.d. spectra of unreacted (**1**), which was separated from the reaction solutions by t.l.c., around 220 nm with the conversion (%) were determined in the asymmetric oxygenation catalysed by the manganese complex (**5**) and are shown in Figure 1(A). The proportion of the L-(+)-isomer of the substrate increased owing to the predominant consumption of the D-(−)-isomer with the catalyst (**5**). On the other hand, in the oxygenation catalysed by (**6**) the L-(+)-isomer (**1**) was consumed predominantly with generation of the L-(+)-isomer (**2**) as shown in Figure 1(B) and (C), respectively. The



Scheme 1



Scheme 2. Manganese porphyrins used as catalysts.

Table 1. Asymmetric oxygenation of the racemates (**1**) to give optically active (**2**), catalysed by chiral manganse porphyrins.[a]

Catalyst		(1),	(2)	
Porphyrin	Oxidn. state of Mn[b]	Conv./ %[c]	Yield/ %	E.e.[d]/ % (Confign.)
(**5**)	II	45	5.9	9.7 (D)
(**5**)	III	37	1.3	9.7 (D)
(**6**)	II	29	2.4	14.9 (L)
(**6**)	III	18	1.0	11.0 (L)
(**7**)	II	9.5	6.1	23.3 (D)
(**8**)	II	15	8.5	1.2 (D)
(**8**)	III	8.8	0.9	8.8 (D)
(**9**)	II	13	10.4	5.8 (D)

[a] The reactions were carried out by keeping tetrahydrofuran (5 cm^3) solutions containing the racemate (**1**) (1.0×10^{-4} mol) and the manganese porphyrin complex (1.0×10^{-5} mol) under atmospheric dioxygen at 298 K for 3 days. [b] Manganese(III) porphyrin complexes are used as chloride salts. [c] Consumption of (**1**), estimated spectrophotometrically; see text for details. [d] Enantiomeric excess.

† The amounts of ring-opening by-products such as (**3**) and (**4**) in Scheme 1 are negligible in comparison with (**2**), and the other products are not ring opening products. Therefore, products other than (**2**) are not discussed in this communication.

‡ The present reaction did not proceed in the absence of the catalyst.

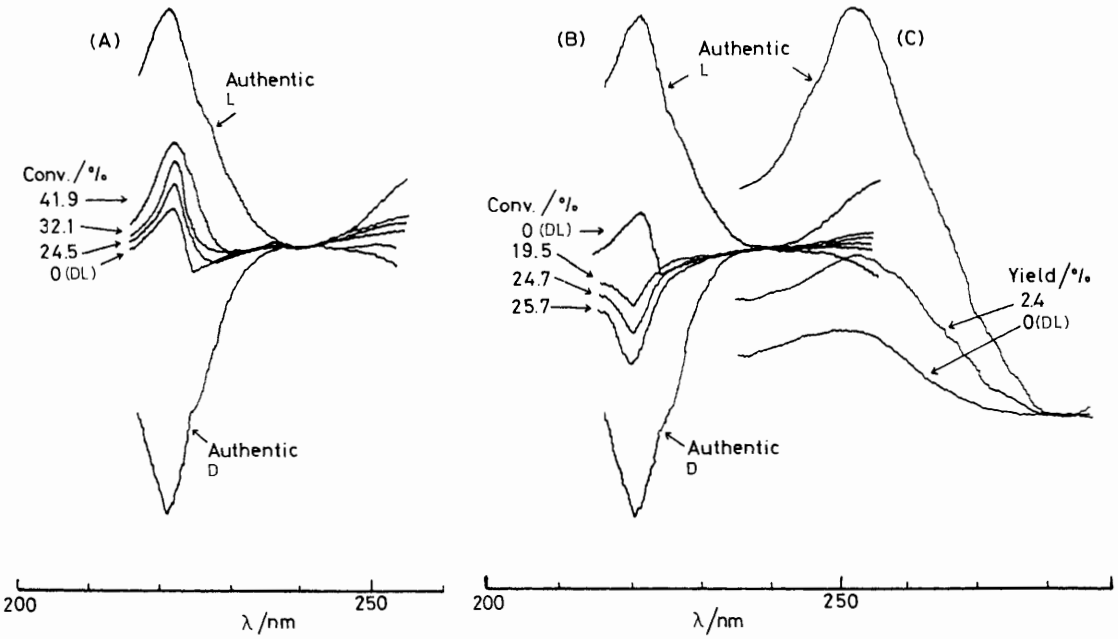


Figure 1. C.d. spectra of (**1**) (A, B) and (**2**) (C) separated from the reaction solution in the catalytic system of the chiral porphyrin complexes (**5**) (A) and (**6**) (B, C).

catalytic activities and selectivities for the asymmetric oxygenation of the racemates (**1**) using the chiral porphyrins (**5**)—(**9**) are summarised in Table 1. The conversions [consumption of (**1**)] using the equatorial type porphyrins (**5**) and (**6**) as catalysts were larger than those with the axial type porphyrins (**7**)—(**9**). Higher conversions of (**1**) and higher yields of (**2**) were observed in the catalytic systems containing Mn^{II} complexes rather than Mn^{III} porphyrin chlorides with the chiral porphyrins of (**5**), (**6**), and (**8**), although no difference of selectivity for (**2**) generation was observed between Mn^{II} and Mn^{III}.

The stereoselectivities were 2.6—19.3% e.e. in the consumption of (**1**) and 1.2—23.3% e.e. in the formation of (**2**). The equatorial manganese(II,III) porphyrin (**6**) possessing menthyl groups and the axial manganese(II) porphyrin (**7**) were found to be effective. The maximum optical yield for the generation of D-(−)-(**2**) was 23.3% e.e. in the catalytic system using the axial complex of (**7**).

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