Enantiomer Discriminating Dehydrogenation of (*R,S*)-(±)-1-Phenylethan-1-ol to Acetophenone Catalysed by Chiral Cobalt(II) Schiff's Base Complexes and Triphenylphosphine

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The oxidation of secondary alcohols to ketones by dioxygen under ambient conditions is catalysed by cobalt(II) Schiff's base complexes (CoL_4) in the presence of a suitable axial ligand (B) [1]. Kinetic evidence [1, 2] strongly suggests that the dioxygen complex ($B \cdot CoL_4 \cdot O_2$) is responsible for the catalytic oxidation, and that hydrogen bonding occurs between the alcohol and coordinated dioxygen prior to reaction. As further evidence for the occurrence of a ternary complex, we now report that when a chiral catalyst is employed a degree of enantiospecific oxidation is observed. When (*R,S*)-(±)-1-phenylethan-1-ol is oxidised to acetophenone the chiral centre is destroyed. This destruction of the two enantiomers should proceed at different rates, leading to partial kinetic resolution, in the presence of a chiral catalyst, if the transition state for the reaction involves both the catalyst and substrate. Hydrogen bonding of racemic 1-phenylethan-1-ol to a chiral catalyst will produce a diastereomeric pair of complexes, and as the two transition states would be expected to have different activation energies, preferential oxidation of one enantiomer of the alcohol should be observed.

Experimental

1,2-diaminopropane was resolved by one fractional crystallisation of the hydrogen L-tartrate acid salts as given by Dwyer *et al.* [3]. The optical purity of the (*R*)-(−)-pn obtained was greater than 99.5%. The chiral cobalt(II) complexes Co(Sal(−)pn), Co(3MeOSal(−)pn), and Co(7MeSal(−)pn) were prepared by standard methods [4] and their structures are shown in Fig. 1. The catalytic reactions were performed either in the following manner or on 1/5 the scale, as described elsewhere [2], and results from both methods were comparable.

Oxygen was bubbled through a solution of the cobalt complex (250 mg) and triphenylphosphine (500 mg) in (*R,S*)-(±)-1-phenylethon-1-ol (50 ml) at 40 °C for 19 h. The reaction mixture was distilled (203 °C/760 mmHg) and the first 40 ml collected.

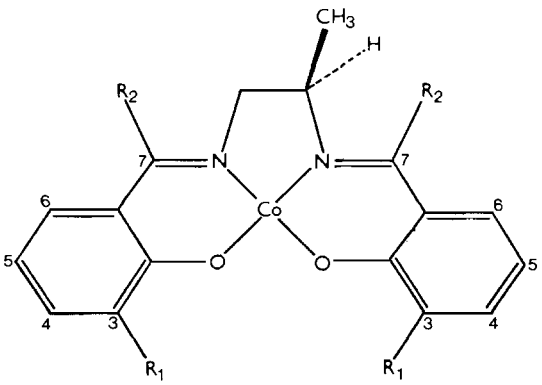

Fig. 1. Schematic structure of catalysts showing absolute configuration for ligands derived from (−)pn. [$R_1 = R_2 = H$, Co(Sal(−)pn); R_1 = MeO, R_2 = H, Co(3MeOSal(−)pn); R_1 = H, R_2 = Me, Co(7MeSal(−)pn)].

The distillate was analysed by GLC for the product, acetophenone. GLC analysis was performed on a Perkin-Elmer F11 dual column instrument using carbowax 20M/chromosorb W as the packing material. The yield of acetophenone was determined by comparison of peak heights and areas with those of synthetic standards. The rotation of the distillate at the sodium D line (589 nm) was determined on a Perkin-Elmer 141 polarimeter using (*R,S*)-(±)-1-phenylethon-1-ol as reference material to set zero. The distillate was also analysed by CD spectroscopy on a Cary 61 instrument for chiral impurities which might give rise to 'false' rotations at 589 nm; none could be detected. The cobalt complexes and free ligands have negative rotations in (±)-1-phenylethon-1-ol at 589 nm.

Results and Discussion

The results of the catalytic oxidation of racemic 1-phenylethanol with chiral catalysts are given in Table I. The chemical yields of 1–4% are similar to those obtained with achiral cobalt(II) Schiff's base complexes as catalysts; the activities of which have been interpreted in terms of the magnitude of electron transfer from cobalt to coordinated dioxygen [5]. It can be seen from Table I that there is always a residual positive rotation in the distillate which implies that (*S*)-(−)-phenylethan-1-ol is oxidised at a faster rate than its enantiomer. The enantiospecificity of the oxidation (%*S*) is conveniently defined in terms of the difference in the amount of each enantiomer oxidized in relation to the yield of acetophenone produced. Alternatively, the enantiospecificity of the reaction can be defined as the ratio of the rate constants for the oxidation of the two

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TABLE I. Experimental Data of Catalytic Oxidations

Cobalt complex[a]	Axial ligand	Chemical yield[b] (%*V*)	Observed rotation[c] (α)	k_S/k_R[d]	%*S*[e]
Co(Sal(−)pn)	$P(OMe)_3$	1.3	+0.020°	1.07	3.5
Co(Sal(−)pn)	PPh_3	3.8	+0.143°	1.18	8.5
Co(3MeOSal(−)pn)	PPh_3	2.8	+0.105°	1.18	8.5
Co(7MeSal(−)pn)	PPh_3	1.7	+0.191°	1.67	25.4

[a]Structure shown in Fig. 1. [b]From GLC analysis of reaction mixtures after 19 h at 40 °C. [c]Rotation of distillate, after reaction period, at the sodium D line with zero set with (±)-1-phenylethon-1-ol. [d]Calculated from *V* and α as given in ref. 6, $k_S/k_R = \ln\{(1 - V)(1 - ee)\}/\ln\{(1 - V)(1 + ee)\}$. [e]Based upon amount of each enantiomer oxidised, $\%S = 100 \times (\%ee)/V$.

enantiomers (k_S/k_R). Both definitions are given in Table I and are calculated [6] from the observed yield (%*V*) and rotation of the distillte (α) by utilising the specific rotation of (*R*)-(+)-1-phenylethon-1-ol ($[\alpha]_D$(neat) = 44.2° [7]).

The differing enantiospecificities of the catalytic oxidations (see Table I) can be accounted for by considering the conformation of the five-membered ring of the catalysts, and the cone angle of the axial ligand. The five-membered propylenediamine ring in the chiral catalyst can exist in two conformations (Fig. 2) with the methyl group either in a pseudo-equatorial (λ) or pseudo-axial (δ) environment. Flipping of the ring, which has a low activation energy, and is rapid at room temperature, will exchange the environments leading to an equilibrium conformation which for Co(Sal(−)pn) slightly favours the δ conformer [8]. Substitution in the aromatic ring is not expected to change the position of equilibrium, and both the unsubstituted and 3-methoxy substituted catalysts produce the same moderate enantiospecificity (see Table I).

The introduction of a methyl substituent into the 7 position produces a striking increase in enantiospecificity (see Table I). There is steric hindrance between a pseudoequatorial methyl group (λ) and substituents in the 7 position of the chelate ligand (Fig. 1) so that in Co(7MeSal(−)pn) the pseudo-axial conformer (δ) is strongly favoured [8]. Inspection of models shows that the methyl group of the λ conformation lies virtually in the plane of the ligand where it would be a poor source of enantiomeric discrimination towards a substrate on the free face of the catalyst. The greatly increased enantiospecificity achieved with the 7-methyl substituted catalyst can be directly attributed to the predominance of the δ conformer in which the pseudo-axial methyl group provides maximum opportunity for enantiomer discrimination on the face of the catalyst.

The reduction in enantiospecificity upon changing the axial ligand from PPh_3 to $P(OMe)_3$ (see Table I) can be accounted for by the steric requirements of these axial ligands. The cone angle of PPh_3 is 145° [9] and the methylgroup of the δ conformer of Co(Sal(−)pn) would be expected to interact strongly with this ligand preventing it from coordinating on the face of the complex bearing the axial methyl group. Trimethylphosphite has a much smaller cone angle (107°, [9]), and this would allow it to bind to either face of the complex without any serious interaction with the methyl group of the δ conformation. The greater enantiospecificity observed with PPh_3 as a ligand arises because the oxidation reaction is constrained to occur on the dissymmetric face of the catalyst by the preference of PPh_3 for the axial site on the other face. In the case of $P(OMe)_3$, oxidations can occur on either face, only on one of which can there be enantiomer differentiating.

A catalytic cycle for the oxidation has been proposed in which hydrogen peroxide, produced in the catalytic oxidation, itself oxidises the alcohol [2]. Further evidence in favour of the catalytic cycle

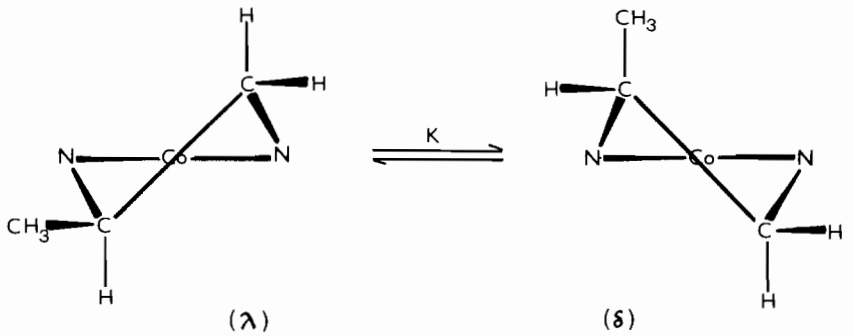

Fig. 2. Drawing showing the two conformations λ and δ of the catalysts five-membered ring.

comes from the chemical yield and enantiospecificity of reactions employing a large excess of PPh_3. When 2 g of PPh_3 (instead of 100 mg) were employed in a 10 ml reaction mixture with 50 mg of Co(Sal(−)pn) the chemical yield, under the standard conditions, was halved to 2.0%, but the rotation of the distillate was barely altered (+0.134°) giving an increased enantiospecificity (k_S/k_R = 1.35; %S = 15.1). These results are consistent with the proposed catalytic cycle [2], since in the reaction with a large excess of PPh_3 the oxidation of the alcohol by hydrogen peroxide is effectively blocked because of competition from PPh_3, which becomes oxidised to triphenylphosphine oxide. As the reaction of hydrogen peroxide with racemic 1-phenylethan-1-ol could not discriminate between the enantiomers, its suppression would be expected to double the enantiospecificity (%S) and halve the chemical yield; which is the result obtained.

Conclusions

Although the enantiospecificities achieved with this catalyst system are not yet preparatively useful, a number of factors which affect enantiospecificity, and which are relevant to the use of other chiral dioxygen complexes as catalysts [10] have been defined, and confirmation of the proposed catalytic cycle [2] has been obtained.

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