Catalysis by Cobalt Schiff's Base Complexes in Highly Selective Conversion of Arylglyoxals to α-Aryl-α-hydroxyacetic Esters

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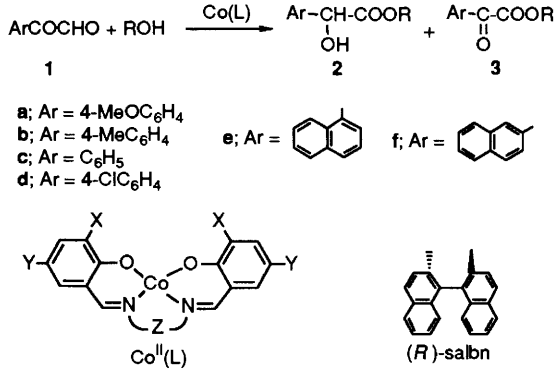
Cobalt Schiff's base complexes catalyse highly selective conversion of arylglyoxals to α-aryl-α-hydroxyacetic esters in alcohols; Lewis acidity of Co^{III} species may be responsible for the catalysis.

In a previous communication, we reported that Co^{II}(salen) [H_2salen = 1,6-bis-(2-hydroxyphenyl)-2,5-diazahexa-1,5-diene] catalysed the oxygenation of phenylacetylene in alcohols such as methanol, ethanol or propan-2-ol exclusively to give acetophenone, and mandelic and phenylglyoxylic esters.[1] The formation of mandelic esters was assumed to involve phenylglyoxal as an intermediate. The well known conversion of phenylglyoxal to mandelic acid is usually seen under strong alkaline conditions.[2] A copper(II) complex has been reported as the first transition metal complex that catalyses the conversion of phenylglyoxal in methanol to methyl mandelate, but the selectivity of the reaction is very low with formation also of many oxidation products including benzoic acid, a C–C bond cleavage product.[3]

We now find that Co^{II}(salen) [= $Co^{II}(L^1)$] as well as the related cobalt(II) Schiff's base complexes [$Co^{II}(L^n)$] catalyse highly selective conversion of arylglyoxals **1** to α-aryl-α-hydroxyacetic esters **2** in propan-2-ol under neutral and aerobic conditions. When a solution of phenylglyoxal **1c** (1 mmol) and $Co^{II}(L^1)$ (0.2 mmol) in a mixture of propan-2-ol (40 ml) and 1,2-dichloroethane (20 ml) was heated at 60 °C under atmospheric pressure of oxygen for 8 h, followed by separation of the metal complex and evaporation, isopropyl mandelate **2c** and isopropylphenylglyoxylate **3c** were obtained in 97 and 3% yield, respectively. The ^{1}H NMR data of the products were identical with those of authentic samples. Similar results were obtained with other alcohols and arylglyoxals, indicating the present reaction is general (Table 1).

The ^{1}H NMR spectrum of commercially available phenylglyoxal monohydrate in $CDCl_3$ shows a 1:7 mixture of the aldehyde and hydrate forms. When the monohydrate was dissolved in an alcohol, the corresponding hemiacetal was mainly formed as judged by the ^{1}H NMR data. No catalyst was needed for this step. Upon addition of $Co^{II}(L^n)$ to the resulting hemiacetal solution under aerobic conditions, the mandelic ester was produced gradually. Therefore, the conversion of arylglyoxals to mandelic esters is reasonably suggested to involve the isomerization of the hemiacetal intermediate catalysed by the cobalt complexes. Since cobalt(II) Schiff's base complexes normally undergo irreversible oxida-

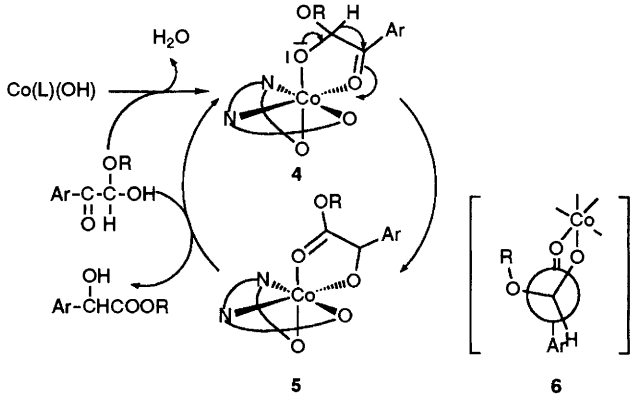


	(L^1)	(L^2)	(L^3)	(L^4)	(L^5)	(L^6)
X	H	H	H	H	Bu^t	H
Y	H	H	H	H	H	H
Z	$(CH_2)_2$	2 Me	2 Pr^n	2 Pr^i	$(CH_2)_2$	$(CHMe)_2$

Table 1 Co(L^n) and Lewis acid catalysed reaction of ArCOCHO **1** with alcohols[a]

Run	1	Co(L^n) or Lewis acid	ROH	T/°C	t/h	k_{obs} × 10^5/s^{-1}	Conversion (%)	Product yield (%) **2**	**3**
1	**1c**	Co(L^1)	Pr^iOH	60[b]	24	—	0	—	—
2	**1c**	Co(L^1)	MeOH	60	24	0.47	35	90	10
3	**1c**	Co(L^1)	EtOH	60	8	4.5	71	94	6
4	**1c**	Co(L^1)	Pr^iOH	60	8	10.3	94	97	3
5	**1c**	Co(L^1)	,,	25	8	5.0	76	99	1
6	**1c**	Co(L^1)	,,	60[c]	24	0.20	23	98	2
7	**1c**	Co(L^1)	Bu^tOH	60	8	8.17	91	99	—
8	**1a**	Co(L^1)	Pr^iOH	60	10	4.0	77	88	12
9	**1b**	Co(L^1)	,,	60	8	6.3	90	90	10
10	**1d**	Co(L^1)	,,	60	7	12.9	99	98	2
11	**1e**	Co(L^1)	,,	60	24	—	99	95	5
12	**1f**	Co(L^1)	,,	60	24	—	98	91	9
13	**1c**	Co(L^2)	,,	60	0.5	232	98	96	4
14	**1c**	Co(L^3)	,,	60	8	10.5	93	97	3
15	**1c**	Co(L^4)	,,	60	24	0.37	31	99	—
16	**1c**	Co(L^5)	,,	60	8	0.74	21	99	—
17	**1c**	Co(L^6)	,,	60	8	0.72	20	98	2
18	**1c**	Co(L^1)	,,	60[d]	8	1.5	46	95	5
19	**1c**	$Al(OPr^i)_3$	,,	60	2	73.0	98	99	Trace
20	**1c**	$CrCl_3$	,,	60	5	10.1	88	99	1
21	**1c**	$FeCl_3$	,,	60	10	4.2	79	98	2

[a] *Conditions*: **1** (1 mmol), catalyst (0.2 mmol), ROH (40 ml), CH_2ClCH_2Cl (20 ml) at 60.0 ± 0.1 °C. Product yields were determined by GLC for runs 1–6, 13–21 and by isolation for runs 7–12. [b] Without catalyst. [c] Under N_2 atmosphere. [d] Pyridine (4 mmol) was added.



Scheme 1

tion rapidly in alcohols to give $Co^{III}(L)(OH)$,[4] the hydroxocobalt(III) complex is likely to be responsible for the reaction under oxygen. The reaction also proceeded under nitrogen, but was much slower than that under oxygen (Table 1, runs 4 and 6).

The reactivity of alcohols in the $Co^{II}(L^1)$ catalysed reaction with **1c** was interestingly in the order: $Bu^tOH \approx Pr^iOH >$ EtOH > MeOH (Table 1, runs 2, 3, 4 and 7). The reaction rate was influenced by the *para*-substituent in **1**: the stronger electron-withdrawing substituent results in the faster reaction (Table 1, runs 4, 8–10). A linear relationship between k_{obs} and σ^+ was observed (ρ = 1.3), suggesting a hydride shift to the positively polarized benzylic carbon.

The reaction rate was also influenced by the nature of the cobalt complex. The observed reactivity of the cobalt complexes was in the order of ligands $L^2 > L^3 > L^1 > L^5 > L^6 > L^4$ (Table 1, runs 4, 13–17). The extremely high reactivity of $Co^{II}(L^2)$ is not clearly understood at the moment. Introduction of bulky groups into the salen ligand results in retardation of the reaction (Table 1, runs 16 and 17). When pyridine, a good coordinating ligand, was added to the reaction system using $Co^{III}(L^1)(OH)$, the reaction was slowed considerably (Table 1, run 18 compared to run 4). These results tell us that the coordination of the substrate as a bidentate ligand to a coordinatively unsaturated cobalt(III) species is important for the present reaction.

Furthermore, the higher reactivity of $Co^{III}(L^1)(OH)$ than $Co^{II}(L^1)$ suggests that Lewis acidity of the complex is responsible for the present reaction. In fact, Lewis acids such as $Al(OPr^i)_3$, $FeCl_3$ and $CrCl_3$ were also catalytically active (Table 1). On the other hand, the addition of a proton acid such as toluene-*p*-sulfonic acid or sulfuric acid to a solution of phenylglyoxal in propan-2-ol gave a complex mixture. Therefore, the exclusive conversion of phenylglyoxals to mandelic esters by the Lewis acid catalysis is interesting and synthetically significant.

All these findings suggest a plausible mechanism for the $Co^{III}(L)(OH)$ catalysed reaction as depicted in Scheme 1; as the hydroxocobalt(III) complex has been shown to act as a base,[4,5] an acid–base equilibrium between the complex and the substrate gives an intermediate of type **4**, which undergoes hydride shift to give **5**. The reaction between **5** and the substrate can maintain the catalytic cycle. This mechanism is supported by the fact that the optically active (*R*)-Co(salbn) in propan-2-ol gave isopropyl (*R*)-mandelate in 13.5% enantiomeric excess.

The reason why the reaction is much faster in propan-2-ol than in methanol is not clear, but a larger nonbonding repulsive interaction between the carbonyl group and the alkoxy group in the intermediate **4** may result in a preferred conformation for the 1,2-hydride shift as shown in **6**.

Further investigation on the detailed mechanism as well as systematic asymmetric syntheses of α-aryl-α-hydroxyacetic esters from arylglyoxals is now underway.

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