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CONVERSION OF 2'-HYDROXYCHALCONES TO FLAVANONES CATALYZED BY COBALT SCHIFF BASE COMPLEX

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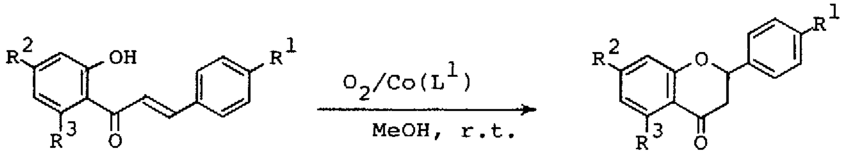
Summary: Co(salpr) catalyzes the conversion of 2'-hydroxychalcones to flavanones in methanol under oxygen. Base catalysis by Co(salpr)(OH) produced in situ is responsible for the reaction, which is found to proceed reversibly.

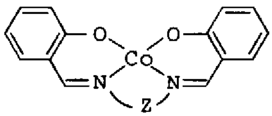
Cobalt(II) Schiff base complexes [Co^{II}(SB)] exhibit dioxygenase-like activity in aprotic solvents, whereas in protic solvents they catalyze monooxygenations of organic molecules.[1-5] The $Co^{II}(SB)-O_2$ oxidation system is also effective for dehydrogenations of alcohols,[4] hydrazones,[6] and amines.[7,8] For all these reactions, hydroxocobalt(III) complexes, Co^{III}(SB)(OH), have been posturated as active key intermediates. The common activation process for the model dioxygenase reactions using Co^{II}(SB) seems to be the formation of substrate anion cobalt(III) complexes sensitive to dioxygen incorporation.[9] Such a substrate anion Co^{III}(SB) complex has recently been documented.[10] Therefore, the significant role of Co(SB) in the model dioxygenase reactions is that the Co^{III}(SB)(OH) complex intermediate functions as a base. However, no direct evidence for such base catalysis of Co^{III}(SB)(OH) has been demonstrated. We now report here that Co(salpr) [salpr = N^1,N^7-4-azaheptamethylenebis(salicylideneiminato)], Co(L^1), catalyzes conversion of 2'-hydroxychalcones to the corresponding flavanones in methanol under oxygen atmosphere, and that the reaction is of reversible promoted by $Co^{III}(L^1)$(OH) as a base. The present results also provide an interesting chemical model for a chalcone synthase.[11]

A solution of chalcone (**1a**) (1 mmol) in methanol (10 ml) containing Co(L^1) (1 mmol) was stirred at room temperature under an oxygen atmosphere for 6 h. The mixture was chromatographed on a silica gel plate being eluted with a 1 : 1 mixture of dichloromethane and hexane to give **1a** (21%) and flavanone (**2a**) (76%), no other products being detected. The structure of **2a** was identical with an authentic sample (IR and ^{1}HNMR). Similar results are obtained with other substituted 2'-hydroxychalcones except dihydroxy derivatives (Table 1).

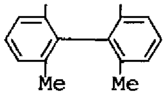
The same results are obtained with $Co^{III}(L^1)$(OH) under nitrogen atmosphere.



1 **2**



Co(L^1): Z = $(CH_2)_3NH(CH_2)_3$ Co(L^2): Z = CH_2CH_2

Co(L^3): Z = 

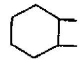
Co(L^4): Z = 

Table 1. Conversion of chalcones (**1**) to flavanones (**2**) promoted by Co(L^1)[a]

1	R^1	R^2	R^3	Reaction time (h)	Conversion (%)	Yield of **2**[b] (%)
1a	H	H	H	6 (24)	79 (79)[c]	76 (77)[c]
1b	OMe	H	H	6 (24)	72 (73)[c]	68 (66)[c]
1c	H	OCH_2OMe	H	6	70	69
1d	OCH_2OMe	OCH_2OMe	H	6	68	67
1e	H	H	OMe	6	65	59
1f	OMe	H	OMe	6	51	49
1g	Cl	H	H	6	65	50
1h	OH	H	H	6	0	0
1i	H	OH	H	6	0	0
1j	H	H	OH	6	93	87
1k	OMe	H	OH	6	85	80

[a] Reaction conditions: chalcone **1** (1 mmol), Co(L^1) (1 mmol), MeOH (10 ml) under 1 atm of oxygen at room temperature. [b] Determined by isolation of **1** and **2**. [c] Values after 24 h reaction.

Since no reaction takes place with $Co^{II}(L^1)$ under nitrogen, the active species in the $Co^{II}(L^1)$ promoted reaction under oxygen should be $Co^{III}(L^1)(OH)$ formed in situ.[12] Interestingly, when 7,4'-bis(methoxymethoxy)flavanone (**2d**) is similarly treated with $Co^{III}(L^1)(OH)$ in methanol at room temperature under nitrogen for 6 h, a mixture of **1d** (55%) and **2d** (45%) was obtained. It is therefore concluded that the present reaction is reversible interconversion promoted by $Co^{III}(L^1)(OH)$, a coordinately saturated hydroxo complex. Coordinately unsaturated hydroxocobalt(III) complexes, $Co^{III}(L^2)(OH)$, $Co^{III}(L^3)(OH)$, and $Co^{III}(L^4)(OH)$ are all inactive. $Co^{III}(L^2)(OH)$ shows catalytic activity only when a donating base ligand such as pyridine or N-methylimidazole (NMI) is added. The nature of solvent is also important. No reaction takes place in dichloromethane or N,N-dimethylformamide. Thus, the reaction of **1c** with $Co^{III}(L^2)(OH)$ in dichloromethane gives the substarte anion cobalt(III) complex, $Co^{III}(L^2)(\mathbf{1c}^-)$[13] quantitatively, although the substrate anion complex from $Co^{III}(L^1)(OH)$ is not isolated in pure form. $Co^{III}(L^2)(\mathbf{1c}^-)$ is quite stable in methanol. However, when NMI is added, the reaction occurs. Time course of the spectral change of this reaction follows first order kinetics (k = $2.9 \times 10^{-5} s^{-1}$ at 350 nm) (Fig. 1), and the final solution gives a mixture of **1c** and **2c**. From these results, a mechanism involving intramolecular cyclization of the substrate anion cobalt(III) complex (**3**) can be proposed for the $Co^{III}(L^1)(OH)$ promoted conversion of chalcones to flavanones (Scheme 1).

The requirement of an alcoholic solvent for the reaction suggests that the protonation of an intermediate (**4**) is important.

The effects of hydroxyl substituent on the reactivity of **1** is interesting. The forma-

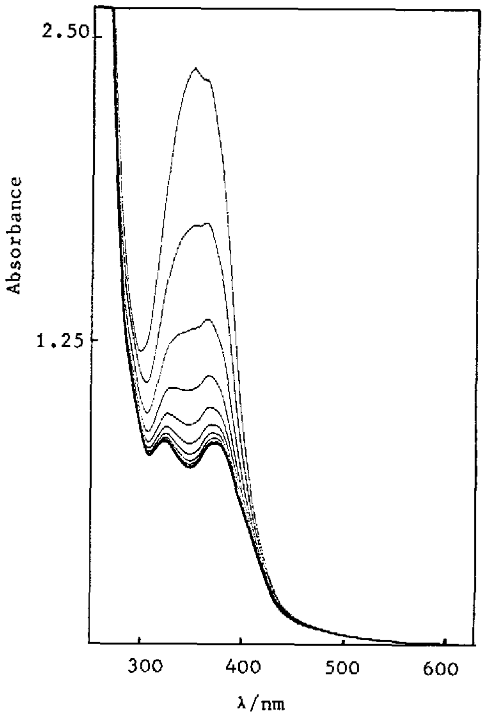
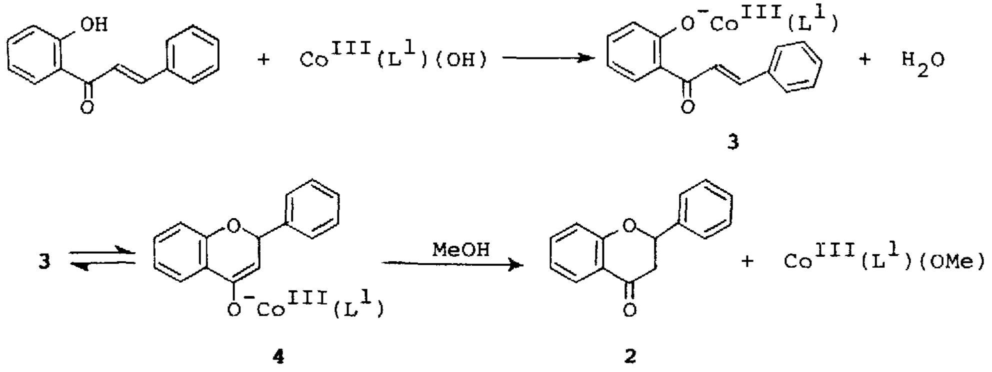


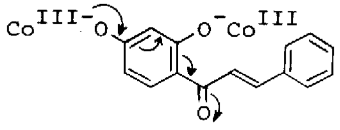
Fig. 1. Spectral change of $Co^{III}(L^2)(\mathbf{1c}^-)$ in methanol. $[Co^{III}(L^2)(\mathbf{1c}^-)] = 8.7 \times 10^{-4}M$, $[NMI] = 1.7 \times 10^{-2}M$ in MeOH at 25.0 ± 0.01 °C, every 30 min.



$$Co^{III}(L^1)(OMe) + H_2O \longrightarrow Co^{III}(L^1)(OH) + MeOH$$

Scheme 1

tion of phenolatocobalt(III) species (**5**, **6**) may be responsible for the non-reactivity of **1h** and **1i** because the intramolecular nucleophilic cyclization is inhibited by resonance effect. Instead, the 6'-hydroxyl group in **1j** and **1k** accelerates the cyclization. This may be due to an intramolecular hydrogen bonding that polarlizes the enone system (**7**).



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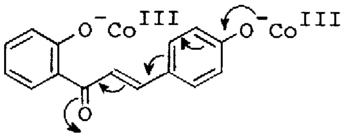

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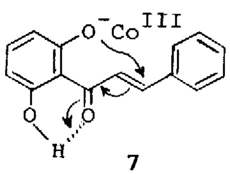

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In general, the 2'-hydroxychalcone - flavanone interconversion is promoted by either a base or an acid.[14,15] On the other hand, coordinately unsaturated Co^{III}(SB)(OH) acts as a superacid catalyst.[16] Therefore, all the findings on the reactivity of Co^{III}(SB)(OH) toward the present interconversion prove that the base catalysis of coordinately saturated Co^{III}(SB)(OH) is responsible for the reaction.

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