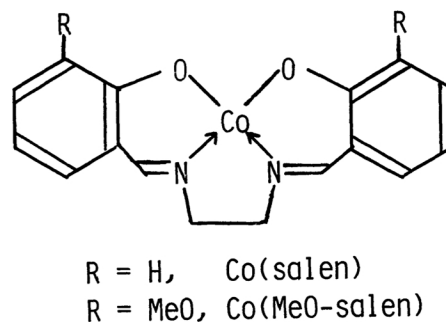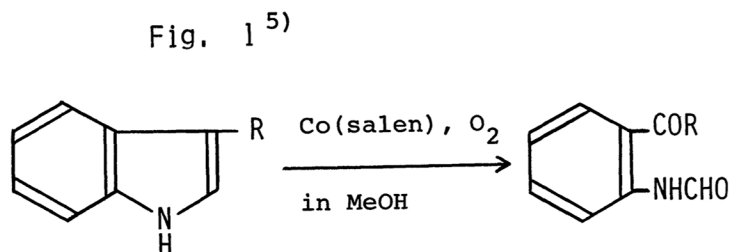# AN EFFECTIVE DEHYDROGENATION OF INDOLINES TO INDOLES
WITH COBALT(II) SCHIFF'S BASE COMPLEXES

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Facile dehydrogenations of indolines to indoles were perfor-
med with the catalytic amount of bis(salicylidene)ethylenediami-
natocobalt(II) and bis(3-methoxysalicylidene)ethylenediaminatoco-
balt(II) under mild conditions in 55-92% yields.

The conversion of an indoline ring to an indole ring is a process of synthe-
tic significance because of the easier accessibility of a functionalized indoline.
Dehydrogenation of indolines to indoles can be accomplished by the chemical oxida-
tion (e.g., with MnO_2, $CuCl_2$-pyridine, chloranil, etc.) and by the catalytic dehy-
drogenation over metallic catalyst (e.g., Pd/C, Raney Ni, etc.).[1] In all these
cases, usually, a considerably large amount of the reagent or catalyst, and/or a
higher reaction temperature are necessary to perform the effective dehydrogenation.

Cobalt Schiff's base complexes such as bis(salicylidene)ethylenediaminatoco-
balt(II) [Co(salen)] and bis(3-methoxysalicylidene)ethylenediaminatocobalt(II)
[Co(MeO-salen)],[2] have been found to act as oxygen carrying catalysts in several
chemical reactions.[3],[4]

Fig. 1[5]

R = H,   Co(salen)
R = MeO, Co(MeO-salen)

The oxygenation of 3-substituted indoles catalyzed with Co(II)-complexes has been studied as a model reaction of the tryptophan 2,3-dioxygenase.[5],[6] (Fig. 1)
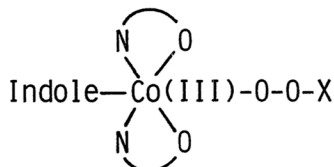
During our investigation on the dehydrogenation of indolines to indoles, we have found that Co(II)-complexes were effective dehydrogenating catalysts. In order to find optimum conditions, the reaction was examined by changing substrate concentration, catalyst amount and reaction media to avoid the oxygenation of resulting indoles. We wish to report now the facile dehydrogenation of simple indolines to indoles catalyzed with Co(II)-complexes under mild conditions.

A typical reaction procedure is as follows. To a solution of indoline (1, 20 mM) in methanol was added Co(salen) (2 mM) and the resulting suspension was bubbled with a fine stream of O_2 at 25°C. The suspension became homogeneous within 1 h except for the case of 1b (vide infra). The reaction mixture was then evaporated and the products were separated by a silica gel chromatography.

The Table summarizes the product yields for each substrate. A longer reaction time and/or a higher concentration of catalyst were necessary in the cases of the indolines having bulky substituents (e.g., 1f and 1g). No dehydrogenation took place without the catalyst in all cases. Active MnO_2, the versatile reagent, was less active than Co(II)-complexes on both substrates, 1a and 1g, which were the best and the worst substrates, respectively, among the N-unsubstituted indolines studied toward the complex catalyzed dehydrogenation.

It is already known[2],[3] that Cobalt Schiff's base complexes absorb the molecular O_2 reversibly in the presence of suitable axial donor ligands such as pyridine, indole, etc. Although an active species of the oxygenation reaction of indole in Co(II)-complex catalysis[5] is not thoroughly clarified, the reaction is supposed to proceed via the abstraction of the hydrogen atom of indole NH by forming an indole-Co(III)-O_2 complex as depicted in Fig. 2.[4],[5] The dehydrogenation of N-unsubstituted indolines catalyzed with Co(II)-complexes may also proceed by the formation of an indoline-Co(III)-O_2 complex which is soluble in methanol (vide supra).

Fig. 2

Indole—Co(III)-O-O-X

X= Co(III) species or an unpaired electron.

N-Methylindoline (1b) resisted to the dehydrogenation catalyzed with Co(II)-complexes.

It is noteworthy that no remarkable subsequent oxygenation of indoles (2)

Table Dehydrogenation of indolines ($\underset{\sim}{1}$) to indoles ($\underset{\sim}{2}$) catalyzed with Co(II)-complexes.[a]
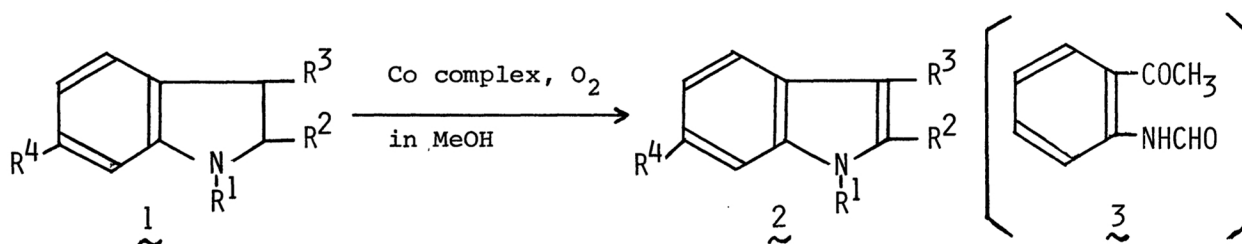
Substrate ($\underset{\sim}{1}$)	Substrate/Co	Reaction Time (h)	Yield of $\underset{\sim}{2}$ (%)[b]	
			Co(salen)	Co(MeO-salen)
a: $R^1=R^2=R^3=R^4=H$ [c]	10/1	5	83	82
b: $R^1=CH_3$, $R^2=R^3=R^4=H$	10/1	24	10 ($\underset{\sim}{1b}$; 74)	8 ($\underset{\sim}{1b}$; 78)
c: $R^1=R^3=R^4=H$, $R^2=CH_3$	10/1	5	79	81
d: $R^1=R^2=R^4=H$, $R^3=CH_3$	10/1	4	60 ($\underset{\sim}{3}$; 4)	64 ($\underset{\sim}{3}$; 3)
e: $R^1=R^2=R^3=H$, $R^4=NO_2$	10/1	5	39 ($\underset{\sim}{1e}$; 52)	---
	4/1	5	92	85
f: $R^1=R^2=R^4=H$, $R^3=(CH_2)_3COOEt$	10/1	18	69	70
	4/1	5	76	78
g: $R^1=R^2=R^4=H$, $R^3=CH_2CH(NHAc)COOEt$	4/1	24	55	55

	Substrate/MnO$_2$		MnO$_2$[d]	
$\underset{\sim}{1a}$	1/8	12	62	
$\underset{\sim}{1g}$	1/8	60	7 ($\underset{\sim}{1g}$; 70)	

a) The dehydrogenation reactions were undertaken using 50 ml reaction solutions as described in the text. The catalytic activity of Co(salen) was checked before use by the following method.[5] To a 20 ml methanol solution of 3-Me-indole ($\underset{\sim}{1d}$) (50 mM) was added Co(salen) (12.5 mM) and the suspension was bubbled with O$_2$ at room temp. for 5 h. Those Co(salen) which showed more than 85% conversion of $\underset{\sim}{1d}$ in the reaction, were used throughout the experiments. Indolines ($\underset{\sim}{1}$) were made after Ref. 7 and all compounds in the table were identified by the direct comparisons with the authentic samples.

b) The average isolated yields of three experiments were given and the yields of the other products or the recoveries of $\underset{\sim}{1}$ were given in the parentheses.

c) The dehydrogenation yields of $\underset{\sim}{1a}$ to $\underset{\sim}{2a}$ by the other methods reported in the literatures are as follows; PdCl$_2$ (0-83%),[8] MnO$_2$ (59,[9a] 56[9b]), Raney Ni (82),[10] Cr/C (33-44),[11] and CuCl$_2$-pyridine (55-60).[12]

d) To a 10 ml benzene solution of $\underset{\sim}{1}$ (1 mmole, a; 119 mg and g; 276 mg, respectively) was added MnO$_2$ (8 mmole, 695 mg) and the reaction mixture was stirred at 25°C.

took place under these conditions. Only in the case of 1d, o-formylaminoacetophe-
none (3)$^{5)}$ was isolated.

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