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OXIDATION OF 2-INDOLINONES WITH COBALT(II) SCHIFF'S BASE COMPLEXES

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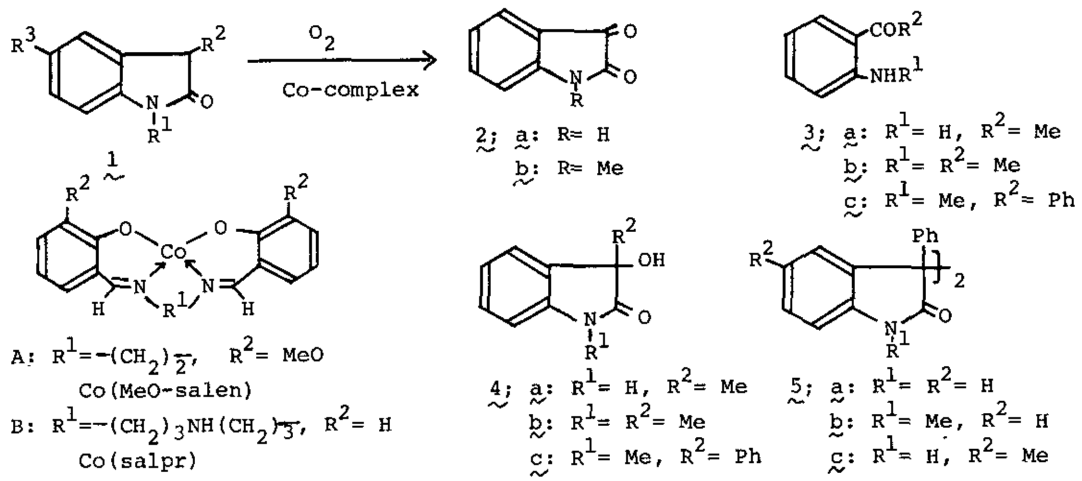
Abstract —— The oxidation of 2-indolinones (1) catalysed with cobalt(II) Schiff's base complexes gave isatins (2), O-aminoketones (3), 3-hydroxy-2-indolinones (4), and dimers (5).

The cobalt(II) Schiff's base complexes such as bis(3-methoxysalicylidene)ethylenediaminatocobalt(II) [Co(MeO-salen)]$^{1)}$ and bis(3-salicylideneaminopropyl)aminecobalt(II) [Co(salpr)]$^{1)}$ interact reversibly with molecular oxygen and have been interested in relation to the biological oxidation systems.$^{2)}$ Nishinaga and his coworkers$^{3)}$ reported the reactions catalysed by these complexes, e.g., oxidation of substituted phenols and oxidation of 3-substituted indoles, providing the non-enzymatic models for the reactions of mono-oxygenase, dioxygenase, and peroxidase. Oxidation of phenols furnished the variety of products depending on the substituents of starting materials, and oxidation of indoles, on the other hand, gave the corresponding O-formylaminoacetophenone derivatives.$^{4)}$

On the oxidation of 2-indolinone (oxindole) which could be represented as 2-hydroxyindole and could exert pseudophenolic properties, there have been reported several examples.$^{5),6),7)}$ In the reaction of 2-indolinones with oxygen in alkaline solution, both ring cleavage and formation of 3-hydroxy-2-indolinone (dioxindole) have occurred.$^{5)}$ In the cases of inorganic oxidative reagents such as $I_2$$^{6)}$ and $K_3Fe(CN)_6$$^{7)}$, 2-indolinones gave dimeric products.

In the present paper, we wish to report the Co(II) Schiff's base complex catalysed oxidation of some 2-indolinones (1). The oxidation proceeded upon treating a MeOH solution of 1 (5 mmole) and Co-complex (0.5 mmole or 1.0 mmole) under a fine stream of oxygen. The reaction mixture was then evaporated down and the residue was purified with silica gel column chromatography.

Table. Oxidation of 2-indolinones(1) with cobalt(II) Schiff's base complexes



2; a: R= H
b: R= Me

3; a: R^1= H, R^2= Me
b: R^1= R^2= Me
c: R^1= Me, R^2= Ph

A: R^1=$-(CH_2)_2-$, R^2= MeO
Co(MeO-salen)

B: R^1=$-(CH_2)_3NH(CH_2)_3-$, R^2= H
Co(salpr)

4; a: R^1= H, R^2= Me
b: R^1= R^2= Me
c: R^1= Me, R^2= Ph

5; a: R^1= R^2= H
b: R^1= Me, R^2= H
c: R^1= H, R^2= Me

Substrate (1)	Co-complex	1/Co (mmole)	Reaction time (h)	Yields of Products (%)
a: R^1=R^2=R^3= H	A	5/0.5	3	2a(73)
b: R^1= Me, R^2=R^3= H	A	5/0.5	3	2b(94)
c: R^1=R^3= H, R^2= Me	A	5/1.0	3	3a(20), 4a(34)
d: R^1=R^2= Me, R^3= H	A	5/1.0	3	3b(24), 4b(56)
	B	5/1.0	24	3b(3), 4b(70) [1d(16)]
e: R^1=R^3= H, R^2=Ph	A	5/0.5	3	5a(70)
	B	5/0.5	3	5a(72)
f: R^1=Me, R^2=Ph, R^3=H	A	5/0.5	3	3c(6), 4c(10), 5b(74)
	B	5/0.5	3	3c(2), 4c(16), 5b(61)
g: R^1=H, R^2=Ph, R^3=Me	A	5/0.5	3	5c(74)

The reaction conditions and results are listed in Table. Oxidation proceeded by both catalysts. No oxidation took place without catalysts. In the case of 1d, Co(salpr) showed moderate activity in comparison with that of Co(MeO-salen). Oxidation products (2-5) were varied as the C(3)-substituent of 2-indolinones (1). Isatins (2) were obtained by the oxidation of C(3)-unsubstituted 1a and 1b. Reaction of 3-methyl-2-indolinones (1c and 1d) gave the corresponding aminoacetophenones (3a and 3b) and 3-hydroxy-2-indolinones (4a and 4b) respectively.

On the other hand, the oxidation of 3-phenyl-2-indolinones (1e-1g) afforded dimeric products (5a-5c).[8] The structures of 5 were deduced from the spectral data described in " EXPERIMENTAL ".

Although the reaction mechanisms of this reaction is not thoroughly clarified, the reaction is supposed to proceed by forming substrate-Co(III)-O_2 complex.[3]

By a similar procedure, 3-phenyl-2-indolinethione gave 2,2'-dithiobis(3-phenylindole)[9] in 90% yield.

EXPERIMENTAL

All melting points are uncorrected. The following instruments were used for obtaining the physical data. ^{1}H-NMR spectra (TMS as internal standard): JEOL JNM-PMX 60; IR spectra: Hitachi 215; UV spectra: Hitachi Model 100-50; MS: Schimadzu LKB 9000.

Oxidation of 2-indolinone(1) with Co-complex

The general procedure is as follows. To a solution of 2-indolinone(1, 5 mmole) in MeOH(100 ml) was added either Co(MeO-salen) or Co(salpr) (each 0.5 mmole or 1 mmole). The resulting suspension[10] was stirred under a fine stream of O_2. The reaction mixture was evaporated down and the residue was purified on a silica gel column with the appropriate solvents to give products(2-5).

Oxidation of 3-phenyl-2-indolinethione to 2,2'-dithiobis(3-phenylindole)

Co(MeO-salen)(0.5 mmole) was added to a solution of 3-phenyl-2-indolinethione(5 mmole) in MeOH(100 ml). The resulting suspension was bubbled with O_2 for 15 min. After the removal of solvent, the residue was extracted with benzene(100 ml) in three portions. After the evaporation of solvent followed by recrystallization, 2,2'-dithiobis(3-phenylindole)[9] was obtained in 90% yield.

Characterization and identification of products

Compounds 2a, 2b, 3a, and 3b were identified with authentic commercial samples. Compounds 3c,[5a] 4a,[11] 4b,[12] 4c,[5a] and 2,2'-dithiobis(3-phenylindole)[9] were identified by the comparison of physical data with the data in literatures.

Dimeric products(5) show the following physical properties.[8] 5a, mp 234-6° C; IR ν_{max}^{KBr} cm^{-1}: 1705; UV λ_{max}^{EtOH} nm(log ε) 288(3.85); ^{1}H-NMR (δ, d_6-DMSO) 6.27(2H, d-like, J=8, ArH), 6.40-7.63(6H, m, ArH); Field desorption(FD) MS m/e(%) 416(M^+, 2),[13] 208 (100); Anal. Calcd for $C_{28}H_{20}N_2O_2$: C, 80.74; H, 4.84; N, 6.73. Found: C, 80.91; H, 5.10; N, 6.63. 5b, mp 215-7° C; IR ν_{max}^{KBr} cm^{-1}: 1705; UV λ_{max}^{EtOH} nm(log ε) 290(3.87);

^{1}H-NMR (δ, $CDCl_3$) 3.00(6H, s, 2 x NMe), 6.25(2H, d-like, J=8, ArH), 6.50-7.67(6H, m, ArH); MS m/e(%) 444(M^+, 4), 222(100); Anal. Calcd for $C_{30}H_{24}N_2O_2$: C, 81.06; H, 5.44; N, 6.30. Found: C, 80.89; H, 5.64; N, 6.16. **5c**, mp 260-2° C; IR ν_{max}^{KBr} cm^{-1}: 1705; UV λ_{max}^{EtOH} nm(log ε) 298(3.77); ^{1}H-NMR (δ, d_6-DMSO) 2.15(6H, s, 2 x Me), 5.97 (2H, s-like, ArH), 6.33-7.67(4H, m, ArH); FD MS m/e(%) 444(M^+, 3),13) 222(100); Anal. Calcd for $C_{30}H_{24}N_2O_2$: C, 81.06; H, 5.44; N, 6.30. Found: C, 80.97; H, 5.62; N, 6.26.

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8) These dimers(**5**) might be mixtures of diastereomers. X-Ray analysis of **5** is now under investigation. Oxidation of **1f** with other inorganic reagents such as $FeCl_3$, $K_3Fe(CN)_6$, and active MnO_2 gave the same compound(**5b**) in 55-65% yields.

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