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Cobalt Schiff Base Complex Catalyzed Dehydrogenation of Amines with *t*-Butyl Hydroperoxide

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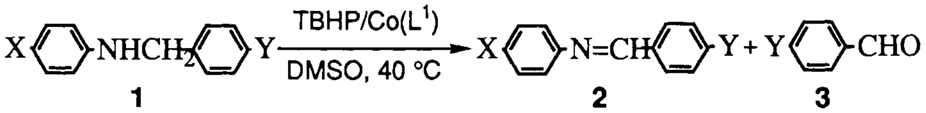
Cobalt Schiff base complex catalyzed oxidation of secondary aromatic amines with *t*-butyl hydroperoxide resulted selectively in dehydrogenation to give the corresponding imines. Proposed mechanism involves electron transfer from the nitrogen atom in the substrate to *t*-butyloxyl or *t*-butylperoxyl radical produced *in situ* from a *t*-butylperoxocobalt(III) complex intermediate.

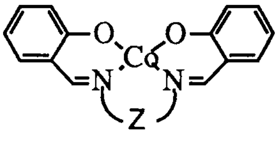
Metal catalyzed oxidations are very important in connection with biological as well as synthetic processes.1) Cobalt(II) Schiff base complexes [Co^{II}(SB)] are of particular interest because they function as artificial metal containing oxidoreductases including dioxygenases, monooxygenases and peroxidases. Co^{II}(SB) complexes also catalyze *t*-butylperoxylation of phenols2) and hydrazones,3) and dehydrogenation of alcohols4) with *t*-butyl hydroperoxide (TBHP). Metal catalyzed dehydrogenation of amines is also important area in organic synthesis.5) In a previous paper we reported the dehydrogenation of secondary amines to imines by the oxidation using the O_2/Co^{II}(salen) system, of which mechanism involves electron transfer from the amine to Co^{III}(salen)(OH) species.6) In a series of studies on Co^{II}(SB) catalyzed oxidation using TBHP as the terminal oxidant, we have examined the oxidation of secondary amines with TBHP. The TBHP/Co^{II}(SB) system is now found to be able to oxidize amine substrates which are unsusceptible to the O_2/Co^{II}(salen) system including tertiary amines,6) where the products are similar to those obtained in the cytochrom p-450 system.

A solution of TBHP (4.8 mmol), amine (**1**) (4.0 mmol), and $Co^{II}(L^1)$ (0.8 mmol) in dimethylsulfoxide (DMSO) (20 ml) was warmed at 40 °C for 8 h. The reaction mixture was then diluted with a saturated brine (200 ml) and extracted with ether. The ether solution was washed with water, dried over sodium sulfate, and evaporated. The resulting residue was chromatographed on a Florisil column with ether as the eluent. The structures of the products were identified by comparison with authentic samples (^{1}H NMR, IR).



1 **2** **3**

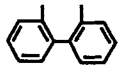
a ; X = Y = H
d ; X = Cl, Y = H
g ; X = H, Y = Me
j ; X = Y = Me
b ; X = OMe, Y = H
e ; X = H, Y = NO_2
h ; X = H, Y = Cl
k ; X = Y = Cl
c ; X = Me, Y = H
f ; X = H, Y = OMe
i ; X = Y = OMe

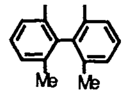


$Co^{II}(L)$

$Co^{II}(L^1)$; Z = CH_2CH_2

$Co^{II}(L^2)$; Z = 

$Co^{II}(L^3)$; Z = 

$Co^{II}(L^4)$; Z = 

$Co^{II}(L^5)$; Z = $C(CH_3)_2C(CH_3)_2$

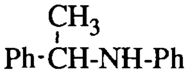
$Co^{II}(L^6)$; Z = $(CH_2)_3NH(CH_2)_3$

Table 1. Oxidation of amines **1** with TBHP catalyzed by $Co^{II}(L^1)$[a]

Run	**1**	[Co]/[**1**]	Reaction time/h	Conversion %	Yield/%[b] **2**	Yield/%[b] **3**
1	**1a**	0	8	0	0	0
2	**1a**	0.2	8	91	94	6
3	**1b**	0.2	0.75	100	95	5
4	**1c**	0.2	4	98	94	6
5	**1d**	0.2	8	97	96	4
6	**1e**	0.2	8	97	90	10
7	**1f**	0.2	8	93	93	7
8	**1g**	0.2	8	96	96	4
9	**1h**	0.2	8	97	98	2
10	**1i**	0.2	0.25	98	100	0
11	**1j**	0.2	4	99	96	4
12	**1k**	0.2	8	94	97	3

a) Reaction conditions: (**1**) (4 mmol), TBHP (4.8 mmol), $Co(L^1)$ (0.8 mmol), DMSO (20 ml), 40 °C. b) Determined by ^1H NMR.

The results obtained in the $Co^{II}(L^1)$ catalyzed dehydrogenation of substituted *N*-benzylanilines (**1**) are summarized in Table 1. As seen from Table 1, no reaction took place without the Cobalt catalyst (Run 1), and the dehydrogenation of **1** was generally catalyzed by $Co^{II}(L^1)$. The *p*-substituent X in the aniline moiety of **1** influenced the reaction rate (Runs 3, 4), whereas nearly no substituent effect was observed with the substituent Y in the benzylic group (Runs 6-9). Similar results were obtained in the stoichiometric reaction of **1** with $Co^{III}(L^1)(OOBu^t)$, indicating

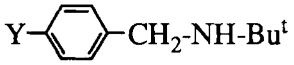


$Ph\text{-}\overset{CH_3}{CH}\text{-}NH\text{-}Ph$

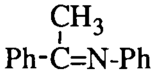
4

$Ph\text{-}CH_2\text{-}NH\text{-}CH_2\text{-}Ph$

5



6



$Ph\text{-}\overset{CH_3}{C}\text{=}N\text{-}Ph$

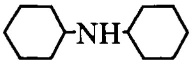
7

$Ph\text{-}CH\text{=}N\text{-}CH_2\text{-}Ph$

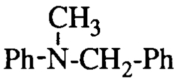
8

$Ph\text{-}CH\text{=}N\text{-}Bu^t$

9

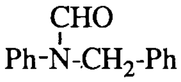


10



$Ph\text{-}\overset{CH_3}{N}\text{-}CH_2\text{-}Ph$

11



$Ph\text{-}\overset{CHO}{N}\text{-}CH_2\text{-}Ph$

12

that the reactive species in the catalytic reaction should be the *t*-butylperoxocobalt(III) complex which is rapidly formed by the reaction of $Co^{II}(L^1)$ with TBHP.7)

The present TBHP/$Co^{II}(L^1)$ system was found to be effective for the dehydrogenation of compounds **4**, **5**, and **6** (Y=H) selectively to give **7** (37% in 8 h), **8** (85% in 4 h), and **9** (95% in 10 h), respectively, although these sterically hindered aniline derivatives and *N*-benzyl aliphatic amines were unsusceptible to the dehydrogenation in the O_2/Co^{II}(salen) oxidation system (no reaction in 24 h). Compound **10**, nevertheless, was not reactive against the TBHP/$Co^{II}(L^1)$ system. Furthermore, compound **11**, which is absolutely stable against the O_2/$Co^{II}(L^1)$ system, was oxidized effectively by the TBHP/$Co^{II}(L^1)$ system (93% conversion in 6 h) to give **1a** (12%), **2a** (38%), **3a** (17%), and *N*-benzylformanilide (**12**) (7%). The results resemble those obtained in the cytochrome p-450 oxidation system.8)

The dehydrogenation is also influenced by the structure of Co^{II}(SB). The conversions of **1a** with TBHP for 6 h using $Co^{II}(L^1)$, $Co^{II}(L^2)$, $Co^{II}(L^3)$, $Co^{II}(L^4)$, $Co^{II}(L^5)$, and $Co^{II}(L^6)$ were 95.4%, 93.8%, 31.0%, 16.6%, 95.6%(1.5 h), and 0.9% respectively, indicating that the reactivity of Co^{II}(L) is in the order: $Co^{II}(L^5) > Co^{II}(L^1) > Co^{II}(L^2) > Co^{II}(L^3) > Co^{II}(L^4) > Co^{II}(L^6)$. On the other hand, in the dehydrogenation of **1a** with the O_2/Co^{II}(SB) system, the sterically hindered complex $Co^{II}(L^5)$ was catalytically inactive. The observed reactivity of Co^{II}(L) may be attributed to the ability of homolytic cleavage of the Co-O bond in $Co^{III}(L)(OOBu^t)$. Furthermore, the results obtained with $Co^{II}(L^5)$ suggest that the dehydrogenation with the present TBHP/Co^{II}(SB) system does not include the coordination of **1a** to the Co^{III} center.

Hammett plots of relative rate ($\log V_X/V_H$), determined by the competition reaction between **1a** and **1b**-**1d** for the oxidation with the TBHP/$Co^{II}(L^1)$ system, against the σ^+ values gave a straight line ($\rho = -1.1$), where V_X and V_H refer to the rates of **1b**-**1d** and **1a**, respectively (Fig.1). The results support the mechanism involving electron transfer from the nitrogen atom of the substrate. Similar results are also obtained with the O_2/$Co^{II}(L^1)$ system ($\rho = -1.8$ against σ^+).6) Time dependent dehydrogenations of *p*-substituted benzylaniline **1** (X = H, Y= MeO, Me, H, Cl, NO_2) and *N*-*t*-butyl-*p*-substituted benzylamine **6** (Y = MeO, Me, H, Cl, NO_2) showed almost no substituent effect.

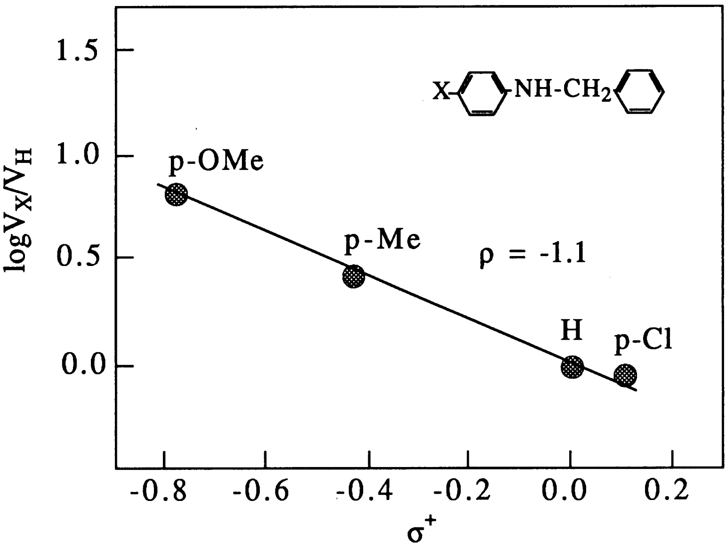


Fig.1. Hammett plots for the $Co^{II}(L^1)$ catalyzed oxidation of **1** (Y=H) with TBHP. Conditions: [1] = 50 mM, $[Co^{II}(L^1)]$ = 10 mM, [TBHP] = 125 mM in DMSO; 40 ± 0.1 °C.

From all these findings, the proposed mechanism involves electron transfer from the nitrogen atom in the substrate to *t*-butyloxyl or *t*-butylperoxyl radical generated from the decomposition of a *t*-butylperoxocobalt(III) complex formed *in situ*. A small value of deuterium isotope effect k_H/k_D = 1.3 observed for the oxidation of $PhNHCD_2Ph$ and the fact that the oxidation of *N*,*N*-dimethylaniline by the TBHP/$Co^{II}(L^1)$ system gave *N*-*t*-butylperoxy-*N*-methylaniline, *N*-methylformanilide, and *N*-methylaniline also support this mechanism.

References

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