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Co(salen) Catalyzed Oxidation of 2,4,6-Trisubstituted Anilines with *tert*-Butylhydroperoxide

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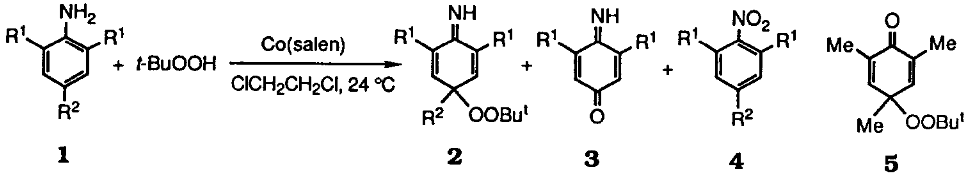
Co(salen) catalyzed oxidation of 2,4,6-trisubstituted (preferentially 2,6-di-*tert*-butylated) anilines with *tert*-butylhydroperoxide gives 4-*tert*-butylperoxy-2,5-cyclohexadien-1-imine and nitrobenzene derivatives. The relative ratio of the products depends on the nature of the substituents in the substrate.

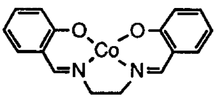
Cobalt(II) Schiff base [Co^{II}(SB)] complexes are quite interesting because of their catalytic activities in oxidation reactions.[1-3] For instance, five-coordinate Co^{II}(SB) complexes in aprotic solvents catalyze the dioxygenase type reactions of phenols, indoles, flavonols, and nitro alkanes.[4] In alcoholic solutions, on the other hand, Co^{II}(SB) complexes catalyze the monooxygenation of phenols, hydrazones, nitroalkanes, alkenes, and alkynes with molecular oxygen.[5] Furthermore, Co(salen) can catalyze the *tert*-butyl hydroperoxide oxidation of phenols giving *tert*-butylperoxyquinol ethers and of alcohols and amines leading to dehydrogenation.[6] In a general investigation of Co^{II}(SB) catalyzed oxidation reactions, we are interested in the oxidation of primary anilines. We now find that 2,4,6-trisubstituted anilines (**1**) are not susceptible to the Co^{II}(SB) catalyzed oxygenation with molecular oxygen, but are readily oxidized with *tert*-butyl hydroperoxide (TBHP) mainly to give 4-*tert*-butylperoxy-2,5-cyclohexadien-1-imines (**2**) and 2,4,6-trisubstituted nitrobenzenes (**3**).

To a solution of 2,4,6-tri-*tert*-butylaniline (**1a**)[7] (130 mg, 0.5 mmol) and Co(salen) (29.6 mg, 0.09 mmol) in 1,2-dichloroethane (DCE) (10 ml) was added TBHP (514 mg of a 70% solution in water, ca. 360 mg TBHP, 4 mmol), and the resulting mixture was stirred at 24 °C for 160 min to complete the reaction. Afterwards, it was filtered through a short neutral alumina column and eluted with DCE to remove the metal complex. The eluent was evaporated and the residue chromatographed on a basic alumina plate (Merck Al_2O_3, 60/No 1103) being developed with a mixture of DCE and hexane (1 : 6) to give 2,4,6-tri-*tert*-butyl-4-*tert*-butylperoxy-2,5-cyclohexadien-1-imine (**2a**) (54%), 2,4,6-tri-*tert*-butylnitrobenzene (**3a**) (30%), and 2,6-di-*tert*-butyl-1,4-benzoquinon-1-imine (**4**) (9%).

Similar results are obtained with other 2,4,6-trisubstituted anilines (**1**) (Table 1). Spectral and analytical data for compounds **2** and **3** are listed in Table 2. The ^{1}H-NMR signals at 1.3 ppm for the *t*-Bu group (R^1) and at 6.3 ppm for the ring protons in **2a-f** are in good agreement with those observed for 4-hydroxy-2,6-di-*tert*-butyl-2,5-cyclohexadien-1-imines.[8] The signal at around 1.2 ppm is reasonably assigned to the *t*-BuOO group as observed for 4-*tert*-butylperoxy-2,5-cyclohexadien-1-one compounds.[9] In the case of **1h** no quinolimine **2** but the quinol **5** was obtained, indicating that quinolimines of type **2** undergo hydrolysis under the reaction conditions, whereas with **2a-f** further hydrolysis of the imino group is hindered by the *t*-Bu groups in the *ortho*-positions. The analytical as well as spectral data for compounds **4** are also in good agreement with their structures (Table 2).



a: $R^1 = R^2 = t$-Bu
b: $R^1 = t$-Bu, $R^2 =$ Me
c: $R^1 = t$-Bu, $R^2 =$ OMe
d: $R^1 = t$-Bu, $R^2 =$ Ph
e: $R^1 = t$-Bu, $R^2 = 4\text{-}MeC_6H_4$
f: $R^1 = t$-Bu, $R^2 = 4\text{-}MeOC_6H_4$
g: $R^1 = t$-Bu, $R^2 =$ Mesityl
h: $R^1 = R^2 =$ Me
i: $R^1 = R^2 =$ Ph



Co(salen)

Table 1. Co(salen) catalyzed oxidation of **1** with TBHP[a]

1	Reaction Time (min)	Conversion (%)	Product Yield (%)[b] **2**	**3**	**4**
1a	160	100	54	9	30
1b	30	100	90	-	-
1c	60	91	-	79	-
1d	110	98	66	-	13
1e	480	92	65	-	23
1f	78	100	53	-	27
1g	72	100	-	10	81
1h	240	100	46(**5**)	-	50
1i	40	100	-	-	73

[a] Reaction conditions: **1** (0.5 mmol), Co(salen) (0.09 mmol), *t*-BuOOH (4 mmol) in CH_2ClCH_2Cl (10 ml) under N_2 at 23-24 °C.
[b] Isolated yield.

The product distribution (Table 1) is largely dependent on the nature of the substituents in **1**. For example, from **1b**, **c**, in which R^1 is of much larger size than R^2, *tert*-butylperoxylation occurs exclusively in the *para*-position to give **2b** or the hydrolysis product **3**. On the contrary, with **1g**, in which the size of R^2 is larger than that of R^1, the oxidation takes place predominantly at the nitrogen atom to give **4g**. When R^1 and R^2 are of equal or comparable size (**1a**, **d-f**, **h**), the products are more homogeneously distributed among types **2** and **4**. Interestingly, **1i** ($R^1 = R^2 =$ Ph) gives only **4i**, providing the first example of a selective formation of a nitro compound by the oxidation of the corresponding aniline.

These results may hypothetically be rationalized by the mechanism shown in Scheme

Table 2. Analytical data for compounds **2** and **4**

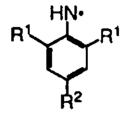
Comp.	M.p.(°C)	^{1}H NMR(CDCl$_3$) δ (ppm)				Calcd.		Found[k]
		R^1	R^2	t-BuO	=CH	Formula	N (%)	N (%)
2a	45-46	1.31[a]	0.91[d]	1.20	6.29	$C_{22}H_{39}NO_2$	4.01	4.01
2b	72-73	1.31[a]	1.27[e]	1.20	6.22	$C_{19}H_{33}NO_2$	4.56	4.46
2d	58-59	1.34[a]	7.2-7.5[f]	1.25	6.38	$C_{24}H_{35}NO_2$	3.79	3.66
2e	55-57	1.32[a]	2.31,[e] 7.1-7.6[g]	1.24	6.35	$C_{25}H_{37}NO_2$	3.65	3.66
2f	56-58	1.33[a]	3.73,[e] 7.0-7.6[g]	1.26	6.34	$C_{25}H_{37}NO_3$	3.51	3.47
4a	157-159	1.37[a]	1.32[d]		7.40[j]	$C_{18}H_{29}NO_2$	4.81	4.65
4d	80-81	1.45[a]	7.51[h]		7.63[j]	$C_{20}H_{25}NO_2$	4.50	4.11
4e	119-120	1.43[a]	2.40,[e] 7.1-7.5[g]		7.57[j]	$C_{21}H_{27}NO_2$	4.30	4.22
4f	104-105	1.45[a]	3.87,[e] 6.9-7.5[g]		7.53[j]	$C_{21}H_{27}NO_3$	4.10	3.79
4g	101-102	1.38[a]	2.03,[b] 2.33[e] 6.95[i]		7.20[j]	$C_{23}H_{31}NO_2$	3.96	3.90
4h	41-42	2.26[b]	2.29[e]		6.80[j]	$C_9H_{11}NO_2$	8.48	8.17
4i	146-147	7.3-7.5[c]			7.52[j]	$C_{24}H_{17}NO_2$	3.99	4.07

[a] t-Bu (*s*, 18H), [b] Me (*s*, 6H), [c] Ph (*m*, 15H), [d] t-Bu (*s*, 9H), [e] Me (*s*, 3H), [f] Ph (*m*, 5H), [g] C_6H_4 (*m*, 4H), [h] Ph (broad *s*, 5H), [i] C_6H_2 (*s*, 2H). [j] Aromatic protons (*s*, 2H). [k] Analytical data other than N: C, ± 0.35%; H, ± 0.20%.

1, which is similar to that proposed for the Co(salen)-catalyzed oxidation of phenols with TBHP.[9] The key species here is the intermediate aminyl radical **6**, which may be produced by the reaction of *tert*-butyloxy radical *t*-BuO• or *tert*-butylperoxy radical *t*-BuOO• with the corresponding aniline **1**, either *via* hydrogen-atom abstraction or electron-transfer to the *oxygen radicals* followed by deprotonation. The oxygen radicals themselves are formed mainly *via* eqns. (1) - (3), eqn. (3) involving decomposition of *in situ* produced Co^{III}(salen)(OOBu^t).[10]

The reaction of the aminyl radical **6** with *tert*-butylperoxy radical should give **2** and an unstable N-*tert*-butylperoxyaniline intermediate **7** which would be readily converted to a nitroso compound **8**, a good radical scavenger. The final formation of **4** may be reasonably understood by assuming the reaction of **8** with *tert*-butylperoxy radical *via* **9**. Indeed, the reaction of 2,4,6-tri-*tert*-butyl-1-nitrosobenzene with TBHP in the presence of Co(salen) in dichloromethane in a separate experiment proceeded rapidly to give **4a** in quantitative yield.[11]

Some aspects of this mechanistic hypothesis are supported by electroanalytical results. Cyclic voltammetric experiments show that anilines with R^1 = Me or *t*-Bu do not react with either Co^{II}(salen) or [Co^{III}(salen)]$^+$. Thus, a direct interaction between the catalyst and the substrate can be excluded in the case of the anilines used in this work.



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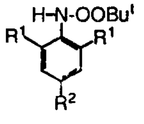

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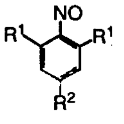

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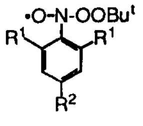

9

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\begin{array}{rcll}
\text{TBHP} + \text{Co}^{\text{II}}(\text{salen}) & \longrightarrow & \text{Co}^{\text{III}}(\text{salen})(\text{OH}) + \text{t-BuO}\bullet & (1) \\
\text{Co}^{\text{III}}(\text{salen})(\text{OH}) + \text{TBHP} & \longrightarrow & \text{Co}^{\text{III}}(\text{salen})(\text{OOBu}^{\text{t}}) + \text{H}_2\text{O} & (2) \\
\text{Co}^{\text{III}}(\text{salen})(\text{OOBu}^{\text{t}}) & \longrightarrow & \text{Co}^{\text{II}}(\text{salen}) + \text{t-BuOO}\bullet & (3) \\
\text{t-BuOO}\bullet & \longrightarrow & \text{t-BuO}\bullet + 1/2\ \text{O}_2 & (4) \\
\mathbf{1} + \text{t-BuO}\bullet & \longrightarrow & \mathbf{6} + \text{t-BuOH} & (5) \\
\mathbf{1} + \text{t-BuOO}\bullet & \longrightarrow & \mathbf{6} + \text{TBHP} & (5a) \\
\mathbf{6} + \text{t-BuOO}\bullet & \longrightarrow & \mathbf{2} + \mathbf{7} & (6) \\
\mathbf{7} & \longrightarrow & \mathbf{8} + \text{t-BuOH} & (7) \\
\mathbf{8} + \text{t-BuOO}\bullet & \longrightarrow & \mathbf{9} & (8) \\
\mathbf{9} & \longrightarrow & \mathbf{4} + \text{t-BuO}\bullet & (9)
\end{array}
$$

Scheme 1

On the other hand, upon mixing Co(salen) and TBHP in dichloromethane a transient reducible species is formed, which may be the $\text{Co}^{\text{III}}(\text{salen})(\text{OOBu}^{\text{t}})$ complex.[10] As a consequence, in the reaction described here, the catalytic activity of the cobalt complex is related to its reaction with TBHP.

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References and Notes

(1) T. Matsuura, *Tetrahedron*, **33**, 2869 (1977).
(2) A. Nishinaga and H. Tomita, *J. Mol. Catal.*, **7**, 179 (1980).
(3) E. C. Niederhoffer, J. H. Timmons, and A. E. Martell, *Chem. Rev.*, **84**, 137 (1984).
(4) A. Nishinaga, *"Protein, Nucleic Acid, and Enzymes,"* Special Issue No. **26**, Ed. by M. Kimura, A. Hanaki, T. Nakajima, Kyoritsu Shuppan Co. Ltd., Publisher, Tokyo, 1983, p. 214.
(5) A. Nishinaga, T. Yamada, H. Fujisawa, K. Ishizaki, H. Ihara, and T. Matsuura, *J. Mol. Catal.*, **48**, 249 (1988). A. Nishinaga, H. Yamato, T. Abe, K. Maruyama, and T. Matsuura, Tetrahedron Lett., 29, 6309 (1988). A. Nishinaga, *"Supramolecular Assemblies: New Developments in Biofunctional Chemistry"*, Ed. by Y. Murakami, Mita Press, Tokyo, 1990, p. 209.
(6) A. Nishinaga, I. Sugimoto, and T. Matsuura, Nippon Kagaku Kaishi, **1988**, 495. K. Maruyama, T. Kusukawa, Y. Higuchi, and A. Nishinaga, *Chem. Lett.*, **1991**, 1093; *" Dioxygen Activation and Homogeneous Catalytic Oxidation"* , Ed. L. I. Simandi, Elsevier Science Publishers B. V., Amsterdam, 1991, p. 489.
(7) H. Kessler and A. Rieker, *Justus Liebigs Ann. Chem.*, **708**, 57 (1967).
(8) J. Bracht and A. Rieker, *Synthesis*, **1977**, 708; A. Rieker and B. Speiser, *J. Org. Chem.*, **56**, 4664 (1991).
(9) A. Nishinaga, S. Yamazaki, H. Nogusa, T. Shimoyama, and T. Matsuura, *Nippon Kagaku Kaishi*, **1985**, 378.
(10) For the isolation of $\text{Co}^{\text{III}}(\text{salen})(\text{OOBu}^{\text{t}})$ in the absence of substrates, its instability in chlorinated solvents and its thermolysis into Co(salen) and t-BuOO•, see A. Nishinaga, H. Tomita, and H. Ohara, *Chem. Lett.*, **1983**, 1751.
(11) See also: K. A. Jorgensen, *J. Chem. Soc., Chem. Commun.*, **1987**, 1405.

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