A convenient synthesis of nickel(II) and cobalt(II) complexes of unsymmetrical salen-type ligands and their application as catalysts for the oxidation of 2,6-dimethylphenol and 1,5-dihydroxynaphthalene by molecular oxygen

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Salen-type ligands 1-4 have been synthesized in high yields, from which the nickel(II) complexes 9-11 and the cobalt(II) complexes 12 and 13 have been prepared and characterized. The complexes have been assessed for their ability to activate molecular oxygen in the catalytic oxidation of phenols, namely, 2,6-dimethylphenol and 1,5-dihydroxynaphthalene. The nickel complexes 9-11 are inactive in the oxidation of the phenols but the cobalt complexes 12 and 13 show high catalytic activity.

Salen-type ligands with N and O atoms are important since their metal complexes find widespread applications as homogeneous catalysts in a variety of reactions. For example, recently, metal complexes prepared from such ligands have become the focus of attention as highly active catalysts for olefin polymerization. Our present efforts are aimed at developing such catalysts for oxidation purposes, a subject of continued commercial interest.

Usually, tetradentate, salen-type chelating ligands are symmetrical and are, therefore, readily synthesized, whereas the preparation of unsymmetrical ligands is by no means trivial. However, the latter offer remarkable structural variation of the metal complexes derived therefrom, which may provide useful catalysts for the activation of molecular oxygen. For example, salen-type manganese complexes serve as activators for peroxide bleaches (percarbonates) in detergents and cleaning products. Herein, we report a convenient and efficient synthesis of some unsymmetrical salen-type ligands, in which N and O ligating atoms are comprised of amine, imine, pyridine, amide, and phenol functionalities. Nickel(II) and cobalt(II) complexes of these ligands have been prepared, characterized and evaluated for their activity as catalysts for the oxidation of phenols.

Materials and Methods

All the reagents were used as commercially supplied. Co(salen) was a generous gift from Du Pont. IR spectra were recorded on Perkin-Elmer 1420 spectrometer. ¹H and ¹³C NMR spectra were run on a Bruker AC 250 spectrometer. The melting points were determined on Büchi SMP 20 melting point apparatus. The structures of the unsymmetrical salen-type ligands are shown in Fig. 1 and their synthesis is outlined in the Schemes 1-3. The corresponding nickel and cobalt complexes are shown in Fig. 2.

Synthesis of the ligand 1

N-(2-Hydroxybenzyl)ethylenediamine (5): Salicylaldehyde (24.4 g, 0.20 mol) was added drop wise to a stirred solution of ethylenediamine (60.0 g, 1.0 mol) in methanol (100 ml) at -5 to 0°C under a nitrogen-gas atmosphere. The bright yellow solution was stirred further for 30 min. Sodium borohydride (2.3 g, 0.06 mol) was added in small lots while stirring and the colourless solution was stirred additionally for 30 min at room temperature (ca 20°C). Methanol and excess ethylenediamine were evaporated (ca 30-60°C at 10 torr) and the residual oil gave colourless needles (22.2 g, 67%) on recrystallization from ether, mp 68-69°C (lit. 4 62-63°C). ¹H NMR (CDCl₃): δ = 2.75 (m, 4H,
Fig. 1—Unsymmetrical salen-type ligands 1-4

Scheme 1—Synthesis of the salen-type ligand 1

Scheme 2—Synthesis of the salen-type ligands 2 and 3
Scheme 3—Synthesis of the salen-type ligand 4

Fig. 2—Nickel (9-11) and cobalt (12-14) complexes

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N-(2-Hydroxybenzyl)-N'-(2-hydroxybenzoyl)ethylenediamine (1): To a solution of N-(2-hydroxybenzyl)ethylenediamine (13.28 g, 0.080 mol) in methanol (100 ml) was added salicylaldehyde (9.76 g, 0.080 mol) and the mixture was refluxed under nitrogen for 30 min. Water (25 ml) was added and the clear orange solution was allowed to cool to room temperature (ca 20°C). The bright yellow flakes were collected, washed with a cold water-methanol mixture (30 ml) and dried (ca 20°C at 1 torr), to afford 19.9 g (92%); mp 107-108°C. Found: C, 71.65; H, 7.02; N, 10.42; calc. for C_{16}H_{18}N_{2}O_{2} (mol. wt. 270.3): C, 71.09; H, 6.71; N, 10.36. IR (KBr): v = 1635 (C=N), 3280 (NH) cm⁻¹. ¹H NMR (CDCl₃): δ = 2.95 (t, J = 6.0 Hz, 2H, CH₂-N), 3.95 (s, 2H, -CH₂-Ar), 6.62-7.37 (m, 8H, aryl-H), 8.32 (s, 1H, -CH=N-) ppm. ¹³C NMR (CDCl₃): δ = 48.7, 52.2, 59.4, 116.7, 117.3, 118.8, 119.1, 119.4, 122.4, 128.7, 129.1, 131.8, 132.8, 158.4, 161.1, 167.0 ppm.

Synthesis of the ligands 2 and 3

N-(2-Aminoethyl)-2-hydroxybenzamide hydrochloride (6): A solution of methyl salicylate (11.4 g, 0.075 mol) in ethanol (15 ml) was added dropwise over 45 min to ethylenediamine (18.0 g, 0.30 mol), while stirring at 100°C under a nitrogen-gas atmosphere and stirred further at this temperature for 2 h. Most of the excess ethylenediamine was evaporated (ca 60°C at 10 torr) and the residue was dissolved in water (75 ml), cooled by means of an ice-bath, and while stirring, acidified by dropwise addition of conc. HCl. The insoluble white solid (2.70 g), N,N'-bis-(2-hydroxybenzoyl)ethylenediamine, was collected and the filtrate was evaporated to give a colourless solid, which was boiled with ethanol (40 ml) and cooled to room temperature. The insoluble material, ethylenediamine dihydrochloride, was removed and washed with ethanol (2x6 ml). The solvent of the combined filtrate and washings was evaporated and the residue was crystallized from a mixture of chloroform and methanol to give pure product as colourless flakes (13.9 g, 83%), mp 152-153°C (lit. 1138-140°C). IR (KBr): v = 1645, 3200, 3420 cm⁻¹. ¹H NMR (CD₃OD-CDCl₃): δ = 3.16 (t, J = 6.0 Hz, 2H, CH₂), 3.68 (t, J = 6.0 Hz, 2H, CH₂), 6.84-7.82 (m, 4H, aryl-H) ppm.

N-(2-Hydroxybenzylidene)-N'-(2-hydroxybenzoyl)ethylenediamine (2): A mixture of N-(2-aminomethyl)-2-hydroxybenzamide hydrochloride (2.17 g, 0.01 mol), ethanol (20 ml) and 1.0 M of aqueous NaOH (10 ml, 0.01 mol) was stirred at ca 50°C to give a clear solution. Salicylaldehyde (1.22 g, 0.01 mol) was
added and the resulting yellow solution was refluxed for 1 h under a nitrogen-gas atmosphere. The solution was cooled to room temperature (ca 20°C) to give a yellow solid (2.56 g, 90%). Recrystallization from a mixture of ethanol and water gave yellow plates, mp 131-132°C. Found: C, 67.73; H, 5.80; N, 9.91; calcd for C_{16}H_{18}N_{2}O_{3} (mol. wt. 284.3): C, 67.59; H, 5.67; N, 9.85. IR (CHCl_3): v = 1600, 1630, 3460, 3690 cm⁻¹. ¹H NMR (CDCl₃): δ = 3.82 (m, 4H, -CH₂-CH₂-), 6.60 (br. s, 1H, NH), 6.77-7.41 (m, 8H, aryl-H), 8.38 (s, 1H, -N=CH-) ppm.

N-(2-Hydroxybenzoyl)ethylenediamine (2): A mixture of N-(2-aminoethyl)-2-hydroxybenzoyl benzamide hydrochloride (5.42 g, 0.025 mol), ethanol (5 ml) and 2.5 M aqueous NaOH (10 ml, 0.025 mol) were stirred at ca 50°C to give a clear solution. The 2-picolinaldehyde (2.68 g, 0.025 mol) and toluene (50 ml) were added and the mixture was heated at reflux for 7 h to remove the water by azeotropic distillation (Dean-Stark apparatus). The solution was cooled to room temperature (ca 20°C), the solid matter was removed, and the toluene evaporated (ca 40°C at 10 torr) to give 6.70 g of a greenish oil. ¹H NMR (CDCl₃): δ = 3.80 (br. s, 2H, CH₂N), 3.88 (m, 2H, CH₂), 6.49 (br. s, 1H, NH), 7.39-8.55 (m, 4H, aryl-H), 8.38 (br. s, 1H, NH) ppm.

N-(2-Pyrindinemethylen)-N'-(2-picolinyl)ethylenediamine (3): A mixture of N-(2-aminoethyl)-2-hydroxybenzoyl benzamide hydrochloride (5.42 g, 0.025 mol), ethanol (5 ml) and 2.5 M aqueous NaOH (10 ml, 0.025 mol) were stirred at ca 50°C to give a clear solution. The 2-picolinaldehyde (2.68 g, 0.025 mol) and toluene (50 ml) were added and the mixture was heated at reflux for 7 h to remove the water by azeotropic distillation (Dean-Stark apparatus). The solution was cooled to room temperature (ca 20°C), the solid matter was removed, and the toluene evaporated (ca 40°C at 10 torr) to give 6.70 g of a greenish oil. ¹H NMR (CDCl₃): δ = 3.80 (br. s, 2H, CH₂N), 3.88 (m, 2H, CH₂), 6.49 (br. s, 1H, NH), 7.39-8.55 (m, 4H, aryl-H), 8.38 (br. s, 1H, NH) ppm.

Synthesis of the ligand 4

N-(2-Acetaminoethyl)-2-pyridinecarboxamide (7): Triethylamine (3.33 g, 0.033 mol) was added drop wise over a period of 20 min to a stirred mixture of picolinic acid (3.69 g, 0.030 mol), ethyl chloroformate (3.6 g, 0.033 mol) and dichloromethane (25 ml) at ca -5°C under a nitrogen-gas atmosphere. The mixture was stirred at ca -5°C for 1 h, a solution of N-acetyl ethylenediamine (3.06 g, 0.030 mol) in dichloromethane (5 ml) was added over 15 min, and stirred at ca 0°C for 1 h and at room temperature (ca 20°C) overnight. The colorless precipitate of triethylamine hydrochloride was removed and the filtrate evaporated. The residual solid was boiled with benzene (60 ml) and the remaining triethylamine hydrochloride was removed by filtration. The benzene solution was concentrated by evaporation (ca 40°C at 10 torr) and allowed to cool to give colourless needles (4.81 g, 77%), mp 89-91°C (lit. 96-99°C). IR (KBr): ν = 1660, 3240, 3305 cm⁻¹. ¹H NMR (CDCl₃): δ = 1.95 (s, 3H, CH₃), 3.48 (m, 2H, CH₂), 3.59 (m, 2H, CH₂), 6.49 (br. s, 1H, NH), 7.39-8.55 (m, 4H, aryl-H), 8.38 (br. s, 1H, NH) ppm.

N-(2-Aminoethyl)-2-pyridinecarboxamide dihydrochloride (8): A mixture of N-(2-acetaminoethyl)-2-pyridinecarboxamide (10.36 g, 0.050 mol), ethanol (85 ml) and conc. HCl (14.7 ml) [2 M in ethanol] was stirred and refluxed under a nitrogen-gas atmosphere for 30 h. The solvent was evaporated (ca 40°C at 10 torr) and the residue recrystallized from ethanol. The colourless needles were washed with acetone (15 ml) and dried (ca 20°C at 1 torr) to afford 7.90 g (66%) of pure product, mp 246-248°C (lit. 262°C). IR (KBr): ν = 1680, 3290 cm⁻¹. ¹H NMR (D₂O): δ = 3.28 (t, J = 6.0 Hz, 2H, CH₂), 3.77 (t, J = 6.0 Hz, 2H, CH₂), 8.09-8.85 (m, 4H, aryl-H) ppm.

N-(2-Hydroxybenzylidene)-N'-(2-picolinyl)ethylenediamine (4): A mixture of N-(2-aminoethyl)-2-pyridinecarboxamide dihydrochloride (7.14 g, 0.050 mol), ethanol (25 ml) and 2.5 M aqueous NaOH (24 ml, 0.06 mol) were stirred for 5 min. Salicylaldehyde (3.66 g, 0.030 mol) was added and the solution was heated to reflux under a nitrogen-gas atmosphere for 1 h. The clear solution was allowed to cool to room temperature (ca 20°C), a yellow solid crystallized, which was washed with water (25 ml) and dried (ca 20°C at 1 torr) to afford 7.12 g (88%) of product. Recrystallization from a mixture of ethanol and water gave yellow prisms, mp 108-109°C. Found: C, 66.65; H, 5.66; N, 15.21; calcd for C_{16}H_{18}N_{2}O: C, 66.90; H, 5.62; N, 15.60.

Preparation of the metal complexes 9-13

The nickel(II) complexes 9-11 were obtained by adding to a warm (ca 60°C) solution of Ni(OAc)₂·4H₂O (1.25 g, 5.0 mmol) in water (10 ml) a solution of the particular ligand (5 mmol) in ethanol (20 ml); the resulting mixture was heated at reflux for 15 min under a nitrogen-gas atmosphere. The mixture was cooled to room temperature (ca 20°C) and the precipitate collected, washed with water (3×10 ml), and dried (100°C at 1 torr) for 6 h. The cobalt complex 12 was prepared similarly from Co(OAc)₂·4H₂O. The complex 13 was obtained by
heating ligand 12 (2.0 g) with pyridine (15 ml) at reflux under a nitrogen-gas atmosphere, followed by cooling the clear solution to room temperature (ca. 20°C). The precipitate was collected and dried (100°C at 1 torr) for 6 h.

**Procedure for the catalytic oxidations**

The particular substrate (0.5 mmol) was added to a solution of the metal complex (0.050 mmol) in acetonitrile (15 ml) and stirred under an oxygen-gas atmosphere (balloon) at ambient temperature (ca. 20°C). The solvent was evaporated (ca. 35°C at 10 torr) and the oxidation products isolated by silica-gel chromatography and characterized by \(^1\)H NMR spectroscopy.

**Results and Discussion**

The targeted unsymmetrical salen-type ligands 1-4 are given in Fig. 1. The dihydrosalen ligand 1 is conveniently synthesized as shown in Scheme 1. Salicylaldehyde was treated with an excess of ethylenediamine and the half-salen intermediate was reduced in situ with sodium borohydride to give \(N\)-(2-hydroxybenzyl)ethylenediamine (5). This procedure for the preparation of 5 is more convenient than the earlier reported one, which uses sodium cyanoborohydride. Condensation of 5 with type ligand 2 in high yield was prepared by modification of the earlier reported procedure. Condensation of the free base of 6 with pyridine carboxaldehyde required forcing conditions.

Salicylaldehyde was treated with an excess of for the preparation of 5 is more convenient than the ethylenediamine and the half-salen intermediate was conveniently synthesized as shown in Scheme 1. Salicylaldehyde proceeded smoothly to give the dihydrosalen 1, which uses sodium cyanoborohydride. Condensation of 5 with \(N\)-(2-aminoethyl)-2-hydroxybenzyl)ethylenediamine (5). This procedure for the preparation of 5 is more convenient than the earlier reported one, which uses sodium cyanoborohydride. Condensation of 5 with salicylaldehyde gave the dihydrosalen 1.

The unsymmetrical salen-type ligand 2 possesses phenolic hydroxy, amide and imine functionalities, whereas 3 bears an additional pyridine group. The synthesis of these compounds is shown in the Scheme 2. The common intermediate, namely \(N\)-(2-aminoethyl)-2-hydroxybenzamide hydrochloride (6) was prepared by modification of the earlier reported procedure. Condensation of the free base of 6 with salicylaldehyde proceeded smoothly to give the salen-type ligand 2 in high yield.

The condensation of the free base of 6 with pyridine carboxaldehyde required forcing conditions. Thus, the reaction in refluxing toluene with azeotropic removal of water gave 3 as an oil in high yield, whose structure was confirmed by \(^1\)H NMR spectroscopy. However, its purification presented problems, since chromatography on silica gel and neutral or basic alumina resulted in partial degradation to pyridine carboxaldehyde.

The novel ligand 4, which contains a phenolic hydroxy group and three different ligating nitrogen atoms, i.e., the imine, pyridine and amide functionalities, was prepared according to sequence given in Scheme 3. \(N\)-(2-Aminoethyl)-2-pyridine carboxamide dihydrochloride (8) was obtained from pyridine-2-carboxylic acid by a slight modification of the reported procedure. Neutralization of the amide 8 with alkali, followed by condensation with salicylaldehyde, gave the salen-type ligand 4 in high yield. The substances 1-4 were characterized by \(^1\)H and \(^{13}\)C NMR and IR spectra and gave satisfactory elemental analyses with the exception of 3. The latter is an oil at ambient temperature and, as already stated above, could not be purified by chromatography, but its \(^1\)H NMR spectrum supports the assigned structure.

The salen-type ligands 1, 2 and 4 gave on treatment with nickel(II) acetate tetrahydrate the corresponding metal complexes 9-11 (Fig. 2) in high yield. Similarly, the cobalt complex 12 was obtained from the ligand 1 and cobalt acetate tetrahydrate. However, when this procedure was used in the preparation of the cobalt complexes derived from the ligands 2 and 4, unexpectedly, a complex mixture was obtained, from which definitive product could not be identified. The cobalt complex 13 was prepared from 12 by treatment with pyridine. The physical properties and analytical data of the complexes are listed in Table 1.

Activation of molecular oxygen by transition metals for the catalytic oxidation of organic substrates has been of continued interest in organic synthesis and also to understand biological oxidation.

<table>
<thead>
<tr>
<th>Complex (Mol. Formula)</th>
<th>Yield</th>
<th>Colour</th>
<th>Mp (°C)</th>
<th>IR cm(^{-1})</th>
<th>Found (Calculated) (%)</th>
<th>C</th>
<th>H</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>9 ((C_{16}H_{10}N_{2}O_{2}))</td>
<td>88</td>
<td>Orange</td>
<td>&gt; 250</td>
<td>1640</td>
<td>59.00</td>
<td>(58.77)</td>
<td>(4.93)</td>
<td>(8.57)</td>
</tr>
<tr>
<td>10 ((C_{16}H_{12}N_{2}O_{2}))</td>
<td>85</td>
<td>Yellow</td>
<td>192-195</td>
<td>1630</td>
<td>56.79</td>
<td>56.36</td>
<td>(4.14)</td>
<td>(8.22)</td>
</tr>
<tr>
<td>11 ((C_{16}H_{12}N_{2}O_{2}))</td>
<td>90</td>
<td>Orange</td>
<td>202-205</td>
<td>1610</td>
<td>55.22</td>
<td>55.27</td>
<td>(4.02)</td>
<td>(12.89)</td>
</tr>
<tr>
<td>12 ((C_{16}H_{12}N_{2}O_{2}))</td>
<td>72</td>
<td>Dark Brown</td>
<td>&gt; 250</td>
<td>1600</td>
<td>55.16</td>
<td>55.66</td>
<td>(5.26)</td>
<td>(8.06)</td>
</tr>
<tr>
<td>13 ((C_{16}H_{12}CoN_{2}O_{2}))</td>
<td>75</td>
<td>Red</td>
<td>&gt; 250</td>
<td>1570</td>
<td>61.98</td>
<td>(62.07)</td>
<td>(5.21)</td>
<td>(10.34)</td>
</tr>
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</table>
ADAM et al.: SYNTHESIS OF Ni(II) & Co(II) COMPLEXES OF SALEN-TYPE LIGANDS

Table 2—Oxidation of 2,6-dimethylphenol and 1,5-dihydroxynaphthalene with molecular oxygen, catalyzed by cobalt complexes 12-14

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Substrate</th>
<th>Convn (%)</th>
<th>Product (Yield) (%)</th>
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<tr>
<td>12</td>
<td>OH</td>
<td>73</td>
<td>(97)</td>
</tr>
<tr>
<td>13</td>
<td></td>
<td>82</td>
<td>(99)</td>
</tr>
<tr>
<td>14</td>
<td></td>
<td>87</td>
<td>(99)</td>
</tr>
<tr>
<td>12</td>
<td>OH</td>
<td>100</td>
<td>(65)</td>
</tr>
<tr>
<td>13</td>
<td></td>
<td>100</td>
<td>(72)</td>
</tr>
<tr>
<td>14</td>
<td></td>
<td>100</td>
<td>(78)</td>
</tr>
</tbody>
</table>

Catalyst:substrate mol ratio was 1:10; stirred in acetonitrile at ambient temperature (ca 20°C) in the presence of O₂ for 7 h. Based on converted material.

processes. For this purpose, Schiff-base metal complexes with salen ligands are well-known to activate molecular oxygen and catalyze the oxidation of electron-rich substrates such as phenols, activated olefins, amines and hydrazones.

In the past, much effort has been expended to improve the catalytic oxidative activity of such metal complexes by variation of the ligand structures. In this context, we have evaluated the salen-type nickel and cobalt complexes for their ability to activate molecular oxygen and whether they may serve as catalysts for the oxidation of phenols. We chose 2,6-dimethylphenol and 1,5-dihydroxynaphthalene as substrates for this purpose. The substrate was stirred under an atmosphere of molecular oxygen in an acetonitrile solution of the metal complex (10 mol %). The results are shown in the Table 2.

Analogous to the parent nickel(II) salen complex, which unfortunately does not activate molecular oxygen, the salen-type nickel complexes were inactive for the oxidation of 2,6-dimethylphenol by oxygen. Polar solvents are known to facilitate the reaction by stabilizing the metal-dioxygen adduct, however, dimethyl formamide in place of acetonitrile also failed to give any oxidation products. Addition of two equivalents of pyridine also did not help to promote oxidative activity.

In contrast, the oxidation of 2,6-dimethylphenol with the cobalt complex gave a high yield of the corresponding benzoquinone and a small quantity of the radical-coupling product, namely, dibenzoquinone. Oxidation by the cobalt complex with an axial pyridine ligand gave improved conversion and a high yield of benzoquinone. For comparison, under these reaction conditions, the salen-type derivatives (Table 2) perform at least as well as the parent Co(salen). Similarly, the oxidation of 1,5-dihydroxynaphthalene with molecular oxygen by cobalt catalysts afforded juglone as oxidation product in high yields.

In summary, a set of unsymmetrical salen-type ligands with a variety of nitrogen-based
functionalities has been made available for the coordination of transition-metal ions. The cobalt complexes serve as effective catalyst for the oxidation of phenols by molecular oxygen.

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References

9 Nestler B, US Pat. 5969171 (to Clariant GmbH) 19 October 1999; Chem Abstr, 130 (1999) 11871; no preparative details have been given.