# Synthesis and first X-ray structures of cobalt(II) and cobalt(III) complexes bearing 2,4-dioxo-alkanoic acid dialkylamide ligands<sup>1</sup>

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Abstract: The aerobic oxidation of 5-hydroxy pentenes to *trans*-tetrahydrofurans (THFs), the Mukaiyama oxidation, has in recent years emerged as a powerful tool in synthetic chemistry. In this report we describe the first crystal structures of 2,4-dioxo-alkanoic acid dialkylamide complexes for both Co(II) and Co(III) salts. The Co(II) structures show an unprecedented arrangement of atoms, with a central Co(II)( $H_2O_{6}$  flanked by two Co(II) atoms each coordinated with three anionic chelating ligands. The dimeric Co(III) structures show two anionic chelating ligands and bridging hydroxyl groups.

Key words: aerobic oxidation, trans-tetrahydrofuran (THF), cobalt, X-ray crystallography, oxidation, coordination.

**Résumé :** L'oxydation aérobique de 5-hydroxypentènes en *trans*-tétrahydrofuranes (THF), l'oxydation de Mukaiyama, est devenue au cours des années récentes un outil puissant. Dans ce travail, on décrit les structures cristallines de sels complexes de Co(II) et de Co(III) de dialkyamides de l'acide 2,4-dioxoalcanoïque. Les structures des sels du Co(II) présentent un arrangement d'atomes, inconnu jusqu'à maintenant, comportant un groupe central Co(II)(H<sub>2</sub>O)<sub>6</sub> flanqué de deux atomes de Co(II) qui sont chacun liés à trois ligands chélatants anioniques. Les structures dimères du Co(III) comportent deux ligands chélatants anioniques et des groupes hydroxyles servant de ponts.

Mots-clés : oxydation aérobique, THF, cobalt, diffraction des rayons X, oxydation, coordination.

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# Introduction

2,4-dioxo-alkanoic Co(III) complexes of acid dialkylamides are useful catalysts for the aerobic oxidation of olefins to peroxides or alcohols (1-5) and for the oxidative cyclization of 5-hydroxy pentenes to tetrahydrofurans (THFs) (6). In recent years, the stereoselective aerobic oxidation of 5-hydroxy pentenes to trans-THFs (henceforth the Mukiayama oxidation, Scheme 1) has emerged as a powerful tool in organic synthesis and has been strategically employed in the total synthesis of natural products by the groups of Wang et al. (7), Takahashi et al. (8), Evans et al. (9), and Pagenkopf and co-workers (10). Surprisingly, despite the obvious synthetic importance of these catalysts, there is little structural information available on transition metal 2,4-dioxo amide complexes, and to the best of our knowledge no X-ray structures of these species have been

Scheme 1. Representative Mukaiyama oxidation.



reported. In this paper we describe crystal structures of two Co(II) complexes and one Co(III) complex.

#### **Experimental**

#### General procedure for ligands 2

To a cooled (0 °C) solution of dialkylamine (10 mmol) and  $Et_3N$  (10 mmol) in  $CH_2Cl_2$  (20 mL) was added ethyl oxalyl chloride (10 mmol). After stirring at room temperature (rt) for 16 h, the reaction mixture was washed with

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Table 1. Crystallographic data collection parameters for 7, 3e, and 9.

Complex	3e	7	9
Chemical formula	C <sub>213</sub> H <sub>218</sub> Co <sub>3</sub> N <sub>6</sub> O <sub>22</sub>	C <sub>141</sub> H <sub>162</sub> Co <sub>3</sub> N <sub>6</sub> O <sub>25</sub>	$C_{98.5}H_{110}Co_2N_4O_{14}$
Formula mass	3390.72	2517.56	1691.77
Crystal dimensions (mm)	$0.32 \times 0.26 \times 0.15$	$0.50 \times 0.14 \times 0.11$	$0.53 \times 0.27 \times 0.15$
Crystal system	Triclinic	Monoclinic	Monoclinic
Space group	$P\overline{1}$	$P2_1/n$	Ia
Ζ	2	2	4
<i>a</i> (Å)	17.9663(1)	16.5500(5)	24.6233(16)
b (Å)	23.9160(2)	20.8953(6)	13.1161(9)
<i>c</i> (Å)	24.1629(2)	19.1655(6)	29.4833(19)
α (°)	67.360(1)	90	90
β (°)	85.866(1)	98.326(2)	98.3545(10)
γ (°)	84.983(1)	90	90
Volume (Å <sup>3</sup> )	9537.27(12)	6557.9(3)	9420.9 (11)
$D_{\rm calcd.} \ ({\rm mg \ cm^{-3}})$	1.181	1.275	1.193
<i>T</i> (K)	153(2)	153(2)	193(2)
Radiation	MoKα ( $\lambda = 0.71073$ )	MoK $\alpha$ ( $\lambda = 0.71073$ )	MoK $\alpha$ ( $\lambda = 0.71073$ )
$\mu (mm^{-1})$	0.324	0.448	0.414
Total reflections collected	74 396	16 105	36 466
Total unique reflections	43 644 $[R(int) = 0.0439]$	$8\ 560\ [R(int) = 0.0606]$	19 200 $[R(int) = 0.0365]$
Observed reflections $[I > 2\sigma(I)]$	16 105	74 396	15 217
$2\theta_{\text{max}}(\alpha)$	54.98	45	52.78
Goodness-of-fit on $F^2$	2.423	1.165	0.987
$R_1 \left[ I > 2\sigma(I) \right]$	0.0847	0.0602	0.0504
$wR_2$ (all data)	0.1576	0.1373	0.129
Largest diff. peak and hole (e $Å^{-3}$ )	1.103 and -0.503	0.486 and -0.320	0.557 and -0.316

UCL (2x) and NaUCO and being and then dried

1 mol/L HCl (2 $\times$ ), satd. NaHCO<sub>3</sub>, and brine and then dried (MgSO<sub>4</sub>). Concentration in vacuo gave **1** as a white solid or colorless oil in quantitative yield, which was used without further purification.

A solution of *t*-BuOK (23 g, 205 mmol, 2.1 equiv.) in THF (180 mL) was added via cannula to a solution of pinacolone (12 mL, 96 mmol, 1.0 equiv.) and amide **1a** (18 g, 96 mmol, 1.0 equiv.) in THF (40 mL) over 40 min at rt. After 3 h, AcOH (20 mL, 350 mmol, 3.6 equiv.) was added over 5 min and the resulting heterogeneous mixture was filtered and the solids were washed with  $CH_2Cl_2$ . The filtrate was washed with NaHCO<sub>3</sub> and brine, dried, filtered, and concentrated. Purification of the resulting oil by flash chromatography (SiO<sub>2</sub>, 50% EtOAc/hexanes) provided the title compound as a slightly yellow solid (18.1 g, 78%).

To a solution of 2 (7.0 mmol) in hexanes or benzene (**3a**) was added Co(II)(2-ethyl-hexanoate)<sub>2</sub> (3.5 mmol) solution in mineral spirits. The reaction mixture was stirred at rt for 8 h and hexane (ca. 70 mL) was added to induce precipitation. The solids were separated by centrifugation or filtration and washed with hexane.

Full characterization of Co(II) complexes by NMR was not possible because the salts are paramagnetic. Combustion analysis is significantly out of range because the number of water molecules within the powder varies and drying generally lead to decomposition. Attempts to record discrete melting points also lead to decomposition. Several of these complexes are known compounds, including **3a**, **3b**, and **3c** (*3a*, 11) (Table 1).

# 3a

Pink amorphous solids. MS (CI) m/z: 540 [M + H]<sup>+</sup>, 242 [ligand + H]<sup>+</sup>.

# 3b

Pink amorphous solids. MS (CI) m/z: 536 [M + H]<sup>+</sup>, 240 [ligand + H]<sup>+</sup>.

# 3c

Pink amorphous solids. MS (CI) m/z: 512 [M + H]<sup>+</sup>, 228 [ligand + H]<sup>+</sup>.

# 3d

Brownish peach colored amorphous solids. MS (CI) m/z: 760 [M + H]<sup>+</sup>.

# 3e

Red crystals. MS (CI) m/z: 1064 [M + H]<sup>+</sup>.

# 4

Pink amorphous solids. MS (CI) m/z: 676 [M + H]<sup>+</sup>.

# 5

Reddish brown brittle foam. MS (CI) m/z: 732 [M + H]<sup>+</sup>.

7

Red crystals. MS (CI) m/z: 732 [M + H]<sup>+</sup>.

# Synthesis and characterization of 9

To a mixture of **3d** (0.76 g, 1 mmol, 1.0 equiv.) in acetone (20 mL) was added  $30\% \text{ w/w} \text{ H}_2\text{O}_2$  (1.2 mL, 10 mmol,

Scheme 2. Synthesis of Co(II) complexes.



10 equiv.) at rt. After 15 h, the solution was concentrated under reduced pressure. TLC showed that the residue showed numerous spots. Flash chromatography over silica gel (25% EtOAc/hexanes) allowed separation of at least six distinct bands, one of which ( $R_f = 0.25$ , 40% EtOAc/hexanes) provided material that eventually crystallized. The crystal for X-ray analysis was grown from a vapor diffusion chamber containing EtOAc, toluene, and hexanes. <sup>1</sup>H NMR (600 MHz,  $C_6D_6$ )  $\delta$ : 7.43 (d, J = 7.3 Hz, 4H), 7.24–7.20 (m, 8H), 7.15–7.08 (m, 8H), 7.00 (d, J = 7.1 Hz, 4H), 6.88–6.81 (m, 10H), 6.75 (t, J = 7.50, 4H), 6.53 (s, 2H), 6.34 (s, 2H), 6.26 (t, J = 7.3 Hz, 2H), 5.58 (d, J = 14.5 Hz, 2H), 5.29 (d, J = 15.4 Hz, 2H), 5.20 (d, J = 14.1 Hz, 2H), 4.28 (d, J =16.8 Hz, 2H), 3.44-3.38 (m, 6H), 3.02 (d, J = 16.5 Hz, 2H), 1.26 (s, 18H), 1.01 (s, 18H), -3.39 (s, 1H), -3.72 (s, 1H). <sup>59</sup>Co NMR (144 MHz,  $C_6D_6$ )  $\delta$ : 13364 (brs). Combustion calcd.: C 67.28, H 6.31, N 3.62; found: C 68.03, H 6.36, N 3.62.

# **Results and discussion**

#### **Cobalt(II) structures**

Our initial efforts to employ the Mukaiyama oxidation in synthesis were complicated by fickle oxidation results as a consequence of inconsistent purity of the Co(II) complex. The first reports on Co(II) 2,4-dioxo-alkanoic acid amide complexes utilized CoCl<sub>2</sub> under aqueous alkaline conditions, but we found that such conditions caused decomposition of the morpholine amide 2a (Scheme 2). The result was that the preparation of catalyst 3a under the aqueous conditions provided a highly contaminated amorphous brown solid and attempts at purification proved fruitless. However, these difficulties were overcome by complexation under neutral conditions in organic solvent. When a solution of the free ligand 2a in benzene was treated with 0.5 equiv. of Co(II)(2-ethyl hexanoate)<sub>2</sub>, the initial dark blue color quickly dissipated and the resulting red solution was treated with hexane to precipitate the complex 3a.

Table 2. Preparation of Co(II) complexes.

Entry	Co(II) Complex	#	Yield <sup>a</sup>
1		<b>3</b> a	99%
2	$Co(II) \left( \begin{array}{c} 0 & \Theta_{0} \\ 0 & 0 \\ 0 & 0 \end{array} \right)_{2}$	3b	75%
3		3c	59%
4	$Co(II) \left( \begin{array}{c} O & O \\ O & O$	3d	59%
5	$Co(II) \left( \begin{array}{c} O & O \\ O & O$	4	99% <sup>b</sup>
6	$Co(II) \left( \begin{array}{c} O & O \\ I & I \\ I & I \\ I \\ O \end{array} \right)_2$	5	27%
7	$Co(II) \begin{pmatrix} O & O \\ Ph & V \end{pmatrix} \begin{pmatrix} Ph \\ Ph & V \end{pmatrix}_2$	6	45%
8	$Co(II) \left( \begin{array}{c} O & O \\ O & O \\ H & O \end{array} \right)_{Me} \left( \begin{array}{c} O & Ph \\ N & Ph \\ N & Ph \end{array} \right)_{2}$	7	76%
9	$Co(II) \left( \begin{array}{c} \Theta \\ \Theta $	3e	23%

Note: The compounds shown are representative of the metal to ligand stoichiometry only, and are not meant to imply structure.

<sup>a</sup>Unoptimized yields of complexation.

<sup>b</sup>Poor solubility.

This modified procedure proved effective for the preparation of a variety of 2,4-dioxo amide complexes and these results are summarized in Table 2. Replacement of the morpholine with piperidine (**3b**), diethylamine (**3c**), or dibenzyl amine (**3d**) gave complexes as microcrystalline pink powders unsuitable for single crystal X-ray analysis. Of these, the dibenzyl amide **3d** displayed the most promising crystalline character, and in entries 5–7 of Table 2 the dibenzyl amide portion of the ligand was conserved while substitutions were made in place of the *tert*-butyl group. The methyl (**4**), isopropyl (**5**), and phenyl (**6**) analogs of **3d** were each prepared successfully, but they too failed to give crystals suitable for X-ray analysis.

A more substantial change was made by installing a methyl group at C(3) and, gratifyingly, the complex 7 was obtained as red crystals and the unusual X-ray structure of 7 is shown in Fig. 1.<sup>5</sup> Selected bond lengths and angles are reported in Table 3. There are three cobalt atoms present in the

<sup>&</sup>lt;sup>5</sup>Supplementary data for this article are available on the journal Web site (canjchem.nrc.ca) or may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, ON K1A 0R6, Canada. DUD 3859. For more information on obtaining material refer to cisti-icist.nrc-cnrc.gc.ca/cms/unpub\_e.shtml. CCDC 203707 (7), 679940 (3e), and 203708 (9) contain the crystallographic data for this manuscript. These data can be obtained, free of charge, via www.ccdc.cam.ac.uk/conts/retriev-ing.html (Or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax +44 1223 336033; or deposit@ccdc.cam.ac.uk).

Fig. 1. (a) View of the complex 7,  $[(C_{21}H_{22}NO_3)_3Co]_2$ -Co(H<sub>2</sub>O)<sub>6</sub>. The complex resides on a crystallographic inversion center at  $\frac{1}{2}$ ,  $\frac{1}{2}$ ,  $\frac{1}{2}$  with Co(H<sub>2</sub>O)<sub>6</sub> at the center, which bridges a pair of (C<sub>21</sub>H<sub>22</sub>NO<sub>3</sub>)<sub>3</sub>Co complexes via O-H···O hydrogen bonds (12). (b) View of 7 showing a single Co-ligand assembly and the central  $Co(H_2O)_6$  with selected atoms labeled. Displacement ellipsoids are scaled to the 30% probability level. Hydrogen atoms and aromatic groups have been removed for clarity.





unit cell, each separated by 4.870 Å. The two outer cobalt atoms are each surrounded by three dioxoamide ligands and their negative charge is balanced by a central  $Co(II)(H_2O)_6$ . The dihedral angle between the amide carbonyl and the acac-like plane is  $118(1)^{\circ}$ , which might be expected to minimize A(1,3) strain with the C(3) methyl group. The unfavorable A(1,3) interaction was also evident in the <sup>1</sup>H NMR spectra of the metal-free ligand  $\mathbf{8}$ , which in CDCl<sub>3</sub> existed as a 1:1 ratio of both the keto and enol forms (Scheme 3). In contrast, the preceding ligands existed primarily in the enol form. The distinctly different structure and behavior of ligand 8 compared with the others caused concern that the structure of 7 may be unique and not representative of the series.

To address concerns that the C(3) methyl may have lead to a structural anomaly, additional complexes more closely resembling 3d were prepared. Of these, the biphenyl analog 3e (Table 2, entry 9) formed crystals suitable for X-ray analysis (Fig. 2). Importantly, the major features of the two structures are conserved, including the arrangement of the three cobalt atoms and the angle of the amide. A minor difference is that the central cobalt in 3e is surrounded by only **Fig. 2.** View of the H-bound complex **3e**,  $[(C_{34}H_{32}NO_3)_3Co]_2$ -Co(H<sub>2</sub>O)<sub>3</sub>, showing the labeling scheme for selected atoms (12). Displacement ellipsoids are scaled to the 30% probability level. Hydrogen atoms and the aromatic groups have been removed for clarity. The three water molecules of the bis Co complex are H-bound to carbonyl oxygen atoms of the adjacent mono Co complex.



Table 3. Selected bond lengths and angles for 7.

Bond lengths (Å)	
C(45)-C(46)	1.450(7)
C(45)–O(7)	1.246(6)
C(46)-C(48)	1.367(7)
C(48)–C(49)	1.535(7)
C(48)–O(8)	1.287(5)
C(49)–O(9)	1.236(6)
C(49)–N(2)	1.339(6)
Co(1)–O(7)	2.021(4)
Co(1)–O(8)	2.075(3)
N(2)-C(57)	1.471(6)
Bond angles (°)	
O(7)-C(45)-C(46)	124.3(5)
C(48)-C(46)-C(45)	121.4(5)
O(8)-C(48)-C(46)	129.2(4)
C(45)-O(7)-Co(1)	132.2(3)
C(48)-O(8)-Co(1)	125.9(3)
O(7)-Co(1)-O(8)	85.73(13)

Scheme 3. Equilibrium disfavors the enol form.



three water molecules, with the coordination sphere being fulfilled by dative bonding from a neighboring ligand. The distance between Co(1) and Co(2) was found to be 4.980 Å, Co(2) and Co(3) are separated by 2.926 Å. Bond lengths and angles of significance are reported in Table 4.

 Table 4. Selected bond lengths and angles for 3e.

Bond lengths (Å)	
Co(3)–O(31)	2.058(2)
Co(3)–O(34)	2.091(2)
C(32d)–C(33)	1.407(4)
C(30d)–C(32)	1.379(4)
C(30d)–O(31)	1.285(3)
C(29)–O(30)	1.236(4)
C(29)–C(30)	1.515(4)
N(1)-C(2)	1.468(4)
N(1)-C(29)	1.349(4)
C(33)–O(34)	1.250(4)
Bond angles (°)	
C(33)-O(34)-Co(3)	125.1(2)
C(30)-O(31)-Co(3)	120.78(9)
O(31)-Co(3)-O(34)	86.88(8)
O(34)-C(33)-C(32)	123.4(3)
O(31)-C(30)-C(32)	127.4(3)
C(30)-C(32)-C(33)	125.8(3)

In both X-ray structures there are neutral donors, including water, surrounding the central cobalt atom. The reactions were run under an argon atmosphere using undried bulk solvents and this was presumably the origin of the water. To determine if additional water would facilitate crystallization, several complexation reactions were simply performed open to air. Remarkably, the preparation of **3d** under these conditions gave larger crystals that were easily obtained by filtration (instead of centrifugation). Importantly, no oxidation to Co(III) was observed under these conditions (TLC), whereas the analogous Co(acac)<sub>2</sub> species oxidize more readily. **Fig. 3.** View of the complex **9**,  $[(C_{34}H_{32}NO_3)_3Co]_2(\mu-OH)_2$ , showing the labeling scheme for selected atoms (12). Nonhydrogen atoms are represented by Gaussian ellipsoids at the 30% probability level. Hydroxyl group hydrogen atoms are shown with arbitrarily small thermal parameters; all other hydrogens and aromatic groups have been removed for clarity.



# Cobalt(III) structure

Obtaining structural information about the Co(III) complexes (which are generated in situ for the Mukaiyama oxidation) might be more helpful in speculating about the nature of the active catalytic species. However, the Co(III) complexes are generally obtained as green oils or glasses. Efforts to grow crystals at -20 °C were promising, but the resultant crystals were not of suitable quality for X-ray analysis. The Co(III) complexes are stable to flash chromatography on silica gel and the complexes elute as numerous bands, some of which are readily separable while others are overlapping. We speculated one origin of these different bands to be diastereomeric complexation, and when separated the individual diastereomers might crystallize more easily. At rt individually eluted bands isomerize within a day or two to multiple species, as monitored by TLC. However, at -20 °C the isomerization is slowed dramatically and crystals suitable for X-ray crystallography were obtained from one of the more polar bands ( $R_f = 0.25$ , 40% EtOAc/hexanes) of compound 9 (the oxidized version of 3d) (Fig. 3). In this binuclear cluster, the two central cobalt atoms are bridged by two hydroxyl groups and each cobalt is surrounded by two chelating ligands. Significant bond lengths and angles have been summarized in Table 5.

#### Use of crystals in oxidative cyclizations

All of the new complexes reported in Table 2 possess some catalytic activity for the oxidation of  $\gamma$ -hydroxyl olefins to tetrahydrofurans. The complexes **3a** and **3d** have emerged as particularly useful catalysts and the decision to employ one versus the other is influenced by product polarity and chromatographic characteristics. Crystals of **9** were dissolved in *i*PrOH and appeared as a single spot by TLC. These crystals successfully catalyzed the oxidation shown in

Table 5. Selected bond lengths and angles for 9.

Bond lengths (Å)	
Co(1)–O(1)	1.903(2)
Co(1)-O(2)	1.904(2)
Co(1)-O(11)	1.888(2)
Co(1)-O(12)	1.887(2)
Co(2)–O(1)	1.903(2)
Co(2)–O(2)	1.918(2)
O(12)–C(13)	1.254(4)
O(11)–C(11)	1.284(4)
O(10)-C(10)	1.234(4)
C(12)–C(13)	1.415(4)
C(11)–C(12)	1.351(5)
C(10)–C(11)	1.541(4)
N(10)–C(10)	1.321(4)
N(10)–C(18)	1.486(4)
Bond angles (°)	
O(1)-Co(1)-O(2)	81.73(9)
O(1)-Co(1)-O(11)	174.77(10)
O(1)-Co(1)-O(12)	89.52(9)
Co(1)-O(1)-Co(2)	98.74(10)
Co(1)-O(2)-Co(2)	98.17(10)
Co(1)-O(11)-C(11)	120.3(2)
Co(1)-O(12)-C(13)	124.1(2)
O(12)-C(13)-C(12)	124.6(3)
O(11)-C(11)-C(12)	128.9(3)
C(11)-C(12)-C(13)	122.4(3)

Scheme 1 (1 atm  $O_2$ , *i*PrOH, 50 °C, 16 h) in yields typically ranging from 70%–90%. Some spots isolated from the Co(III) species via chromatography were found to be inac-

tive under standard Mukaiyama oxidation conditions. Investigations are currently underway to determine the structural differences between the active and inactive Co(III) complexes.

# Conclusions

A modified synthesis for the preparation of Co(II) complexes bearing 2,4-dioxo-alkanoic acid dialkylamide ligands has been reported and the resulting complexes are better precatalysts for the Mukaiyama oxidation compared with those prepared under aqueous alkaline conditions. X-ray structures for two of the Co(II) complexes have been solved and they revealed a unique arrangement of cobalt atoms in the unit cell, where two anionic clusters each containing one Co(II) atom surrounded by three negatively charged dioxoamide ligands flank a central Co(II) atom with neutral donors. Oxidation of the Co(II) salts with  $H_2O_2$  gave green oils or glasses. Separation of the slowly equilibrating mixtures by flash chromatography on silica gel resulted in the isolation of a single diastereomer that lead to crystals suitable for X-ray analysis.

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