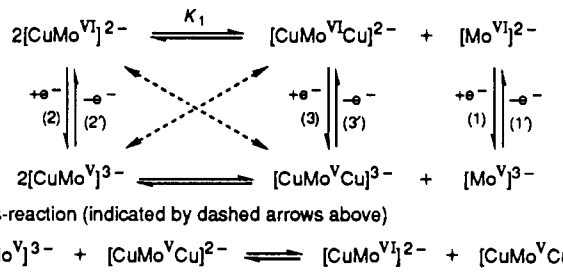
Scheme I. Redox Interconversions[a]



cross-reaction (indicated by dashed arrows above)

$$[CuMo^{V}]^{3-} + [CuMo^{V}Cu]^{2-} \rightleftharpoons [CuMo^{VI}]^{2-} + [CuMo^{V}Cu]^{3-}$$

[a] For simplicity the four sulfur atoms are omitted from each formula.

with the proposed chemical reactions 2–4 being coupled to the reduction processes listed in Table I.

Detailed interpretation is complicated by the presence of equilibrium 1 and the influence of redox cross-reactions. For example, the wave shapes observed for couple (3, 3′) in Figure 3 strongly suggest the presence of such processes. Although the present data at slow scan rates (where the kinetic effects of the following chemical reactions are observed) do not allow quantitative mechanistic interpretation of these effects, it does provide a qualitative indication of the nature of the following chemical reactions. The complexity of the system is illustrated by Scheme I, which details the possible redox interconversions, including cross-reactions.

On the other hand, the fast scan rate data provide a complete thermodynamic description for the six well-defined one-electron couples observed in the present system (Table I).

Acknowledgment. The Wool Research and Development Fund administered by the Australian Wool Corp. is thanked for financial support.

Supplementary Material Available: Figures S1–S3, showing cyclic voltammograms, and Tables S1–S11, listing cyclic voltammetry data for Fc^{+}/Fc, $[MoS_4]^{2-/3-}$ (1, 1′), $[(CN)CuS_2WS_2Cu(CN)]^{2-/3-}$ (3, 3′ and 8, 8′), and $[(CN)CuS_2MS_2]^{2-/3-}$ (2, 2′ and 7, 7′) and rotating disk electrode voltammetry data (i_L versus $\omega^{1/2}$) for processes 1–3 (14 pages). Ordering information is given on any current masthead page.

Contribution from Chemistry Department I, University of Copenhagen, Universitetsparken 5, DK-2100 Copenhagen Ø, Denmark, and Research School of Chemistry, The Australian National University, G.P.O. Box 4, Canberra, ACT 2601, Australia

Oxidation of Chelated Amino Acids to Imine Derivatives with Thionyl Chloride

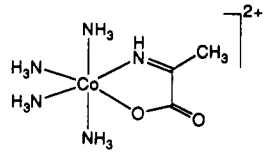
Anders Hammershøi,*[1a] Richard M. Hartshorn,*[1b] and Alan M. Sargeson*[1b]

Received December 27, 1989

Various (α-amino acidato)cobalt(III) complexes have been treated with $SOCl_2$ in DMF. Provided the amino acid side chain does not contain functionalities that react with $SOCl_2$, the complex undergoes a facile oxidation to give the related α-imino acidato complex. A mechanism is proposed for these reactions.

Introduction

A considerable body of literature now exists on the enhanced reactivity of coordinated molecules toward both inter- and intramolecular nucleophiles.[2,3] The activating effect has been attributed to the ability of the metal ions to polarize bonds in the ligand, thus making it more susceptible toward attack by nucleophiles. For instance, the hydrolysis of acetonitrile is enhanced $\geq 10^6$-fold on coordination to cobalt(III), rhodium(III), and iridium(III). Moreover, the effect extends to the reduction of coordinated nitriles, which has been achieved by BH_4^-,[5] while a similar reduction of the free nitrile requires a considerably more potent reducing agent such as $LiAlH_4$. Coordinated imines are similarly activated, so that the nitromethane anion rapidly adds to the 2-iminopropionato complex **1** to give chelated α-nitro-



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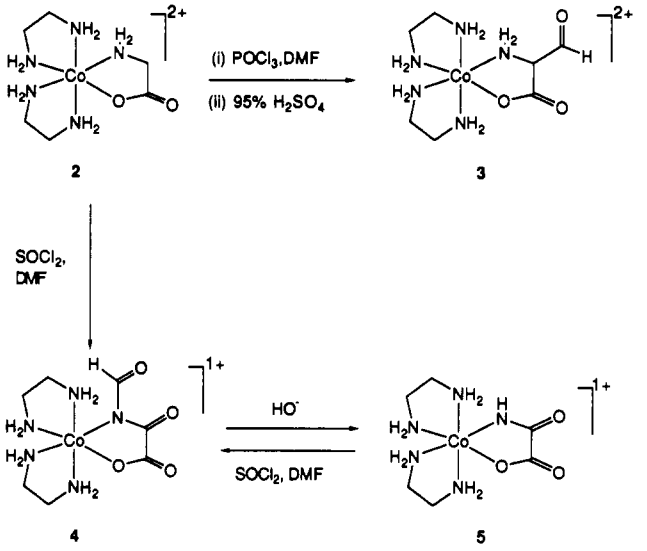
methylalanine.[4] It was considered for some time that this increased reactivity of coordinated ligands toward nucleophiles would be accompanied by a corresponding decrease in reactivity toward electrophiles. For this reason much effort has been spent investigating the reactions of coordinated ligands with nucleophiles, while not much has been done on reactions with highly electrophilic reagents, despite the fact that the metal ions may be employed to protect some sites and activate others in a ligand. Work using the Vilsmeier–Haack adduct derived from $POCl_3$ and DMF indicates that the metal ion can influence such electrophilic reactions in a useful way,[6–8] and presumably other electrophiles would also

Scheme I



2 **3** **4** **5**

(1) (a) University of Copenhagen. (b) The Australian National University.
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0020-1669/90/1329-4525$02.50/0

have interesting properties. This paper explores the reactions of $SOCl_2$, a highly electrophilic reagent, with coordinated amino acid ligands.

Bidentate N,O-attachment of an α-amino acid to a metal center such as cobalt(III) serves to protect the ligating groups and to activate the proton(s) on the α-carbon atom. By coordinating to the metal ion, the amine nitrogen atom gains some ammonium ion character. In addition, the metal-bound carboxylate ion has some ester character, and these two features, together with the higher positive charge of the complex overall, combine to activate the proton(s) on the adjacent carbon atom.[9,10] Carbanion formation is thereby facilitated. Thus, treatment of the glycinato complex $[Co(en)_2(Gly)]^{2+}$ (**2**) with $POCl_3$ in DMF followed by hydrolysis introduces a formyl group in a Vilsmeier–Haack-type formylation reaction.[6-8] If chiral starting material is used, then the resulting *C*-formylglycinato complex **3** constitutes a useful starting point for stereospecific synthesis of C-3-modified alanine derivatives.[8]

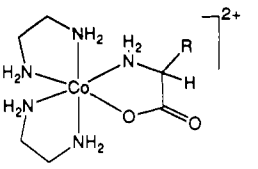
In contrast, when $[Co(en)_2(Gly)]^{2+}$ (**2**) was treated with $SOCl_2$ in lieu of $POCl_3$, the product isolated was identified crystallographically as the *N*-formyloxamato complex **4**.[11] The glycine moiety is oxidized by $SOCl_2$, and the sulfur reagent is reduced to elemental sulfur.

The oxamato complex **5** can be obtained by base hydrolysis of the *N*-formyl derivative **4**, and treatment of this complex with $SOCl_2$ in DMF regenerates the *N*-formyloxamato complex **4**.[11,12] Scheme I summarizes this chemistry. A possible implication of this result is that N-formylation of the oxamato complex **5** may well be the final step in the reaction sequence leading to the formation of the *N*-formyl derivative **4**. If this assumption is correct, then the mechanistic problem presented by this reaction reduces to one of identifying the route by which the glycinato complex **2** is converted to the oxamato complex **5**. One obvious possibility is that the initial oxidation product is the related α-imino acidato complex, which could then have been further oxidized.

In order to test this hypothesis, the alaninato complex **6a** was subjected to the same treatment. The chelated imino acidato complex **7a** that would result from oxidation of the alaninato complex **6a** is a known, stable compound,[13] which would not be expected to undergo further oxidation. On the basis of this rationale, a number of simple amino acidato complexes (**6a–h**) have been prepared and submitted to such reaction conditions. The complexes chosen for this study did not contain side chain functionalities that were likely to react irreversibly with $SOCl_2$. The reactions of other complexes with such substituents, such as those of serine and threonine, will be dealt with elsewhere.

Experimental Section

^1H and ^{13}C NMR spectra were recorded in D_2O with a JEOL JNM-FX 200 Fourier transform spectrometer, using sodium 3-(trimethylsilyl)propanesulfonate (TPS) as an internal standard. Chemical shifts (δ, positive downfield) are given in ppm. In the ^1H NMR spectra, only signals associated with nonexchangeable protons are quoted, since signals due to exchangeable protons change in position and intensity from sample to sample as pD varies. Visible spectra were measured with a Hewlett-Packard HP 8450A spectrophotometer. Molar absorptivities (ϵ, M^{-1} cm^{-1}) were obtained in 0.1 M HCl unless otherwise specified. Cation-exchange resins AG 50W-X2, 200–400 mesh (Bio-Rad), and SP Sephadex C-25 (Pharmacia) were used throughout. The dimensions of resin columns are given as diameter × length. Following chromatography on SP C-25 resin, solutions could be desalted by adsorption onto AG 50W-X2 resin, washing thoroughly with 1 M HCl, and then eluting with more concentrated acid solutions. The concentration of solutions by removal of solvent was carried out at reduced pressure (~20 Torr) in a Büchi rotary evaporator using a water aspirator and water bath (<50 °C). Elemental analyses were performed by the ANU Analytical Services Unit. All chemicals were analytical grade. Commercial CF_3SO_3H was distilled before use. $SOCl_2$ was distilled over linseed oil, and *N*,*N*-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) were dried over 3-Å molecular sieves.



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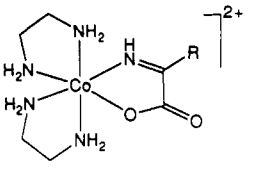
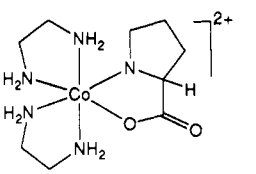


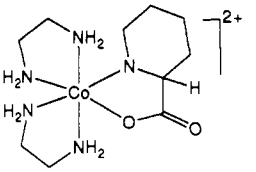
7

a : R = CH_3
b : R = $CH_2C_6H_4OH$
c : R = $CH(CH_3)_2$
d : R = $CH_2CH_2CO_2H$

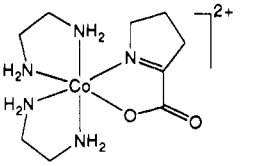
g : R = $CH_2CH_2SCH_3$
h : R = $CH_2CH_2CH_2CH_2NH_3$
i : R = CH_2CO_2H
j : R = CH_2CONH_2



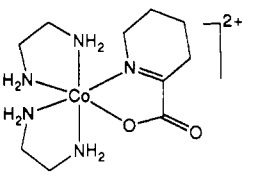
6e



6f



7e



7f

$[Co(en)_2(amino\ acidato)]^{2+}$. Complexes **6** were prepared as diastereoisomeric mixtures by published methods. The glutamato (**6d**) and aspartato (**6i**) complexes were prepared as their perchlorate salts by the method of Legg and Steele[14] and converted into the chloride salt by cation-exchange chromatography on AG 50W-X2 resin. Other complexes were prepared by using a method similar to that employed by Chong et al.[13] Perchlorate salts were used for the reactions with $SOCl_2$ if they were soluble in DMF. Otherwise, the trifluoromethanesulfonate salts, prepared in the usual way,[15] were employed. Satisfactory elemental analyses and ^1H NMR spectra were obtained for all the amino acidato complexes.

$[Co(en)_2(NH{=}C(CH_3)CO_2)]Cl_2{\cdot}H_2O$ (7a). $[Co(en)_2(S\text{-}Ala)](CF_3SO_3)_2$ (**6a**) (0.5 g) was dissolved in DMF (10 mL). The solution was thoroughly cooled (<−5 °C) in an ice–salt bath before $SOCl_2$ (1.5 mL) was added dropwise, with stirring. Initially, an orange precipitate formed, which slowly redissolved on continued addition of $SOCl_2$. The solution was stirred for a further 30 min at room temperature before being quenched by careful addition to H_2O (500 mL). After 15 min of stirring (to allow the precipitated sulfur to coagulate), the solution was filtered and adsorbed onto a column (4 × 10 cm) of AG 50W-X2 resin. The column was washed with H_2O (500 mL) and 0.5 M HCl (500 mL) before being eluted with 2 M HCl. The resulting orange-red eluate was evaporated and the residue taken up in the minimum volume of 1 M HCl. Precipitation by dropwise addition of ethanol gave 0.4 g (85%) of the solid α-imino acidato complex as its chloride salt (**7a**). Anal. Calcd for $CoC_7H_{20}N_5O_2Cl_2{\cdot}H_2O$: Co, 16.64; C, 23.74; H, 6.26; N, 19.78; Cl, 20.02. Found: Co, 16.5; C, 23.9; H, 6.3; N, 19.9; Cl, 20.3. Visible spectrum (λ (nm), ϵ_{max}: 476, 115. ^1H NMR δ: 2.7–3.0 (br) (en methylenes); 2.52 (s) (β-CH_3). ^{13}C NMR δ: 22.6 (CH_3); 44.7, 45.4, 46.0, 46.6 (en methylenes); 173.7 (C=NH); 186.6 (Co—O—C=O).

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$[Co(en)_2(NH{=}C(CH_2C_6H_4OH)CO_2)]Cl_2{\cdot}2H_2O$ (7b). $[Co(en)_2(S\text{-}Tyr)](CF_3SO_3)_2{\cdot}3H_2O$ (**6b**) (1 g) was dissolved in DMF (7 mL), and the solution was cooled in an ice–salt bath. $SOCl_2$ (2.5 mL) was added and the solution stirred at room temperature for 21 h, during which time sticky lumps of coagulated sulfur were produced. The reaction was quenched by addition to H_2O (1 L), and the resulting orange solution was filtered and adsorbed onto a column (4 × 10 cm) of SP Sephadex C-25 resin. After the column was washed with H_2O (500 mL), elution with 0.1 M NaCl gave a diffuse orange band, a purple band, and another orange band, in that order. Each fraction was separately adsorbed onto short (4 × 4 cm) column of AG 50W-X2 resin, which was then washed with 0.5 M HCl to remove Na^+ ions and eluted with 2 M HCl. On evaporation to dryness, the ^1H NMR spectra of the two orange fractions were identical. These products were therefore combined and recrystallized from 3 M HCl by slow addition of acetone to give $[Co(en)_2(NH{=}C(CH_2C_6H_4OH)CO_2)]Cl_2{\cdot}2H_2O$ (**7b**) 0.35 g (54%). Anal. Calcd for $CoC_{13}H_{24}N_5O_3Cl_2{\cdot}2H_2O$: Co, 12.69; C, 33.63; H, 6.08; N, 15.09; Cl, 15.27. Found: Co, 12.7; C, 33.9; H, 5.8; N, 14.6; Cl, 15.5. Visible spectrum (λ (nm), $\epsilon)_{max}$: 476, 123. ^1H NMR δ: 2.4–3.0 (br) (en methylenes); 4.13 (s) (β-CH_2); 6.98, 7.25 (AB quartet, J_{AB} = 8.6 Hz) (aromatic CH). ^{13}C NMR δ: 41.5 (β-CH_2); 44.7, 45.4, 46.1, 46.4 (en methylenes); 117.2 (*m*-CH); 124.1 (R—C); 132.4 (*o*-CH); 156.2 (C—OH); 173.1 (C=NH); 188.5 (Co—O—C=O). The evaporated purple fraction containing ring-opened $[Co(en)_2(NH_2CH(CH_2C_6H_4OH)\text{-}COOH)Cl]Cl_2$ was recrystallized by dissolution in the minimum volume of hot H_2O followed by cooling overnight in the refrigerator. Anal. Calcd for $CoC_{13}H_{27}N_5O_3Cl_3{\cdot}2.5H_2O$: Co, 11.51; C, 30.51; H, 6.30; N, 13.69; Cl, 20.78. Found: Co, 10.6; C, 30.5; H, 6.6; N, 13.7; Cl, 19.7. ^1H NMR δ: 2.6–3.0 (br) (en methylenes); 3.13 (m) (β-CH_2); 3.87 (m) (α-CH); 6.91, 7.22 (AB quartet, J_{AB} = 8.3 Hz) (aromatic CH). ^{13}C NMR δ: 39.9 (β-CH_2); 45.3, 45.6, 45.7, 46.0 (en methylenes); 59.8, 59.9 (α-CH, diastereoisomers); 116.7 (*m*-CH); 127.7 (R—C); 131.8 (*O*-CH); 155.9, (C—OH); 176.7 (Co—O—C=O). In solution, this complex slowly re-forms the tyrosinato chelate (**6b**).

$[Co(en)_2(NH{=}C(CH(CH_3)_2)CO_2)](ClO_4)_2{\cdot}1.5H_2O$ (7c). $[Co(en)_2(S\text{-}Val)](ClO_4)_2$ (**6c**) (2.5 g) was dissolved in DMF (8 mL) and the solution cooled in an ice–salt bath. $SOCl_2$ (3.5 mL) was added dropwise, with stirring. The reaction mixture was stirred for 1 h, by which time it had achieved a gelatinous quality. The reaction was quenched by cautious addition to H_2O (2 L) and the mixture stirred for 30 min to coagulate the sulfur, which was then removed by filtration. The resulting orange solution was adsorbed onto a column (5 × 20 cm) of SP Sephadex C-25 resin and washed with H_2O (1 L). Elution with 0.1 M NaCl gave a minor purple band followed by a major orange band; the latter was adsorbed onto a short AG 50W-X2 column, washed with 0.5 M HCl, and eluted with 1 M HCl. The eluate was taken to dryness and dissolved in warm H_2O, and the product was precipitated by the addition of $NaClO_4{\cdot}H_2O$. The solid was collected at the pump, washed with ethanol and diethyl ether, and air-dried, yielding 1.95 g of the α-imino acidato complex (**7c**). Anal. Calcd for $CoC_9H_{24}N_5O_{10}Cl_2{\cdot}1.5H_2O$: Co, 11.35; C, 20.82; H, 5.24; N, 13.49; Cl, 13.66. Found: Co, 11.9; C, 20.6; H, 4.9; N, 13.5; Cl, 13.9. Visible spectrum (λ (nm), $\epsilon)_{max}$: 478, 114. ^1H NMR δ: 1.29 (d), 1.34 (d) (γ-methyls); 2.6–3.0 (br) (en methylenes); 3.14 (m) (β-CH). ^{13}C NMR δ: 18.9, 19.4 (γ-methyls); 35.0 (β-CH); 44.7, 45.4, 45.9, 46.3 (en methylenes); 172.6 (C=NH); 193.5 (Co—O—C=O).

In a separate experiment, using a smaller amount of complex (1.5 g), the reaction mixture was quenched with H_2O (30 mL) and the precipitated sulfur centrifuged and collected. The yield of sulfur was 25% on a molar basis, i.e. 50% of the expected value.

When the reaction was quenched after only 10 min, a second orange band could be separated on the Sephadex column. After the fraction was desalted on AG 50W-X2 resin and the resulting solution was taken to dryness, this species was identified as the starting material by ^1H NMR spectroscopy. The $(\Delta S,\Lambda R)$:$(\Lambda S,\Delta R)$ ratio of this diastereoisomeric mixture was approximately 2:1 as opposed to the 1:1 mixture in the starting material. Treatment of this starting material (1 g) with slightly more than 1 equiv of $SOCl_2$ (0.2 mL) in DMF (10 mL) leads to a quantitative recovery of the valinato complex with a $(\Delta S,\Lambda R)$:$(\Lambda S,\Delta R)$ ratio of approximately 2:1, as determined by ^1H NMR spectroscopy.

$[Co(en)_2(NH{=}C(CH_2CH_2CO_2H)CO_2](ClO_4)_2$ (7d). $[Co(en)_2(S\text{-}Glu)](CF_3SO_3)_2{\cdot}0.5CF_3SO_3H$ (**6d**) (0.9 g) was dissolved in DMF (8 mL), and the solution was cooled in an ice–salt bath. $SOCl_2$ (2 mL) was added and the solution stirred at room temperature for 15 min before quenching by careful addition to H_2O (1 L). After 30 min of stirring, the solution was filtered (to remove the sulfur) and adsorbed onto a Sephadex column (4 × 10 cm). A single orange fraction was eluted with 0.1 M NaCl and adsorbed onto a short AG 50W-X2 column for desalting. The complex was eluted with 2 M HCl and the eluate taken to dryness on a rotary evaporator. The residue was dissolved in H_2O (5 mL), and $NaClO_4{\cdot}H_2O$ (2 g) was added. The volume was reduced by passing a stream of air over the surface of the solution until the $NaClO_4$ began to crystallize. Enough H_2O was added to redissolve the crystals; then ethanol was added dropwise to the point of turbidity, and the solution was cooled overnight in the freezer. The solid that deposited was collected and recrystallized in the same manner. The orange product was washed with ethanol and diethyl ether and air-dried. Further material could be obtained by desalting the mother liquor on Dowex and repeating the crystallization procedure to yield the *diperchlorate* (**7d**), 0.45 g. Anal. Calcd for $CoC_9H_{22}N_5O_{12}Cl_2$: C, 20.70; H, 4.25; N, 13.41. Found: C, 20.6; H, 4.3; N, 13.1. Visible spectrum (λ (nm), $\epsilon)_{max}$: 478, 134. ^1H NMR δ: 2.6–2.9 (br) (en methylenes); 2.99 (m), 3.12 (m) (β,γ-methylenes). ^{13}C NMR δ: 29.9, 31.2 (β,γ-methylenes); 44.8, 45.4, 46.1, 46.6 (en methylenes); 173.0 (C=NH); 176.4 (CO_2H); 187.4 (Co—O—C=O).

$[Co(en)_2(\overline{N{=}C(CH_2CH_2CH_2)CO_2})]Cl_2{\cdot}0.5H_2O$ (7e). $[Co(en)_2(S\text{-}Pro)](CF_3SO_3)_2$ (**6e**) (0.5 g) was dissolved in DMF (6 mL), and the solution was cooled in an ice–salt bath. $SOCl_2$ (0.6 mL) was added rapidly, with stirring, resulting in the formation of a precipitate that slowly redissolved. The reaction mixture was removed from the cooling bath and the stirring continued for 15 min before it was added cautiously to H_2O (300 mL). After 30 min of stirring, the orange solution was filtered to remove the sulfur and adsorbed onto a column (4 × 10 cm) of SP Sephadex C-25 resin. A single orange fraction was eluted with 0.2 M NaCl, desalted on AG 50W-X2 resin, and taken to dryness. The residue (0.36 g) was taken up in a small volume of 3 M HCl, an equal volume of ethanol added, and the solution left in the freezer, whereupon orange crystals of the α-imino acidato complex (**7e**) formed slowly. Anal. Calcd for $CoC_9H_{22}N_5O_2Cl_2{\cdot}0.5H_2O$: Co, 15.88; C, 29.13; H, 6.25; N, 18.87; Cl, 19.10. Found: Co, 16.7; C, 29.1; H, 6.2; N, 18.6; Cl, 19.9. ^1H NMR δ: 2.46 (m) (γ-CH_2); 2.7–3.0 (br) (en methylenes); 3.15 (m) (β-CH_2); 4.27 (m) (δ-CH_2). ^{13}C NMR δ: 22.4 (γ-CH_2); 35.1 (β-CH_2); 44.7, 45.5, 46.1, 47.1 (en methylenes); 59.8 (δ-CH_2); 171.0 (C=N–); 187.1 (Co—O—C=O).

As an alternative method for the isolation of this complex, the residue resulting from chromatography and desalting of the reaction mixture was taken up in the minimum volume of H_2O, and $NaClO_4{\cdot}H_2O$ was added. A precipitate of the chloride–perchlorate double salt of the α-imino acidato complex (**7e**) formed immediately and was collected and washed with ethanol and diethyl ether. A further crop was obtained by slow evaporation of the mother liquor. Anal. Calcd for $CoC_9H_{22}N_5O_6Cl_2{\cdot}0.5H_2O$: Co, 13.83; C, 25.37; H, 5.20; N, 16.43; Cl, 16.64. Found: Co, 14.1; C, 25.5; H, 5.3; N, 16.3; Cl, 16.7. Visible spectrum (λ (nm), $\epsilon)_{max}$: 480, 120.

$[Co(en)_2(\overline{N{=}C(CH_2CH_2CH_2CH_2)CO_2})]Cl_2{\cdot}H_2O$ (7f). $[Co(en)_2(Pip)](CF_3SO_3)_2{\cdot}H_2O$ (**6f**) (Pip = pipecolinate) (0.5 g) was dissolved in DMF (10 mL), the solution was cooled in an ice–salt bath, and $SOCl_2$ (2 mL) was added. After 3 h, further $SOCl_2$ (1 mL) was added and the solution stirred for 18 h. The reaction was quenched by dropwise addition to H_2O (1 L). The solution was stirred for 45 min to allow for the precipitation and coagulation of sulfur before it was filtered and adsorbed onto a SP Sephadex C-25 column (4 × 10 cm). Elution with 0.067 M NaH_2PO_4/Na_2HPO_4 (1:1) buffer resulted in the formation of three bands: a diffuse yellow band (discarded), a weak purple band (discarded), and a major orange band. The orange fraction was desalted on AG 50W-X2 resin in the usual way, yielding a solid (0.31 g) when the HCl eluate was taken to dryness. This material was recrystallized from H_2O by slow evaporation in air to yield orange crystals of the α-imino acidato complex (**7f**). Anal. Calcd for $CoC_{10}H_{24}N_5O_2Cl_2{\cdot}H_2O$: Co, 14.95; C, 30.47; H, 6.65; N, 17.77; Cl, 17.99. Found: Co, 15.2; C, 30.3; H, 6.7; N, 17.6; Cl, 18.0. Visible spectrum (λ (nm), $\epsilon)_{max}$: 484, 121. ^1H NMR δ: 1.7–2.1 (br) (γ,δ-methylenes); 2.7–3.0 (br) (en, β-methylenes); 3.83 (br) (ϵ-CH_2). ^{13}C NMR δ: 17.4, 22.8 (γ,δ-methylenes); 30.5 (β-CH_2); 44.4, 45.3, 45.9, 46.6 (en methylenes); 52.2 (ϵ-CH_2); 173.7 (C=N); 182.5 (Co—O—C=O).

$[Co(en)_2(NH{=}C(CH_2CH_2SCH_3)CO_2)](ClO_4)_2$ (7g). $[Co(en)_2(S\text{-}Met)](ClO_4)_2{\cdot}H_2O$ (**6g**) (14 g) suspended in DMF (200 mL) was cooled in an ice–salt bath. $SOCl_2$ (30 mL) was added dropwise, with stirring. The reaction mixture was stirred for 30 min before it was quenched by cautious addition to iced H_2O (5 L). The resulting solution was stirred until the ice melted, diluted 2-fold, and then adsorbed onto a SP Sephadex C-25 column (10 × 25 cm). A diffuse band eluted as the mixture was loaded onto the column. Thorough washing with H_2O and then elution with 0.1 M $NaClO_4$ removed the remains of this diffuse band (which was discarded) and then revealed three bands. The first, a purple fraction, was discarded. The second fraction was collected and desalted on AG 50W-X2 resin, and the HCl eluate was taken to dryness. The orange residue was taken up in the minimum volume of H_2O and precipitated by the addition of $NaClO_4{\cdot}H_2O$. The solid was collected and recrystallized from H_2O to give the α-imino acidato complex (**7g**). Anal.

Calcd for $CoC_9H_{24}N_5O_{10}SCl_2$: Co, 11.24; C, 20.62; H, 4.61; N, 13.36; S, 6.12; Cl, 13.53. Found: Co, 11.65; C, 20.36; H, 4.73; N, 13.51; S, 5.90; Cl, 13.28. Visible spectrum (λ (nm), $\epsilon)_{max}$: 478, 113. ^{1}H NMR δ: 2.18 (s) (S—CH_3); 2.7–3.0 (br) (en, β-methylenes); 3.17 (t) (γ-CH_2). ^{13}C NMR δ: 14.9 (S—CH_3); 29.1 (γ-CH_2); 34.8 (β-CH_2); 44.8, 45.5, 46.0, 46.5 (en methylenes); 173.0 (C=NH); 187.0 (Co—O—C=O). The third and final band was desalted on Dowex, and a ^{1}H NMR spectrum of the residue indicated that this complex was $[Co(en)_3]^{3+}$.

$[Co(en)_2(NH{=}C(CH_2CH_2CH_2CH_2NH_3)CO_2)]Cl_3\cdot H_2O$ (7h). $[Co(en)_2(S\text{-Lys})](CF_3SO_3)_2\cdot H_2O$ (**6h**) (0.62 g) was dissolved in DMF (7 mL). The solution was cooled in an ice–salt bath before $SOCl_2$ (2 mL) was added dropwise to the stirred solution. The reaction mixture was stirred for a further 10 min before being poured into H_2O (1 L). The orange solution was filtered, adsorbed onto a SP Sephadex C-25 column (4 × 10 cm), and washed with H_2O. A single orange band was eluted with 0.3 M NaCl and desalted on AG 50W-X2 resin. The HCl eluate was taken to dryness and the residue dissolved in the minimum volume of H_2O. Slow addition of ethanol gave the α-imino acidato complex (**7h**) as the trichloride salt. Anal. Calcd for $CoC_{10}H_{28}N_6O_2Cl_3\cdot H_2O$: Co, 13.16; C, 26.83; H, 6.75; N, 18.77; Cl, 23.75. Found: Co, 12.89; C, 26.73; H, 6.53; N, 18.25; Cl, 22.35. Visible spectrum (λ (nm), $\epsilon)_{max}$: 476, 115. ^{1}H NMR δ: 1.7–2.0 (br) (γ,δ-methylenes); 2.7–3.0 (br) (en methylenes); 2.90 (t) (β-CH_2); 3.08 (t) (ϵ-CH_2). ^{13}C NMR δ: 21.9, 26.8 (γ,δ-methylenes); 35.3 (β-CH_2); 39.7 (ϵ-CH_2); 44.7, 45.4, 45.9, 46.5 (en methylenes); 173.0 (C=NH); 188.6 (Co—O—C=O).

Reaction of $[Co(en)_2(S\text{-Asp})](CF_3SO_3)_2$ (6i) and $[Co(en)_2(S\text{-Asn})](CF_3SO_3)_2$ (6j) with $SOCl_2$. These complexes were treated with $SOCl_2$ in a manner similar to that for the other amino acidato complexes, over a period of 15 min. Chromatography of the quenched reaction mixture on Sephadex SP-C25 cation-exchange resin revealed a large number of bands. The ^{1}H NMR spectra of the desalted eluates implied that some of these fractions were still mixtures. As there was no major product, and a large number of minor ones, work on these complexes was abandoned.

Results

The ^{1}H NMR spectra of the chelated amino acids (Ala, Tyr, Val, Glu, Pro, Pip, Met, Lys) are quite similar to those of the free ligands. There are minor changes in chemical shifts and an increase in complexity due to the presence of diastereoisomers, but the resonances are readily assigned on the basis of broad similarities to those of the free amino acid. In some cases, e.g. the alaninato (**6a**) and valinato (**6c**) complexes, the resonances have been assigned previously to specific diastereoisomers.[16] In these cases integration of the spectra showed that approximately equal amounts of each diastereoisomer were produced in each preparation. This is in agreement with the results obtained in the synthesis of the serinato complex.[13]

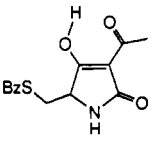
Treatment of these α-amino acid chelates with $SOCl_2$ in DMF gave the related α-imino acidato complexes and a significant amount of sulfur was produced as a byproduct. The synthesis of the α-imino acidato complexes were usually clean and, generally speaking, gave good yields (>80%, ~50% for the tyrosinato complex). The only common impurities in the reaction mixture were small amounts of starting material, which could be difficult to separate chromatographically from the product, and some purple products assigned as amino chelate ring-opened species. These latter complexes resulted from displacement of the coordinated carboxylate by chloride, but were readily separated on SP Sephadex C-25 resin. Lengthening the reaction time eliminated the starting material but, as in the case of the tyrosinato complex (**6b**), resulted in more of the ring-opened species. Large amounts of the ring-opened species were usually indicative of long reaction times or overheating of the reaction mixture by too rapid addition of $SOCl_2$. Thorough preliminary cooling and slow (dropwise) addition of the $SOCl_2$ minimized this problem.

The recovery of starting material from the reaction of the $[Co(en)_2(Val)]^{2+}$ (**6c**) complex with $SOCl_2$ led to an important observation concerning the relative amounts of recovered diastereoisomers. The starting material contained equal amounts of ΔS and ΛS diastereoisomers, but if the complex was treated with slightly more than 1 equiv of $SOCl_2$, a quantitative recovery of $[Co(en)_2(Val)]^{2+}$ (**6c**) with a $(\Delta S,\Lambda R)$:$(\Lambda S,\Delta R)$ diastereoisomeric ratio of approximately 2:1 resulted. This implies that the α-carbon centers of the amino acidato complexes (**6**) mutarotate under the reaction conditions applied via α-proton exchange.

The major exceptions to the above general comments were the aspartato (**6i**) and asparaginato (**6j**) complexes, which both gave rise to a variety of products (>6). No serious attempt was made to isolate and characterize the products in these complex mixtures.

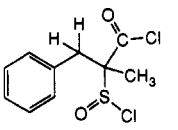
Discussion

Several examples of $SOCl_2$ acting as a dehydrogenating agent exist. In a total synthesis of holomycin, Büchi and Lukas[17] found that the pyrrolinone **8** gave the dehydrogenated product **9** on



8 **9**

treatment with $SOCl_2$. Elemental sulfur was also produced in this reaction. In a second example, treatment of 2-methyl-3-phenylpropanoic acid with $SOCl_2$ gave rise to the dehydro acid chloride.[18] This reaction was presumed to proceed via the sulfinyl chloride **10**, which arises from $SOCl_2$ attack on the enolized acid



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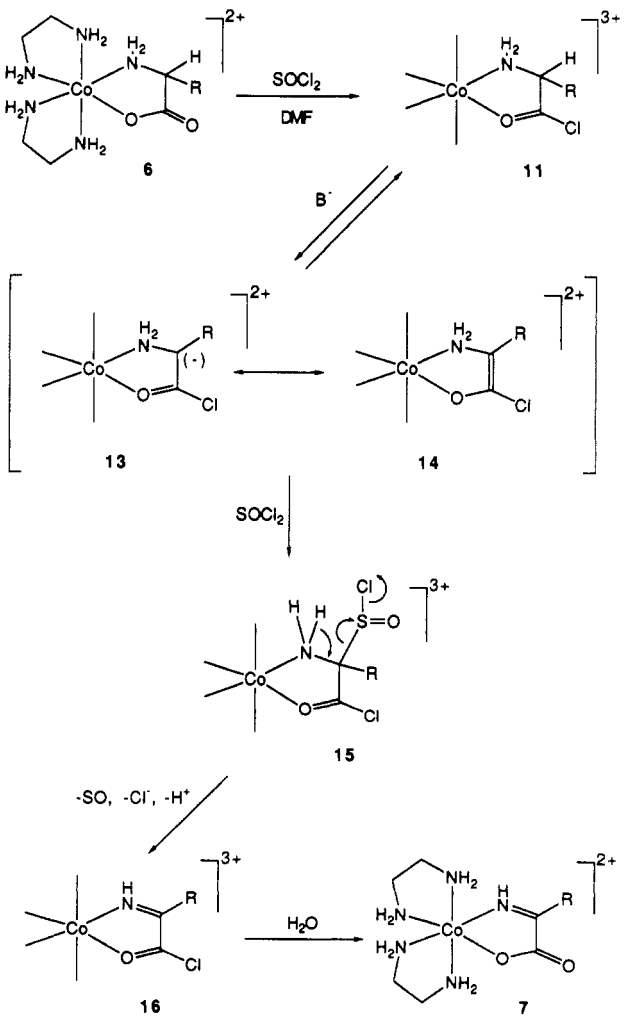
Scheme II

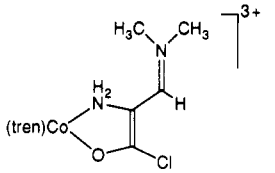


6 **11** **13** **14** **15** **16** **7**

(17) Büchi, G.; Lukas, G. *J. Am. Chem. Soc.* **1964**, *86*, 5654.
(18) Krubsack, A. J.; Higa, T. *Tetrahedron Lett.* **1968**, 5149.

chloride. A more complex system following a similar pathway has also been described.[19]

The general mechanism shown in Scheme II is proposed for the oxidation of the amino acidato complexes. Here, the initial step in the formation of the α-imino acidato complexes **7a–h** is reaction of the carboxylate functionality to give the chelated acid chlorides **11a–h**. $SOCl_2$ is a standard reagent in the preparation of acid chlorides from carboxylic acids, while similar reactions are presumed to be involved in the formation of chelated amino acid esters from amino acidato complexes on treatment with $SOCl_2$ in alcoholic solvents.[20] In addition, the formylation of $[Co(tren)(Gly)]^{2+}$ by treatment with $POCl_3$ in DMF is argued to proceed via the acid chloride, since the dimethyliminium acid chloride intermediate (**12**) has been isolated and crystallographically characterized.[6] Formation of the acid chloride activates the proton(s) on the α-carbon still further, and the second step involves a reversible deprotonation of this α-carbon to give the carbanion **13**, which is stabilized as the enol **14**.



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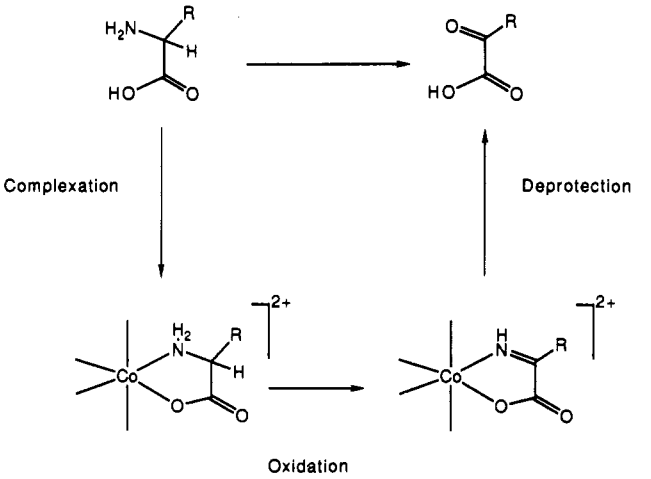
Two pieces of evidence support the proposal of an intermediate with carbanionic character in this reaction. First, the reactions of $[Co(tren)(Gly)]^{2+}$ and $[Co(en)_2(Gly)]^{2+}$ (**2**) with $POCl_3$ in DMF give, after hydrolysis, the chelated *C*-formylglycine complexes but *no* chelated *N*-formylglycine complexes were seen.[7,8] This implies that the α-protons of the chelated acid chlorides (**11a–h**) are at least not much less acidic than the amine protons. Second, indirect evidence is obtained from the diastereoisomeric ratio of the recovered valinato complex (**6c**) as mentioned above. The 2:1 stereochemical ratio in the recovered material is, within experimental error, the equilibrium distribution obtained on mutarotation of chelated valinato complex in aqueous base.[9] The possibility of this ratio arising as a result of a kinetic phenomenon was eliminated by obtaining a quantitative recovery of starting material with this same 2:1 diastereoisomeric ratio from the reaction of the valinato complex (**6c**) with slightly more than 1 equiv of $SOCl_2$. The addition of CF_3SO_3H to a DMF solution of the valinato complex (**6c**) does not lead to mutarotation, making an acid-catalyzed path unlikely. The conclusion is therefore that treatment with $SOCl_2$ in DMF leads to formation of the carbanion (**13c**) or its equivalent (**14c**), preceded by proton loss.

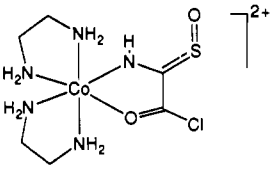
Once the carbanion (**13**) has formed, $SOCl_2$ may add to afford the α-sulfinyl chloride (**15**). Extrusion of sulfur monoxide and loss of HCl, as shown in Scheme II, results in the chelated α-imino acid chloride (**16**), which is then hydrolyzed to the observed α-imino acidato complexes (**7a–h**) during the isolation procedures. Sulfur monoxide is known to be in equilibrium with elemental sulfur and sulfur dioxide,[21] and this disproportionation, therefore, accounts for the observed sulfur. Consequently, the maximum theoretical yield of sulfur is 50%. Only half this amount was recovered, but this is ascribed to the chemistry of the sulfur oxides being rather complicated.[22]

The key feature of these oxidation reactions would appear to be the reaction of $SOCl_2$ at the activated α-carbon of the chelated amino acid chloride. If this reaction were to take place on the aspartato and asparaginato complexes, **6i** and **6j**, then the presumed products, **7i** and **7j**, would contain further acidic protons. The reaction of $SOCl_2$ with activated substrates has much precedent, and many possible pathways, as detailed in a review by Oka.[23] The large number of products observed in the reactions of the aspartato and asparaginato complexes could therefore be explained by an initial oxidation reaction, followed by further reactions, employing a number of the available reaction pathways.

Scheme III



An immediate question is whether this mechanism can be applied to the oxidation of $[Co(en)_2(Gly)]^{2+}$ with $SOCl_2$ in DMF. Formation of the chelated acid chloride (**11**, R = H) would be the first step in the $[Co(en)_2(Gly)]^{2+}$ oxidation. Deprotonation to form the carbanion would follow as the α-protons are presumably activated to a similar degree to those of the other acid chloride complexes (**11a–j**). Reaction with $SOCl_2$ should then give the α-sulfinyl chloride (**15**, R = H). The next step for most amino acidato complexes is the removal of an amine proton as a trigger for the extrusion of sulfur monoxide and loss of Cl^- from the α-sulfinyl chloride. However, by postulating deprotonation of the α-carbon rather than the amine nitrogen atom in the formation of the α-sulfinyl chloride, we are, in effect, saying that the proton or protons on the α-carbon are of the same order of acidity as the amine protons. This means that the remaining proton on the α-carbon of the α-sulfinyl chloride (**15**, R = H) derived from the glycinato complex (**2**), is probably even more acidic, due to the presence of another electron-withdrawing substituent on the α-carbon atom, and would therefore be lost in preference to the amine proton. Loss of HCl from the α-sulfinyl chloride (**15**, R = H) could therefore be expected to occur with formation of the sulfine complex (**17**) and not the α-imino acidato



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complex (**7**, R = H) as the initial step in the formation of the *N*-formyloxamato complex (**4**).

Conclusion

Bis(ethylenediamine)cobalt(III) complexes of α-amino acids (**6a–h**) can be oxidized to their related α-imino acidato complexes (**7a–h**) on treatment with $SOCl_2$ in DMF. The metal ion plays a major role in this process. First, it acts as a protecting group for the amine and moderates the reactivity of the carboxylate group. Second, it significantly activates the proton on the α-carbon, as described in the Introduction, which is critical for the reaction to proceed. Provided any side chain functionality is not too reactive toward $SOCl_2$, in either the starting material or the product, this reaction appears to be quite general for chelated amino acids. Previously, α-imino acidato complexes of this type have been obtained either by intramolecular attack by coordinated

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(20) Buckingham, D. A.; Foster, D. M.; Sargeson, A. M. *J. Am. Chem. Soc.* **1968**, *90*, 6032.
(21) Zeise, H. *Z. Phys. Chem. Abt. B* **1942**, *51*, 120.
(22) Schenk, P. W.; Steudel, R. *Inorganic Sulfur Chemistry*; Elsevier Publishing Co.: Amsterdam, London, New York, 1968; Chapter 11.
(23) Oka, K. *Synthesis* **1981**, 661.

ammonia on the corresponding monodentate α-keto carboxylate[3] or by elimination reactions on chelated *O*-acetylserinate or *S*-methylcysteinate to produce the chelated 2-iminopropanoate.[13] The chemistry described here provides an easy way of producing α-imino acidato complexes, provided side chain functionalities do not give undesired reactions with $SOCl_2$. Since the α-imino acidato chelate is a protected keto acid, this reaction could therefore constitute a relatively general synthesis of α-keto acids from their related α-amino acids (Scheme III). Should the free keto acid be required, then the complex could be decomposed by one of a variety of methods[24-26] and the keto acid isolated from the resulting mixture.

Analysis of the mechanism proposed here for the oxidation of non-glycine α-amino acidato complexes in the context of the reaction of $[Co(en)_2(Gly)]^{2+}$ (**2**) with $SOCl_2$ leads to the conclusion that these α-amino acidato complexes (**6a-j**) may not be good models for the $[Co(en)_2(Gly)]^{2+}$ complex (**2**) in this reaction. The structural difference, one α-proton instead of two in $[Co(en)_2(Gly)]^{2+}$, leads to other mechanistic possibilities, which are presently being explored.

Acknowledgment. Financial support for this work (to A.H.) from The Danish Natural Sciences Research Council is gratefully acknowledged. We are also grateful to the ANU Analytical Service for microanalyses.

Registry No. **6a**, 129448-02-8; **6b**, 129448-03-9; **6c**, 129448-04-0; **6d**, 129448-05-1; **6e**, 129448-06-2; **6f**, 129519-70-6; **6g**, 129466-73-5; **6h**, 129519-71-7; **6i**, 129466-74-6; **6j**, 129448-09-5; **7a**, 95098-08-1; **7b**, 129447-95-6; **7c**, 129447-97-8; **7d**, 129447-99-0; **7e**, 129448-00-6; **7f**, 129448-01-7; **7g**, 129448-08-4; **7h**, 129466-72-4; *S*-Ala, 17807-53-3; *S*-Tyr, 12557-24-3; *S*-Val, 17333-21-0; *S*-Glu, 138-18-1; *S*-Pro, 17781-82-7; Pip, 22560-49-2; *S*-Met, 44805-37-0; *S*-Lys, 17781-81-6.

(24) Clark, C. R.; Tasker, R. F.; Buckingham, D. A.; Knighton, D. R.; Harding, D. R. K.; Hancock, W. S. *J. Am. Chem. Soc.* **1981**, *103*, 7023.
(25) Knighton, D. R.; Harding, D. R. K.; Friar, M. J.; Hancock, W. S.; Reynolds, G. D.; Clark, C. R.; Tasker, R. F.; Buckingham, D. A. *J. Am. Chem. Soc.* **1981**, *103*, 7025.
(26) Keyes, W. E.; Legg, J. I. *J. Am. Chem. Soc.* **1976**, *98*, 4970.

Contribution from the Department of Chemistry, University of Calgary, Calgary, Alberta, Canada T2N 1N4

A Theoretical Study on the Insertion of Ethylene into the Cobalt-Hydrogen Bond

Louis Versluis, Tom Ziegler,* and Liangyou Fan

Received April 3, 1990

Two of the important elementary reaction steps in the hydroformylation process catalyzed by $HCo(CO)_3$ have been investigated by theoretical calculations based on the density functional theory. The first step involved the formation of the π complex $HCo(CO)_3(\eta^2\text{-}C_2H_4$ (I) from $HCo(CO)_3$ and C_2H_4. A total of three stable conformations of I were considered. All had a trigonal-bipyramidal structure. The most stable has C_2H_4 coordinated equatorially with the C=C olefin bond in the basal plane. The second (**1b**), which is 20 kJ/mol higher in energy, is also coordinated equatorially but has the C=C bond perpendicular to the basal plane. The third structure with C_2H_4 in the apical position (**2a**) is, on the other hand, 56 kJ/mol less stable than **1a**. The ethylene dissociation energy in **1a** was calculated to be 70 kJ/mol. The second step investigated involves the insertion of C_2H_4 into the Co-H bond of $HCo(CO)_3$, leading to the ethyl complex II. The most stable conformation of II, **4b**, has the ethyl group in the axial position and a β-hydrogen in the equatorial position interacting in an agostic manner with cobalt. Only 28 kJ/mol higher in energy is a second structure, **4a**, with the ethyl group in the equatorial position and a β-hydrogen in the axial position interacting in an agostic manner with cobalt. A third structure, **4c**, with the ethyl group in the axial position, but lacking an agostic interaction, was 39 kJ/mol higher in energy than **4b**. The energy profile for the insertion process was investigated by an approximate linear transit procedure, and it was found that the process (**1b** → **4a**) is exothermic (ΔE = -8 kJ/mol) with a modest activation barrier of not more than 6 kJ/mol.

Introduction

The oxo or hydroformylation reaction discovered in 1938 by Roelen is used on a large industrial scale[1] to convert olefins and synthesis gas into aldehydes. The process employs homogeneous catalysts based on cobalt[1] or rhodium.[2] The most commonly used (pre)catalyst is $HCo(CO)_4$, which is generated in situ from the hydrogenation of $Co_2(CO)_8$ by H_2.

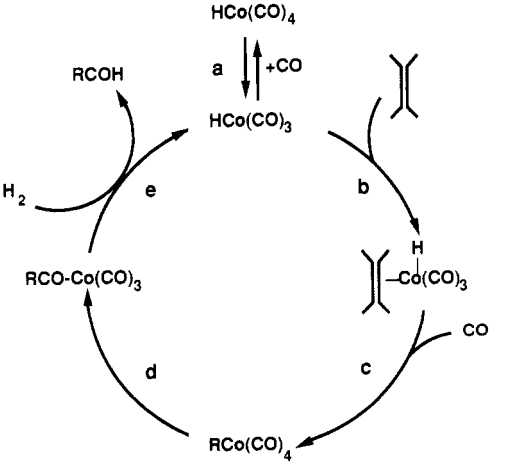
A mechanism for the cobalt-based hydroformylation process was first proposed by Heck and Breslow[3] in 1961 (see Scheme I). The catalytic cycle in Scheme I consists of a number of elementary reaction steps (a-e), of which steps a and d have been investigated in a previous theoretical study.[4]

We shall here focus our interest on the coordination of olefin to the cobalt fragment, eq 1 (step b of Scheme I), as well as on the insertion process of C_2H_4 into the cobalt-hydrogen bond, eq 2 (step c of Scheme I).

$$HCo(CO)_3 + C_2H_4 \rightarrow HCo(CO)_3\text{-}C_2H_4 \quad (1)$$

$$HCo(CO)_3\text{-}C_2H_4 \rightarrow Co(CO)_3\text{-}C_2H_5 \quad (2)$$

Scheme I



Not only is the study of these reactions important for the hydroformylation process as discussed here, but it is, on a more general basis, also relevant to the catalytic hydrogenation and isomerization of olefins, since the same elementary reaction steps have been proposed for these processes.[5] Experimental findings

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