Chemical Properties of Metallocarboxylic Acids of Transition Metals

Sir:

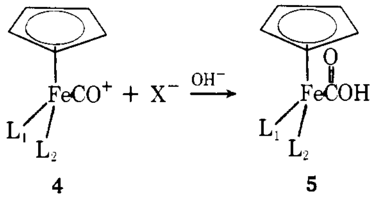
The sequence of steps involving conversion of a metal carbonyl **1** to a metallocarboxylic acid **2** and subsequent loss of CO_2 to generate a metal species in a reduced form **3** appears to be a key feature in many reductions in which carbon monoxide acts as the reducing agent (eq 1).

$$\underset{\mathbf{1}}{\overset{+(n)}{\text{LMCO}}} \xrightarrow{\text{OH}^-} \underset{\mathbf{2}}{\overset{+(n-1)}{\text{LMCOOH}}} \rightarrow \underset{\mathbf{3}}{\overset{+(n-1)}{\text{LMH}}} + \text{CO}_2 \qquad (1)$$

Metallocarboxylic acids were first proposed as intermediates by Halpern and co-workers in the reduction of Hg(II) ions[1] and Ag(I) ions[2,3] by CO. This reaction sequence has also been suggested in the reduction of other metal ions by CO, e.g., complexes of Ni(II),[4] Cu(II),[5] Rh(III),[6] and Co(III),[7] and also in the extensive area whereby metal carbonyl complexes are converted to metal carbonyl hydrides upon treatment with base.[8,9] The sequence also appears to be part of the catalytic cycle involved in the metal catalyzed reduction of organic substrates by CO, e.g., the Reppe modification of the hydroformylation reaction,[10] the reduction of nitro arenes to amines by CO and water,[11] and the reduction of quinones to quinols.[12] It is also involved in the conversion of CO and H_2O to H_2 and CO_2, catalyzed by several homogeneous transition metal systems.[10,13]

Despite the apparent widespread applications of eq 1, very little is known about metallocarboxylic acids as functional groups, nor have the effects of the ligands (L) upon the formation and decomposition of metallocarboxylic acids, as given in eq 1, been studied. Only two reports of the isolation of a stable molecule containing the MCOOH group have appeared; M = Ir[14] and Pt.[15] We report here the isolation of an iron-carboxylic acid system and the profound effect on the chemistry of the FeCOOH functionality depending on the nature of the other ligands on iron.

The three cyclopentadienyliron carbonyl cations **4a–c**, having increasing substitution of CO ligands by phosphine, have been treated with aqueous NaOH or KOH in an attempt to generate the corresponding metallocarboxylic acids **5**.



4 **5**

a, $L_1 = L_2 = CO$
b, $L_1 = CO$; $L_2 = Ph_3P$
c, $L_1 + L_2 = Ph_2PCH_2CH_2PPh_2$ (diphos)

Treatment of cold aqueous solutions of the BF_4^- salt of the cation **4a** with an equimolar amount of KOH gave rise to a yellow precipitate, presumably of the carboxylic acid **5a**; the material rapidly decomposed to yield the cyclopentadienyliron dicarbonyl dimer with evolution of H_2 and CO_2. Apparently, **5a** decarboxylates to give $C_5H_5Fe(CO)_2H$, which can be identified in a benzene extract of the reaction mixture, and which is known to decompose to hydrogen and the $C_5H_5Fe(CO)_2$ dimer.[16]

Treatment of the chloride salt of **4b** with an equimolar amount of KOH in a benzene-water mixture, followed by addition of cold pentane to the benzene layer, afforded a stable yellow microcrystalline precipitate of the metallocarboxylic acid **5b** (mp 130 °C dec). Included in the IR spectrum of the material in Nujol are absorptions at 2700, 1930, and 1565 cm^{-1} associated with -OH, FeC≡O, and -COOH groups, respectively. Treatment of the chloride salt of **4b**, or the carboxylic acid **5b**, with excess KOH yields the potassium salt of the acid **5b** as a yellow, microcrystalline precipitate. The potassium salt, when treated with aqueous HCl (pH 2.0), reforms the carboxylic acid **5b**. However, **5b** and its potassium salt react with stronger HCl solutions (pH <2.0) to form the chloride salt of the cyclopentadienyliron dicarbonyl cation **4b**; in the IR spectrum this cation has two characteristic strong metal carbonyl absorptions at 2060 and 2010 cm^{-1} and none associated with a ketonic type carbonyl group.

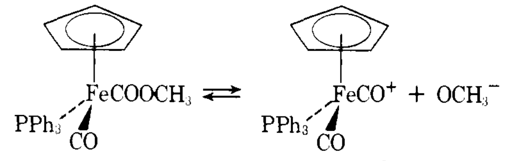
Most striking is the difference in the IR absorption spectrum of the acid **5b** in solvents of different dielectric constant (*E*). In benzene ($E = 2.3$) only one MCO absorptions is observed at 1935 cm^{-1}, consistent with the covalent formulation **5b**; however, in formamide ($E = 109.5$) two MCO absorptions at 2080 and 2030 cm^{-1}, characteristic of the cation **4b**, are the only absorptions appearing in the metal carbonyl region. In the latter solvent the "acid" exists entirely as the cation **4b** having a hydroxide counterion.

We conclude that this particular metallocarboxylic acid is amphoteric toward acids and bases and, depending on conditions, may be readily induced to ionize in the two ways indicated in eq 2.

$$\text{MCO}^+ + \text{OH}^- \rightleftarrows \text{MCOOH} \rightleftarrows \text{MCOO}^- + \text{H}^+ \qquad (2)$$

This peculiar mode of spontaneous ionization involving heterolytic cleavage of a carbon–oxygen bond, which has no precedence in purely organic carboxylic acids, is also observed in the corresponding methyl ester. Treatment of the chloride salt **4b** with equimolar amounts of NaOMe in methanol, followed by evaporation of the solvent, affords the ester **6a** as a yellow crystalline solid. In solvents of low polarity, e.g., C_6H_6, CS_2, and $CHCl_3$, the compound exhibits in the IR spectrum a single MC≡O absorption at 1935 cm^{-1} and a ketonic absorption at 1605 cm^{-1}; however, in formamide there are only two MC≡O-type absorptions at 2080 and 2030 cm^{-1}, indicative of the ionic form **6b**.

In solvents of intermediate polarity, absorptions due to both species **6a** and **6b** are seen, indicating establishment of the equilibrium given in eq 3; in acetone containing 15% formamide the IR absorption intensities indicate 50% ionization of the ester. Evaporation of the solvent from a solution in methanol, in which both **6a** and **6b** are present, affords only the solid covalent form, **6a**. Also, evaporation of a solution of the ester **6a** in CD_3OD leads to the corresponding perdeuteriomethyl ester. This facile transesterification reaction presumably proceeds via the unique S_N1 type reaction given in eq 3.



(3)

6a **6b**

The ^1H NMR of the analogous isopropyl ester confirms these conclusions. When dissolved in acetone the two methyl groups of the $-CH(CH_3)_2$ moiety in the ester are nonequivalent and appear as two separate doublets (at δ 0.90 and 0.82, $J = 6.0$ Hz for each) due to the attachment of this fragment to the chiral Fe atom in the covalent form analogous to **6a**. However, in formamide, the methyl groups are now equivalent and appear as a single doublet (δ 0.70, $J = 6.0$ Hz) indicating separation of the isopropyl fragment from the iron atom and loss of chirality.[17]

This facile ionization now affords a simple explanation for

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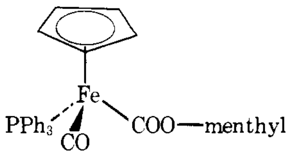
the observation that, whereas epimerization about the chiral iron center of the optically pure menthyl ester **7** does not occur upon heating in benzene, nonetheless only the racemate of the methyl ester **6a** was obtained upon transesterification of **7** by simple dissolution for a few minutes in methanol at room temperature.[18]



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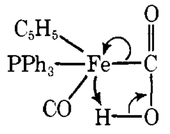
The reactions of the chloride salt of the bisphosphine cation **4c** are also surprising. No apparent reaction occurs between **4c** and aqueous NaOH. Passage of an aqueous solution of the chloride salt **4c** twice through a column of anion-exchange resin previously treated with excess NaOH, followed by addition of a concentrated NaOH solution to the eluate and extraction with ethyl acetate, afforded yellow needles of the ionic hydroxide **4c** (X = OH), mp 89–91 °C. The compound displays a single intense IR absorption at 1980 cm^{-1} identical with that seen for the corresponding chloride salt of **4c.** Treatment of **4c** (X = OH) with aqueous NaCl produces an immediate precipitate of the corresponding chloride (**4c,** X = Cl).

Even the BH$_4^-$ anion does not readily react with the carbonyl groups of the cation **4c.** Thus, treatment of the chloride salt of **4c** with NaBH$_4$ gave an immediate yellow precipitate of the borohydride salt of the cation, as a yellow powder, mp 132–133 °C. This borohydride salt also possessed the strong absorption at 1980 cm^{-1} in the IR spectrum, characteristic of the cation **4c.** In aqueous methanol, the borohydride salt rapidly reduced acetone and benzaldehyde to isopropanol and benzyl alcohol respectively.

Finally, with respect to the mechanism of the decarboxylation of metallocarboxylic acids, we have observed that benzene solutions of the carboxylic acid **5b** rapidly decompose with liberation of CO$_2$ upon warming. In contrast, solutions of the potassium salt of the acid in dry formamide do not decompose upon heating to 100 °C. With this particular system, at least, a concerted elimination of CO$_2$, as shown in **8**, is indicated in preference to one involving loss of CO$_2$ via a metallocarboxylic anion. Both types of mechanisms have been proposed for other systems in which decarboxylation of intermediate metallocarboxylic acids is inferred.[9,19]



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(17) The IR absorption spectrum of the isopropyl system in perdeuterioacetone containing 20% formamide includes absorptions at 1935 (vs) and 1605 (m) cm^{-1} and at 2080 (vs) and 2030 (vs) cm^{-1}, corresponding to the covalent and ionic form, respectively; the intensities of the absorptions indicate approximately equal concentrations of each form. The ^{1}H NMR of the isopropyl system in this same solvent mixture at 25 °C consists of two cyclopentadienyl absorptions of equal intensity at δ 4.50 and 5.50, related to the covalent and ionic forms; the two methyl groups of the isopropyl residue in the covalent form appear as doublets at δ 0.62 and 0.82 (J = 6.0 Hz), while the single methyl absorption of the ionic form consists of a doublet at δ 1.05 (J = 6.0 Hz).
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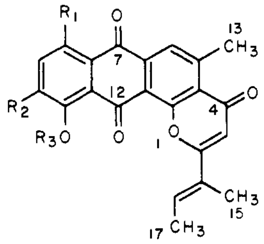
4*H*-Anthra[1,2-*b*]pyran Antibiotics. Total Synthesis of the Methyl Ether of Kidamycinone

Sir:

In connection with our studies toward development of new methods for synthesis of anthracycline antibiotics,[1-4] we have accomplished an efficient regioselective synthesis of the methyl ether of kidamycinone (**1b**), i.e., the methyl ether of the aglycone[5] (**1c**) of the anticancer antibiotic kidamycin (**1a**).[6]



1a. R$_1$ = angolosomine, R$_2$ = N,N-dimethylvancosamine, R$_3$ = H
1b. R$_1$ = R$_2$ = H, R$_3$ = CH$_3$
1c. R$_1$ = R$_2$ = R$_3$ = H

Kidamycin[6] (**1a**), neopluramycin,[7] pluramycin A,[7] hedamycin,[8] and indomycins[9] are a family of antibiotics which have a functionalized 4*H*-anthra[1,2-*b*]pyran nucleus as a common structural feature. Because of their complexity, full structural elucidation has been achieved only for **1a** and that required X-ray analysis.[6]

The synthetic plan followed for preparation of *O*-methylkidamycinone (**1b**) was regioselective construction of the hexasubstituted anthracene **4a,** followed by annelation of the pyrone portion from the *o*-hydroxyl and acetyl functionalities of **4a.** Efficient construction of anthracene **4a** was achieved using the synthetic strategy and complementary ring annelation methodologies previously reported by us.[1,3] The anion of 7-methoxy-3-phenylsulfonyl-1(3*H*)-isobenzofuranone (**2**)[3] (lithium diisopropylamide (LDA), tetrahydrofuran (THF), −78 °C) readily condensed with methyl crotonate to give, after methylation (K$_2$CO$_3$/dimethyl sulfate), regioselectively constructed naphthoate **3a**[10,11] as an oil in 83% yield. Reaction of **3a** with 1 equiv of *N*-bromosuccinimide in CCl$_4$ gave bromomethyl compound **3b** (mp 84–87 °C) which upon treatment with sodium thiophenoxide in ethanol yielded the corresponding sulfide **3c** (mp 91–92 °C) in 89% overall yield from **3a**. Oxidation (*m*-chloroperbenzoic acid/CH$_2$Cl$_2$, −78 °C)