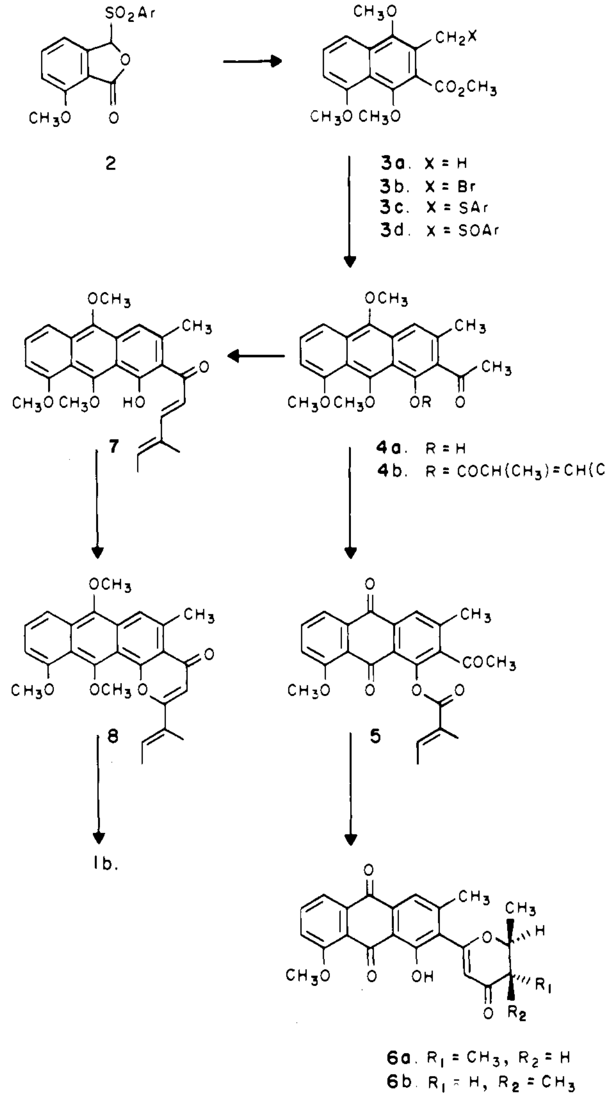

of sulfide **3c** to sulfoxide **3d** (mp 114-116 °C) was accomplished in 95% yield. The anion of sulfoxide **3d** (LDA/THF, −78 °C) was condensed with 3-penten-2-one to give, after thermal elimination of sulfenic acid, regioselectively constructed anthracene **4a**[11] in 71% yield (mp 132-134 °C). Construction of the pyrone portion of **1b** from the *o*-hydroxyl and acetyl functionalities present in anthracene **4a** was undertaken next. Attempted transfer of the acyl group of tigloyl ester **4b** to the methyl ketone using sodium hydride in dioxane was unsuccessful. Following oxidation ($CuBr_2$/THF) of **4b** to **5**, successful transfer of the tigloyl moiety was accomplished by base treatment (NaH/dioxane). The 1,3-diketone intermediate was immediately cyclized (HOAc/HCl). No **1b** resulted; instead, alternate cyclization products **6a** and **6b** were produced in 76 and 22% yield, respectively.

An alternative route to **1b** from **4a** was devised. Conversion of **4a** to a dilithium anion (2.2 equiv of LDA) followed by condensation with tiglaldehyde gave dienone **7**[11] in 75% yield. After a lengthy study, conditions were found (SeO_2/*tert*-amyl alcohol)[12] whereby dienone **7** underwent cyclization and dehydrogenation to **8** (mp 150-152 °C). The structure of **8** was confirmed from its ^{1}H NMR spectrum. The 5-methyl group was shifted from 2.38 ppm in **7** to 2.98 ppm in **8** as a consequence of its proximity and coplanarity with the deshielding cone of the carbonyl group at C-4. Further confirming features were the shift of the vinyl hydrogen of the propenyl side chain from 5.85 ppm in **7** to 7.29 ppm in **8** and the appearance in **8** of the C-5 hydrogen at 6.46 ppm. Oxidation[13] of **8** (AgO/HNO_3) cleaved the 7,12-dimethoxyl groups, furnishing *O*-methylkidamycinone **1b**[11,14] in 83% yield (mp 251-252 °C).

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(10) Satisfactory analyses were obtained for all compounds.
(11) Unless otherwise noted, all ^{1}H NMR spectra were determined in CCl_4 with tetramethylsilane internal standard: **3a,** δ 2.27 (s, 3 H), 3.75 (s, 3 H), 3.77 (s, 3 H), 3.87 (s, 3 H), 3.90 (s, 3 H), 6.74 (d, $J = 8$ Hz, 1 H), 7.28 (t, $J = 8$ Hz, 1 H), 7.60 (d, $J = 8$ Hz, 1 H); **4a,** δ 2.43 (s, 3 H), 2.59 (s, 3 H), 3.96 (s, 6 H), 3.99 (s, 3 H), 6.66 (d, $J = 8$ Hz, 1 H), 7.25 (t, $J = 8$ Hz, 1 H), 7.39 (s, 1 H), 7.25 (t, $J = 8$ Hz, 1 H), 7.72 (d, $J = 8$ Hz, 1 H); 7, δ 1.77 (d, $J = 7$ Hz, 1.5 H), 1.84 (s, 4.5 H), 2.38 (s, 3 H), 3.90 (s, 3 H), 3.94 (s, 3 H), 3.96 (s, 3 H), 5.85 (br q, $J = 7$ Hz, 1 H), 6.41 (d, $J = 16$ Hz, 1 H), 6.63 (d, $J = 8$ Hz, 1 H), 6.98 (d, $J = 16$ Hz, 1 H), 7.21 (t, $J = 8$ Hz, 1 H), 7.43 (s, 1 H), 7.71 (d, $J = 8$ Hz, 1 H), 10.50 (s, 1 H); **8,** δ 1.98 (d, $J = 7$ Hz, 1.5 H), 2.02 (s, 4.5 H), 2.98 (s, 3 H), 3.88 (s, 3 H), 4.03 (s, 3 H), 4.08 (s, 3 H), 6.46 (s, 1 H), 6.84 (d, $J = 8$ Hz, 1 H), 7.19–7.40 (br m, 1 H), 7.50 (d, $J = 8$ Hz, 1 H), 7.80 (s, 1 H), 7.88 (d, $J = 8$ Hz, 1 H); **1b,** δ 2.01 (s, 4.5 H), 2.04 (d, $J = 6$ Hz, 1.5 H), 2.98 (s, 3 H), 4.05 (s, 3 H), 6.35 (s, 1 H), 7.2–7.5 (m, 2 H), 7.68 (t, $J = 8$ Hz, 1 H), 7.88 (d, $J = 8$ Hz, 1 H), 7.91 (s, 1 H). UV for **1b:** λ_{max}^{EtOH} 216 nm (ϵ 27 600), 237 (33 800), 268 (28 200), 320 (5900), 384 (7500).
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A High-Field Mössbauer Study of the Iron Sites in Mixed-Valent Biferrocene Monocation

Sir:

In an attempt to elucidate the electron-exchange mechanisms and differences in apparent exchange rate in biferrocene(1+) and bis(fulvalene)diiron(1+) (BFDFe(1+)), we have studied biferrocene, biferrocene(1+), biferrocene(2+), and ferricenium ion using Mössbauer spectroscopy in external magnetic fields at low temperature. Our results are not consistent with the accepted view of biferrocene(1+) as consisting of a ferrocene-like Fe(II) and a ferricenium-like Fe(III)[1,2] and point to the need for a re-formulation of the electronic structure of these systems.

Biferrocene monocation and dication are paramagnetic,[3,4] with the formally mixed-valent (Fe(II),Fe(III)) monocation displaying intense absorption in the near-infrared region of the electronic spectrum, often attributed to intervalent charge

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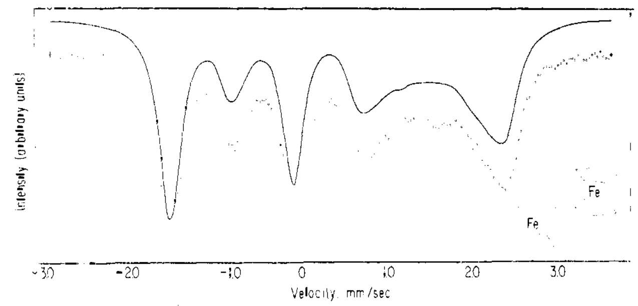

Figure 1. Iron-57 Mössbauer spectrum of a powdered sample of biferrocene at 4.2 K and 60-kOe longitudinal applied field. Velocities are relative to metallic iron. A computer simulated spectrum for V_{zz} positive, $e^2qQ/2 = 2.32$ mm/s, $\eta = 0.0$, and $H_n = 60$ kOe is shown as a solid line.

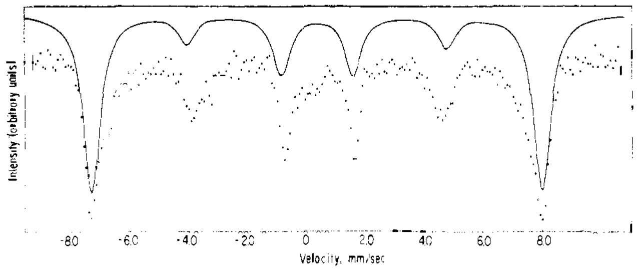

Figure 2. Iron-57 Mössbauer spectrum of a powdered sample of ferricenium hexafluorophosphate at 4.2 K in 60-kOe longitudinal applied field. Velocities are relative to metallic iron. The solid line is a computer simulated Mössbauer spectrum for $e^2qQ/2 = 0.20$, $\eta = 0$, and $H_n = 474$ kOe. Residual $\Delta m = 0$ transitions were simulated by assuming an angle of 28° between H_n and the direction of γ-ray propagation.

transfer.[5] ESCA[6] and Mössbauer studies[2,7] on the monocation have been interpreted in terms of distinct Fe(II) and Fe(III) sites, and the molecule is considered to be a class II mixed-valent species. On the other hand, ESCA[8] and Mössbauer[1,8] studies on the BFDFe monocation give evidence for a single iron site and are interpreted in terms of fully delocalized valence electrons[9] or a class III mixed-valent species.[8] The reason for the different rates of electron transfer has been a subject of debate for several years.

The zero-field ^{57}Fe Mössbauer spectrum of biferrocene consists of a single quadrupole doublet with splitting at 4.2 K, $\Delta E_Q = 2.32$ mm/s, and isomer shift (with respect to iron-metal), $\delta_{Fe} = 0.39$ mm/s. Our results are in agreement with previously reported values for ΔE_Q and δ_{Fe}[10] and compare with measurements in ferrocene (298 K, $\Delta E_Q = 2.36$ mm/s, $\delta_{Fe} = 0.45$ mm/s).[10] The biferrocene spectrum at 4.2 K and a longitudinal applied field $H_0 = 60$ kOe is shown in Figure 1, together with a computer simulation assuming $e^2qQ/2 = 2.32$ mm/s, the sign of the principal component of the electric field gradient tensor V_{zz} positive, the asymmetry parameter $\eta = 0$, and the field at the nucleus $H_n = H_0$. This spectrum is comparable with the spectrum for ferrocene in an external magnetic field obtained by Collins[11] and indicates that the iron atoms in biferrocene are electronically equivalent to the iron in ferrocene.

The spectrum of the ferricenium ion at 4.2 K in zero field consists of a broadened single line or unresolved quadrupole doublet[10,11] with isomer shift $\delta_{Fe} = 0.44$ mm/s. The spectrum of ferricenium PF$_6$ at 4.2 K and $H_0 = 60$ kOe is shown in Figure 2. The overall splitting of the spectrum indicates a large induced hyperfine interaction in addition to the applied field ($\bar{H}_n = \bar{H}_0 + \bar{H}_{hf}$). Measurements at various fields up to 80 kOe show that this interaction is equivalent to 414 kOe and has a positive sign. The residual absorption at the positions of the $\Delta m = 0$ transitions indicate that $\bar{H}_{hf}$ is not parallel to $\bar{H}_0$, which is due to an anisotropic g factor. The Mössbauer spectrum of the dication, biferrocene(2+) at 4.2 K and 60 kOe is virtually identical with that of ferricenium PF$_6$, with a slightly reduced hyperfine interaction of + 406 kOe, and indicates that the iron atoms in biferrocene(2+) are electronically equivalent to the iron site in ferricenium ion.

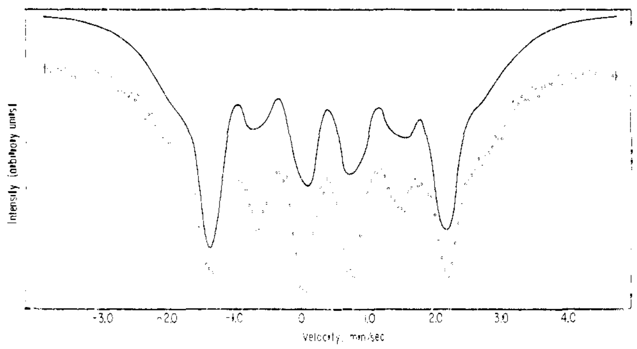

Figure 3. Iron-57 Mössbauer spectrum of a powdered sample of biferrocene(1+) hexafluorophosphate at 4.2 K in a 60-kOe longitudinal applied field. Velocities are relative to metallic iron. The solid line is a computer simulated Mössbauer spectrum generated by summing two spectra with (a) V_{zz} positive, $e^2qQ/2 = 1.85$ mm/s, $\eta = 0.90$, $H_n = 58$ kOe; and (b) V_{zz} positive, $e^2qQ/2 = 0.48$ mm/s, $\eta = 0.90$, and $H_n = 138$ kOe.

The zero-field 4.2 K spectrum of biferrocene(1+) PF$_6$ consists of two quadrupole doublets[1,2] with parameters for the inner and outer doublets, $\Delta E_Q = 0.50$ mm/s, $\delta_{Fe} = 0.40$ mm/s, and $\Delta E_Q = 2.08$ mm/s, $\delta_{Fe} = 0.39$ mm/s, respectively. The outer doublet has been attributed to the ferrocene portion of the molecule, while the inner doublet has been ascribed to the ferricenium portion. Thus, if we accept this interpretation we might expect the magnetic field spectrum to consist of a superposition of a ferrocene-like spectrum (Figure 1) and a ferricenium-like spectrum (Figure 2). However, this is not what is observed. The 4.2 K, $H_0 = 60$ kOe spectrum is shown in Figure 3. The primary features of the spectrum are the six resolved lines which arise from the splitting of the outer quadrupole doublet into two apparent triplets. Careful inspection of the spectrum reveals non-Gaussian shape for the outermost lines. This may be ascribed to a second spectrum arising from the inner quadrupole doublet. Also shown in Figure 3 is a computer simulation[12] based on the following assumptions. For the first spectrum, $H_n = 58$ kOe, $e^2qQ/2 = 1.85$ mm/s, V_{zz} positive, and in contrast to ferrocene, $\eta \approx 1$. For the second spectrum $H_n = 138$ kOe, $e^2Q/2 = 0.48$ mm/s, V_{zz} positive, and $\eta = 0.9$. Because the spectrum is not resolved, the sign of V_{zz} and the magnitude of η could not be determined with precision. As can clearly be seen, both portions of the spectrum differ significantly from the spectra observed in biferrocene and biferrocene(2+).

The Mössbauer spectroscopy of the biferrocene series seems to distinguish three situations: (i) for biferrocene a low-spin iron(II) in an electronic environment that produces an axially symmetric electric field gradient at the iron nucleus, as in ferrocene; (ii) for biferrocene(2+) a low-spin iron(III) in an electron environment that produces a large, positive hyperfine interaction at the iron nucleus, as in ferricenium ion; (iii) for biferrocene(1+) (formally a mixed-valent iron(II) and iron(III) system) the two sites are distinguishable, but the iron(II) site has a very asymmetric electric field gradient tensor and no magnetic hyperfine interaction and the other site has a small magnetic hyperfine interaction. This latter situation would arise if the unpaired electron occupies a predominantly ligand-based orbital which is asymmetric with respect to the two iron sites. Such an orbital might involve the π-electron system of the fulvalene bridging ligand (see inset in Figure 1), which can be asymmetric for trans iron sites. In the BFDFe series in which the iron sites are cis, an unpaired electron in the fulvalene bridge system would be symmetric with respect to both irons and should produce a Mössbauer spectrum with a small or zero hyperfine field and an asymmetric electric field gradient tensor. Preliminary measurements of the monocation BFDFe(1+) BF_4 are consistent with this hypothesis. Complete results will be published in a subsequent report.

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(12) The experimental spectrum in Figure 3 is a superposition of many spectra corresponding to the various orientations of the principal components of the electric field gradient tensors in the polycrystalline absorber with respect to the external field direction (parallel to the γ-ray propagation direction). The computer simulation mimics this by calculating spectra for discrete orientations and summing with appropriate weighting factors. The solid line in Figure 3 is a composite assuming two sites, with appropriate summation of calculated spectra for each site, and corresponding to the two quadrupole splittings observed in zero field. For a general description of the calculations, see Collins, R. L.; Travis, J. C. "Mössbauer Effect Methodology", I. Gruverman, Ed.; Plenum Press: New York, 1967; Vol. 3, p 123.

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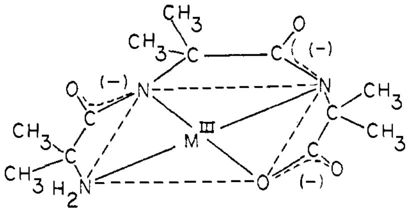
Thermally Stable Copper(III)- and Nickel(III)-Tripeptide Complexes and Their Photochemical Decomposition in Acid Solution

Sir:

Previously, we have reported numerous examples of deprotonated peptide complexes containing copper[1,2] and nickel[3,4] in trivalent oxidation states. These complexes exhibit variable stability in solution, persisting from seconds to hours.[3,5-7] However, both the copper(III) and the nickel(III) complexes undergo self-oxidation-reduction, catalyzed by either acid or base,[6,8,9] in which the ligand is oxidized and the metal ion is reduced. This lack of long-term stability over a wide range of pH often complicates or limits investigations of the reactions of these complexes with other species.

The decomposition products of the copper(III) and nickel(III) complexes of tetraglycine[6,8,9] show that ligand oxidation occurs at the methylene groups. Although tripeptide complexes are in general less stable than tetrapeptide or pentapeptide complexes, studies in this laboratory have shown that the substitution of methyl groups for methylene hydrogens tends to increase the stability of peptide complexes. Thus, copper(III) and nickel(III) complexes of glycylglycylalanine are significantly more stable than their triglycine analogues.

In the present study an amino acid, α-aminoisobutyric acid (Aib), with no methylene hydrogens was used to synthesize the tripeptide and its copper and nickel complexes. Structure I proposed for the $M^{III}(H_{-2}Aib_3)$ complexes is consistent with the structures of many other peptide complexes.[10] Electron spin resonance studies indicate that in solution axial coordination of water molecules occurs with the nickel(III) complex.[7] These complexes of Aib_3 are unusually resistant to decomposition in acid. In the absence of light or reducing agents the copper(III) and nickel(III) complexes show no decomposition over periods of weeks to months in 0.05-0.5 M $HClO_4$. Even in 5 M $HClO_4$ the complexes will last for days to weeks. The inertness of the complexes in acid indicates a remarkable kinetic stability of copper(III) and nickel(III) coordinate bonds toward solvent substitution and an even more remarkable resistance of the peptide coordination to acid attack. In addition the complexes are resistant to self-redox. They are, however, very sensitive to photochemical decomposition by visible radiation. The photolysis causes oxidative decarboxylation of the tripeptide and the formation of acetone.



I

Tri-α-aminoisobutyric acid was prepared by a combination of conventional techniques, starting with the benzyloxycarbonyl amino acid (CbzAib)[11] and the amino acid benzyl ester (AibOBz).[12] Carbodiimide coupling[13] was used to form the dipeptide derivative from these precursors. The dipeptide benzyl ester was formed by reaction of the $CbzAib_2OBz$ with HBr-saturated acetic acid.[14] It was then coupled with another equivalent of CbzAib, again using *N,N′*-dicyclohexylcarbodiimide. The free peptide was isolated by catalytic hydrogenation[13,15] of the Cbz tripeptide benzyl ester. Anal. Calcd for $C_{12}H_{23}N_3O_4$: C, 52.73; H, 8.48; N, 15.37. Found: C, 52.93; H, 8.50; N, 15.34.

Solid samples of $Cu^{III}(H_{-2}Aib_3)$ were prepared by dissolving the pure tripeptide in dilute NaOH, reacting it with freshly precipitated $Cu(OH)_2$, and electrolyzing the copper(II) complex solution by passing it through an electrochemical flow cell.[16] The neutral copper(III) complex was collected in dilute $HClO_4$ in the dark and at low temperatures. Ionic species were separated from this solution by passing it through a Retard-Ion (Bio-Rad) resin. The eluant was then lyophilized, yielding solid $Cu^{III}(H_{-2}Aib_3)$. Anal. Calcd for $CuC_{12}H_{20}N_3O_4$: C, 43.2; H, 6.00; N, 12.6. Found: C, 43.5; H, 6.25; N, 12.5.

A similar procedure was used for $Ni^{III}(H_{-2}Aib_3)$ with special care to avoid basic conditions once nickel(III) was obtained. Anal. Calcd for $NiC_{12}H_{20}N_3O_4$: C, 43.8; H, 6.08; N, 12.8. Found: C, 43.6; H, 6.25; N, 12.9.

Table I outlines some of the properties which characterize the copper(III) and nickel(III) complexes of Aib_3. The ultraviolet-visible (UV-vis) spectra are similar to those of other tripeptide complexes,[4,17] where two intense charge-transfer bands are seen. In general copper(III) has one band at 260-280 and another band with a lower absorptivity at 380-400 nm. Nickel(III) tripeptides typically have bands at 250-260 and 340-360 nm. The reactivity of the Aib_3 complexes with various reducing agents gives further evidence that the trivalent metal complexes are present. Ascorbic acid, hydroquinone, and Fe(II) all react quantitatively with these complexes. This property was utilized in determining their molar absorptivities by spectrophotometric redox titrations.

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