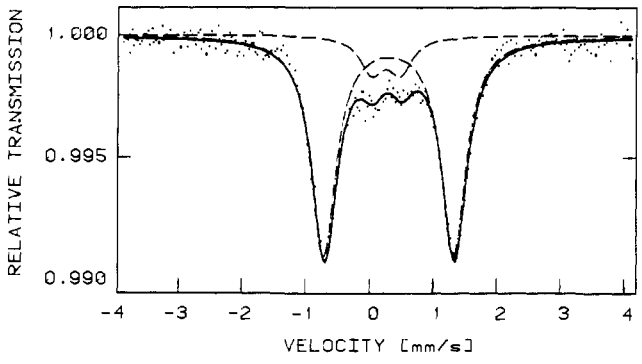

Figure 3. Mössbauer spectrum of $[Fe(O_2)TPpivP(SC_6HF_4)]^-[K\text{-}2.2.2.]^+$ at 77 K. The sample is 85 ± 5% pure and may contain 15 ± 5% iron(III).

at 1139 cm^{-1}. This band is not present in the CO adduct or in the five-coordinate material (Figure 2). Substituting $^{18}O_2$ for natural oxygen would shift this absorption to the 1073-cm^{-1} region. Unfortunately, this part of the spectrum is obscured by a near total absorption of chlorobenzene so the initial experiments could only indirectly confirm the attribution of the O–O stretching vibration: when $^{18}O_2$ was used, there was indeed no absorption at this wavelength but we could not detect the oxygen-18 stretching vibration. A careful search for a different good solvent led to the use of fluorobenzene (Figure 2). The experiments carried out in this solvent revealed the appearance of the $^{18}O_2$ stretch at 1076 cm^{-1}, in good agreement with the calculated value of 1073 cm^{-1} for a pure harmonic oscillator.

Finally, Mössbauer spectroscopy confirms the formulation of **3** as an O_2 adduct. The studies carried out on the anion $[FeTPP(SC_6H_5)]^-$ at low temperature have shown that a species displaying the Mössbauer features of an oxy adduct are indeed observed when oxygen is admitted to the solid sample: a quadrupole doublet with IS = 0.312 $mm\cdot s^{-1}$, ΔE_q = 2.015 $mm\cdot s^{-}$, and Γ_{expt} = 0.272 $mm\cdot s^{-1}$ was observed at 77 K. These values are similar to those reported for oxy-P-450.[12] They are quite insensitive to the nature of the sixth ligand and have the same magnitude for oxyhemoglobin[13] and the oxyhemoglobin model compounds reported by Collman et al.[14] However, despite repeated attempts under various conditions of pressure and temperature, we could not obtain more than about 40% oxygenation on bulk samples of 100 mg.[5]

The sample used in the present study, $[Fe(O_2)TPpivP(SC_6HF_4)]^-$, was obtained by exchanging CO in the carbonyl adduct **2**. A solution of **2** was purged with oxygen for 30 min, pentane was added, and the resulting oil was frozen and transferred to the sample holder. The Mössbauer spectrum, reproduced in Figure 3, shows that 85 ± 5% exchange has taken place. There is about 15% of a second species, probably iron(III) (vide infra). The parameters obtained at 77 K are nearly the same as for the TPP adduct, namely, IS = 0.30, ΔE_q = 2.04, and Γ_{expt} = 0.48 $mm\cdot s^{-1}$ (±0.02 $mm\cdot s^{-1}$). Present efforts are directed at obtaining a pure sample. A complete Mössbauer study of all three complexes will be reported later.

Prolonged exposure of **3** to an oxygen atmosphere or UV irradiation at 190 nm results in the formation of a new species with absorptions at 419 and 505 nm. This spectrum is typical of five-coordinate iron(III), and Mössbauer spectroscopy indeed confirms that an iron(III) species is formed under these circumstances (≃30% in 6 h). A material with an identical UV–visible spectrum, $FeTPpivP(SC_6HF_4)$, **4**, can be synthesized in a manner similar to Holm's preparation.[2] The above-mentioned observations suggest that the oxy complex **3** is degraded following the reaction $[Fe^{II}(O_2)TPpivP(SC_6HF_4P)]^- \rightleftarrows Fe^{III}TPpivP(SC_6HF_4) + O_2^-$.[20]

Interestingly, solutions of **3** can be reduced to the iron(II) complex **1** upon slight warming when the oxygen atmosphere is pumped off, even though there seems to be no excess thiolate left. In a separate experiment, solutions of **4** were reacted under argon at −30 °C with solutions of $[K^+\text{-}2.2.2.]O_2^-$, resulting in the immediate formation of **3**, as shown by the identity of UV–visible spectra. This parallels the results of Valentine et al.[15]

That superoxide ions are formed upon degradation of the oxy complex **3** constitutes a further similarity with the behavior of cytochrome P-450.[16] Current ESR experiments should further confirm this point.

The evidence presented above shows that an oxy adduct mimicking the properties of oxy-P-450 can be obtained. The reversibility of the oxygenation–carbonylation reaction demonstrates the presence of sulfur bonding to iron.[17] The decreased frequency of the O–O stretching vibration relative to that reported for oxyhemoglobin models[18] (1163 cm^{-1}) would similarly indicate the presence of a larger charge on iron.[19] This complex undoubtedly constitutes a model for the oxy state of cytochrome P-450. Its good thermal stability will facilitate further studies on other putative intermediates in the P-450 cycle.

Acknowledgment. This work has been supported by the CNRS (ATP No. 4097) and by the Deutsche Forschungsgemeinschaft.

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Synthesis and Structure of $[FeCo_3(CO)_{12}AuPPh_3]$: A Trimetallic Trigonal-Bipyramidal Cluster. Gold Derivatives as Structural Analogues of Hydrides

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The stereochemical influence of the hydride ligand and the structures of transition-metal hydrides have been topics of considerable controversy and discussion.[1,2] Overlooked has been a close structural relationship between certain hydrido–metal complexes and $AuPPh_3$ derivatives exemplified by such pairs of compounds as the complexes $[Co(CO)_4AuPPh_3]$ and $[Co(CO)_4H]$ with capped tetrahedral geometries,[3,4] the complex $[Fe(CO)_4\{AuPPh_3\}_2]$, which we have shown to have the same bicapped tetrahedral geometry as the hydride $[Fe(CO)_4H_2]$,[4,5] and the double-bridged Os_3 clusters $[Os_3(CO)_{10}(\mu\text{-}X)(\mu\text{-}L)]$ with X = Cl or Br and L = H or $AuPPh_3$.[6,7,8]

The structural similarities may seem to be surprising at first because it would seem that a gold phosphine group and a hydride

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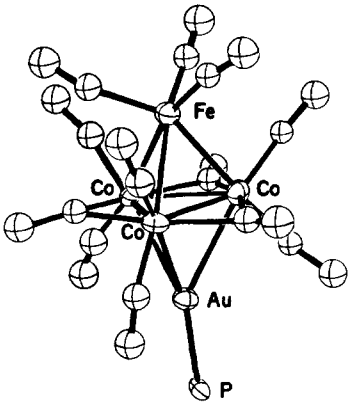
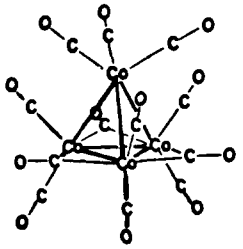


Figure 1. ORTEP plot of the $[FeCo_3(CO)_{12}AuPPh_3]$ molecule. The phenyl groups are ommitted for clarity. The iron atom has not been directly distinguished but is assigned by analogy to its location in **4** (see text).

would have little in common from either an electronic or steric viewpoint. Upon closer examination, however, they are not so different. Gold atoms are large, but there is no steric problem since with longer bonds they are further away from a transition metal. Hydrogen bonds to a metal by using its 1s orbital; gold uses primarily its 6s orbital. The bonds formed between gold atoms and transition-metal anions are very polar and carbonyl infrared spectra indicate that the electron density on the transition metal tends to be intermediate between that of the free anion and its hydride.

The first mixed-metal clusters ever reported were the cluster anion $[FeCo_3(CO)_{12}]^-$, **1**, and the hydride $[HFeCo_3(CO)_{12}]$, **2**, synthesized by Chini and co-workers more than 20 years ago.[9] Their basic structures were recognized to be analogues of $[Co_4(CO)_{12}]$,[10,11] **3**, but there was considerable discussion regarding



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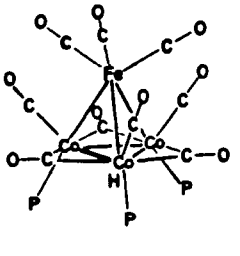

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the location of the hydrogen atom in the hydride.[12-14] The controversy was ended when the structure of a trimethyl phosphite derivative, $[HFeCo_3(CO)_9\{P(OMe)_3\}_3]$, **4**, was determined by Kaesz[15] and confirmed in a neutron study by Koetzle and Bau.[16] They found a C_{3v} structure similar to that of **3**, with the hydride bridging the three Co atoms.

We have now prepared the gold derivative $[FeCo_3(CO)_{12}AuPPh_3]$, **5**, by the direct reaction of the cluster anion $[FeCo_3(CO)_{12}]^-$, **1**, with an equivalent amount of (triphenylphosphine)gold(I) nitrate in acetone. The product has an intense purple color and an infrared spectrum similar [2075 (w), 2005 (s), 1975 (m), 1930 (s), 1820 (m)] to that of the parent anion.[9]

An X-ray diffraction study of **5** has revealed that the molecule crystallizes in space group $P2_1$ with $a = 9.174$ (2) Å, $b = 15.103$ (2) Å, $c = 12.708$ (3) Å, $\alpha = 108.08$ (2)°, $V = 1674$ Å^3, ρ_{calcd} = 2.04 g cm^{-3}, and $Z = 2$. Diffraction data were collected on an Enraf-Nonius CAD4A diffractometer using Mo Kα radiation. The structure was solved by Patterson and difference Fourier methods and refined by least-squares methodology to final indices of $R = 3.8\%$ and $R_w = 4.2\%$ for the 1915 data in the range $0 < 2\theta < 50°$ with $F_o > 3\sigma(F_o)$.

Table I. Selected Average Bond Distances (Å) and Angles (Deg) for $[FeCo_3(CO)_{12}AuPPh_3]$, **5**, $[HFeCo_3(CO)_9\{P(OMe)_3\}_3]$,[7,8] **4**, and $[Co_4(CO)_{12}]$,[3] **3**

	5	4	3
Fe–Co	2.56 (8)	2.560 (2)	
Co–Co	2.52 (8)	2.488 (12)	2.49 (2)
Au–Co	2.714 (7)	1.734 (4) H–Co	
Fe–C	1.79 (14)	1.798 (9)	
Co–C_{trm}	1.75 (6)	1.755 (8)	1.9 (2)
Co–C_{br}	1.94 (7)	1.954 (13)	2.07 (11)
Co–Fe–Co	59.0 (2)	58.1 (3)	59.8 (1.3)
Fe–Co–Co	60.5 (13)	60.9 (1)	60.1 (7)
Au–Co–Fe	112.9 (15)	83.8 (5) H–Co–Fe	
Co–Au–Co	55.3 (3)	91.8 (2) Co–H–Co	
C–Fe–C	96 (2)	96 (2)	102 (2)
Fe–Co–$C_{cis\text{-}trm}$	78 (3)	81 (3)	92.8 (9.8)
Fe–Co–$C_{trans\text{-}trm}$	173 (2)	174 (3) Fe–Co–P	162.4 (5.8)
Fe–Co–C_{br}	84 (3)	82 (2)	82.6 (3.3)

The structure consists of a trigonal-bipyramidal array of metal atoms with the gold atom at one apical position. We could not on the basis of our data distinguish the Fe atom from the Co atoms but have assigned the Fe atom to the opposite apical position by analogy to its location in **4**. The $FeCo_3(CO)_{12}$ portion of the molecule has a structure similar to that of **3** with the same general arrangement of CO ligands, but the various bond angles, Table I, are much closer to those in the trimethyl phosphite substituted hydride **4**. In particular, the average Fe–Co–C angle for the cis-terminal CO ligands is substantially less in the capped compounds (Au, 78°; H, 81°) than in **3** with a Co–Co–C angle of 93°. However, the angles to the trans-terminal CO or phosphite ligands are greater in the capped compounds (Au, 173°; H, 174°) vs. **2** (162°). The average Fe–Co bond distances (2.56 Å) are identical in **4** and **5** and the average Co–Co distances are similar (Au, 2.52 Å; H, 2.49 Å). We believe that the structure of **5** is likely to be even closer to that of the parent hydride, $[HFeCo_3(CO)_{12}]$, **2**, than it is to the phosphite derivative.

The compound **5** contains the first example of a Au atom triply bridging three transition-metal atoms. The average Au–Co bond length of 2.714 Å is 0.21 Å longer than the 2.50 Å single-bond distance found in $[Co(CO)_4AuPPh_3]$.[3] In a neutron diffraction study of **4** the Co–H distances averaged 1.734 Å, also about 0.2 Å longer than the expected single-bond distance (1.52 Å).[2,16]

It should be possible to prepare gold phosphine analogues of most transition-metal hydrides with the obvious exceptions of cluster interstitials. Investigations of the structures of the gold analogues may in some cases be more appropriate than studies of the hydrides themselves. This will be true in cases where the hydride is unstable. For example, the compounds $[V(CO)_6H]$ and $[WC_5H_5(CO)_3H]$ are quite reactive and good crystallographic studies have not been possible, but structures of the analogous gold derivatives have been determined[17,18] and are likely good hydride models.

Gold derivatives may also prove to be useful as analogues of heavy metal or cluster hydrides in which the location of the hydrogen cannot be determined by X-ray diffraction. Finally a gold derivative of a fluxional hydride might serve as a model of one single stabilized isomer.

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Supplementary Material Available: A table of the positional and thermal parameters and their estimated standard deviations (2 pages). Ordering information is given on any current masthead page.

Cell-Free Biosynthesis of Penicillins. Conversion of Peptides into New β-Lactam Antibiotics

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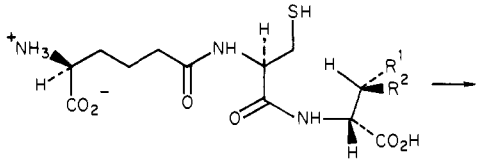
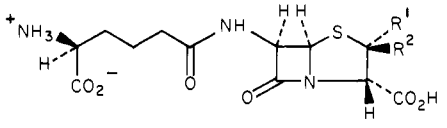
The efficient conversion of (L-α-amino-δ-adipyl)-L-cysteinyl-D-valine (**1**) to isopenicillin N (**2**) by a partially purified cell-free system from *Cephalosporium acremonium* has been studied in detail during investigations of the mechanism of formation of the pencillin ring system.[1,2] We now report the results of experiments with structural analogues[1] of tripeptide **1** designed to evaluate the substrate specificity of this conversion. The results of these experiments have shown, for the first time, that the cyclase enzyme system, which converts **1** to **2**, is able to accept and transform modified substrates into new penicillins. Furthermore, these substrates act as inhibitors of the conversion of the natural substrate **1** into isopenicillin N.



1, $R^1 = R^2 = CH_3$
3, $R^1 = CH_3$; $R^2 = CH_3CH_2$
4, $R^1 = CH_3CH_2$; $R^2 = CH_3$
5, $R^1 = H$; $R^2 = CH_3$



2, $R^1 = R^2 = CH_3$
11, $R^1 = CH_3$; $R^2 = CH_3CH_2$
12, $R^1 = CH_3CH_2$; $R^2 = CH_3$
14, $R^1 = H$; $R^2 = CH_3$

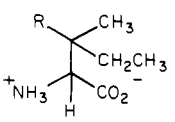
The L,L,D-tripeptides **3**, **4**, and **5** were synthesized by standard procedures[3,4] and separately incubated with a cell-free system from *C. acremonium* C-91.[1] The extent of conversion to bioactive products was assayed with *Staphylococcus aureus* NCTC 6571. Under these conditions each peptide was converted into a penicillinase-sensitive antibiotic, presumed to be an analogue of isopenicillin N. However, the extent of conversion under the conditions used was much less than the virtually quantitative yield from the natural substrate **1**. After 60-min incubation a significant proportion of these analogues remained unchanged and they behaved as inhibitors of the natural substrate (see Table I).

Table I. Conversion of Peptides to Penicillins in Extracts of *C. acremonium*

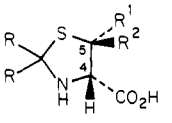
peptide	product	% yield[a]	% inhibition[b]
1	2	100	
3	11	36	40
4	12	4	75
5	14[c]	10	78

[a] Peptides (1 mM) and cell-free extract (4–10 mg/mL protein) were incubated at 27 °C. Yields after 60 min were estimated by bioassay (*S. aureus* NCTC 6571) on the assumption that penicillins 11, 12 and 14 had about 50% of the specific antibacterial activity of isopenicillin N (**2**).[5] Since conversion of 1 to **2** was quantitative within 30 min. the yields shown may provide an overestimate of the relative rates of conversion of the peptide analogues of 1. [b] Inhibition is defined as the decrease (%) in the bioactivity generated after 30 min when a peptide analogue (1 mM) was incubated with the cell extract (1–2 mg/mL protein) for 15 min at 27 °C before addition of the natural substrate (1) (0.4 mM). [c] Predominant product.

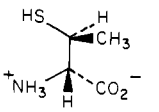
The nature of the biosynthesis products was determined as follows. Oxidation (performic acid, 4 °C, 5 h) of the incubation mixture from **3**, followed by electrophoresis on paper (pH 1.8), gave a sulfonic acid[6] (cadmium ninhydrin positive) which comigrated with the more mobile of a diastereomeric pair of sulfonic acids **6** produced by similar oxidation of a diastereomeric mixture



6, R = SO_3H
7, R = SH



8, $R = CH_3$; $R^1 = CH_3$; $R^2 = CH_3CH_2$
9, $R = CH_3$; $R^1 = CH_3CH_2$; $R^2 = CH_3$
10, $R = CD_3$; $R^1 = CH_3CH_2$; $R^2 = CH_3$



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of β-mercapto-DL-isoleucine **7**[7]. This result, coupled with the antibiotic activity and penicillinase sensitivity, is consistent with a stereospecific conversion of **3** into a penicillin bearing a 2-ethyl substituent. The stereochemistry was determined as follows. Fractional crystallization (acetone, ethanol) of the thiazolidine mixture **8** and **9** prepared by reaction of **7** with acetone (reflux) gave one diasteromer, **8**, mp 182–184 °C (dec),[8] which was oxidized (performic acid) to a sulfonic acid which comigrated with that derived from the biosynthetic experiment (electrophoresis on paper, pH 1.8). The relative configuration of **8** was established by observation of an NOE (300 MHz, D_2O) on the C-5 ethyl group on irradiation of the C-4 (δ 4.38) hydrogen. The minor isomer **9**, corresponding to the less mobile sulfonic acid, gave an NOE (18%) on C-4 (δ 4.45) hydrogen upon irradiation of the C-5 (δ 1.47) methyl group. This NOE was also observed in **10**, the deuterated analogue, thereby removing the possibility of misassignments of the methyl groups. Thus the relative stereochemistry of **8** is as shown and hence that of the new penicillin corresponds to **11**.

Incubation of **4**, derived from D-alloisoleucine, gave a smaller yield (Table I) of a bioactive, penicillinase-sensitive product. The latter was oxidized to a sulfonic acid and shown (electrophoresis)

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