reaction 2 (ΔH^0_2 = −18.5 ± 0.8 kcal/mol).[20] Reversible dimerization of **2** through C–C bond formation to produce a 1,2-ethanedionyl bridged complex (eq 2) can be viewed as being related to formyl radical coupling (2HĊO → H(O)C–C(O)H). However, dimerization of (TMP)Rh–ĊO must involve substantially larger electronic and structural rearrangement of the Rh–CO unit compared to that required for HĊO as evidenced by the small ΔH^0 for reaction 2. Rehybridization and reduction of the CO fragment of **2** is completed only when a second covalent bond is formed with the carbonyl center as occurs in the formation of **3**. This work also supports previous indications that the carbonyl carbon in (por)Rh–ĊO species functions as a site for one-electron reactions such as hydrogen atom transfer from a metallohydride to produce a metalloformyl species[10] and reaction with a second metalloradical to form dimetal ketone complexes.[11,12] Rhodium porphyrin systems are currently unique in providing metalloradical activated carbonyl species at equilibrium, where one-electron reactions at the carbonyl center can be more fully exploited.

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(20) 2(TMP)Rh–ĊO ⇌ ((TMP)Rh–(CO))$_2$; K_2 = [((TMP)Rh–CO)$_2$]/[(TMP)Rh–CO]^2; [((TMP)Rh–CO)$_2$] = [((TMP)Rh–CO)$_2$]$_0$ − $^1/_2$[(TMP)Rh–CO]; $I_{(2)}$ = EPR intensity for **2** adjusted for the temperature dependence of the electron spin populations; $I_{(2)}$[(TMP)Rh–CO] = X; K_2 = [[((TMP)Rh–CO))$_2$]$_0$ − $^1/_2X$]/X^2; $X \ll$ [((TMP)Rh–CO)$_2$] = C; $K_2 = C/X^2$; $X = C'(I_{(2)})$; $K_2 \simeq C/C'^2(I_{(2)})^2 = C''I_{(2)}^{-2}$; ln K_2 = −2 ln $I_{(2)}$ + ln C''. The slope of the linear relationship between −2 ln $I_{(2)}$ and $1/T$ yields $-\Delta H_2^0/R$ (ΔH_2^0 = −18.5 ± 0.8 kcal/mol). Estimating ΔS_2^0 as ≃ −28 cal/mol K yields an estimate for ΔG_2^0 (ΔG_2^0 (298 K) ≃ −10.2 kcal/mol; K_2 (298 K) ≃ 3 × 10^7). These thermodynamic estimates demonstrate that the dissociation of **3** into **2** within the range of temperature and concentrations studied (230–290 K) is less than 0.5%.

Novel Trimetallic Complexes of Rhodium with Bis(difluorophosphino)methylamine: The Crystal and Molecular Structure of $[Rh_3(\mu\text{-}Cl)_3(\mu\text{-}H_3CN(PF_2)_2)_3]$

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The coordination chemistry of bis(difluorophosphino)methylamine is notable for the number of unusual structures that can be formed.[1-3] Until very recently when the mixed-valence complex $[Rh_2Cl_2(PF_3)(\mu\text{-}H_3CN(PF_2)_2)_3]$ was reported,[4] the chemistry of this ligand with rhodium and iridium has been conspicuous by its absence. We wish to report findings in this area which include the synthesis of the first *trinuclear* complex of $MeN(PF_2)_2$, $[Rh_3(\mu\text{-}Cl)_3(\mu\text{-}MeN(PF_2)_2)_3]$, shown to adopt an unprecedented cone-shaped structure.

Reaction of $MeN(PF_2)_2$ with $[RhCl(CO)_2]_2$ forms a dark green-black solution which becomes dark red-orange upon concentration under reduced pressure.[5] An X-ray crystallographic analysis[6] of the product obtained (**1**) revealed that instead of the anticipated binuclear "A-frame" species, **1** is *trimeric* with a novel *cone*-shaped structure. The inner coordination sphere of **1** is depicted in Figure 1 and although possessing no crystallographically imposed symmetry, **1** is very close to having C_{3v} symmetry. The average Rh–Rh separation of 3.0964 (4) Å is comparable to that found in binuclear Rh(I) complexes of the "A-frame" type[7,8] and does not require the presence of metal–metal bonding. It is significantly longer than the value of 2.785 (1) Å found in $[Rh_2Cl_2(PF_3)(\mu\text{-}MeN(PF_2)_2)_3]$.[4] The coordination about each metal is approximately square-planar, and there are no unusual metrical parameters.

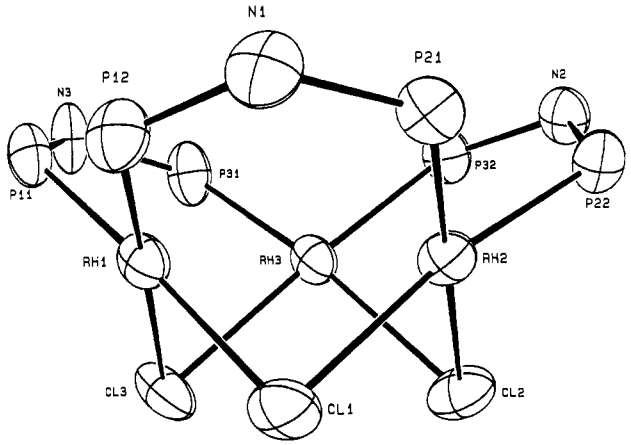

Figure 1. A perspective view of the inner coordination sphere of $[Rh_3(\mu\text{-}Cl)_3(\mu\text{-}MeN(PF_2)_2)_3]$. Thermal ellipsoids are drawn at the 50% probability level.

The structure adopted by **1** represents a new type for closed trinuclear complexes. The closest analogy available appears to be $[Rh_3(\mu\text{-}H)_3(P(OPr^i)_3)_6]$,[9] but, although all three metals there also have square-planar coordination, the dihedral angles between these planes and the Rh_3 plane vary considerably. More important, one bridging hydride ligand lies on the *opposite* side of the Rh_3 plane from the other two, while in **1** all three bridging chloride ligands are on the same side of the Rh_3 plane. Two other similar but less closely related species are $[Pt_3H(\mu_3\text{-}S)(\mu\text{-}DPPM)_3]BPh_4$[10] and $[Pt_3(\mu_3\text{-}CO)(dmpm)_3]PF_6$.[11] Here however two of the bridging diphosphine ligands in the former are more nearly *equatorial* than axial with respect to the Pt_3 plane, while, in the latter, all three are within 0.62 Å of this plane.

Complex **1** reacts readily with carbon monoxide and with 3 equiv of *tert*-butylisocyanide as evidenced by color changes from orange to dark blue-green and dark red-violet, respectively. A slower reaction of **1** occurs with hexafluorobut-2-yne to yield a light orange adduct (**2**) which analyzes for $[Rh_3Cl_3(C_4F_6)(H_3CN(PF_2)_2)_3]$.[12] No apparent reaction occurs under moderate conditions with either dimethylacetylene dicarboxylate or dihydrogen. In **2**, a band of medium intensity at 1612 cm^{-1} suggests the alkyne is bound as a dimetalated olefin.[13] Consistent with the expected unsymmetrical structure the ^1H NMR spectrum shows two resonances for the fluorophosphine methyl groups.[14]

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(5) A solution of 0.400 g (0.806 mmol) of $[RhCl(COD)]_2$ (COD = cycloocta-1,5-diene) in 20 mL of diethyl ether was stirred under carbon monoxide for 30 min. Dropwise addition of 0.270 g (1.612 mmol) of $MeN(PF_2)_2$ in 1 mL of hexane produced a dark yellowish green solution accompanied by gas evolution. Concentration of the solution under reduced pressure resulted in a color change to dark red orange. Filtration, dilution with hexane, and cooling at −10 °C produced dark red orange, air stable crystals.
(6) Crystal data for **1**: $C_3H_9N_3P_6F_{12}Cl_3Rh_3$, fw = 916.06; monoclinic space group $C2/c$, a = 17.323 (2) Å, b = 10.998 (2) Å, c = 23.226 (3) Å; β = 93.03 (1)°; V = 4419 (2) Å^3; Z = 8; d_{calcd} = 2.76 g/cm^{-3}; absorption coefficient = 30.8 cm^{-1}; Mo Kα radiation (graphite monochromated); scan range θ = 3–26°; 4322 unique data with 3811 ≥ 3$\sigma(I)$. Solution by direct methods (MULTAN) with full-matrix refinement to convergence (271 variables); R = 0.030, R_w = 0.038, GOF = 2.72.
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The carbonyl adduct **3** is extremely labile, a feature which has made complete characterization difficult. Thus briefly flushing a solution of **3** with nitrogen rapidly causes a color change to orange,[15] and the ^1H and ^{31}P NMR spectra of this solution are identical with those of **1**.[16] This ready recovery of **1** from **3** strongly suggests that the latter remains trinuclear and its infrared and NMR spectra[17] indicate a symmetrical structure. The addition of 3 equiv of *tert*-butylisocyanide to **1** produces a single species, **4**, as indicated by the ^1H and ^{31}P NMR spectra[18] which are invariant over the temperature range 298-224 K. Given the stoichiometry of the reaction and the lack of evidence in the ^{31}P NMR spectrum for unsymmetrical substitution or the presence of more than one species (i.e., fragmentation of the trimer) we believe that **4** is also a symmetrical adduct of **1**. Although fluxionality in **4** cannot be conclusively ruled out, the invariance of the NMR spectra with temperature would require a high degree of fluxionality which does not seem likely based on previous experience with isocyanide complexes of the "A-frame" type.[19] Unfortunately, attempts to determine if *intermolecular* exchange of isocyanide ligands occurs were frustrated by further reaction of **4** with the added isocyanide to ultimately form $[Rh(CNBu^t)_4]^+$.

The ready recovery of **1** from **3** and the apparent formation of a single species from **1** and 3 equiv *tert*-butylisocyanide suggests that **3** and **4** be formulated as $[Rh_3Cl_3L_3(MeN(PF_2)_2)_3]$ (L = CO, $CNBu^t$). In the absence of structural data we cannot say whether these ligands have simply added to the metal atoms or whether cleavage of the chloride bridges has also occurred. The high value of ν_{CO} in **3** tentatively suggests the latter.

The results obtained here underscore the unpredictable complexing tendencies of $RN(PR'_2)_2$ (R = Me, Et; R' = F, OMe, OPr^i, OCH_2-) ligands. Thus with rhodium alone it is possible to obtain monomers,[20] a variety of symmetrical[20-22] and unsymmetrical[4,21] dimers, and even trimers depending on the nature of the substituents on both nitrogen and phosphorus. We are continuing to explore these interesting systems and will report further details in the future.

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Supplementary Material Available: Tables of positional parameters, bond lengths, interbond angles, anisotropic thermal parameters, and calculated hydrogen atom positions (8 pages). Ordering information is given on any current masthead page.

(14) ^1H NMR ($(CD_3)_2CO$) δ 3.19 (3 H, t (J = 7.3 Hz)), 3.02 (6 H, m). The complex was insufficiently soluble to obtain a satisfactory ^{31}P NMR spectrum.

(15) Evaporation of the solution of **3** with a CO stream yields a dark greenish blue solid which rapidly becomes orange in vacuo. Adduct **3** is thus quite labile even in the solid state.

(16) ^1H NMR ($CDCl_3$) δ 2.99 (t, J_{P-H} = 7.4 Hz); ^{31}P NMR ($CDCl_3/CH_2Cl_2$) δ 135 ($AA'X_2X_2'M$).

(17) IR spectrum ν_{CO} = 2056 cm^{-1} (Nujol), 2064 cm^{-1} (CH_2Cl_2 solution); ^1H NMR ($CDCl_3$, 224 K) δ 3.04 (t, J_{P-H} = 7.0 Hz); ^{31}P NMR ($CDCl_3$, 224 K) δ 135 (m). Although not well-resolved, the ^{31}P NMR spectrum appears as a symmetrical multiplet which is clearly different from that of **1**. The symmetrical appearance together with the single terminal carbonyl stretching frequency indicates the presence of a single species with a symmetrical disposition of carbonyl ligands. On warming the ^{31}P resonance broadens presumably because of CO exchange and on flushing with nitrogen becomes that observed for authentic **1**.

(18) IR spectrum ν_{CN} = 2210, 2171 cm^{-1} (toluene); ^1H NMR ($CDCl_3$, 298 K) δ 2.94 (9 H, t (J_{P-H} = 7.1 Hz)), 1.49 (27 H, s); ^{31}P NMR ($CDCl_3$, 298 K) δ 137 (m). The ^1H and ^{31}P NMR spectra are invariant down to 224 K, and the latter appears as a *symmetrical* complex multiplet. Because of the large number of spins involved, a simulation was not feasible, but the symmetrical appearance strongly argues for chemical equivalence of all phosphorus atoms, a conclusion consistent with the single chemical shifts observed for the ligand methyl groups and for the *tert*-butyl groups.

(19) Loss of isocyanide occurred on drying the apparently crystalline samples of **4** obtained from these solutions which prevented obtaining reliable analyses. This loss was evident from ^{31}P NMR spectra of the dried solid which showed a mixture of **1** and **4** to be present.

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An Approach for Studying the Active Site of Enzyme/Inhibitor Complexes Using Deuterated Ligands and 2D NOE Difference Spectroscopy

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Obtaining detailed structural information on enzyme/inhibitor complexes by NMR spectroscopy is a formidable problem due to the difficulties in analyzing the large number of broad, overlapping NMR signals. In order to simplify the proton NMR spectra of ligand/macromolecule spectra, several experimental approaches have been proposed.[1-5] Recently, we have described[4,5] a method for studying enzyme/inhibitor complexes with use of isotope-editing techniques[6] in which only those protons attached to the isotopically labeled nuclei (^{13}C, ^{15}N) of the ligand are detected. By using these techniques, we were able to determine the conformation of a tightly bound inhibitor of porcine pepsin and help define its active-site environment.[5]

In this communication, we present a simple, alternative method for providing the same type of structural information on large, enzyme/inhibitor complexes that has several practical advantages over previously proposed techniques. The method involves the subtraction of two-dimensional NOE spectra of two enzyme/inhibitor complexes prepared with either a protonated or a deuterated inhibitor. At short mixing times, only NOEs involving ligand protons that have been replaced by deuterium are observed in the 2D NOE difference spectrum.

The technique is illustrated by using the same pepsin/inhibitor (Figure 1) complex (MW = 35 kD) that has been previously studied by isotope-editing procedures.[5] This system was chosen to be able to evaluate the reliability of the method. Figure 2A depicts a contour map of a 2D NOE spectrum of the protonated inhibitor (Figure 1) complexed to pepsin minus a 2D NOE spectrum of pepsin bound to the inhibitor perdeuterated at P_3. The 2D NOE difference spectrum is markedly simplified compared to the individual 2D NOE data sets (not shown), making it possible to interpret the data. NOEs between ligand protons (e.g., $P_3H^\alpha/P_3H^{\beta 3}$, $P_3H^\alpha/P_3H^{\delta 1}$) help define the P_3 side-chain conformation of the bound inhibitor, and NOEs between the ligand and enzyme (boxed NOEs) provide structural information on the active site. For example, the NOEs observed between the P_3 methyl groups of the ligand and enzyme indicate that the P_3 side

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