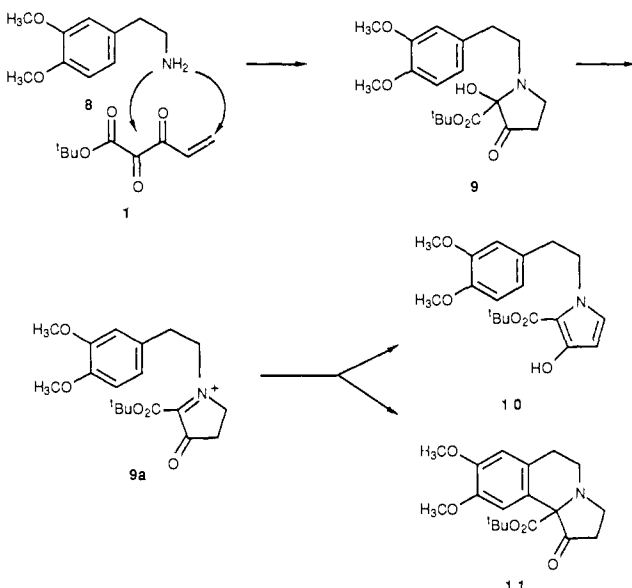**Figure 1.** UPLOT drawing of the vinyl tricarbonyl hydrate **1**.

dehydrating agents such as silica gel to the corresponding 2-carbalkoxy-3-hydroxypyrrole **7** (77%).[9]

Reaction of **1** with reagents having multiple donor sites is illustrated in the two-step formation of the dihydroisoquinoline derivative **11** from dimethoxyphenylethyl amine **8**. The initially
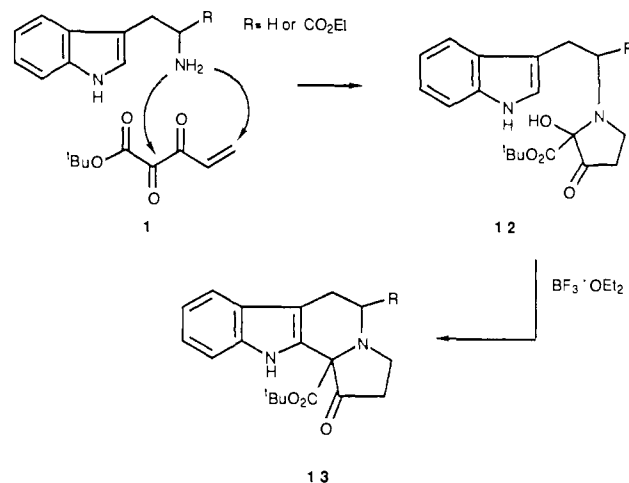

formed pyrrolidinone **9** can be converted on treatment with mild acid to the pyrrole derivative **10**. With POCl₃, however, cyclization of **9** takes place to form the tricyclic product **11** (41%), most probably through the iminium salt **9a**. We are investigating the conversion of **1** to **11** as the first step in the synthesis of alkaloids in the erythrina family.

A noteworthy example of the behavior of the vinyl tricarbonyl **1** as a trielectrophile is found in its reactions with tryptamine or tryptophan ethyl ester, leading to the formation of the tetracyclic system **13**. Here, carbinolamine **12** is formed initially by a double addition of the primary amine to the α,β-unsaturated ketone and the central carbonyl group. Treatment of **12** with BF₃·Et₂O yields the tetracylic system **13**, in 73% yield from the vinyl tricarbonyl. In further reports, we will describe the use of this unusually reactive and versatile polyelectrophile in the formation of other systems, including indolizidines, tricyclic β-lactams, and cyclopentanones.

(8) To the vinyl tricarbonyl **1** (65 mg, 0.32 mmol) in 5 mL of CH₂Cl₂ was added benzylamine (34 mg, 0.32 mmol), and the reaction mixture was stirred at room temperature for 30 min. The solvent was removed in vacuo, and the oil was purified on a silica gel column (Et₂O/pentane, 1:3), yielding 90 mg (93%) of pyrrolidinone **6**: ¹H NMR (90 MHz, CDCl₃) 7.32 (m, 5 H), 4.23 (br s, 1 H), 3.83 (s, 2 H), 3.06 (t, 2 H, *J* = 7 Hz), 2.53 (t, 2 H, *J* = 7 Hz), 1.48 (s, 9 H); MS, CI, *m/z* (rel intensity) 291 (2.8), 217 (13.7), 191 (100).

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13

Characterization of a Novel μ_4-Peroxide Tetrairon Unit of Possible Relevance to Intermediates in Metal-Catalyzed Oxidations of Water to Dioxygen

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At some stage in the mechanism of oxygen evolution from water (eq 1), two oxygen atoms must approach one another to provide

$$2H_2O \rightarrow O_2 + 4H^+ + 4e^- \qquad (1)$$
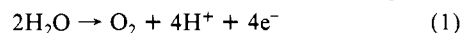
a stereochemical pathway for O–O bond formation. In Photosystem II,[1–3] this coupling is postulated to occur at a tetramanganese center,[4] for which several model complexes have been synthesized.[5] These models offer limited insight into the critical O–O bond forming step, however. Recently, we reported a compound, [Fe₆O₂(OH)₂(O₂CPh)₁₂(H₂O)(1,4-dioxane)] (**1**),[6] in which one could envision oxidative coupling of two closely positioned [2.46 (1) Å] hydroxide ligands mutually supported by four central iron atoms of a hexanuclear cluster. We now wish to describe the synthesis and properties of a novel μ_4-peroxide analogue, [Fe₆(O)₂(O₂)(O₂CPh)₁₂(OH₂)₂] (**2**), prepared by simple ligand substitution of one peroxide for two bridging hydroxides (eq 2; the curved lines denote benzoate groups). Compound **2**

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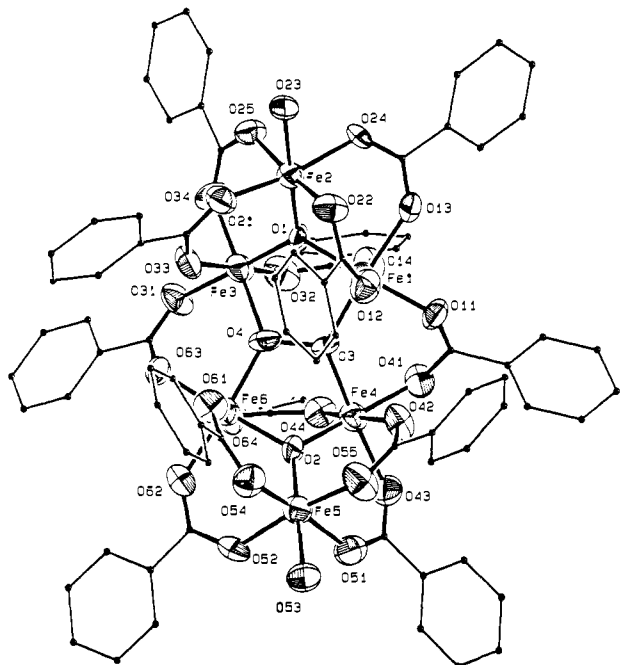(6) Micklitz, W.; Lippard, S. J. *Inorg. Chem.* **1988**, *27*, 3067.

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Figure 1. ORTEP drawing of **2** showing the 50% probability thermal ellipsoids and atom labels for the iron atoms and the oxygen atoms. Carbon atoms are represented as small spheres for clarity. Selected interatomic distances (Å) and angles (deg) are as follows: O(3)–O(4), 1.480 (12); Fe(1)–O(1), 1.899 (8); Fe(2)–O(1), 1.875 (7); Fe(3)–O(1), 1.908 (5); Fe(4)–O(2), 1.911 (8); Fe(5)–O(2), 1.866 (8); Fe(6)–O(2), 1.907 (8); Fe(1)–O(3), 1.997 (7); Fe(4)–O(3), 2.002 (9); Fe(3)–O(4), 2.010 (10); Fe(6)–O(4), 2.030 (9); Fe(1)–O(1)–Fe(2), 122.5 (3); Fe(1)–O(1)–Fe(3), 115.0 (4); Fe(2)–O(1)–Fe(3), 122.4 (4); Fe(4)–O(2)–Fe(5), 123.1 (4); Fe(4)–O(2)–Fe(6), 114.9 (4); Fe(5)–O(2)–Fe(6), 121.7 (4); Fe(1)–O(3)–Fe(4), 129.9 (4); Fe(1)–O(3)–O(4), 114.9 (6); Fe(4)–O(3)–O(4), 114.4 (5); Fe(3)–O(4)–Fe(6), 129.9 (4); Fe(3)–O(4)–O(3), 112.7 (6); Fe(6)–O(4)–O(3), 114.8 (6).

is significant, for it reveals features of a possible key intermediate in metal-catalyzed oxidations of water to dioxygen.[7]
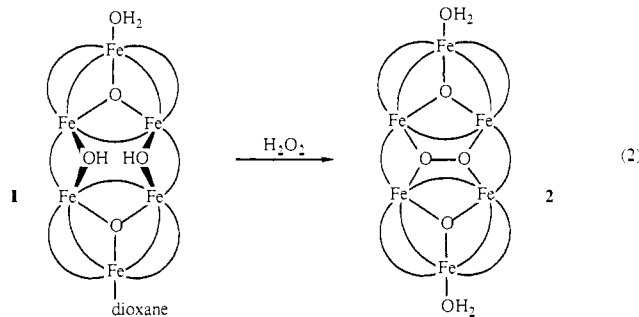
Dropwise addition of 1.0 mL of aqueous 30% H_2O_2 to a stirred slurry of 1.0 g (0.85 mmol) of orange "basic iron(III) benzoate"[8] in 100 mL of acetone yielded an intense red solution after 1 h. Filtration of any unreacted material and crystallization at −10 °C gave **2**·2CH₃CN in 90% yield.[9,10] A portion of this material was also analyzed for elemental composition and by IR, Raman,

¹H NMR, ESR, UV–vis spectroscopic and magnetic measurements.[10] Recrystallization from CH₃CN/acetone yielded triangular prisms of **2**·3(CH₃)₂CO·2H₂O·CH₃CN which proved to be suitable for X-ray diffraction studies.

The structure of **2** is illustrated in Figure 1.[11] It consists of two $[Fe_3O(H_2O)(\mu\text{-}O_2CPh)_5]^{2+}$ units bridged by two $(\mu\text{-}O_2CPh)^-$ groups and a $\mu_4\text{-}O_2^{2-}$ ion. The most interesting aspect of the structure is the central $\{Fe_4(O_2)\}$ unit. Charge balance requires the O–O fragment formally to be a peroxide ion. The observed Fe–O and O–O bond lengths compare favorably to those expected for such a moiety, mean Fe–O = 2.01 (1) Å compared to 1.99 (2) Å in compound **1**; O–O = 1.480 (12) Å compared to 1.48 (1) Å in the only other known μ_4-peroxo-bridged complex, K₄-$[Mo_4O_{12}(O_2)_2]$.[12] A unique aspect of the coordination in **2** arises from the planarity of the peroxo group oxygen atoms. Although $(\mu_4\text{-}X_2)M_4$ connectivity has been observed once before when X = O[12] and several times for X = S,[13] all of the structurally characterized examples involve pyramidal geometries for the chalcogen atoms. In the absence of any notable electronic effects, the planarity in **2** may be attributed to the steric constraints of the remainder of the molecule, as must the twist of only 5° about the O–O bond vector.

Low-temperature ESR studies[10] of **2** in drop-frozen THF solutions indicate a diamagnetic ground state and suggest that **2** is not prone to dissociation into trinuclear units. By using the Evans NMR method,[14] a room temperature effective magnetic moment of 2.70 μ_B per iron was found for **2**,[10] consistent with antiferromagnetic coupling of two $\{Fe_3O\}^{7+}$ units. By contrast, compound **1** exists in a trimer–hexamer equilibrium in THF at room temperature.[15] The O–O stretching vibration in **2** gives rise to a resonance enhanced Raman band at 853 cm⁻¹, comparable to values reported for other metal-coordinated peroxide ion structure types.[16]

Compound **2** has been isolated as a characterized solid by direct reaction of **1** with hydrogen peroxide.[9] In addition, when 20 μL of a 30% solution of $[^{16}O]H_2O_2$ in $[^{18}O]H_2O$ was added to 2 mL of a 5 mM solution of $[^{18}O]$**1** in THF, the 853 cm⁻¹ resonance Raman band was observed. This result is consistent with predominant conversion of **1** to **2** by ligand substitution and not formal outer-sphere oxidation. This substitution reaction may proceed by dissociation of **1** into reactive trinuclear units.

If the functional unit in Photosystem II were comprised of a nearly parallel pair of spin-coupled binuclear manganese centers, water coordination and dioxygen evolution could occur with little nuclear reorientation or ligand sphere rearrangements during the critical O–O bond-forming step. Furthermore, a planar μ_4-peroxo intermediate or transition state, such as that found in compound **2**, could lower the potential for subsequent oxidation to O_2.[7] In Photosystem II there is evidence that all four electrons are ejected from the metal core before the $H_2O \rightarrow O_2$ chemical transformation steps are initiated.[17] A similar result is observed for water

(7) A detailed stereoelectronic model for the oxygen-evolving complex of Photosystem II will be described elsewhere.

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(9) Compound **2** was also obtained via two other routes, namely, (i) reaction of a CH₃CN solution of (NEt₄)₂[Fe₂OCl₆] (1.0 mmol) and Zn-(O₂CPh)₂ (5.0 mmol) with aqueous H_2O_2 (30%, 1.8 mmol), followed by slow evaporation in air (yield 84%), and (ii) reaction of **1** (0.1 mmol) in CH₃CN (40 mL) with aqueous H_2O_2 (30%, 1.8 mmol) (yield 57%).

(10) Anal. ($C_{88}H_{70}N_2O_{30}Fe_6$) C, H, N, O, Fe; IR (KBr, cm⁻¹) 1564, 1536 (ν_{as}, COO), 1410 (ν_s, COO); Raman (THF, 514 nm) 853 cm⁻¹, ν(O–O); ¹H NMR (250 MHz, 297 K, 15 mM in acetone-d_6) δ 2.85, 5.55, 5.87, 6.03, 7.78 (br), 8.32 (br), 10.03, 10.43, 10.70, 11.08; X-band ESR, 4.2 K, silent; electronic spectrum (acetone) [λ_{max}, nm (ϵ_M/Fe cm⁻¹ M⁻¹)] 408 (744), 456 (592), 534 (265); magnetic susceptibility, solution (295 K, 1.3 mM in acetone-d_6), 2.70 μ_B/Fe.

(11) Crystal data for **2**·3(CH₃)₂CO·2H₂O·CH₃CN ($C_{95}H_{89}NO_{35}Fe_6$, M_r = 2139.8) at 298 K: triclinic, space group $P\bar{1}$, a = 16.361 (3) Å, b = 19.602 (5) Å, c = 20.513 (5) Å, α = 104.15 (2)°, β = 106.57 (2)°, γ = 101.99 (2)°, V = 5835 Å³, Z = 2, ρ_{obsd} = 1.26 g/cm³, ρ_{calcd} = 1.22 g/cm³. For 4863 unique, observed reflections and 564 variable parameters the current discrepancy indices are R = 0.052, R_w = 0.065.

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oxidation by the catalyst $[(H_2O)(bpy)_2RuORu(bpy)_2(OH_2)]^{4+}$.[18,19] In keeping with these observations, we have thus far been unable to demonstrate the direct 2 e⁻ oxidation of **1** to **2**.

Supplementary Material Available: Table of atomic positional and thermal parameters for $2 \cdot 3(CH_3)_2CO \cdot 2H_2O \cdot CH_3CN$ (6 pages). Ordering information is given on any current masthead page.

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(19) This catalyst system also might operate by forming a μ_4-peroxo-bridged dimer of the binuclear ruthenium centers in the crucial O–O oxidative coupling step.

Palladium-Mediated Coupling between Organic Disulfides and Nucleic Acid Constituents
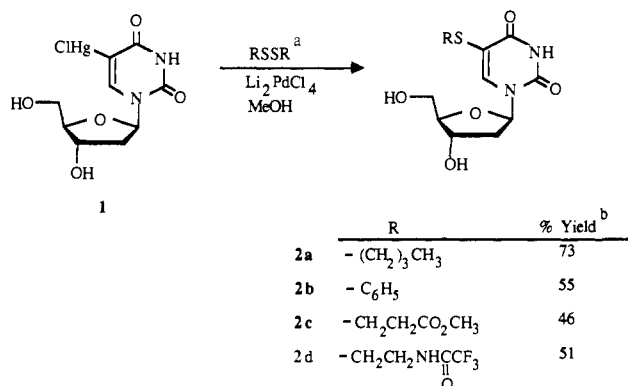
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C-5 pyrimidine nucleosides and nucleotides have found notable applications as antiviral agents[1,2] and as constituents of modified nucleic acids useful as biochemical tools and diagnostic probes.[3–10] Pyrimidine dideoxyribonucleoside triphosphates modified at C-5 have recently found use in an automated rapid method for DNA sequencing.[11] In these applications C-5 serves as the site for attachment of linker arms to haptens, fluorophores,[12] metal ligands,[13] enzymes,[14] biotin,[3] or functional groups capable of facilitating the cleavage of complementary sequences. Among the unique advantages of C-5 as a site for attaching linker arms to

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Scheme I

	R	% Yield[b]
2a	$-(CH_2)_3CH_3$	73
2b	$-C_6H_5$	55
2c	$-CH_2CH_2CO_2CH_3$	46
2d	$-CH_2CH_2NHCCF_3$ (with $\overset{O}{\underset{\parallel}{}}$)	51

[a] All reactions were run overnight at room temperature with 2 mmol 5-HgCldU, 4 mmol Li_2PdCl_4, and 5 mmol RSSR in 40 mL of methanol solvent. [b] Yield of product after purification by silica gel chromatography eluting with 90% chloroform/10% ethanol.

nucleic acids are the lack of interference with binding of the modified sequence to complementary sequences and the flexibility to either modify a nucleic acid directly at the polynucleotide level, incorporate C-5 substituted nucleoside 5'-triphosphates enzymatically, or incorporate the modified nucleoside phosphoramidites in conventional automated synthesis.

We have previously described synthetic methodology for linking olefins at C-5 of pyrimidine nucleosides via palladium-mediated reactions of either mercurated or halogenated nucleosides.[15] The reaction has been extended to the modification of nucleoside 5'-triphosphates[16] and to nucleic acids.[17] A variation on this reaction allows linkage of terminal alkynes to suitably protected 5-iodopyrimidine nucleosides.[18] Both the alkene and alkyne versions of the palladium-mediated coupling reaction frequently give side products that may result from participation by solvent, lack of regioselectivity, or intramolecular participation by a nucleophilic group on the nucleoside.

We now wish to report the discovery of a novel reaction that may prove to be at least as versatile as the palladium-mediated coupling reactions of alkenes and alkynes. The only observed nucleoside containing side product is unmodified nucleoside. The reaction involves combining an organic disulfide with a methanol solution of lithium palladium chloride in which is suspended 5-(chloromercurio)-2'-deoxyuridine (**1**).[19] After stirring overnight at room temperature an insoluble palladium thiolate complex can be removed by filtration to yield a methanol solution of the product.

The disulfides shown in Scheme I were found to react with 5-(chloromercurio)-2'-deoxyuridine (**1**) to give 5-(alkylthio)- or 5-(arylthio)-2'-deoxyuridine (**2**).[20] Initially, when only 1 equiv of Pd(II) and 1 equiv of the mercurionucleoside was used the only disulfides to react were neutral ones (butyl and phenyl disulfides). Disulfides with polar functional groups did not react very well, if at all. These disulfides included 3,3'-dithiodipropionic acid, dimethyl 3,3'-dithiodipropionate, N,N'-bis(trifluoroacetyl)cystamine, and 2,2'-dithiodiethanol. When the amount of Pd(II) was doubled, all of the more polar disulfides gave good yields of product, with the exception of 2,2'-dithiodiethanol. Since the trifluoroacetyl-protecting group is easily removed from an amino group in concentrated ammonia, the N,N'-bis(trifluoroacetyl)-

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(20) All new compounds were characterized by ¹H and ¹³C NMR spectroscopy, high resolution FAB mass spectrometry, and ultraviolet spectroscopy.