

Figure 2. Parent ion signal for protoporphyrin IX dimethyl ester,  $\beta$ -estradiol, and adenine vs. amount desorbed per laser pulse.

glass cup or tube forms part of the first electrode (repeller plate) of a linear (30 cm) time-of-flight mass spectrometer. The ions are detected by an electron multiplier with two preamplifiers (EG&G ORTEC Model 9301 and 474) which feed a transient digitizer (LeCroy 9400) so that the entire mass spectrum can be recorded from a single laser shot. Typically, an average over 200 laser shots is taken. From the spectrum is subtracted a "gas-phase background spectrum" obtained with the desorption laser off. The sample container can be rapidly introduced ( $\sim 1$  min) into the time-of-flight mass spectrometer (pressure  $\sim 10^{-7}$  torr) through a vacuum interlock.

Protoporphyrin IX dimethyl ester,  $\beta$ -estradiol, and adenine were obtained from Sigma Chemical Co. and were used without further purification. Chloroform solutions are placed inside the spinning glass cup or tube and the solvent is removed under a rough vacuum ( $10^{-1}$  torr) to produce a nearly uniform film.

Typical laser desorption/multiphoton ionization mass spectra of protoporphyrin IX dimethyl ester,  $\beta$ -estradiol, and adenine are shown in Figure 1. Note that in each case the spectrum shows almost exclusively the parent ion, indicating that fragmentation is negligible. A calculated detection limit ( $S/N = 2$ ) of  $4 \times 10^{-17}$  mol is obtained for protoporphyrin IX dimethyl ester. These results demonstrate ultrahigh sensitivity of our methodology, which is comparable to that of TOF secondary ion mass spectrometry (SIMS).<sup>20-22</sup> In contrast to this work in which the desorption step is separated from the ionization step,<sup>23</sup> the ionization process in other techniques, such as SIMS, fast atom bombardment (FAB), plasma desorption, field desorption (FD), and direct laser desorption/ionization, depends sensitively on the nature of the matrix.<sup>21</sup>

The linear dependence of signal on sample concentration is investigated with fixed  $\text{CO}_2$  laser power ( $50 \text{ kW/cm}^2$ ), fixed Nd:YAG laser power ( $300 \text{ kW/cm}^2$ ), and fixed time delay ( $70\text{--}90 \mu\text{s}$ , depending on the molecule) between  $\text{CO}_2$  laser pulse and Nd:YAG laser pulse. The results for protoporphyrin IX dimethyl ester,  $\beta$ -estradiol, and adenine are shown in Figure 2 where the

parent ion peak height is plotted against the desorption amount per  $\text{CO}_2$  laser pulse. The desorption amount is calculated on the basis of the amount deposited on the substrate, the new area exposed per laser shot, and the assumption that all irradiated molecules are desorbed. The sample concentration ranges from nanomoles to subfemtomoles. It should be noted that the linearity covers more than 5 orders of magnitude of sample concentration. The complete desorption by the  $\text{CO}_2$  laser has been demonstrated within the concentration range given in the figure. In contrast to other mass spectrometric methods for the analysis of molecular adsorbates,<sup>24,25</sup> the ability of the present two-step laser method to cover so wide a dynamic range of quantitation appears to be unprecedented.

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### Synthesis and X-ray Crystal Structure of $(\mu_3\text{-COCH}_3)(\mu_2\text{-CH}_2)(\text{Cp})(\text{MeCp})\text{Fe}_2\text{Mn}(\text{CO})_5$ , the First Carbyne-Methylene Cluster. Carbon-Carbon Coupling To Give a Methoxyvinyl Cluster

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The study of transition-metal cluster compounds that incorporate two different  $\sigma$ -bound organic fragments, compounds that we call difunctional clusters, is attracting increasing attention.<sup>1,2</sup> This work is important with respect to both uncovering new modes

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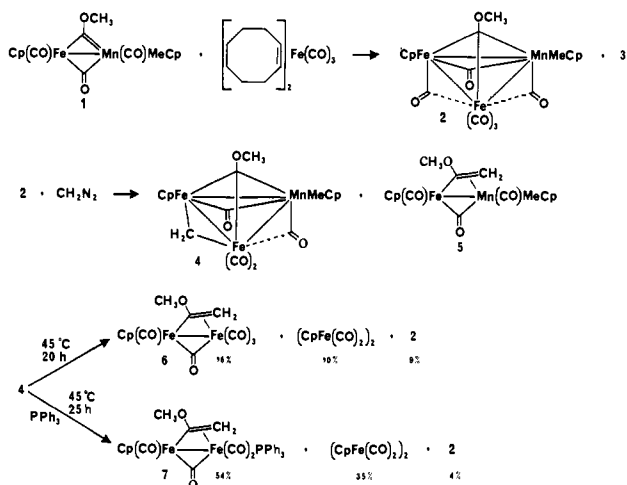
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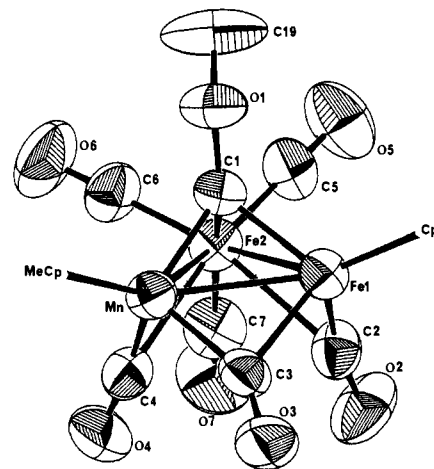
## Scheme 1



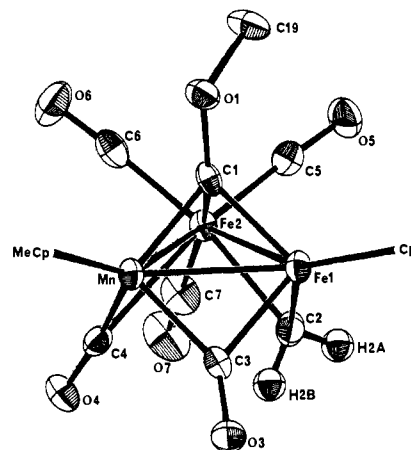
of cluster-mediated carbon-carbon bond formation<sup>2</sup> and helping our understanding of surface-catalyzed reactions such as the Fischer-Tropsch reaction. We recently reported the synthesis of the first heterodinuclear methoxycarbonyl complex, Cp(CO)Fe(μ-COCH<sub>3</sub>)(μ-CO)Mn(CO)MeCp (**1**) (Cp = η<sup>5</sup>-C<sub>5</sub>H<sub>5</sub>; MeCp = η<sup>5</sup>-CH<sub>3</sub>C<sub>5</sub>H<sub>4</sub>), and its thermal decomposition to yield MeCpMn(CO)<sub>3</sub> and via methyl migration the 16-electron fragment CpFe(CO)CH<sub>3</sub>.<sup>3</sup> Incorporation of a μ-methylene into **1** via reaction with diazomethane proved to be slower than thermal decomposition of **1**, so elaboration of the cluster was attempted in order to stabilize it. We report here (1) the high yield conversion of **1** into a heterotrinnuclear μ<sub>3</sub>-methoxycarbonyl cluster, (2) the successful incorporation of a methylene fragment into the trinuclear cluster to give the first μ<sub>3</sub>-methoxycarbonyl, μ<sub>2</sub>-methylene difunctional cluster, and (3) thermal and ligand-induced intramolecular coupling of the methylene and carbonyl ligands to give methoxyvinyl compounds.

Reaction of **1** and Grevels' reagent (cyclooctene)<sub>2</sub>Fe(CO)<sub>3</sub><sup>4</sup> gave an 80% yield of the new heterotrinnuclear methoxycarbonyl cluster **2**, as well as a minor amount (ca. 5%) of the recently reported<sup>5</sup> (also as a minor byproduct) triiron methoxycarbonyl cluster (μ<sub>3</sub>-COCH<sub>3</sub>)(Cp)Fe<sub>3</sub>(CO)<sub>8</sub> (**3**) (Scheme I). Key spectroscopic data<sup>6</sup> in support of structure **2** include a signal in the <sup>1</sup>H NMR due to the methoxy group at δ 4.14 and signals in the <sup>13</sup>C NMR due to the capping carbonyl carbon at 348.5 ppm,<sup>21,5,7</sup> the bridging carbonyl at 264.8 ppm, and the terminal carbonyls at the relatively low-field positions<sup>3</sup> of 239.3 (MnCO) and 227.7 (FeCO) ppm. A single-crystal X-ray diffraction study<sup>6</sup> of **2** (Figure 1) revealed the presence of a nearly symmetrical metal triangle with a μ<sub>3</sub>-carbonyl cap. The bridging (by NMR) carbonyl is clearly semibridging,<sup>8</sup> while the "terminal" carbonyls are bent roughly 20° from linearity and thus clearly interact with the Fe(CO)<sub>3</sub> center despite the carbon-Fe(2) distances of ~2.5 Å. This interaction presumably accounts for the downfield shifts<sup>3</sup> of these weakly semibridging<sup>5,8b</sup> carbonyl ligands.

Reaction of **2** with excess diazomethane occurred slowly at room temperature to give the desired carbonyl-methylene cluster **4** in roughly 15% yield, along with a comparable amount of the unexpected methoxyvinyl cluster **5**,<sup>9</sup> as the major isolated products



**Figure 1.** ORTEP drawing of **2**. Selected bond distances (Å) and angles (deg): Mn-Fe(1), 2.580 (2); Mn-Fe(2), 2.634 (2); Fe(1)-Fe(2), 2.603 (2); C(1)-Mn, 1.931 (8); C(1)-Fe(1), 1.972 (8); C(1)-Fe(2), 1.876 (8); C(1)-O(1), 1.352 (9); C(1)-O(1)-C(19), 123.06 (86); C(2)-Fe(1), 1.763 (10); C(2)-Fe(2), 2.455 (10); Fe(1)-C(2)-O(2), 160.46 (89); C(3)-Fe(1), 2.034 (9); C(3)-Mn, 1.859 (10); Fe(1)-C(3)-O(3), 129.60 (74); Mn-C(3)-O(3), 147.53 (79); C(4)-Mn, 1.792 (10); C(4)-Fe(2), 2.517 (10); Mn-C(4)-O(4), 163.79 (96).



**Figure 2.** ORTEP drawing of **4**. Selected bond distances (Å) and angles (deg): Mn-Fe(1), 2.550 (1); Mn-Fe(2), 2.655 (1); Fe(1)-Fe(2), 2.507 (1); C(1)-Mn, 1.913 (6); C(1)-Fe(1), 1.894 (6); C(1)-Fe(2), 1.950 (6); C(1)-O(1), 1.364 (8); C(1)-O(1)-C(19), 119.55 (50); C(2)-Fe(1), 1.916 (7); C(2)-Fe(2), 2.057 (7); C(2)-H(2A), 0.905 (91); C(2)-H(2B), 0.902 (92); Fe(1)-C(2)-Fe(2), 78.15 (27); H(2A)-C(2)-H(2B), 90.1 (7.2); C(3)-Fe(1), 1.990 (6); C(3)-Mn, 1.894 (7); Fe(1)-C(3)-O(3), 134.35 (53); Mn-C(3)-O(3), 143.56 (54); C(4)-Mn, 1.811 (7); C(4)-Fe(2), 2.512 (7); Mn-C(4)-O(4), 162.74 (60).

(Scheme I). Key data<sup>6</sup> for **4** include two new doublets in the <sup>1</sup>H NMR for the methylene bridge, each integrating as one hydrogen at δ 7.75 and 7.10 ( $J_{\text{HH}} = 1.6 \text{ Hz}^{10}$ ), and signals in the <sup>13</sup>C NMR

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at 358.1 and 151.4 ppm for the carbyne and methylene carbons.<sup>11</sup> The presence of <sup>13</sup>C peaks at 265.8 and 240.7 ppm, but not near 230 ppm, suggested that the methylene group was bridging the iron atoms. An X-ray diffraction study<sup>6</sup> of **4** (Figure 2) confirmed this fact; otherwise the overall structure of **4** is remarkably similar to that of **2**. The methylene ligand bridges the two iron atoms only somewhat asymmetrically, however, especially compared to the weakly semibringing carbonyls of **2** and **4**. The structure of **5**, which like **1** exists as a mixture of cis and trans isomers, was confirmed by independent synthesis via photolysis of Cp(CO)<sub>2</sub>FeC(OMe)=CH<sub>2</sub><sup>12</sup> and MeCpMn(CO)<sub>2</sub>(THF); it is apparently the first heterodinuclear  $\mu$ - $\sigma$ , $\pi$  methoxyvinyl complex and only the second  $\mu$ -methoxyvinyl compound of any kind.<sup>13</sup>

Thermal decomposition of **4** was complete in 20 h at 45 °C, giving as the only tractable products [CpFe(CO)<sub>2</sub>]<sub>2</sub>, **2**, and methoxyvinyl compound **6** due to carbon-carbon bond formation between the carbyne and methylene ligands (Scheme I). The structure of **6** was confirmed by independent synthesis via the rapid room temperature reaction of Cp(CO)<sub>2</sub>FeC(OMe)=CH<sub>2</sub> and (cyclooctene)<sub>2</sub>Fe(CO)<sub>3</sub>.<sup>14</sup> Carbonylation of **4** was cleaner but slower, being complete in 24 h at 75 °C or in 8 days at 45 °C, giving **5** (9%), **6** (4%), MeCpMn(CO)<sub>3</sub> (80%), [CpFe(CO)<sub>2</sub>]<sub>2</sub> (60%), and **2** (16%). A much cleaner reaction took place between **4** and PPh<sub>3</sub> under similarly mild conditions, yielding methoxyvinyl cluster **7** as the major product (Scheme I). The timing of the PPh<sub>3</sub> incorporation into **7** is unknown, since **7** forms over the course of a few hours by room temperature reaction of PPh<sub>3</sub> with **6**. A crossover experiment involving reaction of **4** and its deuterated bis-MeCp analogue ( $\mu$ -<sup>3</sup>-COCD<sub>3</sub>)( $\mu$ -<sup>2</sup>-CD<sub>2</sub>)(MeCp)<sub>2</sub>Fe<sub>2</sub>Mn(CO)<sub>5</sub> (**8-d<sub>5</sub>**) yielded as the only vinyl products **7** and its MeCp/C-(OCD<sub>3</sub>)=CD<sub>2</sub> analogue **9-d<sub>5</sub>**.<sup>15</sup> The PPh<sub>3</sub>-induced ligand coupling is therefore intramolecular.

In conclusion, we have demonstrated the stepwise and rational synthesis of a heterotrinnuclear difunctional cluster and mild intramolecular cluster-mediated carbon-carbon bond formation. This is the first demonstration of intramolecular coupling via a crossover study in which the new fragment remains cluster-bound. The most closely related examples are due to Shapley, in which methylene-ketene coupling to give an  $\eta^4$ -oxaallyl fragment on a ruthenium cluster was induced by CO,<sup>2a</sup> and Dickson, in which methylene- $\mu$ , $\eta^2$ -alkyne coupling to give an  $\eta^1$ , $\eta^3$ -allyl fragment on a rhodium cluster occurred at room temperature.<sup>2b</sup> More typically, complete cluster destruction occurs,<sup>2c-e</sup> or in cases where the new fragment remains cluster-bound, the carbon-carbon bonds formed (such as in carbyne-carbyne coupling) lack stereochemical information.<sup>2d,h-n</sup> The coupling reaction described here, along with the metal atom "markers" inherent in the heteronuclear system, should permit kinetic and stereochemical studies that may shed light on the detailed mechanism. Such work is in progress.

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Petroleum Research Fund, administered by the American Chemical Society, Research Corporation, the UCLA Committee on Research, and the Universitywide Energy Research Group is gratefully acknowledged. We thank a referee for several helpful comments.

**Supplementary Material Available:** Spectroscopic data for **2** and **4-7** and tables of crystallographic data for **2** and **4** and details of the solutions (25 pages); tables of structure factors for **2** and **4** (19 pages). Ordering information is given on any current masthead page.

## Enzymatic Second-Order Asymmetric Hydrolysis of Keturolac Esters: In Situ Racemization

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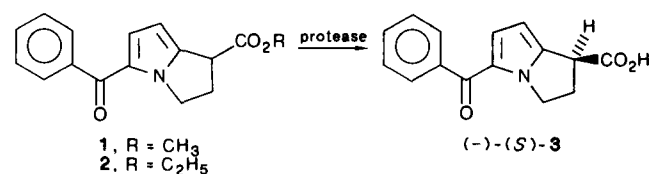
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The enantiospecific hydrolyses of racemic carboxylic esters by hydrolytic enzymes are common biochemical procedures for the resolution of chiral carboxylic acids. As in all conventional resolution processes, enzymic or nonenzymic, the maximum obtainable yield of one pure enantiomer is 50%.

However, if a reaction could be conducted under conditions wherein the substrate may be racemized in situ, it should then be possible to transform the substrate completely to the desired enantiomeric pure product. This approach not only obviates the tedious recycling steps of the undesired remaining ester, but, more importantly, the enantiomeric excess of the product ( $ee_p$ ) is now independent of the extent of conversion,  $c$ , and the process becomes apparently more enantiospecific.<sup>1</sup> This type of enzymatic second-order asymmetric transformation<sup>2</sup> has thus far only been achieved in a very limited number of cases in the amino acid field.<sup>3</sup> In this paper, we report the first successful application of this concept to the enzymatic asymmetric hydrolysis of carboxylic esters.

Keturolac, 5-benzoyl-1,2-dihydro-3*H*-pyrrolo[1,2-*a*]pyrrole-1-carboxylic acid (**3**), is a compound of considerable therapeutic importance because of its potent antiinflammatory and analgesic activities.<sup>4</sup> More recently, it was reported that the (-)-*S* isomer of **3** is considerably more potent than the (+)-*R* isomer in animal studies.<sup>5</sup> The esters **1** and **2** were selected as model substrates for our enzymic studies, for we envisaged that the chiral center could be easily racemized under mildly basic conditions as a consequence of the resonance stabilization of the anion.



Our continuing interest in the application of commercial microbial lipases for the preparation of optically active compounds led us to first examine their abilities in catalyzing the enantio-

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(15) The methoxy methyl was 99+% and the methylene 95.5% deuterated in **8-d<sub>5</sub>**. The initial crossover reaction mixture was 0.02 M each **4** and **8-d<sub>5</sub>** and 0.08 M PPh<sub>3</sub>. The mixture of **7** and **9-d<sub>5</sub>** was analyzed by <sup>1</sup>H NMR; at 500 MHz, the methoxy signals are separated by 22 Hz, and the *E* and *Z* methylene hydrogens by 14 and 19 Hz, respectively. Greater than ~5% crossover at either the methyl or methylene site would have been detected.

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