

Diels-Alder adducts in a 2:1 ratio.

The propensity for cyclobutane chemoselection in cation radical cycloadditions of electron-rich alkenes and styrenes to some dienes, though by no means universal, contrasts with the consistent cyclohexane chemoselection observed in diene/diene cycloadditions. This divergent behavior, though not yet completely understood, is considered to derive, at least in part, from the fact that, whereas Diels-Alder addition to electron-rich alkenes and styrenes requires complete deconjugation of the donor substituent from the cation radical site in the adduct, the cyclobutane-forming process does not. This unusual circumstance is engendered by the fact that the adduct cyclobutane cation radicals almost certainly have a "long-bond" structure (e.g., **10**), in which the donor substituent is still highly stabilizing, rather than a fully closed cyclobutane structure. Both theoretical<sup>6,7</sup> and experimental<sup>5</sup> studies have strongly implicated long-bond structures as the sole minimum for  $\sigma$  cyclobutane cation radicals, and this is especially true when donor substituents such as alkoxy are attached. In contrast, the  $\pi$  cyclohexene cation radical moiety in the Diels-Alder adducts is expected (and has been calculated<sup>8</sup>) to have a normal (i.e., closed)  $\pi$  cation radical structure. It is, consequently, not implausible to suggest that cyclobutane cation radical adducts (with retained substituent stabilization and considerable relief of cyclobutane ring strain as a result of the long-bond structure) can, in many cases, achieve stability greater than the corresponding cyclohexene cation radical adduct. This order of product stabilities could then be reflected in the transition states for cyclization as product development control. Extended basis set (3-21G) ab initio reaction-path calculations now in progress as well as further experimental studies should shed further light on the basis for the novel cyclobutane chemoselection.

Thermal rearrangement of vinylcyclobutanes is well-known to give cyclohexenes, providing an indirect route to the Diels-Alder adducts as an additional synthetic option.<sup>9</sup> However, in view of the special facility of the "anionic oxy" vinylcyclobutane rearrangement,<sup>10</sup> the cycloaddition of **1** to  $\beta$ -chloroethyl vinyl ether (**2d**) was performed under ET conditions.<sup>11</sup> Treatment of **3d** with *n*-butyllithium in ether/HMPA gave **3** (X = OH) in 70% yield.<sup>12</sup> Rearrangement of the latter afforded the Diels-Alder adduct **4** (X = OH) in 60% unoptimized yield (Scheme III).<sup>10</sup>

The conversion of **1** and **2a** to **3a** on a preparative scale is illustrative of the general procedure for selective cyclobutane formation:

A solution of 10 g of **1** (74 mmol) and 64 g of **2a** (887 mmol) dissolved in anhydrous acetonitrile (120 mL) containing 26 mol % (2.5 g) of 1,4-dicyanobenzene (ET) was irradiated through a Pyrex filter under argon atmosphere for 56 h at room temperature by a 450-W Hanovia medium-pressure mercury vapor lamp housed in a water-cooled immersion jacket. Evaporation of the solvent, removal of the ET by extraction of the crude into pentane, and column chromatography (silica gel, pentane) yielded 10.9 g (71%) of **3a** as an oil.<sup>13</sup>

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(13) This product and all others mentioned in this paper were fully characterized by GC/MS, high-resolution MS, and <sup>1</sup>H and <sup>13</sup>C magnetic resonance spectroscopy. Wherever carbonyl or hydroxyl groups are present, infrared spectral data also support the assignment. All products were obtained as diastereomeric mixtures, but these were not separated, except in the case of **4** (X = OH), where careful silica gel chromatography yielded both isomers cleanly.

## Carbon Dioxide Chemistry. The Synthesis and Properties of *trans*-[Mo(CO)<sub>2</sub>(PMe<sub>3</sub>)<sub>4</sub>]: The First Stable Bis(carbon dioxide) Adduct of a Transition Metal

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The coordination of a CO<sub>2</sub> molecule to a transition-metal center is considered to be the first step in its activation,<sup>1</sup> since it is through coordination that the electronic structure and the reactivity of the molecule are modified. We have recently reported<sup>2</sup> that the reaction of *cis*-[Mo(N<sub>2</sub>)<sub>2</sub>(PMe<sub>3</sub>)<sub>4</sub>] (**1**) with CO<sub>2</sub> yields a carbon dioxide complex of composition [Mo(CO)<sub>2</sub>(PMe<sub>3</sub>)<sub>4</sub>] (**2**) in addition to the disproportionation products [Mo(CO)<sub>3</sub>(CO)(PMe<sub>3</sub>)<sub>4</sub>] (**3**) and [Mo(CO)<sub>3</sub>(CO)(PMe<sub>3</sub>)<sub>2</sub>]<sub>2</sub> (**4**). For **2** no clear distinction could be made between the two structural possibilities envisaged, namely a bis CO<sub>2</sub> adduct [Mo(CO)<sub>2</sub>(PMe<sub>3</sub>)<sub>4</sub>] and a head-to-tail dimer [Mo(C<sub>2</sub>O<sub>4</sub>)(PMe<sub>3</sub>)<sub>4</sub>]. In this paper we report a straightforward high-yield preparation<sup>3</sup> of **2** and present chemical and spectroscopic evidence that demonstrate this compound is the first stable bis CO<sub>2</sub> adduct of a transition metal, *trans*-[Mo(CO)<sub>2</sub>(PMe<sub>3</sub>)<sub>4</sub>].

Complex **2** is a yellow, moderately air-stable solid<sup>4</sup> that can be heated in vacuo at ca. 50 °C for 4–5 h without decomposition, although it decomposes quickly at higher temperatures (70–80 °C). In solution it is only moderately stable, decomposing slowly at 25 °C, even under N<sub>2</sub>, although decomposition is prevented by addition of PMe<sub>3</sub>. Since we have been unable to obtain crystals suitable for X-ray analysis, a detailed investigation of its chemical and spectroscopic properties has been undertaken.

While the addition of MeI or I<sub>2</sub> to solutions of **2** produces CO<sub>2</sub> (detected by GC), the coordinated CO<sub>2</sub> cannot be displaced by N<sub>2</sub> or C<sub>2</sub>H<sub>4</sub>. Interaction with CO, however, affords *cis*-[Mo(CO)<sub>2</sub>(PMe<sub>3</sub>)<sub>4</sub>] and CO<sub>2</sub>, and reaction with COS yields [Mo(S<sub>2</sub>CO)(CO)<sub>2</sub>(PMe<sub>3</sub>)<sub>2</sub>], which can also be obtained from *cis*-Mo(N<sub>2</sub>)<sub>2</sub>(PMe<sub>3</sub>)<sub>4</sub> and COS. This strongly favors formulation of **2** as a Mo(0) species, a proposal also supported by spectroscopic data. Thus the <sup>31</sup>P NMR spectrum consists at 20 °C of a broad unresolved signal which becomes a sharp singlet at 50 °C and converts at –60 °C into a pattern of lines characteristic of an AA'BB' spectrum ( $\delta_A$  1.88,  $\delta_B$  –3.25;  $^2J_{AB}$  = 144.4,  $^2J_{AB'}$  = –17.8,  $^2J_{AA'}$  = 14.5,  $^2J_{BB'}$  = 23.3 Hz). From these data a *trans* geometry, **2**, similar to that found for the ethylene complex analogue *trans*-[Mo(C<sub>2</sub>H<sub>4</sub>)<sub>2</sub>(PMe<sub>3</sub>)<sub>4</sub>],<sup>5</sup> can be proposed for this compound.<sup>6</sup> In agreement with this, the room-temperature <sup>13</sup>C NMR spectrum of **2\*** (50% enriched in <sup>13</sup>C) shows a quintet at  $\delta$  206.1 ( $^2J_{PC}$  = 17.9 Hz) in the region expected for coordinated carbon dioxide.<sup>7</sup> Furthermore, the <sup>31</sup>P NMR of **2\*** recorded at 60 °C clearly shows

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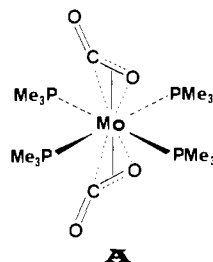
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(3) Compound **2** has been independently prepared by M. L. H. Green.

(4) In a typical preparation a solution of 0.68 g (ca. 1.5 mmol) of **1** in 150 cm<sup>3</sup> of petroleum ether was pressurized in a 250 cm<sup>3</sup> capacity Fischer-Porter vessel, with 5 atm of CO<sub>2</sub>. The mixture was left aside for ca. 12–18 h and the resulting yellow solid filtered off and washed with petroleum and diethyl ether (yield 0.57 g, 80%). The compound can be recrystallized from toluene or tetrahydrofuran.

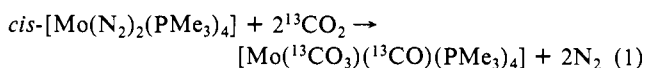
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the three central lines of the 1:4:6:4:1 quintet that would be expected for an isotopic mixture of **2** and **2\*** containing approximately 50% of molecules of **2** having one  $^{13}\text{CO}_2$ , 25% with two  $^{13}\text{CO}_2$ , and 25% with two  $^{12}\text{CO}_2$ . From the separation of the outer lines a value of 17.5 Hz can be computed for  $^2J_{\text{PC}}$ , in excellent agreement with the  $^{13}\text{C}$  data already discussed. The IR spectrum has a strong band at  $1670\text{ cm}^{-1}$  ( $1620\text{ cm}^{-1}$  in  $^{13}\text{C}$ -enriched **2\***) in the region expected for coordinated  $\text{CO}_2$ .<sup>7,8</sup>

As reported previously,<sup>2</sup> the reaction of **1** with  $\text{CO}_2$  may yield, in addition to **2**, the disproportionation products **3** and **4**. Using  $^{13}\text{CO}_2$ , we have now confirmed our initial IR assignments of bands due to coordinated CO and  $\text{CO}_3^{2-}$  in these complexes and demonstrated that both groups form in a metal-induced  $\text{CO}_2$  reductive disproportionation (eq 1). A reasonable mechanism for the



formation of complexes **2-4** should address the question of under what conditions the coordinated  $\text{CO}_2$  molecule is "sufficiently activated" to give the disproportionation products and should explain the facts that (a) free  $\text{PMe}_3$  drastically diminishes the yield of **2** in favor of **3**, (b) **2** is stable toward disproportionation even under 5 atm of  $\text{CO}_2$  and in the presence of free  $\text{PMe}_3$ , and (c) polar or aromatic hydrocarbon solvents also favor disproportionation. These observations are consistent with the formation of an intermediate species " $\text{Mo}(\text{CO}_2)(\text{N}_2)(\text{PMe}_3)_4$ ", which would yield **2** by coordination to a second molecule of  $\text{CO}_2$ , following prior dissociation of  $\text{N}_2$ . Alternatively,  $\text{N}_2$  substitution by solvent or  $\text{PMe}_3$  blocks the available coordination site at the Mo center and activates the coordinated  $\text{CO}_2$  through an increase in the back-donation from the metal, thus favoring disproportionation. This process might involve formation of a Herskovitz type head-to-tail dimer,<sup>9</sup> but if the coordinated  $\text{CO}_2$  is sufficiently activated toward electrophilic attack by free  $\text{CO}_2$ , it could be viewed as an  $\text{O}^{2-}$  transfer<sup>10</sup> from coordinated to free  $\text{CO}_2$ , with the subsequent formation of two Mo-O bonds (to yield **3**) providing the additional thermodynamic driving force. Since in **2** the back-donation from the  $\text{MoP}_4$  fragment is shared by two  $\text{CO}_2$  molecules, it becomes clear that a sufficient perturbation of the electronic structure of the coordinated  $\text{CO}_2$  molecule, i.e., sufficient activation, is a necessary requirement for the disproportionation reaction to take place.

In conclusion we believe that the stability of **2** is due to a delicate balance of steric and electronic effects. The importance of the former is shown by the tendency of **2** to decompose by dissociation of  $\text{PMe}_3$  (as found for  $\text{trans-}[\text{Mo}(\text{C}_2\text{H}_4)_2(\text{PMe}_3)_4]^{11}$ ) and by our failure<sup>11</sup> to observe adduct formation with the bulkier phosphines  $\text{PMe}_2\text{Ph}$  and  $\text{PET}_3$ , while the influence of the electronic factors is demonstrated by the preferred formation of the disproportionation products when the electron density at the metal is increased by solvent or  $\text{PMe}_3$  coordination. We also believe that

the remarkable strength of the Mo-CO<sub>2</sub> bonds, as compared to other transition-metal-carbon dioxide bonds,<sup>1</sup> is due to the intense back-bonding from the molybdenum center to the coordinated  $\text{CO}_2$  molecules and to the oxophilic nature of molybdenum.

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### DNA Breakage by a Perhydrate Complex of *cis,cis,trans*-Pt<sup>IV</sup>Cl<sub>2</sub>(NH<sub>3</sub>)<sub>2</sub>(OH)<sub>2</sub>

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The coordination compound *cis*-dichlorodiammineplatinum(II) (CDDP, **1**) is in wide clinical use for the treatment of various types of cancer.<sup>1</sup> The drug is believed to derive its cytotoxic effects by direct interaction with guanine bases of cellular DNA.<sup>2</sup> Although the majority of the platinum-based antitumor agents which have been studied to date are platinum(II) complexes, certain complexes of platinum(IV) are also known to exhibit antitumor effects.<sup>3</sup> One such compound, *cis,cis,trans*-Pt<sup>IV</sup>Cl<sub>2</sub>((CH<sub>3</sub>)<sub>2</sub>CHNH<sub>2</sub>)<sub>2</sub>(OH)<sub>2</sub> (CHIP, **2**), is currently undergoing clinical trials in the United States as a potential second generation CDDP analogue. The results of this study strongly suggest that the DNA breakage observed in the earlier investigations with CHIP (**2**) was due to lattice hydrogen peroxide.<sup>4-6</sup>

In an effort to more clearly define the chemical and biochemical events which underlie the mechanism of action of platinum-(IV)-based antitumor agents, we have studied the hydrogen peroxide oxidation products of CDDP (**1**). Two products have been isolated: the well-characterized *cis,cis,trans*-Pt<sup>IV</sup>Cl<sub>2</sub>(NH<sub>3</sub>)<sub>2</sub>(OH)<sub>2</sub><sup>7,8</sup> (**3**) and a previously unreported perhydrate (**4**) whose formulation includes 1.0 H<sub>2</sub>O<sub>2</sub> per platinum(IV) complex.

Reaction of **1** with an excess of 30% H<sub>2</sub>O<sub>2</sub> at 50 °C results in the formation of a pale yellow solid (**4**). The IR spectrum of **4**<sup>9</sup> exhibits strong bands at 3460 and 3475 cm<sup>-1</sup> assigned to OH

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