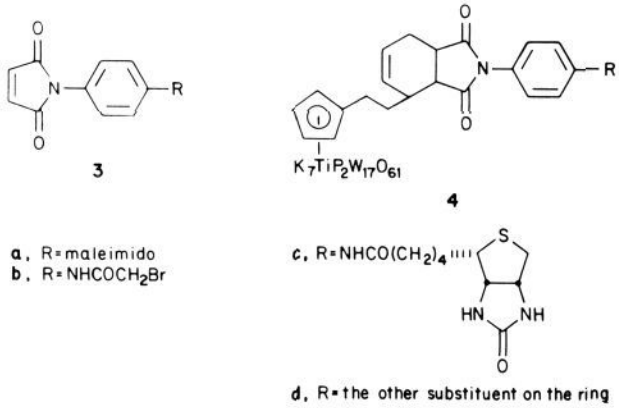
Figure 1. Bright-field TEM of "dimeric" HPT **4d**. The spacing between the dots is about 2–3 nm (different orientations of the dimers) and is consistent with the separation indicated from an inspection of molecular models of an extended conformation of **4d**. The bar represents 20 nm.

The presence of the 1,3-diene unit in HPT **2a** permits the ready attachment of various protein-reactive groups[14] via a Diels–Alder reaction with 4-substituted phenylmaleimide dienophiles. Thus, maleimides **3a–c**[15] were allowed to react (60 °C, 6 h) with 1 equiv



of **2a** (K^+ salt) in DMF, CD_3CN, and Me_2SO-d_6, respectively, giving maleimide **4a**,[16] bromoacetamide **4b**,[16] and the biotinylated derivative **4c**[16] in near quantitative yield. The reaction of 2 equiv of **2a** with **3a** gave the "dimeric" HPT **4d**[16] containing two modified Dawson units.

An electron micrograph (not shown) of HPT **2d** (K^+ salt)[17] taken on a Philips 420 with a ST lens at 40-kV with a 40-μm objective aperture at magnification 210000× consisted of dense dots clearly visible above backgroud. Stability in the beam is high: an exposure taken after 5 min in the beam (beam current giving satisfactory density after 2 s) was indistinguishable from that taken after 2 s. A morphologically unique image consisting of dumbbells results from **4d** (Figure 1), opening the way for differential labeling of multisubunit complexes with these reagents.[18]

Acknowledgment. This research was supported by PHS Grant GM 27137 from the National Institute of General Medical Sciences. We thank Prof. R. Finke for many fruitful discussions.

(14) Lundblad, R. L.; Noyes, C. M. "Chemical Reagents for Protein Modification"; CRC Press: Boca Raton, FL, 1984. Means, G. E.; Feeney, R. E. "Chemical Modification of Proteins"; Holden-Day: San Francisco, 1971.

(15) **3a**, Aldrich Co. **3b**, mp 234–236 °C (EtOAc),[7] prepared by acylation of (*p*-aminophenyl)maleimide with bromoacetyl bromide. **3c**·$^1/_3H_2O$, mp 247–250 °C (DMF–ether),[7] prepared by acylation of (*p*-aminophenyl)maleimide with *d*-biotin activated by reaction with methyl chloroformate according to: Green, N. M.; Konieczny, L.; Toms, E. J.; Valentine, R. C. *Biochem. J.* **1971**, *125*, 781.

(16) Formation of the desired adduct was clear from the 360-MHz ^1H NMR spectrum. A satisfactory C, H, and N analysis was obtained on the corresponding TMA salts of **4a–d**.

(17) Prepared by the addition of $C_5H_5TiCl_3$ (173 mg) to an aqueous solution (15 mL) of α_2-$K_{10}P_2W_{17}O_{61}$ (3.368 g)[10] using methodology similar to that of Knoth (see ref 9) in the $PW_{11}O_{39}^{7-}$ series. HPT **2d** (TMA salt);[7] **2d** (K^+ salt); ^1H NMR (D_2O) 6.73 ppm (s); ^{31}P NMR (D_2O) −10.10 (s), −13.21 ppm (s) (external H_3PO_4); ^{183}W NMR (D_2O) −90.70 (2 W), −129.50 (2 W), −167.26 (1 W), −175.85 (2 W), −180.14 (2 W), −191.89 (2 W), −194.26 (2 W), −195.38 (2 W), −215.87 ppm (2 W) (external Na_2WO_4).

(18) Starting with 3,5-dimaleimidobenzoic acid we have also prepared an analogous carboxy-functionalized "dimeric" HPT, characterized as the $(TMA)_{15}$ salt.[7]

Synthesis, Structure, and Reactions of a η^5-CpCo(η^4-bisketene) Complex

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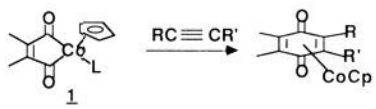
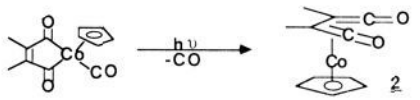
A recent manuscript from this laboratory described the synthesis of η^5-CpCo(dimethylmaleoyl)(L) (**1**) (L = CO, PPh_3, C_5H_5N, Et_2S) and the reaction of certain of these compounds with alkynes to produce a wide range of highly functionalized η^5-CpCo(η^4-1,4-benzoquinone) complexes (eq 1) which can be cleaved to the



(1)

free quinones under mild conditions.[2] It was presumed that dissociation of the ligand L was a necessary prerequisite to reaction with alkynes. In our study of the parent compound **1**, L = CO, the carbon monoxide ligand was found to be very thermally stable but to readily dissociate upon photolysis with a 150-W flood lamp. Photolysis in the presence of an alkyne produced the quinone complex in high yield; however, in the absence of an alkyne a new, reactive cobalt species was produced. Spectroscopic data suggested this new compound was a cobalt complex of a bisketene and an X-ray crystal structure determination confirmed this suspicion. The synthesis, structure, and reactions of this first metal-complexed bisketene are described herein.

Photolysis of 2 mmol of a 0.004 M solution of maleoylcobalt complex **1**, L = CO, in a 1:1 benzene–acetonitrile (nitrogen saturated—with continuous nitrogen purge) for 24 h with a 150-W GE flood lamp placed directly below the reaction vessel led to slow CO evolution accompanied by a color change from bright yellow to deep red. Evaporation of solvent on a rotary evaporator, addition of 50 mL of benzene, brief heating and reevaporation, and repeating the procedure from the addition of benzene gave a residue of crude product. Trituration with hexane yielded 313 mg (66%) of yellow η^5-CpCo(η^4-dimethylbisketene) (**2**) (eq 2).



(2)

An additional quantity of complex (12%) can be obtained from the hexane wash by concentration and chromatography (1:1 Et_2O–hexane; 10 g of flash grade SiO_2).

The dramatic structural reorganization shown in eq 2 was evident from the infrared data (**1**, L = CO, 2025, 1683, 1650 cm^{-1}; **2**, 1810, 1760 cm^{-1}) and NMR spectra (**1**, L = CO, ^1H NMR δ 5.09 (s, 5 H), 1.96 (s, 6 H); ^{13}C NMR δ 240.6, 168.4, 91.8, 12.0; **2**, ^1H NMR δ 5.02 (s, 5 H), 1.91 (s, 6 H); ^{13}C NMR δ 225.9 (CO carbons), 86.8 (olefinic carbons), 51.3 (Cp carbons), 10.8 (CH_3 groups). We could not find one of the ^{13}C resonances of **1**, L = CO, even after extensive pulsing under various conditions. A ^{13}C NMR spectrum of **1**, L = Et_2S (δ 262.0, 166.5, 88.9, 33.2, 13.1, 11.1) confirmed that the very low field signal was due to the acyl carbons and that the CO carbon resonance was missing in the spectrum of **1**, L = CO. Bisketene complex **2** could be crystallized from cold hexane (dec 115 °C) and gave satisfactory elemental analysis. Confirmation of the proposed structure was secured by an X-ray structure determination on a suitable single crystal obtained by slow crystallization from hexane (distilled from CaH_2 under nitrogen). An ORTEP of the molecule is shown in Figure 1 with representative bond distances and angles given in the caption. It is obvious that the cobalt atom lies well below the plane

(1) Fellow of the Alfred P. Sloan Foundation, 1983–1987.

(2) Liebeskind, L. S., Jewett, C. F., Jr. *J. Organomet. Chem.* **1985**, *285*, 305

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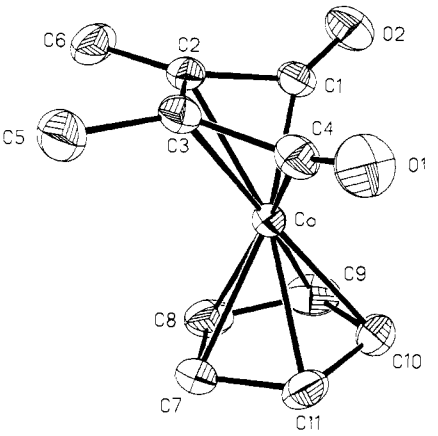
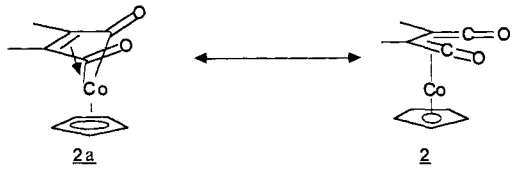


Figure 1. ORTEP diagram of η^5-CpCo(η^4-dimethylbisketene) showing 30% probability thermal ellipsoids with numbering scheme for the atoms. $R = 0.0409$, $R_w = 0.0438$. Distances: Co-C1, 1.868 (4) Å; Co-C2, 2.045 (3) Å; Co-C3, 2.065 (4) Å; Co-C4, 1.860 (4) Å; C1-C2, 1.455 (5) Å; C2-C3, 1.415 (5) Å; C3-C4, 1.445 (5) Å. Angles: C2-C1-O2, 137.8 (3)°; Co-C1-O2, 145.5 (3)°; C3-C4-O1, 138.5 (4)°; Co-C4-O1, 142.8 (3)°.

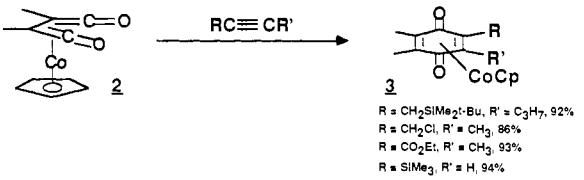
of the four carbons defining the bisketene backbone, and the fact that the bonds between these carbon atoms have similar lengths (1.455, 1.415, 1.445 Å) suggests some diene-like bonding for the structure of **2**.[3] However, the C-C-O bond angles (145.5°, 142.8°) indicate substantial rehybridization of the carbonyl carbon from sp toward sp^2 and the slightly shorter bond length for C2-C3 (compared to C1-C2 and C3-C4) both argue for a significant contribution of limiting geometry **2a** to the structure of this



2a **2**

bisketene complex.[3] Other studies relevant to this work include the characterization of η^2-monoketene complexes,[4] vinylketene complexes,[5] a diiminocobaltacyclopentene complex,[6] and a η^4-bis(*tert*-butylimino)diphenylbuta-1,3-diene complex.[7]

Bisketene complex **2** reacted under mild conditions with a variety of alkynes to give excellent isolated yields of η^5-CpCo-(η^4-1,4-benzoquinone) compounds **3** which are all very polar, air-stable, red-brown solids (eq 3).[2,8] Triphenylphosphine,



(3)

R = CH_2SiMe_2t-Bu, R' = C_3H_7, 92%
R = CH_2Cl, R' = CH_3, 86%
R = CO_2Et, R' = CH_3, 93%
R = $SiMe_3$, R' = H, 94%

pyridine, and diethyl sulfide all reacted quickly to convert the bisketene complex back to the maleoylcobalt structure **1**.[9] Although it is tempting to suggest a direct reaction of alkynes with **2** to give the quinone complexes **3**, the facile conversion of **2** back to the maleoyl form **1** with simple ligands implies that quinone complex formation may occur from a maleoylcobalt species **1** with L = alkyne. The reactions of bisketene complex **2** obviously have a bearing on the mechanism of our previously published studies of quinone complex formation from **1**.[2]

Bisketene complex **2** is stable in the solid state and can be stored in that form; however, in solution exposed to air slow decomposition occurs. On heating a benzene solution of **2** to 80 °C under nitrogen in a sealed system, decomposition occurs to give η^5-$CpCo(CO)_2$,[10] η^5-$(CpCoCO)_3$,[10] η^5-CpCo(η^4-duroquinone),[11] and η^5-CpCo(CO)(dimethylmaleoyl) **1**, L = CO. These results point to decarbonylation of the bisketene complex as the major mode of thermal decomposition, since the liberated CO and 2-butyne (possibly complexed) can react with **2** to give the latter two observed products.

In a preliminary set of reactions we have prepared the η^5-C_5Me_5 analogues of **1**, L = CO, and **2** and found the pentamethyl bisketene complex to be more stable toward decomposition than its nonmethylated analogue. Attempts to convert both of the bisketene complexes into other interesting compounds (reaction with RLi, with Wittig or Tebbe reagents) and a study of the reaction chemistry of the functionalized quinone complexes are currently under way. Complete experimental details for the chemistry described in this manuscript can be found in the supplementary material.

Acknowledgment. This investigation was supported in part by PHS Grants CA 26374 and CA 40157 awarded by the National Cancer Institute, DHHS, and in part by the National Science Foundation under Grant CHE-8305055.

Supplementary Material Available: Experimental details for the synthesis and reactions of bisketene complexes and complete data for the X-ray crystal structure determination (25 pages). Ordering information is given on any current masthead page.

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(9) Identified by comparison with known compounds prepared according to the procedures described in ref 2.

(10) Identified after chromatography by comparison of infrared data with the values described in: Vollhardt, K. P. C.; Bercaw, J. E.; Bergman, R. G. *J. Organomet. Chem.* **1975**, *97*, 283.

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Resonance Raman Spectroscopy of Metalloproteins under Extreme Conditions: Cryogenic Diamond-Cell Study of Azurin

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There are numerous cases in the physiological functioning of proteins where volume changes or other transformations that may be induced or affected by pressure are known to be important. Considerable spectrophotometric study (primarily of hemoglobin and its derivatives) has been devoted to such phenomena at hydrostatic pressures in the 1-8 kbar range (ref 1 and references therein). However, protein behavior under the extreme pressures available by current diamond-cell technology has not been investigated. In particular, no structure-specific spectroscopic probes (e.g., vibrational spectroscopy) have been utilized to determine whether the structural integrity of any protein remains intact under

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