close to that reported for $cp_2V(CH_2O)$,[1] with the two bent cp ligands making a cavity in the equatorial plane for the formaldehydo fragment. The C–O bond length [1.360 (9) Å] is very close to those of the other formaldehydo complexes,[1,2] except for that in $[Os(CO)_2(PPh_3)_2(\eta^2\text{-}CH_2O)]$ [1.59 (1) Å].[2a] The Mo–O bond [2.056 (4) Å] is significantly shorter than the Mo–C bond distance [2.252 (8) Å], similar to the vanadocene derivative.[1] A significant structural feature is the hydrogen bonding formed from the oxygen atoms interacting with the hydrogens from C1 and C7 of an adjacent molecule [C1···O, 3.318 (8); H1···O, 2.330 (69) Å; C1–H1···O, 163 (4)°; C7···O, 3.439 (8); H7···O, 2.404 (64) Å; C7–H7···O, 158 (5)°].[10]

Diphenylacetylene was displaced in complex I by carbon dioxide carrying out the reaction in toluene[11] at room temperature. Complex III was isolated as crystalline solid,

$$\underset{\text{I}}{cp_2Mo(PhC{\equiv}CPh)} + CO_2 \xrightarrow{PhC{\equiv}CPh} (1/n)\underset{\text{III}}{[cp_2Mo(CO_2)]_n} \quad (2)$$

having a C=O stretching band at 1745 cm^{-1} in solution (THF), which is shifted down to 1705 cm^{-1} in the solid state (Nujol).[11]

A view of complex III is shown in Figure 2, with the most relevant bond distances and angles.[12] In the asymmetric unit there are two crystallographic independent molecules, $[cp_2Mo(CO_2)]$ denoted by A and B, whose geometries are not significantly different. The two cp ligands are bent to make a cavity in the equatorial plane for the CO_2 unit η^2-C,O bonded to the metal. Structural parameters for the cp_2Mo unit are as reported for complex II. Mo–C and Mo–O bond distances in the $[Mo(CO_2)]$ fragment are very close and very similar to those found in $[Mo(CO_2)_2(CN\text{-}i\text{-}Pr)(PMe_3)_3]$.[13] The M–O bond distance in complex III is significantly longer than that found in II. Both C–O bond distances maintain a double-bond character with the longest one [C11A–O1A, 1.288 (14) Å] involved in the interaction with the metal, while the other one is C11A–O2A = 1.201 (14) Å. These distances compare very well with those reported for $[Ni(PCy_3)_2(CO_2)]$ [1.22 (2) and 1.17 (2) Å][14] and $[(\eta^5\text{-}C_5H_4Me)_2Nb(CH_2SiMe_3)(CO_2)]$ [1.283 (8) and 1.216 (8) Å].[15] It is worthy to note that the molecules are held together by a network of CH···O contacts which can be considered as hydrogen bonds (Figure 3, supplementary material).[10,16]

Carbon dioxide in complex III can be viewed as experiencing bifunctional activation: the electron-rich active site is the Mo atom and weakly acid hydrogen atoms interacting at the oxygens complete the activation.[17] Such a bifunctional interaction would be responsible for the difference in the C–O stretching frequency going from solid state (1705 cm^{-1}, Nujol) to the solution (1745 cm^{-1}, THF).[11] This feature may have interesting suggestions on how fixation of CO_2 occurs in bifunctional systems containing protonic acids, including solvents, and how to devise strategies for the fixation of CO_2. Complex III is a rather unique complex of CO_2, since the metallic fragment to which CO_2 is bonded is rather robust and it is not a phosphine-type ligand, which can be involved in promoting transformations of CO_2-like deoxygenation.

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Supplementary Material Available: Tables of positional and thermal parameters and bond distances and angles and a listing of structure factor amplitudes for complexes II and III and Figure 3 showing the hydrogen bonding framework in complex III involving molecules A and B (12 pages). Ordering information is given on any current masthead page.

(9) Crystal data: $C_{11}H_{12}MoO$, M_r = 256.2, monoclinic, space group $C2/c$ (from systematic absences and structural analysis), a = 13.576 (2) Å, b = 6.825 (1) Å, c = 20.751 (3) Å, β = 104.21 (1)°; V = 1863.9 (5) Å^3, Z = 8; D_c = 1.826 g cm^{-3}; λ(Mo Kα) = 0.7107 Å, μ(Mo Kα) = 13.3 cm^{-1}; crystal dimensions 0.10 × 0.24 × 0.50 mm. Intensities of 3617 reflections were measured at room temperature ($2.5 < \theta < 26.0$) on a Philips 1100 diffractometer by using Mo Kα radiation, 1947 independent reflections, agreement between equivalent reflections =0.026. The structure was solved by the heavy-atom method and refined by full-matrix least squares. All calculations were carried out using the SHELX-76 program. For 1414 unique observed reflections [$I > 3\sigma(I)$] the final R value is 0.031.

(10) Berkovitch-Yellin, Z.; Leiserowitz, L. *Acta Crystallogr., Sect. B* **1984**, *B40*, 159-165.

(11) A toluene (50 mL) or THF (50 mL) solution of I (2.0 g) was reacted at room temperature and atmospheric pressure with carbon dioxide. The reaction is very slow. After a week a weak band appeared at 1745 cm^{-1}, while some crystalline solid precipitated. The amount of crystalline solid increased by cooling the solution at −15 °C (0.41 g). The unreacted starting complex I can be recovered from the mother solution. Anal. Calcd for $C_{11}H_{10}O_2Mo$: C, 48.89; H, 3.70. Found: C, 49.27; H, 3.73. By gentle heating and under 20 atm of CO_2 the reaction is significantly faster and the yield higher. The CO band falls at 1705 (Nujol) and 1745 cm^{-1} (THF solution). Its solubility in THF is rather poor. The reaction of I with CO_2 can be followed by IR and the appearance of the band at 1745 is very slow. When dissolved by gentle heating in THF, complex III shows a strong band at 1745 cm^{-1}. With continued heating in vacuo, a band at 1700 cm^{-1} appeared, which increased slowly with time. This change cannot be reversed by restoring the CO_2 atmosphere. We did not clearly identify the new species having the band at 1700 cm^{-1} in solution.

(12) Crystal data: $C_{11}H_{10}MoO_2$, M_r = 270.2, monoclinic, space group $P2_1/c$ (from systematic absences), a = 7.754 (3) Å, b = 13.04 (6) Å, c = 19.045 (7) Å, β = 100.70 (4)°; V = 1892 (1) Å^3, Z = 8, D_c = 1.896 g cm^{-3}; $F(000)$ = 1072, λ(Mo Kα) = 0.7107 Å, μ(Mo Kα) = 13.2 cm^{-1}; crystal dimensions 0.32 × 0.22 × 0.35 mm. Intensities of 4707 reflections were measured at room temperature ($3.0 < \theta < 25.0$) on a Philips PW 1100 diffractometer using Mo Kα radiation resulting in 3440 independent reflections (agreement between equivalent reflections 0.070). The structure was solved by the heavy-atom method and refined anisotropically by full-matrix least squares. All calculations were carried out using the SHELX-76 program. For 2153 unique observed reflections [$I > 3\sigma(I)$] the final R value is 0.054.

(13) Alvarez, R.; Carmona, E.; Gutierrez-Puebla, E.; Marin, J. M.; Monge, A.; Poveda, M. L. *J. Chem. Soc., Chem. Commun.* **1984**, 1326-1327.

(14) Aresta, M.; Nobile, C. F. *J. Chem. Soc., Dalton Trans.* **1977**, 708-711.

(15) Bristow, G. R.; Hitchcock, P. B.; Lappert, M. F. *J. Chem. Soc., Chem. Commun.* **1981**, 1145-1146.

(16) The metal-bonded oxygen atoms are involved in the formation of one hydrogen bond; the uncoordinating ones form two hydrogen bonds. The environment of the two molecules is, however, different. Molecule A forms centrosymmetric dimers through the hydrogen bonds C9A–H9A···O2A and is linked to adjacent B molecules through four hydrogen bonds involving both cyclopentadienyl rings. Molecule B is linked through hydrogen bond only to molecules A and only one of the two cyclopentadienyl rings is engaged in the formation of hydrogen bonds.

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Dithioether-Containing Cyclic Peptides

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The design and synthesis of cyclic analogues of linear peptide hormones and neurotransmitters have attracted considerable interest in recent years. This interest often has been motivated by the desire to develop analogues with increased receptor selectivity, antagonist activity, or prolonged duration of action and is generally based upon evidence for or suspicion of a biologically active conformation of the native peptide that includes some specific folded structure. The rationale for the cyclic analogue then is to stabilize this proposed folded conformation. Among the many approaches utilized for preparing cyclic peptides,[1] several successful examples have employed pairs of cysteine and/or penicillamine (β,β-dimethylcysteine) residues with subsequent cyclization through the side chains to yield conformationally restricted disulfide-containing peptides.[2-5] These successes notwithstanding, cyclization via disulfide bond formation suffers from one major drawback. Generally, for a given native peptide relatively few residues can be replaced without drastic activity losses. Thus,

(1) Hruby, V. J. *Life Sci.* **1982**, *31*, 189-199.

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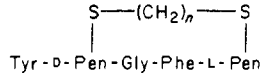
allowable positions in the linear sequence for substitution by amino acids with sulfhydryl side chains are limited. Since readily available amino acids with sulfhydryl side chains are limited to cysteine and penicillamine (β-sulfhydryls) and homocysteine (γ-sulfhydryl) one is restricted, for fixed substitution within the primary sequence, to cyclic structures of n to $n + 2$ atoms where n is determined by the number of intervening amino acid residues in the primary sequence. Thus even in cases in which a folded conformation may be biologically important the disulfide cyclization may impose too severe a conformational constraint. We present here a more general approach which allows the examination of a larger set of cyclized peptides by utilizing sulfhydryl side chains to form dithioethers. This variable conformational restriction approach can be employed to evaluate the importance of folded structures for bioactivity of a given native peptide and to develop cyclic analogues in which the appropriate degree of folding is stabilized.



I, $n = 2$
II, $n = 3$

[D-Pen^2,L-Pen^5]Enkephalin (Tyr-D-Pen-Gly-Phe-L-Pen), a cyclic disulfide-containing analogue of the native, linear enkephalins, Tyr-Gly-Gly-Phe-Met (or Leu), which is highly selective for the δ opioid receptor,[5] served as the parent peptide for the present study. The protected, resin-bound pentapeptide *N*-(*tert*-butyloxycarbonyl)-Tyr-D-Pen(S-*p*-MeBzl)-Gly-Phe-L-Pen-(*S*-*p*-MeBzl)-resin was synthesized by solid-phase methodologies using Merrifield resin (chloromethylated polystyrene cross-linked with 1% divinylbenzene) as previously described.[5] Cleavage from the resin and concomitant deprotection were achieved by reaction with anhydrous HF containing 10% anisole at 0 °C for 1 h. Following evaporation the peptide was extracted from the resin with 50% acetic acid and the solution freeze dried. The cyclic dithioether-containing peptides I and II were obtained by modification of the procedure employed by Frankel and Gertner for the synthesis of homologues of djenkolic acid.[6] The free sulfhydryl-containing peptide (0.1 mmol) was added to 400 mL of anhydrous liquid ammonia and treated with sufficient sodium to maintain a blue color for 90 s. The solution was decolorized by addition of NH_4Cl and 0.12 mmol of 1,2-dibromoethane (for I), or 1,3-dibromopropane (for II) dissolved in 10 mL of anhydrous ether was added dropwise over 0.5 h. The solution was allowed to reflux for 2 h and then evaporated under a nitrogen stream. The product was dissolved in 30% acetic acid and purified by HPLC (Vydac C-18 column, 1 cm × 25 cm) using the solvent system 0.1% trifluoroacetic acid in H_2O/0.1% trifluoroacetic acid in acetonitrile (75/25). Yields of 20% were obtained for both I and II and in each case unreacted, free sulfhydryl-containing peptide was the major component recovered.

The purified products, I and II, were tested for the presence of free sulfhydryls through reaction with 5,5′-dithiobis(2-nitrobenzoic acid)[7] with and without prior incubation with disulfide-reducing agents (2-mercaptoethanol, dithiothreitol, or $NaBH_4$). In all cases these tests were negative, indicating the absence of free sulfhydryls or disulfides. Analysis by fast atom bombardment mass spectrometry yielded the appropriate molecular weights for I (MW = 673) and II (MW = 687).

To the best of our knowledge, I and II constitute the first examples of the use of dithioether bridges to form cyclic peptides. This approach should be of general utility in the design and synthesis of cyclic peptides with variable ring size. Pharmacological and conformational analyses of I and II are in progress.

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Synthesis of a 1,3-Dioxa-2,4-diboretane: An Oxoborane Precursor

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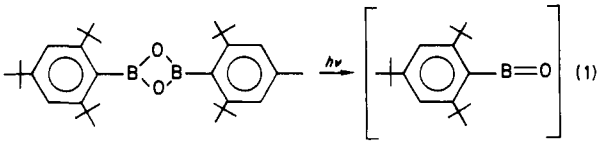
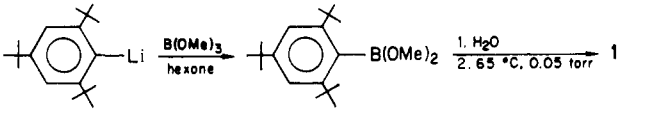
We report here the synthesis of a 1,3-dibora-2,4-dioxetane **1** and its photolysis to give trapping products consistent with intermediate formation of the oxoborane **2** (eq 1).



(1)

1 **2**

Although there is much current interest in species containing multiple bonds to boron,[1] no reports of oxoboranes (boranones, RB=O) have yet appeared.[2] Photolytic cleavage of a 1,3-dioxa-2,4-diboretane seemed a likely route to boranones, but these compounds were also unknown, except for a coordination compound with bridging methoxyl groups.[3] Dehydration of organodihydroxyboranes usually leads to the six-membered ring boroxines;[4] when very bulky groups are attached to boron dehydration may not take place.[5] However, hydrolysis and dehydration of (2,4,6-tri-*tert*-butylphenyl)dimethoxyborane (**3**), prepared from (2,4,6-tri-*tert*-butylphenyllithium[6] (**4**) and trimethoxyborane, led to dioxadiboretane **1** (eq 2).



4 **3**

(2)

In a typical experiment 5.2 g of **3** was stirred in a mixture of 50 mL of heptane, 50 mL of toluene, and 100 mL of water with 20 mg of tetrahexylammonium bromide for 48 h at 25 °C. The organic layer was separated and the solvents were evaporated under vacuum; heating of the residue to 65 °C at 0.05 torr produced 3.3 g (76%) of nearly pure **1** as a yellowish oil.[7] The same

(1) See, for example: Paetzold, P.; von Plotho, C.; Schmidt, G.; Boese, R.; Schrader, B.; Bougeard, D.; Pfeiffer, O.; Gleiter, R.; Schäfer, W. *Chem. Ber.* **1984**, *117*, 1089. Klusik, H.; Berndt, A. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 877. Nöth, H.; Staudigl, R.; Wagner, H.-U. *Inorg. Chem.* **1982**, *21*, 706.
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(3) Goubeau, J.; Lücke, K. E. *Liebigs Ann. Chem.* **1952**, *575*, 37. A compound for which a 1,3-dioxa-2,4-diboretane structure was originally proposed (Hawkins, R. T.; Lennarz, W. J.; Synder, H. R. *J. Am. Chem. Soc.* **1960**, *82*, 3053) was later shown to have the common six-membered ring boroxine structure.[4]
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(5) Hunter, D.; Steinberg, H. U.S. Patent 3 359 298, 1969; *Chem. Abstr.* **1969**, *70*, 353.
(6) Pearson, D. C.; Frazer, M. G.; Frazer, V. S.; Washburn, L. C. *Synthesis* **1976**, 621; Staab, H.; Meissner, B. *Ann. Chem.* **1971**, *753*, 80.

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