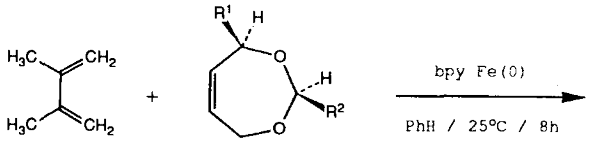
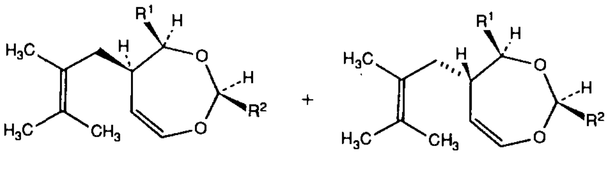
4] ene products **2** and **3** (R^1 = H, R^2 = C_6H_5). The isoprene reaction catalyzed by dmph·Fe(0) is also slightly more anti selective, yielding a 30:70 syn/anti mixture.

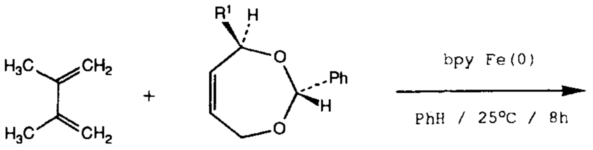
While the parent acetals **1** are achiral, homochiral 2,4-disubstituted 1,3-dioxepins can be easily prepared by starting with the asymmetric reduction of an appropriate propargylic ketone.[11] Acetalization of 2-substituted *cis*-1,4-but-2-ene diols with benzaldehyde dimethyl acetal yields a thermodynamic mixture of *cis*- and *trans*-phenyl acetals.[12] The 56:44 mixture of diastereomers **5** and **6** (R^1 = C_2H_5 or CH_2Ph, R^2 = Ph) can be separated by chromatography on silver nitrate impregnated silica gel and the unwanted isomer reequilibrated to the thermodynamic mixture. Each of the phenyl acetal diastereomers **5** and **6** reacts with 2,3-dimethyl-1,3-butadiene in the presence of bpy·Fe(0) to yield (40–60%) a [4 + 4] ene product, **7** and **9**, respectively (eq 2 and 3). Each coupling reaction proceeds highly diastereoselectively (>95:5), with the isomeric all-cis [4 + 4] ene products **7** and **9** differing only with respect to the regiochemistry of carbon–carbon bond formation. Most significantly, the stereochemistry of carbon–carbon bond construction proceeds independent of the stereochemistry of the substituent (R^1) at the 4-position of the 1,3-dioxepin ring and is directed greater than 95% syn with respect to the remote phenyl substituent. The acetal substituent is critical to the asymmetric induction. In contrast to the reactions of **5a** and **5b**, the bpy·Fe(0)-catalyzed reaction of the unsubstituted acetal **5c** (R^1 = C_2H_5, R^2 = H) proceeds in poor yield (10%) and with low stereoselectivity to give a 2:3 mixture of **7c** and **8c**.



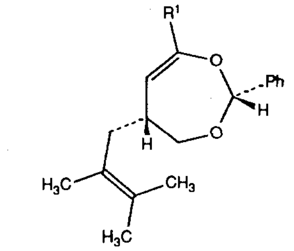
5a R^1 = C_2H_5, R^2 = Ph
b R^1 = CH_2Ph, R^2 = Ph
c R^1 = C_2H_5, R^2 = H



7 **8** (2)



6a R^1 = C_2H_5, R^2 = Ph
b R^1 = CH_2Ph, R^2 = Ph



9 (3)

Further studies of the effect of remote substituents on the stereochemistry of this new carbon–carbon bond-forming reaction and on the applications of this methodology to asymmetric synthesis are in progress.[13]

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[11] (a) Midland, M. M.; Tramontano, A.; Kazubski, A.; Graham, R. S.; Tsai, D. J. S.; Cardin, D. B. *Tetrahedron* **1984**, *40*, 1371–1380. (b) Soulier, J.; Farines, M.; Bonafus-Bastouill, A.; Laguerre, A. *Bull. Soc. Chim. Fr.* **1975**, 1763–1766. (c) Eliel, E. L.; Badding, V. G.; Rerick, M. N. *J. Am. Chem. Soc.* **1962**, *84*, 2371–2377.

[12] The energy difference between the lowest energy conformers of **5** and **6** is estimated by MM2 to be +0.10 kcal/mol, consistent with the slight thermodynamic preference for formation of the cis diastereomer. The structural assignments of **5** and **6** are based upon the detailed analysis of the 300-MHz ^{1}H NMR spectra and from NOE experiments. In an NOE difference experiment (irradiating the acetal proton), the methine hydrogen in **5**, but not in **6**, shows a strong signal enhancement, confirming the cis relationship between those two protons.

[13] We thank the National Institutes of Health (GM 34927), the donors of Petroleum Research Fund, administered by the American Chemical Society, and the University of Utah Research Committee, for support of this work.

The Synthesis, Reactions, and Molecular Structure of Zirconocene–Alkyne Complexes

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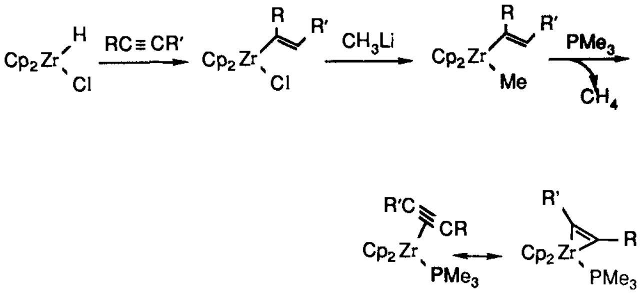
Transition metal complexes of alkynes have been reported for a large number of metals, including examples of both early and late transition metals.[1] We have recently reported the preparation and reaction chemistry of the zirconocene complexes of cyclohexyne[2a] and benzyne.[2b] We have now developed a general route to zirconocene complexes of both terminal and internal acyclic alkynes and herein we report on their synthesis and reactions. In addition we have determined the X-ray crystal structure of the trimethylphosphine adduct of the zirconocene complex of 1-hexyne **2b** which shows several interesting differences in structure from the cyclohexyne and benzyne complexes and which is, to our knowledge, the first structurally characterized acyclic alkyne complex of zirconium to be reported.

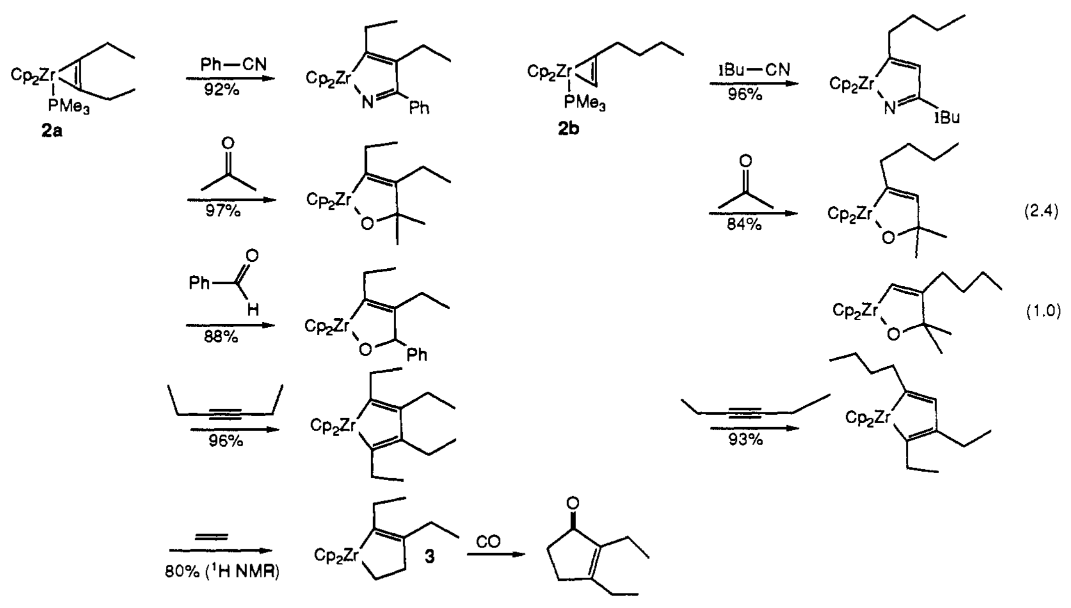
Zirconocene alkyne complexes can be prepared as shown in Scheme I. Hydrozirconation of an alkyne[3] followed by the addition of methyllithium produces intermediate **1** which loses methane,[4] and the resulting alkyne complex is trapped with trimethylphosphine. These complexes can be isolated in ca. 70% yield and can be further purified by recrystallization from ether/hexane at low temperature.

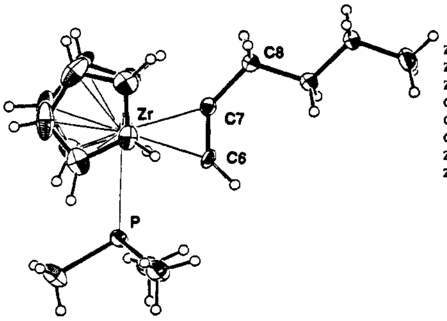
The X-ray crystal structure of **2b** is shown in Figure 1. Of note is the C6–C7–C8 bond angle of 135.8 (3)°. This should be compared with the corresponding angles of 126.0 (1.2)° and 122.1

Scheme I



Scheme II





Zr-P	2.6576(11) Å
Zr-C6	2.244(3)
Zr-C7	2.211(3)
C6-C7	1.286(5)
C7-C8	1.491(5)
C6-C7-C8	135.8(3)°
Zr-C6-C7	71.81(19)
Zr-C7-C6	74.64(20)

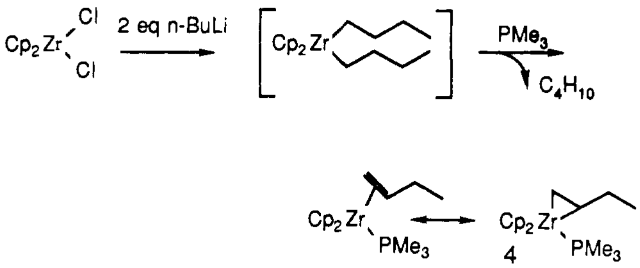
Figure 1.

(5)° in the cyclohexyne and benzyne complexes, respectively. The C–C "triple" bond distance in **2b** is identical, within experimental error, with that found for the cyclohexyne complex.[2a] This suggests that the 135.8 (3)° value more accurately reflects the bond order in these complexes and that the lower value observed for the cyclohexyne complex (and to a lesser extent, the benzyne complex[2b]) is due to the ring strain which prohibits the bond angles from splaying farther outward.

In the cyclohexyne and benzyne complexes loss of the coordinated alkyne and subsequent addition of another molecule of phosphine is disfavored by the high energy of the free alkynes. The stability of **2a,b** is presumably due to the ability of the alkyne to remove excess electron density from the metal by back-bonding. This is reflected in the bond angles and the triple-bond length in **2b** which more closely resemble a metallacyclopropene than a metal–alkyne complex. This situation has previously been noted in other early transition metal–alkyne complexes.[1,2]

Like the related complexes which we have prepared,[2] **2a,b** couple readily with nitriles, alkynes,[5] ketones, aldehydes, and ethylene[6] as shown in Scheme II. Whereas no regiochemical amibiguity exists for the coupling reactions of **2a**, the reactions of **2b** fall into two categories. First, if in the newly formed metallacycle all ring carbons are sp^2 hybridized, the 3,5 isomer is formed exclusively. If in the newly formed metallacycle either carbon 3 or 4 is sp^3 hybridized, then a mixture results. Here the difference is presumably due to steric repulsion in the transition state leading to product formation caused by the enforced planarity of the contiguous substituents which prevents the formation of the 3,4 regioisomer in the former case. Of special note, from a synthetic perspective, is that metallacycle **3** can be carbonylated to the corresponding cyclopentenone in a manner similar to that employed by Negishi in bicyclic cases.[6a,8]

Scheme III



We have also begun preliminary work on the synthesis of zirconocene complexes of alkenes. As shown in Scheme III, treatment of zirconocene dichloride with 2 equiv of *n*-butyllithium at −78 °C,[8,9] followed by addition of trimethylphosphine and allowing the reaction mixture to warm to room temperature causes the formation of the *n*-butene complex **4** in ca. 85% yield.

We are continuing work on the synthesis of complexes of both strained and unstrained unsaturated organic molecules using zirconium and other early transition metals. In addition, we are investigating the use of other ligands as alternatives to tri-

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(5) There are a number of examples of group 4 metallocene-induced reductive coupling of two alkynes; cf.: Nugent, W. A.; Calabrese, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 6422 and references therein.

(6) For examples of group 4 metallocene-induced reductive coupling of an olefin with an alkyne, cf.: (a) Negishi, E.; Holmes, S. J.; Tour, J. M.; Miller, J. A. *J. Am. Chem. Soc.* **1985**, *107*, 2568. (b) Erker, G.; Kropp, K. *J. Am. Chem. Soc.* **1979**, *101*, 3659.

(7) All yields refer to isolated yields with the exception of the reaction of **2a** with ethene where the yield was determined by ¹H NMR.

(8) Negishi, E.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1986**, *27*, 2829.

(9) Negishi has found that dibutylzirconocene generated in this manner in the presence of an alkyne causes displacement of the butene and serves as a clean zirconocene source.[8]

methylphosphine and are continuing to develop methods to convert our initial metallacycles to synthetically useful organic compounds.

Acknowledgment. The workers at MIT gratefully acknowledge the financial support of the National Institutes of Health (GM-34917), the Research Corporation, Firmenich S. A., and Dr. Alfred Bader. S.L.B. is the recipient of a Distinguished New Faculty Grant from the Camille & Henry Dreyfus Foundation, Inc., which he gratefully acknowledges. B.T.W. is the recipient of an American Chemical Society Organic Division Graduate Fellowship sponsored by the Dow Chemical Co. for which he is grateful. J.C.H. thanks the Marshall H. Wrubel Computing Center for a generous gift of computing time. We also acknowledge Professor E. Negishi and co-workers (Purdue University) for the mutual exchange of unpublished information on their related work.

Supplementary Material Available: Experimental procedure for the preparation of **2b**, NMR and high-resolution mass spectral data for the compounds shown in Schemes II and III, and tables of final positional and thermal parameters and bond distances and angles (13 pages); tables of calculated and observed structure factors (12 pages). Ordering information is given on any current masthead page.

Subsite-Specific Functionalization of the $[4Fe\text{-}4S]^{2+}$ Analogue of Iron-Sulfur Protein Clusters

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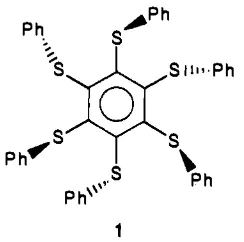
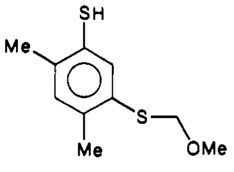
Structural and reactivity features are now known to be developed at specific iron subsites of protein-bound $Fe_4(\mu_3\text{-}S)_4(S\cdot Cys)_4$ clusters. Thus, siroheme in sulfite reductase is coupled to one cluster subsite by a bridging cysteinyl sulfur atom,[1] exogenous iron in the reconstitution $Fe_3S_4 \rightarrow Fe_4S_4$ is incorporated at one (at most two) subsite(s) of the product cluster,[2,3] substrate binds at this site in aconitase,[4,5] and a $CoFe_3S_4$ cluster has been produced by use of Co(II) in reconstitution.[6] One implication of these results is that the subsite voided in the oxidative transformation $Fe_4S_4 \rightarrow Fe_3S_4$ is that recovered in reconstitution. Analogue clusters $[Fe_4S_4L_4]^{2-}$ (L = RS^-, halide) exhibit statistical subsite reactions[7] and thus are unsuitable for probing subsite-specific features. We report here entry to clusters with one differentiated subsite and illustrative subsite-specific reactions thereof.

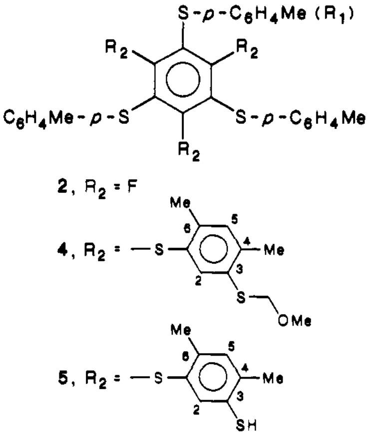
The cavitand concept[8] and the alternating up-down stereochemistry of the "legs" of crystalline hexasubstituted benzenes such as **1**[9,10] (notation,[11] *ababab*) have been combined in the synthesis of a new type of semirigid tridentate ligand.[12] Reaction of 1,3,5-tribromo-2,4,6-trifluorobenzene[13] and *p*-tolyl thiocuprate[10b] (DMF, 140 °C, 36 h) gave **2** (56%). The sodium salt of thiol **3** [from 1,3-dimercapto-4,6-dimethylbenzene[14] + 2 equiv of NaH + 2 equiv of $ClCH_2OMe$ (DMF, 25 °C) followed by 1 equiv of NaSEt[15] (DMF, 160 °C, 60%)] combined with template **2** under conditions similar to those of MacNicol et al.[16] (DMEU, 70 °C, 5 days) gave bright yellow **4** (41%). Deprotection [$Hg(OAc)_2$, H_2S] afforded yellow, air-sensitive trithiol **5** (97%, 17% based on 1,3,5-$C_6H_3F_3$). Equimolar ligand substitution reaction 1 in situ[12a] gave the ethanethiolate *mono*substituted cluster **6** (identified by ^{1}H NMR), which in reaction 2 afforded $(Ph_4P)_2[Fe_4S_4(L\cdot S_3)Cl]$ (**7**, 58%, from DMF/ether). The structure of anion **7**[12b] (Figure 1) proves formation of the desired cluster. The three R_2 legs of **7** lie on the same side of the planar central ring, with angles C_{ring}–S–C = 103.1 (1)–106.2 (1)°, binding three irons atoms; the remaining iron subsite is bound to chloride. Cluster atom S(4)



1



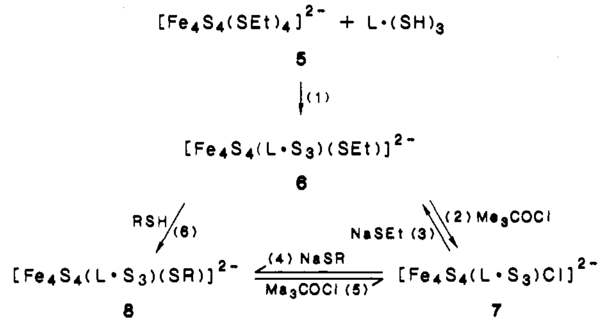
3



2, R_2 = F

4, R_2 = —S—

5, R_2 = —S—



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(12) Experimental: (a) All operations and measurements were carried out anaerobically. ^{1}H and ^{13}C NMR spectra were determined at 500 and 125.8 MHz, respectively. Reactions 1–6 were run in DMF or acetonitrile at ~25 °C. (b) X-ray diffraction data of **7** were collected at ~25 °C with use of monochromatized Mo Kα radiation. The structure was solved by standard methods and refined with all rings but the central ring as semirigid bodies and all non-hydrogen atoms described anisotropically. Space group $P\bar{1}$; a = 13.537 (3) Å, b = 15.099 (4) Å, c = 24.550 (6) Å, α = 94.42 (2)°, β = 92.73 (2)°, γ = 101.84 (2)°, Z = 2; unique data [$F^2 > 3\sigma(F^2)$], 7238; $R(R_w)$ = 5.3 (5.9)%.

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