active than **1** as time-dependent inhibitors of *E. coli* AdoMetDC, showing the importance of the steric factors in the inactivation process.

In conclusion, inactivation of *E. coli* AdoMetDC by **1** represents the first example of potent enzyme-activated irreversible inhibition of a pyruvoyl enzyme. Inactivation studies on AdoMetDC prepared from rat tissues will be described elsewhere.

Acknowledgment. We thank Annie Clauss for technical assistance in the synthesis of the described compounds.

Registry No. 1, 123642-27-3; **2**, 6117-80-2; **3**, 123642-28-4; **4**, 123642-29-5; 5′-(methylamino)-5′-deoxy-2′,3′-*O*-isopropylideneadenosine, 34245-49-3; adenosylmethionine decarboxylase, 9036-20-8.

(15) These compounds were 5′-[(3-amino-4-pentenyl)methylamino]-5′-deoxyadenosine; 5′-[(3-amino-4-pentynyl)methylamino]-5′-deoxyadenosine; 5′-[(3-amino-4,5-hexadienyl)methylamino]-5′-deoxyadenosine; 5′-[(3-amino-4-fluorobutyl)methylamino]-5′-deoxyadenosine. Detailed data regarding these compounds will be published elsewhere.

Synthesis and X-ray Crystal Structure of the Zirconocene Complex of a Cyclopentyne and Its Use To Prepare Bicyclic Cyclopentenones

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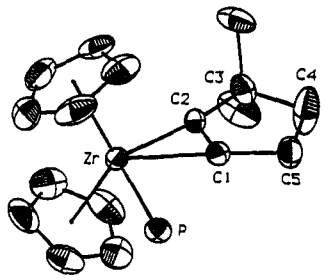
Received August 1, 1989

Cyclohexyne is the smallest cyclic alkyne to be prepared in a form stabilized by complexation to a transition metal.[2-4] We now describe the preparation, characterization by X-ray crystallography, and a preliminary study of the reactivity of the zirconocene complex of 5,5-dimethylcyclopentyne stabilized as its trimethylphosphine adduct.

We recently reported the preparation of the zirconocene complex of cyclohexyne **2**.[2] Compound **2** was formed via loss of methane from **1** with $\tau_{1/2}$ = 40 min at 20 °C (Scheme I). Studies of the reactions of **2** indicated that this compound experienced little angle distortion, the strain being relieved by the π-backbonding from the electron-rich zirconium center. The ease of formation of **2** and its relatively unstrained structure suggested that zirconocene complexes of even smaller cyclic alkynes ought to be accessible. Thus, we were surprised when (1-cyclopentenyl)methylzirconocene (**3**) did not lose methane to form the corresponding cyclopentyne complex **4**, even upon prolonged heating at elevated temperatures (120 °C). Subsequent work indicated that having sufficient overlap of the vinyl C–H bond with the Zr-centered LUMO was the key to inducing methane loss.[5,6] In order to probe whether a derivative of **3** could be prepared which possessed the necessary interaction of the C–H bond with the LUMO, we synthesized (5,5-dimethylcyclopentenyl)methylzirconocene (**5**). Thermolysis of **5**, at 90 °C ($\tau_{1/2}$ = 4 h), in the presence of excess trimethylphosphine provides a 48% isolated yield of complex **6**, which has been characterized by ^{1}H, ^{13}C, and ^{31}P NMR, X-ray crystallography, IR, and combustion analysis. The X-ray crystal structure of **6** is shown in Figure 1. It is interesting to note that the presence of the geminal dimethyl groups at C-3 does not cause a perceptible lengthening, in the solid state, of the C2–Zr bond relative to the analogous bond in **2**.[2] We believe, however, that the presence of these methyl groups in **5** effects the necessary overlap by causing the movement of C3 away from the Cp_2Zr fragment, with a concomitant decrease in the distance between C1 and the Cp_2Zr unit as shown in Scheme I.[7]

Complex **6** and its ligand-free version **7**, which can be generated and used in situ, manifest a number of important and synthetically useful differences in reactivity as compared to **2**. In particular, **2** fails to react with olefins at room temperature. The corresponding ligand-free complex of **2**, generated in situ, reacts at room temperature with 1-hexene to give a ca. 1:1 mixture of regioi-

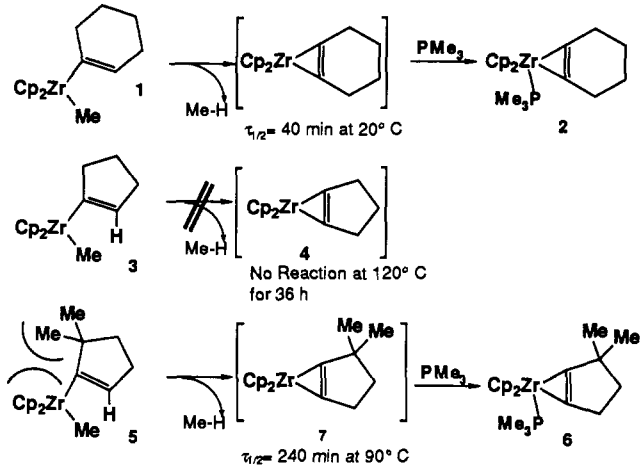


Selected Bond Lengths and Angles

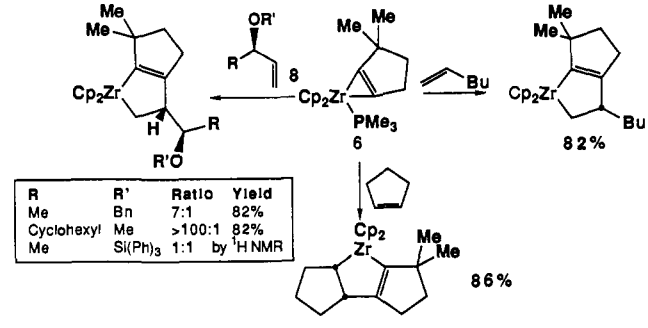
Zr-C1	2.201(4)Å
Zr-C2	2.169(4)
C1-C2	1.295(6)
C1-C5	1.528(6)
C2-C3	1.515(6)
Zr-P	2.698(2)
C1-Zr-C2	34.5(2)°
C1-C2-C3	114.4(4)
C2-C1-C5	111.1(5)

Figure 1.

Scheme I



Scheme II



R	R'	Ratio	Yield
Me	Bn	7:1	82%
Cyclohexyl	Me	>100:1	82%
Me	$Si(Ph)_3$	1:1 by ^{1}H NMR	

(1) Camille & Henry Dreyfus Teacher-Scholar Awardee, 1989–1994; American Cancer Society Junior Faculty Research Awardee, 1987–1989; Eli Lilly Grantee, 1988–1990; Alfred P. Sloan Research Fellow, 1988–1990; Union Carbide Innovation Recognition Awardee, 1989.

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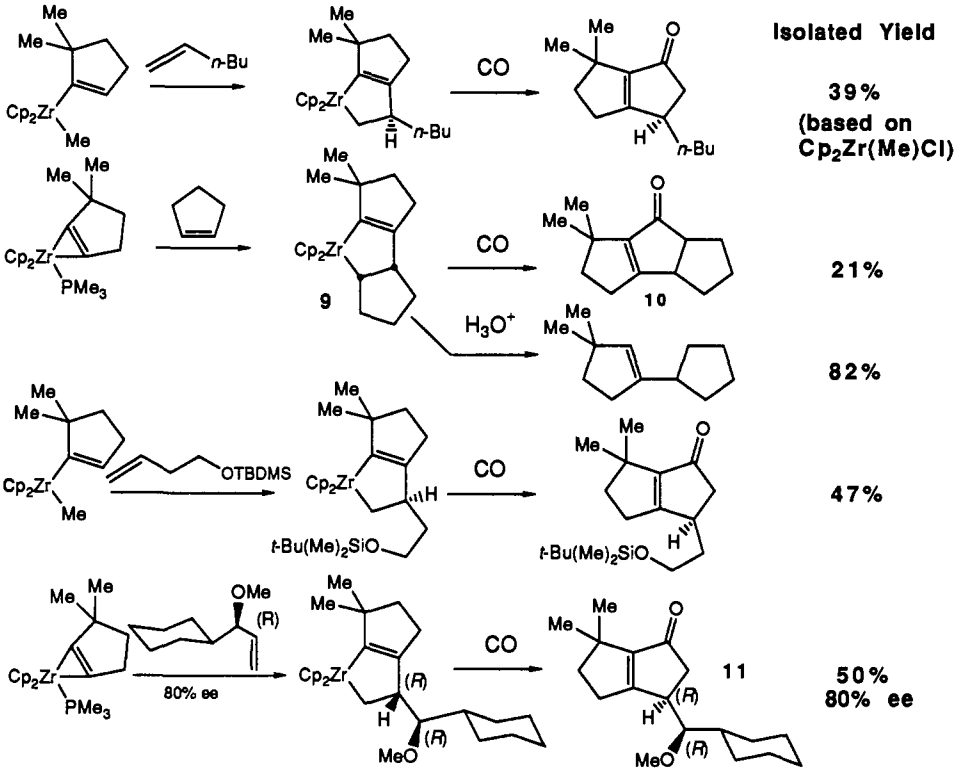
Scheme III



someric metallacycles. In contrast, both **6** and **7** give only the one isomer shown (Scheme II) when exposed to 1-hexene at room temperature and 90 °C, respectively. In all the cases we have examined, the zirconocene unit ends up on the carbon α to the geminal dimethyl group. This appears to be controlled by the approach of the olefin from the less hindered side of **7**. Additionally, the olefin substituent is placed at the sterically less congested β-carbon in an analogous manner to what is seen for other insertion reactions involving zirconocene complexes of arynes.[8] As well as inserting simple olefins, **6** and **7** react in a highly diastereoselective manner with chiral allylic ethers of general structure **8**. The degree of diastereoselectivity is extremely dependent on the relative sizes of R and R′. For example, for R = Me and R′ = Bn, a 7:1 mixture of diastereoisomers is formed in 82% yield. Increasing the size of R′ (to Ph_3Si) relative to R (Me) gives a 1:1 mixture of diastereomers by ^1H NMR. However, in the case where R = cyclohexyl and R′ = Me, only one isomer is detected. The metallacycles produced via these reactions may be transformed, without isolation, directly into bicyclic cyclopentenones in good overall yield, as is shown in Scheme III.[9,10] One exception is metallacycle **9**, which, although it is produced in high yield, to date has been converted to the tricyclic ketone **10** in only modest yield. While the yield for the conversion of **5** to **10** is 21%, overall it represents a rapid, one-pot method for the construction of the tricyclic ketone from remarkably simple precursors.[11]

Of the greatest interest is the reaction of (*R*)-(+)-1-cyclohexyl-1-methoxy-2-propene (80% ee) with **6**, followed by carbonylation, to produce cyclopentenone **11** in 50–54% isolated yield as a single diastereomer (80% ee).[12] This represents the first transition-metal-induced intermolecular carbon–carbon bond formation via a formal reductive coupling of an olefin and an alkyne with ~100% asymmetric induction caused by an existing chiral center on one of the substrates.[13] The relative stereochemistry of **11** was determined by X-ray crystallography.[12] Since the configuration at the stereogenic center of the substrate is unchanged in the product, this allows the assignment of the absolute configuration of **11** as *R,R*.

In summary, we have prepared and structurally characterized the first transition-metal complex of a cyclopentyne. Moreover, we have shown that it can be transformed into metallacycles with high to complete diastereoselectivity. These intermediates can, without isolation, be transformed into bi- and tricyclic cyclopentenones in what constitutes an overall brief and efficient pathway.

We are continuing to explore the chemistry of **6** and related species and are probing the source of the observed diastereoselectivity in the insertion reactions described above.

Acknowledgment. We thank Eli Lilly, the American Cancer Society, the National Institutes of Health (GM-34917), and Firmenich SA for their generous financial assistance. We also gratefully acknowledge Professor Jeremy Burdett (University of Chicago) for making insightful suggestions and Professor Martin A. Bennett (Australian National University) for disclosing unpublished information.

Supplementary Material Available: Experimental section containing the preparation and spectroscopic characterization of representative compounds, along with crystallographic data and procedures, ORTEP diagrams of **6** and **11**, tables of bond distances and angles for **6** and **11**, and a table of final positional and thermal parameters for **6** and **11** (35 pages); listing of structure factors for **6** and **11** (55 pages). Ordering information is given on any current masthead page.

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(12) Details are given in the supplementary material.

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