

**THE ZIRCONOCENE INDUCED COUPLING OF BENZYNE WITH NITRILES: SYNTHESIS,
STRUCTURE AND REACTIONS OF NOVEL AZAMETALLACYCLOPENTENES**

Stephen L. Buchwald*, Ann Sayers, Brett T. Watson and John C. Dewan

Department of Chemistry

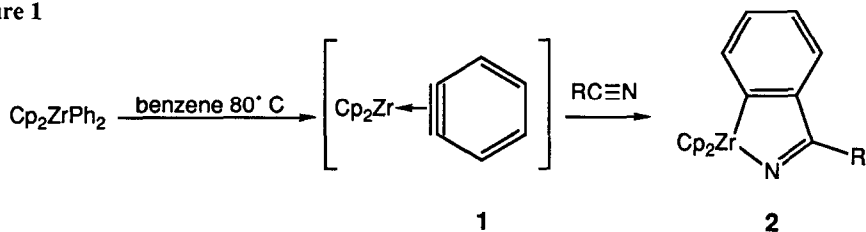
Massachusetts Institute of Technology

Cambridge, Massachusetts 02139

Abstract: A series of novel azazirconacyclopentenes have been prepared by the thermolysis of diphenylzirconocene in the presence of one equivalent of a wide variety of nitriles. An X-ray crystal structure shows these metallacycles to be dimeric in the solid state.

Diphenylzirconocene has previously been shown to generate the nascent zirconocene-benzynes complex **1** on gentle thermolysis in benzene (80°C).¹ **1** had been trapped by several olefins, but these reactions required a large excess of trapping reagents.¹ We have found that if the thermolysis is carried out in the presence of one equivalent of any of a wide variety of nitriles, the unique metallacycles **2** (figure 1) are formed as highly crystalline solids in good to excellent yields.² We have previously shown that the trimethylphosphine adduct of **1** also reacts with nitriles to form **2**.³ An X-ray crystal structure for **2**, R=n-propyl (a dimer in

Figure 1



the solid state) is shown in figure 2. This dimer possesses a center of symmetry located midway between the two zirconium atoms. Included, as well, are the most important bond lengths and angles.

In table 1 are shown a few of the many examples of the metallacycles prepared so far.^{4a} Also shown are the yields of ketones produced from hydrolyses of metallacycles **2**. Of special note is that the reaction seems unperturbed by the presence of common functional groups such as olefins (even conjugated) or a ketal. The yields of this hydrolysis procedure range from good to excellent. The overall transformation for this reaction sequence is equivalent to a Friedel-Crafts acylation.⁵ In simple cases standard Friedel-Crafts chemistry provides a facile route to the phenone products. Our method, however, should prove superior in instances where the substrates or products are acid sensitive (e.g., entries 7-9).

A few nitriles react with **1** to give "abnormal" products. These fall into two classes. The first, shown in

Table 1

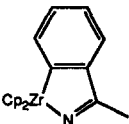
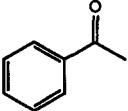
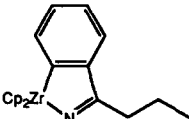
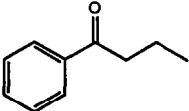
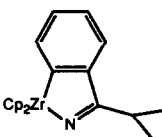
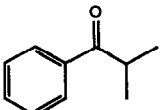

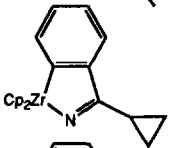
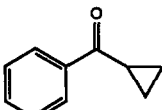

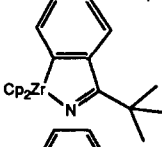
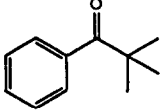
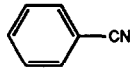
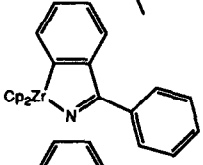
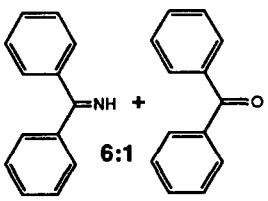
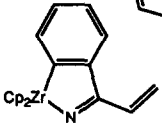
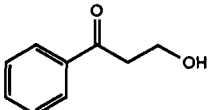
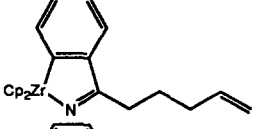
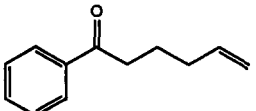
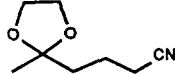
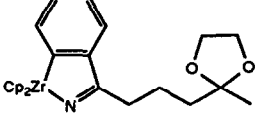
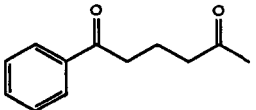
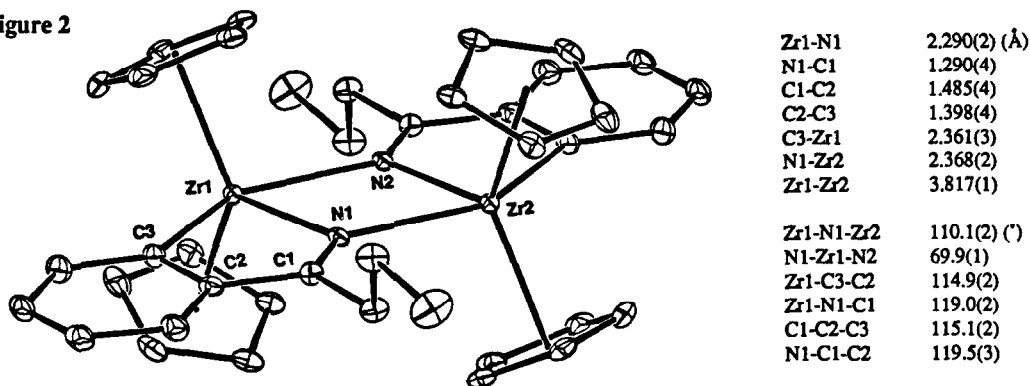
Entry	Nitrile	Metallacycle	Yield (%)	Hydrolysis Product	Yield (%)
1	<chem>CH3CN</chem>		87		70
2	<chem>CCCC#N</chem>		88		93
3	<chem>CC(C)C#N</chem>		87		92
4			91		90
5			not isolated		74
6			93		93
7	<chem>C=CC#N</chem>		76		54 ^{6a}
8	<chem>C=CCCC#N</chem>		83		86 ^{6b}
9			99		65 ^{6c}

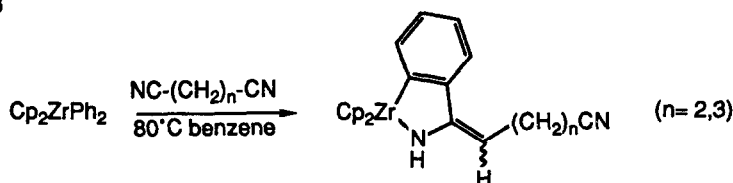
figure 3, is the formation of the enamino metallacycles, isomers of the imine metallacycles. These are formed if

Figure 2



another cyano group is present in the molecule. These metallacycles, which are the only products observed,

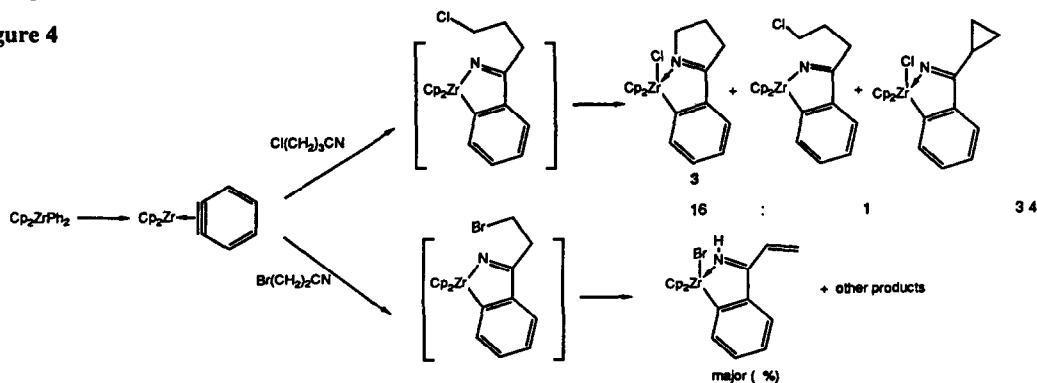
Figure 3



appear to be formed as only one of the two possible geometric isomers (^1H , ^{13}C NMR) but we have yet to prove the stereochemical disposition of R". These two examples are the only ones in which we see any of the enamino regioisomer. In addition we have been unable to find conditions to convert one isomer into the other.

The second class of "abnormal" products is observed when there is a ω -halo substituent on the R group. In figure 4 are shown the products obtained from the reaction of the zirconocene-benzyne complex with nitriles of this type. In each instance the initially formed metallacycle is converted to a new product. Of special note

Figure 4



is the case $\text{R}=(\text{CH}_2)_2\text{CH}_2\text{Cl}$ where intramolecular alkylation occurs to form dihydropyrrole 3.7

In summary, we have demonstrated the generality of the zirconocene-induced coupling of an alkyne (benzyne) with nitriles. The initially formed metallacycles have been characterized structurally and have been shown to have interesting and synthetically useful chemistry. We are currently investigating the synthesis and reactions of substituted analogues of **1** as well as continuing our efforts to devise novel transformations based on these metallacycles.

Acknowledgement. We would like to thank the National Institutes of Health (GM-34917), the Research Corporation and Alfred Bader for their generous support of this research. SLB is the recipient of a Distinguished New Faculty Grant from the Camille & Henry Dreyfus Foundation, Inc. which he gratefully acknowledges. BTW is the recipient of an American Chemical Society Organic Division Graduate Fellowship sponsored by the Dow Chemical Company for which he is grateful. We would also like to thank the Biomedical Research Support Shared Instrumentation Grant Program, Division of Research Resources, for funds to purchase the X-ray diffraction equipment (NIH grant S10 RR02243).

References

1. Erker, G.; Kropp, K. *J. Am. Chem. Soc.* **1979**, *101*, 3659; Kropp, K.; Erker, G. *Organometallics* **1982**, *1*, 1247.
2. (a) For examples of group 4 metallocene induced couplings of alkynes with olefins and other alkynes Cf. Negishi, E.; Swanson, D.R.; Cederbaum, F.E.; Takahashi, T. *Tetrahedron Lett.* **1987**, *28*, 917; Negishi, E.; Cederbaum, F.E.; Takahashi, T. *Tetrahedron Lett.* **1986**, *27*, 2829; Negishi, E.; Holmes, S. J.; Tour, M.; Miller, J. A. *J. Am. Chem. Soc.* **1985**, *107*, 2568; Nugent, W. A.; Calabrese, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 6422.
 b) Bercaw has reported the decamethyltitanocene-induced coupling of acetonitrile with ethylene: Cohen, S. A.; Bercaw, J. E. *Organometallics* **1985**, *4*, 1006.
3. Buchwald, S.L.; Watson, B.T.; Huffman, J.C. *J. Am. Chem. Soc.* **1986**, *108*, 7411.
4. Typical procedure for the synthesis of azametallacycles:
 To diphenyl zirconocene (2.25 g, 6.0 mmol) in a schlenk flask under argon is added, via syringe, dry benzene (25 mL) followed by acetonitrile (314 μ L, 0.246 g, 6.0 mmol). The schlenk flask is fitted with an air cooled condenser and the reaction is heated at 80 $^{\circ}$ C for 17 h. During this period, the product metallacycle had crystallized from solution. The supernatant liquid is removed by decantation and the crystals are washed with a small portion of benzene, followed by washing with hexane and drying under vacuum. The resulting metallacycle is isolated as yellow nuggets (1.88 g, 92% yield): mp (sealed capillary) 291-296 $^{\circ}$ C (dec); IR (KBr): 1566, 1537; 1 H NMR(250 MHz, C $_6$ D $_6$): δ 7.00-7.47 (m, 4H partially obscured by solvent), 5.62 (s, 10H), 2.33 (s, 3H). Anal. Calcd. for C $_{18}$ H $_{17}$ NZr: C, 63.86; H, 5.06; N, 4.14. Found: C, 63.97; H, 5.10; N, 4.15.
5. March, J. *Advanced Organic Chemistry*, 3rd Ed., Wiley: New York, 1985.
6. a) Rocek, J.; Martinez, A. M.; Cushmac, G. E. *J. Am. Chem. Soc.* **1973**, *95*, 5425.
 b) Tapio, H. *Synthesis*, **1980**, 36.
 c) Narasaka, K.; Soai, K.; Aikawa, Y.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 779.
7. 2-phenyl-1-pyrroline,**8** derived from **3**, can be isolated in 64% yield after hydrolysis of the crude reaction mixture followed by flash chromatography on silica gel.
8. Kemppainen, A. E.; Thomas, M. J.; Wagner, P. J. *J. Org. Chem.* **1976**, *41*, 1294.

(Received in USA 20 April 1987)