# Reactions of Zirconacyclopentadienes with Nitrosobenzene. Characterization of Zirconacycle Intermediates and Formation of *N*-Phenylpyrroles

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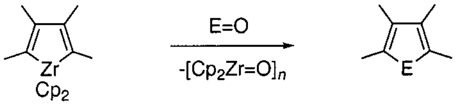
*Summary: Nitrosobenzene inserts into the Zr−C bond of zirconacyclopentadienes to give seven-membered zirconacyclic rings. The resulting insertion products are readily converted to N-phenylpyrroles and (in one case) a 3,3-spiroindole derivative.*

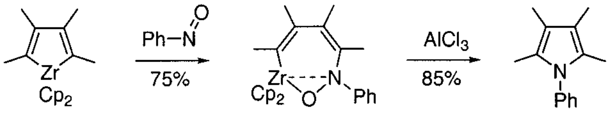
Zirconocene-coupling methods are now well-established as important synthetic routes to a variety of heterocyclic compounds and functionalized molecules.[1] In one manifestation of this chemistry, a zirconocene reagent couples with two alkynes to produce a zirconacyclopentadiene in high yield and high regioselectivity. These zirconacyclopentadienes are useful synthons for heterocycles, which are obtained by reactions with main-group-element dihalides in procedures originally developed by Nugent and Fagan.[2] However, for the synthesis of heterocycles by this method, product yields can depend strongly on reaction conditions and the nature of substituents on the halide derivative and the zirconacycle. For this reason, a number of modifications to the original synthetic method have been explored.[3] Previously, we found that zirconocene coupling reactions involving $SO_2$ may be used to produce thiophene-1-oxides in high yield in reactions that feature "oxo transfer" (oxygen transfer to zirconium; eq 1, E = SO).



(1)

Thus, $SO_2$ reacts cleanly with a range of zirconacyclopentadienes to afford thiophene 1-oxides and zirconocene oxide, $[Cp_2ZrO]_n$,[4] and this method results in significantly higher yields than can be obtained with thionyl chloride as the sulfoxide-transfer reagent.[2c] This strategy has recently been employed by Xi in the synthesis of cyclopentadienes, via reactions of zirconacyclopentadienes with aldehydes in the presence of $AlCl_3$ (eq 1, E = RCH).[5] In further investigations of such oxo-transfer reactions, we have found that nitrosobenzene reacts with zirconacyclopentadienes via insertion into a Zr−C bond, and this insertion chemistry has been used to produce pyrroles (eq 1, E = RN)[6] and an unexpected indole derivative.

**Scheme 1**



**1a** **2a** **3a**

Tetramethylzirconacyclopentadiene[2c,7] (**1a**) reacted with nitrosobenzene in toluene at −78 °C to form an insertion product (**2a**) in 75% yield (Scheme 1). The zirconacycle **2a** was isolated as light yellow, air-stable crystals by flash column chromatography ($Al_2O_3$, hexane/ether) followed by recrystallization from acetonitrile at −30 °C. The molecular structure of **2a** (Figure 1) consists of a seven-membered ring resulting from insertion of the N=O double bond into the zirconacycle of **1a** and a strong Zr···N interaction. At room temperature this reaction also produced **2a** (60%), as well as tetramethylfuran (30%), azoxybenzene (15%), and azobenzene (10%) (by $^1H$ NMR spectroscopy and GC-MS). In the presence of $AlCl_3$ (1 equiv), the selectivity of this process toward production of **2a** is dramatically improved (to >90%).

The slow thermolysis of **2a** in benzene-$d_6$ at 80 °C occurred over ca. 2 weeks and produced tetramethyl-*N*-phenylpyrrole[8] (**3a**) in 90% yield. This reaction is dramatically accelerated by the addition of a Lewis acid such as $AlCl_3$, trimethylsilyl triflate, or $B(C_6F_5)_3$. For example, when 1 equiv of $AlCl_3$ was added to a benzene-$d_6$ solution of **2a** at room temperature, the conversion to **3a** and $Cp_2ZrCl_2$ occurred within 10 min and was essentially quantitative. With 1 equiv of $B(C_6F_5)_3$ as the added Lewis acid, the reaction was somewhat slower,

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[3] See for example: Ura, Y.; Li, Y.; Tsai, F.-Y.; Nakajima, K.; Kotora, M.; Takahashi, T. *Heterocycles* **2000**, *52*, 1171−1189.

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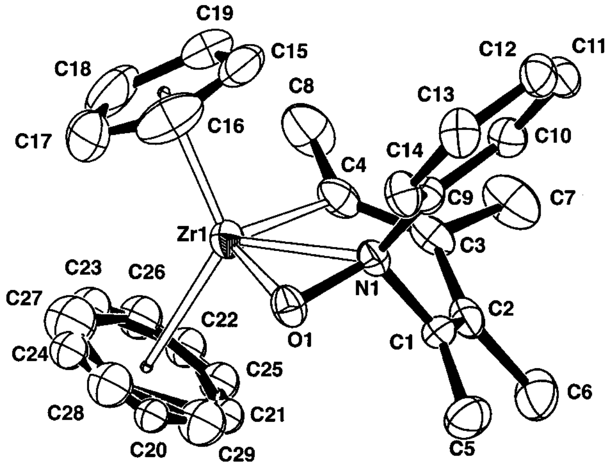
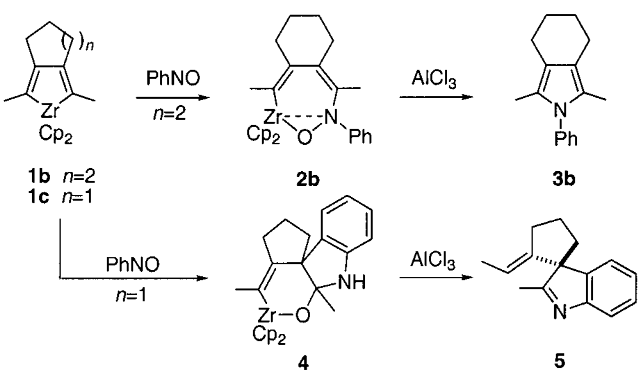


**Figure 1.** ORTEP diagram of **2a**.

**Scheme 2**



such that only a 55% yield of **3a** (as the only product) was observed after heating at 60 °C in benzene-$d_6$ for 24 h.

The most convenient synthetic route to the pyrrole involves adding both PhNO and $AlCl_3$ (1 equiv) to the zirconacyclopentadiene **1a**. When this reaction was carried out at 0 °C in toluene, the pyrrole **3a** was produced in an isolated yield of 85%.

It is interesting to compare our results involving nitrosobenzene to those of Xi and Li, who reported similar chemistry for isoelectronic benzaldehyde. In the latter case, zirconacyclopentadienes were found to be unreactive toward benzaldehyde at room temperature.[5] This appears to reflect a higher reactivity for nitrosobenzene toward insertion.[9] Note, however, that Xi proposed a different mechanism for the reaction with benzaldehyde, involving transmetalation to form an aluminacyclopentadiene, which then reacts with the aldehyde. In the reactions with nitrosobenzene, transmetalation is probably not involved, since Lewis acids which cannot undergo this process also accelerate the conversion to products. We propose that the role of the Lewis acid in both reactions (involving nitrosobenzene and benzaldehyde) is to facilitate insertion of the E=O functionality into the Zr−C bond (with E−C bond formation). In addition, the Lewis acid clearly plays a role in promoting the elimination of $[Cp_2ZrO]_n$ from the initial insertion product.

The synthesis of pyrroles from zirconacyclopentadienes appears to be quite sensitive to steric factors, such that bulkier groups in the α-position of the metallacycle (e.g., Et, $SiMe_3$, and Ph) prevent the insertion

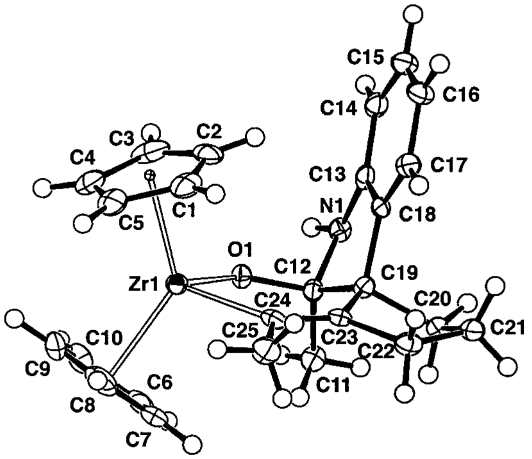


**Figure 2.** ORTEP diagram of **4**.

of PhNO or lead to other products. For example, the reaction of tetraethylzirconacyclopentadiene[7] with PhNO (with or without $AlCl_3$ present) in toluene produced a complex reaction mixture. Heating PhNO with $Cp_2Zr[1,4\text{-}(Me_3Si)_2\text{-}2,3\text{-}Ph_2C_4]$[10] did not give an insertion product, but eventually the free alkyne $Me_3SiC{\equiv}CPh$ was observed. For tetraphenylzirconacyclopentadiene,[7] the major product from the reaction with PhNO was tetraphenylfuran (mp 184−186 °C, lit.[11] mp 185−186 °C; 40−50% yield).

Bicyclic zirconacyclopentadienes **1b**[12] and **1c**[13] were found to readily undergo insertions with nitrosobenzene (Scheme 2). In the case of the six-membered ring ($n$ = 2, **1b**), the insertion to give **2b** proceeded in moderate yield (40%), and its thermolysis gave the tetrahydroisoindole derivative **3b** in 92% yield (from **2b**). The $AlCl_3$-promoted formation of **3b** led to an isolated yield of 59% (from **1b**). In contrast, the reaction of **1c** ($n$ = 1) with nitrosobenzene took a different course, to afford the zirconacycle **4** in 64% yield after recrystallization from ether. The structure of **4** was confirmed by an X-ray crystallographic analysis (Figure 2). Zirconacycle **4** was efficiently converted to the indole derivative **5** (95%, by $^1H$ NMR, benzene-$d_6$ solution) by heating at 80 °C for 12 h or by the reaction with $AlCl_3$ at room temperature for 1 h. It is also possible to obtain **5** directly from the reaction of zirconacyclopentadiene **1c** with nitrosobenzene in the presence of $AlCl_3$ without isolation of **4**, in good yield (70%). Compound **5** was fully characterized by various means, including mass spectrometry and NMR spectroscopy. In particular, the $^1H$ and $^{13}C$ NMR spectra are consistent with the 3,3-spiroindole structure shown in Scheme 2. The $^{13}C$ NMR shift of 68.6 ppm ($C_6D_6$) for the spiro carbon atom and other spectroscopic features agree with the corresponding values reported for a closely related spiroindole derivative.[14] A tentative assignment of the product as the *E* isomer is based on a relatively upfield shift for

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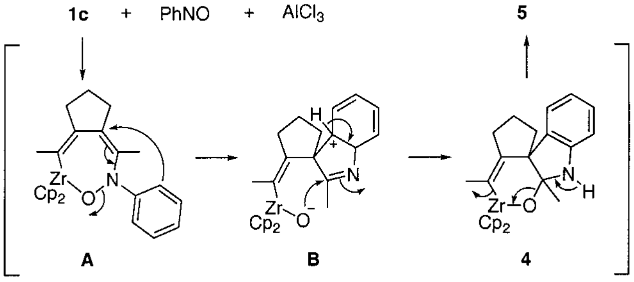
**Scheme 3**



the vinyl proton (4.67 ppm), which may be due to its proximity to the aromatic ring system of **5**.

A possible mechanism to account for the formation of zirconacycle **4** and the following transformation to indole **5** is given in Scheme 3. Insertion of nitrosobenzene into the Zr−C bond occurs as it does for **1a** and **1b**, to generate intermediate **A**. Due to strain in the five-membered ring, intermediate **A** could undergo N−O bond scission and electrophilic substitution on the benzene ring. Subsequent recyclization and proton transfer in **B** would then give zirconacycle **4**. Finally, elimination of $[Cp_2ZrO]_n$ and proton transfer could give **5**. Attempts to observe an intermediate in this transformation (by $^1H$ NMR spectroscopy) were not successful. Some support for the proton-transfer step of this mechanism was observed by monitoring the thermolysis of **4**. In rigorously dry chloroform-*d*, pure **4** remained unchanged for several days at elevated temperature (80 °C). However, in wet chloroform-*d*, the transformation to product is complete within 12 h at 40 °C.

In summary, we report the synthesis of two pyrroles from simple zirconacyclopentadiene starting materials, using an oxo-transfer reaction. This chemistry has also produced an unexpected indole derivative. Future efforts will address the further development of this synthetic method.

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**Supporting Information Available:** Text and tables giving synthesis, characterization, and crystallographic details for **2**−**5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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