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Cyclization of adiponitrile in the reaction with diphenylzirconocene

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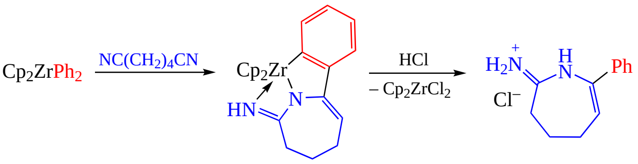
Intramolecular cyclization of adiponitrile with the formation of an amidinate functional group in zirconium coordination sphere was found. The obtained complex can be protolyzed with HCl in dioxane to afford a new representative of amidines, namely, 7-phenyl-1,3,4,5-tetrahydro-2*H*-azepin-2-imine in hydrochloride form.

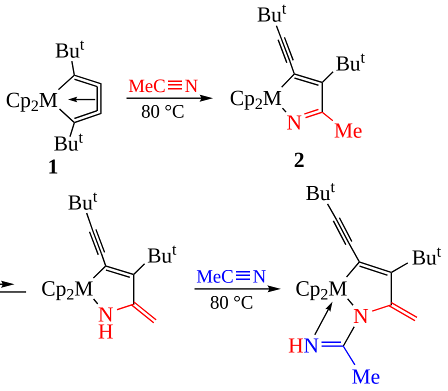


Keywords: zirconium, adiponitrile, cyclization, amidines, amidinate, azepines.

Amidines belong to important class of compounds in modern organic chemistry. These strong bases are used in organic synthesis and as ligands in coordination chemistry[1] and protein chemistry.[2,3] Also, amidines are essential units of the economically significant anti-infective agents of the pentamidine series.[4,5] However, the gradual increase in tolerance to existing drugs forces us to look for new drugs. Thus, the search for new synthetic methods for the preparation of amidines is an urgent task.

Several years ago, we began to study the reactions of seven-membered zirconacyclocumulene complexes with nitriles[6,7] and found that the reaction with acetonitrile produced a zirconaazacyclopentadiene[6] metallacycle which, in turn, reacted with another equivalent of nitrile upon prolonged heating[7] with the formation of zirconamidinate complex. Further study of five-membered zircona- and hafnacyclocumulenes **1** showed a similar reactivity in the case of acetonitrile[8] (Scheme 1).

According to our preliminary assumption,[7] complexes **2** underwent imine–enamine tautomerization, and the addition of the second equivalent of nitrile to **2′** occurred at the NH-bond of the tautomer to form an amidinate complex **3**. However, calculation of the reaction parameters for complex **4** with acetonitrile showed that enaminization is not preferred (path A).

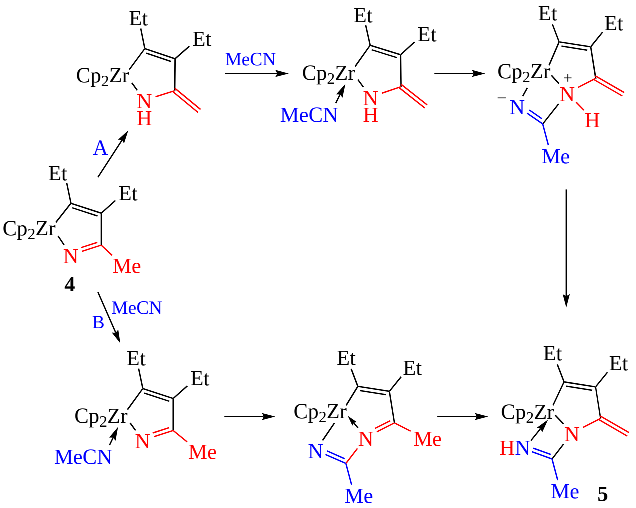


Scheme 1

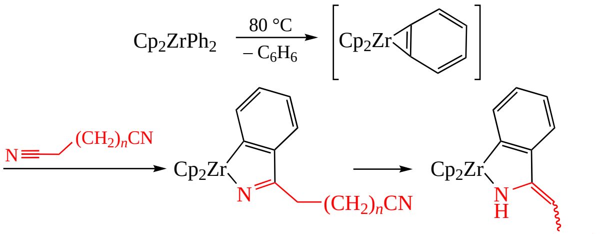
More probable, the attack of the nitrile occurred first, then the migration of the proton (path B) and the formation of **5** took place (Scheme 2).[7]

Interestingly, Buchwald reported[9] on the reactions between diphenylzirconocene and various nitriles leading to zirconaazacyclopentadienes **6** and **6′** (Scheme 3). According to the authors, the products of these reactions were observed in the enamine tautomer form **6′** 'if another cyano-group is present in the molecule'. Moreover, products **6′** were found only in the form of one of two possible geometric isomers.

In an attempt to find enamine metallacycles, we repeated the Buchwald's reaction with adiponitrile. Starting phenyllithium[10] and diphenylzirconocene[11] were synthesized according to the literature. The reaction of diphenylzirconocene with nitrile was performed in toluene at 80 °C for 2.5 h. In fact, this reaction proceeded in a different way and did not lead to complex **6′** but gave a tricycle **7** with an amidine functional group as a result of intramolecular cyclization of dinitrile in the coordination sphere of zirconium (Scheme 4).

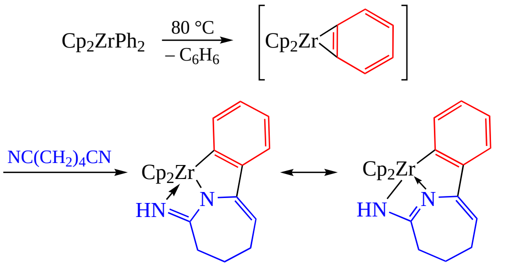


Scheme 2



6 $n = 3, 4$ **6′**

Scheme 3



7 **7′**

Scheme 4

Complex **7** was isolated as a white solid crystalline stable compound with 82% yield. In the ^{1}H NMR spectrum of complex **7** in C_6D_6, along with the CH_2 multiplets (δ 1.51 and 1.91–1.94, 2.26 ppm), and the singlet for the Cp rings (5.65 ppm), multiplets for the phenylene fragment are observed (7.19–7.26, 7.38–7.40, 7.68–7.70 ppm), as well as the triplet for the vinyl hydrogen of the seven-membered ring (5.54 ppm, J 5.1 Hz), and a broad signal for the NH proton (3.93 ppm). In the ^{13}C NMR spectrum, along with other signals, there is a resonance of the *C*=C(N)C atom (98.2 ppm), as well as signals for quaternary carbons associated with the heteroatom ‘N’ [174.7 ppm (N=$\underline{C}$–N)], and ‘Zr’ (183.5 ppm).

Single crystals of complex **7** contained one molecule of co-crystallized benzene per two molecules of **7**.[†] According to X-ray diffraction data, the complex consists of four fused cycles located in the bisector plane of dihedral angle between the η^5-C_5H_5 rings of zirconocene fragment (Figure 1). Four-, five-, and six-membered cycles are practically planar. The C(1)–N(1) [1.316(2) Å] and C(1)–N(2) [1.338(2) Å] distances of the amidinate fragment are close in value indicating the presence of a **7′** resonance structure for complex **7** (see Scheme 4). A similar coordination feature is characteristic of previously obtained amidinates.[7,8]

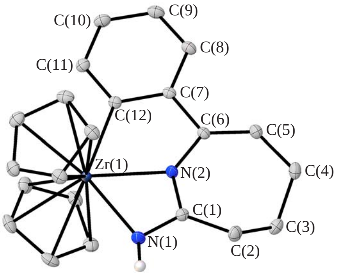
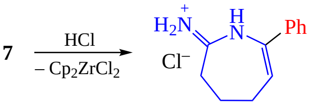


Figure 1 ORTEP representation of the molecular structure of complex **7** with thermal ellipsoids drawn at the 50% probability level. Hydrogen atoms [except the hydrogen atom attached to the N(1)] are omitted for clarity. Selected bond lengths (Å) and angles (°): Zr(1)–N(1) 2.298(1), Zr(1)–N(2) 2.2143(8), N(1)–C(1) 1.316(2), N(2)–C(1) 1.338(2), N(2)–C(6) 1.312(4), C(6)–C(7) 1.491(2), C(7)–C(12) 1.419(1), C(6)–C(5) 1.348(1), Zr(1)–N(1)–C(1) 95.20(9), N(1)–C(1)–N(2) 109.1(1), C(1)–N(2)–Zr(1) 98.41(8).

The obtained complex can be protolyzed with HCl in dioxane with the formation of 7-phenyl-1,3,4,5-tetrahydro-2*H*-azepin-2-imine hydrochloride **8** and Cp_2ZrCl_2 (Scheme 5). In the ^{1}H NMR spectrum of **8** in CD_3OD, along with the multiplets for CH_2 groups (δ 2.34–2.38 and 2.67–2.71 ppm), multiplets for the phenylene fragment (7.37–7.43, 7.48–7.51 ppm), as well as the triplet for the vinylic proton of the seven-membered ring (6.38 ppm, J 6.9 Hz) are observed. The IR spectrum contains a strong band for $\delta_{NH} + \nu_{C=N}$ vibrations (1662 cm^{-1}), two medium-intensity bands for CH_2 vibrations (2870, 2931 cm^{-1}), as well as a broad band of H-bondend NH group (ν_{NH} 3244 and 3429 cm^{-1}).



8

Scheme 5

In summary, the reaction of Cp_2ZrPh_2 with adiponitrile does not produce enamine complexes mentioned by Buchwald. Instead, intramolecular cyclization of the dinitrile in the zirconium coordination sphere with the formation of complex **7** occurs. Protolysis of the resulting HCl complex in dioxane leads to promising amidine of tetahydroazepine family.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2024.06.026.

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[†] *Crystal data for* **7**. $C_{25}H_{25}N_2Zr$ (M = 444.69 g mol^{-1}): monoclinic, space group $C2/c$, a = 25.0016(8), b = 12.4893(4) and c = 16.1038(5) Å, V = 3968.9(2) Å^3, Z = 8, T = 100 K, μ(MoK$_\alpha$) = 0.567 mm^{-1}, d_{calc} = 1.488 g cm^{-3}, 52038 reflections measured (3.86° ⩽ 2θ ⩽ 60°), 5803 unique (R_{int} = 0.0473, R_{sigma} = 0.0241) which were used in all calculations. The final R_1 was 0.0232 [$I > 2\sigma(I)$] and wR_2 was 0.0608.

CCDC 2339278 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.