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Synthesis of Stable Primary Enamines from (Butadiene)zirconocene and Benzylic Nitriles

Gerhard Erker*, Dorothee Kowalski, and Ralf Noe
Organisch-Chemisches Institut der Universität Münster, Corrensstraße 40, D-48149 Münster, Germany

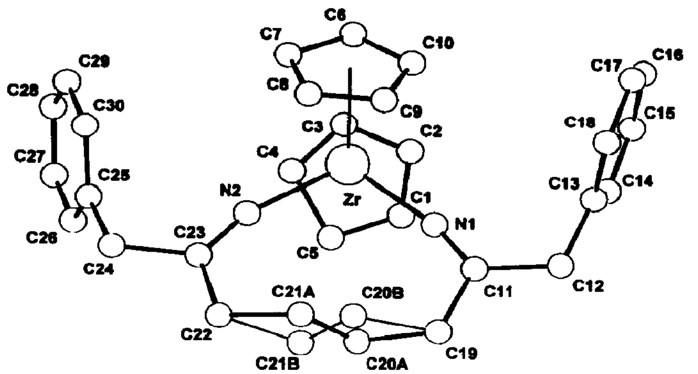
Carl Krüger and Matthias Nolte
Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, D-45470 Mülheim a. d. Ruhr, Germany

Abstract: (Butadiene)zirconocene adds two molar equivalents of benzyl cyanide to give the chiral nine-membered metallacycle 4. Controlled hydrolysis (CH_3OH) of 4 yields the stable conjugated primary enamine 2,7-diamino-1,8-diphenyl-2,4,6-octatriene (6) (≥70% isolated). (2-Pyridyl)acetonitrile reacts similarly with the (butadiene)zirconocene reagent. Subsequent controlled hydrolysis now produces a non-conjugated primary enamine, namely 2,7-diamino-1,8-di(2-pyridyl)-1,4,7-octatriene (9). In this case, conjugative stabilization of a primary enamine is overcome by functional group stabilization by the 2-pyridyl substituent at the β-enamine position.

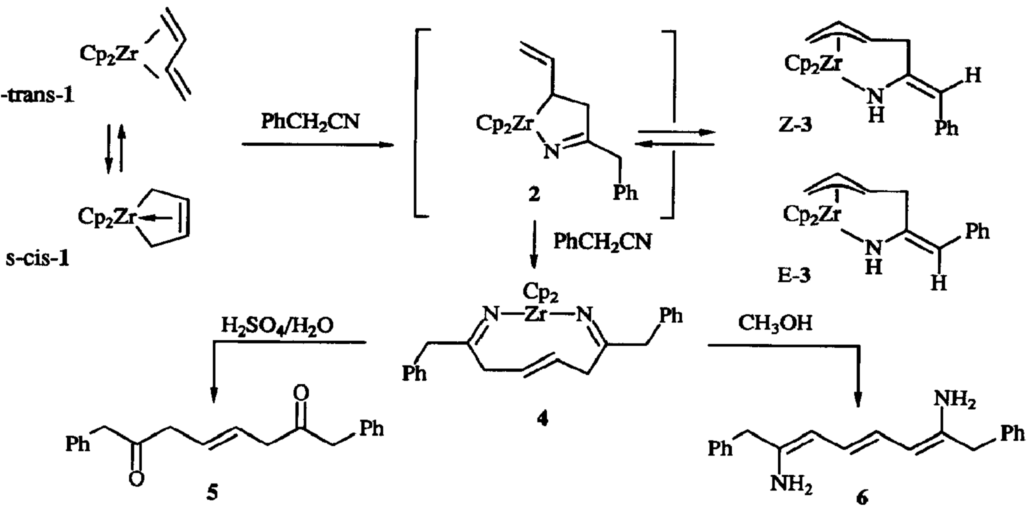
Primary enamines are in equilibrium with their imine tautomers, and this equilibrium usually lies on the imine side unless the enamine is stabilized by electron-withdrawing substituents attached at the alkenamine β-carbon.[1] We have recently demonstrated that conjugated primary enamines (1-aminobutadienes) are thermodynamically >3 kcal/mol more stable than their corresponding imines, so that the dienamines are the only isomers detected within the ^{1}H NMR accuracy under equilibrium conditions. We have used a template coupling reaction[2] (see below) to prepare simple substituted butadiene amines (from CC-coupling of butadiene with a nitrile and a ketone at the Cp_2Zr-backbone)[3] and also very stable 1,6-diaminohexatrienes (from CC-coupling of butadiene with two nitrile molecules, followed by controlled hydrolysis). The latter reaction was used to prepare 1,6-diaryl- and 1,6-di-tert-butyl-substituted 1,6-diamino-1,3,5-hexatrienes.[4] We here report the first example of such a template synthesis leading to the formation of a stable 1,6-diaminohexatriene that has only primary hydrocarbyl substituents attached at the terminal positions of the tail-to-tail connected conjugated primary dienamine systems.

(Butadiene)zirconocene was treated with benzyl cyanide. Under ^{1}H NMR control the formation of the 1:1 addition product is observed. The expected primary product 2 was not found. It had apparently rearranged to the more stable isomers Z-3 and E-3 (observed as an 80:20 mixture). Under preparative conditions benzyl cyanide was treated with the (butadiene)zirconocene reagent in a 2 : 1 molar ratio. This led to the formation of a mixture of nine-membered metallacycles (N-metallated imine and enamine isomers) (isolated in >90% yield). The major component of the mixture was identified as the zirconium-bis-imido complex 4. It was identified by X-ray diffraction and spectroscopically. Complex 4 contains a very rigid metallacyclic framework that is characterized by very large carbon–nitrogen–zirconium angles [Zr–N(2)–C(23) 164.1(4)°, Zr–N(1)–C(11) 165.1(3)°] and short Zr–N bonds [Zr–N(2) 2.052(4) Å, Zr–N(1) 2.034(3) Å] indicating pronounced nitrogen to zirconium backbonding. Complex 4 contains a trans-configurated C=C double bond inside the nine-membered metallacycle (found to be 70:30 disordered in the X-ray crystal structure analysis).[5] Thus, complex 4 is chiral, consequently it exhibits dynamic NMR spectra. From the variable temperature ^{1}H NMR spectra we have calculated a Gibbs activation energy of $\Delta G^{\ddagger}$ (300 K) = 14.5 ± 0.5 kcal mol^{-1} for the ring topomerization reaction of 4.[6]

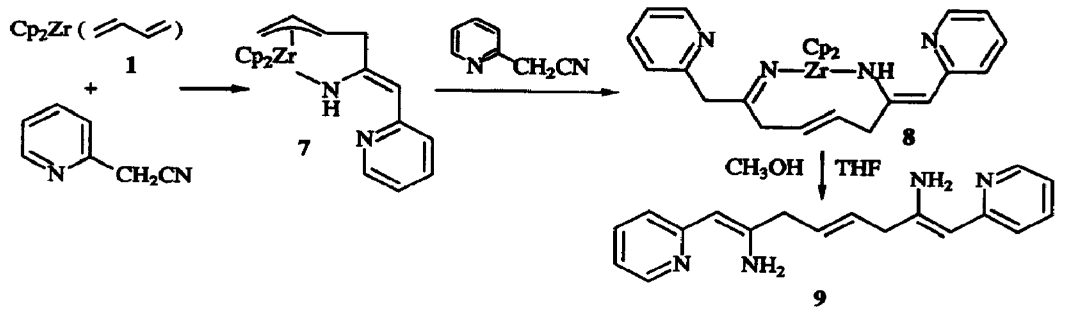
Figure 1. SCHAKAL plot of the molecular structure of 4.



Straightforward hydrolysis of complex 4 with 2N sulfuric acid yields 1,8-diphenyl-2,7-dioxo-trans-4-octene (5). However, the nitrogen was retained when the demetallation of 4 was carried out by treatment with a small quantity of methanol. The stable conjugated primary enamine (2Z,4E,6Z)-2,7-diamino-1,8-diphenyl-2,4,6-octatriene (6) was obtained and isolated in >70% yield [$-NH_2$: ^1H NMR: $\delta = 2.78$; IR: $\tilde{\nu} = 3457, 3374$ cm^{-1}; UV: $\lambda_{max} = 330$ nm ($\varepsilon = 5200$)].[7]



The reaction of (butadiene)$ZrCp_2$ with 2-(cyanomethyl)pyridine in a 1:1 molar ratio gave a single metallacyclic (π-allyl)zirconium enamido isomer to which we ascribe the structure 7 from its spectroscopic data. Subsequent coupling with a second nitrile equivalent leads to a metallacyclic nine-membered ring product 8 which has the enamido zirconocene moiety of the intermediate 7 retained. Complex 8 was prepared on a preparative scale and isolated in >70% yield from the reaction between (butadiene)zirconocene and 2-(cyanomethyl)pyridine in a 1:2 ratio.



The reaction of 8 with methanol in tetrahydrofuran again produced a stable primary enamine in high yield (9, >70% isolated) as the only reaction product. However, in this case, this does not contain the 2,7-diamino-2,4,6-octatriene moiety as in 6. Here the strongly electron withdrawing 2-pyridyl substituent dominates the enamine stabilization and directs the system into the formation of two stable pyridyl-substituted enamines that are isolated from each other by the connecting $CH_2CHCHCH_2$ chain, as found in the obtained product 2,7-diamino-1,8-di(2-pyridyl)-1,4,7-octatriene (9).

These examples nicely show that the diaminohexatriene system does not need any kinetic stabilization by bulky substituents at its ends to be stable and easily isolated. The rather small energetic contribution of the butadiene conjugation[8] is indeed sufficient to make the primary enamine system more favourable than any of its imine tautomers.[9] Nevertheless, the thermodynamic stabilization by conjugation is apparently smaller than the stabilizing substituent effects that carbonyls or analogous groups exert in the β-position of an enamine. From the direct competition it is evident that the polyene conjugation effect is inferior to the 2-pyridyl substituent effect for enamine stabilization and consequently, the non-conjugated bis-enamine is obtained when 2-(cyanomethyl)pyridine is used in our template synthesis whereas the substituted 1,6-diaminohexatriene is the stable conjugated primary enamine product of the analogous reaction sequence starting from benzyl cyanide.

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7. Experimental: (a) *2,7-Diamino-1,8-diphenyl-2,4,6-octatriene* (**6**): A solution of benzylnitrile (0.46 ml, 4.00 mmol) in 10 ml of toluene was added during 3 h to a solution of 551 mg (2.00 mmol) of (butadiene)zirconocene at ambient temperature. After 16 h of stirring the mixture is filtered and the filtrate evaporated in vacuo to give 970 mg (95%) of **4**. Crystals of **4** were obtained from toluene at -30°C. Anal. Calcd. for $C_{30}H_{30}N_2Zr$ (509.8) C 70.68, H 5.93, N 5.49. Found C 69.78, H 6.02, N 5.50. X-ray crystal structure analysis: monoclinic space group $P2_1/n$, a = 8.139(1) Å, b = 33.916(3) Å, c = 9.950(1) Å, β = 112.22(1)°, V = 2542.9 Å^3, Z = 4, 11023 reflections collected, $\pm h$, $\pm k$, $+l$, 5219 independent reflections, 4563 observed reflections, 296 refined parameters, R = 0.047, R_w = 0.044. Details of the X-ray crystal structure determination can be obtained from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen, on quoting the depository number CSD 58335, the names of the authors, and the journal citation. 1.30 g (2.55 mmol) of **4** was dissolved in 20 ml of tetrahydrofuran; 0.5 ml of methanol was added and the mixture filtered through alumina (act. 1) after 1 h. Solvent was removed in vacuo to yield 544 mg of **6** (73%), m. p. 104°C (decomp., DSC). ^{1}H NMR ([D$_6$]benzene): δ 2.78 (br. s, 4H, NH_2), 3.19 (s, 4H, C*H*$_2$Ph), 5.12 (m, 2H, 3-H, 6-H), 6.04 (m, 2H, 4-H, 5-H), 7.05–7.14 (m, 10H, Ph), coupling constants (Hz): ^3J = 14.5 (4-H, 5-H), 11.3 (3-H, 4-H). Anal. Calcd. for $C_{20}H_{22}N_2$ (290.4) C 82.72, H 7.64, N 9.65. Found C 82.70, H 7.29, N 9.32.

   (b) *2,7-Diamino-1,8-di(2-pyridyl)-1,4,7-octatriene* (**9**): (2-Pyridyl)acetonitrile (1.50 ml, 13.7 mmol) in 10 ml of toluene was added dropwise to a solution of 1.88 g (6.82 mmol) of (butadiene)zirconocene in 30 ml of toluene. After 16 h a precipitate is filtered off and the solution concentrated in vacuo to a volume of 10 ml. The product **8** is collected by filtration and washed with pentane, yield 2.54 g (73%), m. p. 114°C (decomp., DSC). IR (KBr): $\tilde{\nu}$ 3463 cm^{-1} (NH). ^{1}H NMR ([D$_6$]benzene): δ 2.65 (br. m, 2H, CH_2), 3.20 (d, 2H, CH_2), 3.42 (s, 2H, CH_2-Pyr), 5.15 (m, 2H, CH=CH), 5.25 (s, 1H, =CHPyr), 5.80 (s, 10H, Cp), 6.71, 7.08, 8.43 (m, 8H, Pyr), 10.04 (br. s, 1H, NH). Anal. Calcd. for $C_{28}H_{28}N_4Zr$ (511.8) C 65.71, H 5.51, N 10.95. Found C 64.60, H 5.58, N 10.63. 613 mg (1.20 mmol) of **8** was dissolved in 20 ml of tetrahydrofuran. Methanol (0.3 ml) was added and the mixture filtered over alumina (act. 1) after 1.5 h. Solvent was removed in vacuo and the residue washed with pentane to yield 251 mg (72%) of **9**, m. p. 85°C (DSC). IR (KBr): $\tilde{\nu}$ 3457, 3250 cm^{-1} (NH_2). ^{1}H NMR ([D$_6$]benzene): δ 2.81 (m, 4H, CH_2), 4.88 (s, 2H, C*H*=C(NH_2)), 5.58 (m, 2H, CH=CH), 6.34 (br. s, 4H, NH_2), 6.67, 7.28, 8.23 (m, 8H, Pyr). Anal. Calcd. for $C_{18}H_{20}N_4$ (292.4) C 73.94, H 6.89, N 19.16. Found C 72.85, H 6.51, N 18.17.
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