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Solubilized zirconocene dihydride as a promotor of alkene coupling reactions

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Abstract

The THF-soluble bis(methoxyethyl)zirconocene dihydride **3** displayed novel reactivity patterns and was used to reductively couple alkenes, dienes, and enynes. A plausible mechanism involves the formation of a 14-electron zirconium(II) and zirconacyclopentane species. © 2000 Published by Elsevier Science Ltd.

Keywords: zirconocene dihydride; zirconium(II); reductive cyclization; intra- and intermolecular coupling.

The reductive coupling of two unsaturated substrates can be mediated by low-valent metals from the two extremes of the transition series (Ni, Ti, Zr).[1] The intermediate metallacycle can be transformed into a variety of useful products.[2] The reductive coupling of alkenes mediated by a zirconocene(II) equivalent provides fairly stable zirconacycles, which react with protons, halogens,[3] isocyanides,[4] oxygen,[5] carbon monoxide,[6] ketones[7] and other electrophiles[8] to afford mono- and bicyclic organic compounds with high regio- and stereoselectivities.[9] Ligands and ligand substituents strongly effect the reactivity of zirconocene complexes. The modification of the cyclopentadiene ring of polymeric and insoluble zirconocene dihydride changes its solubility and promotes new reaction pathways. While Cp_2ZrH_2 is essentially unreactive toward alkenes and alkynes, the reaction of $(\eta^5\text{-}C_5Me_5)ZrH_2$ with propyne to form monocyclic zirconacyclopentenes was reported in 1985.[10] In this paper, we report the reaction of alkenes with zirconocenes containing alkyl ether attachments to the Cp ring that increase solubility and reactivity of the early transition metal complex and promote a reaction manifold reminiscent of zirconocene(II) chemistry.

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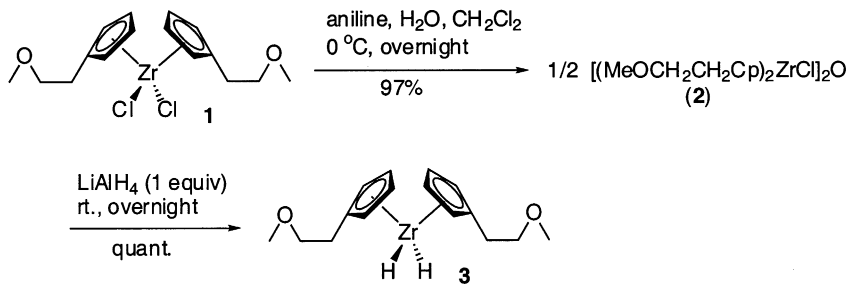
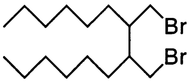
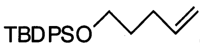
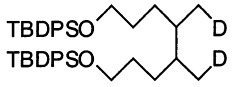
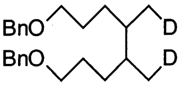
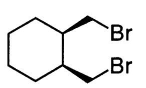
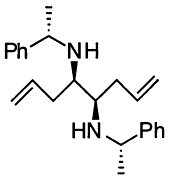
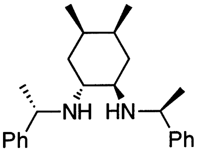
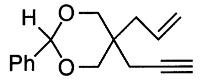
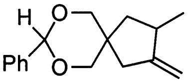
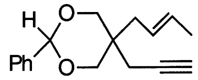
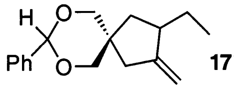
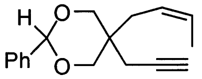
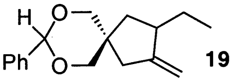


Scheme 1. Preparation of bis(methoxyethyl)zirconocene dihydride **3**

After reaction of the known zirconocene dichloride **1**[11] with aniline and water, the resulting oxo-bridged compound **2** was reduced with 1 equiv. of $LiAlH_4$ to give the zirconocene dihydride complex **3** (Scheme 1).[12] As expected, the ^1H NMR of **3** showed two resonances for the hydride protons at 4.07 and −2.86 ppm. Treatment of terminal alkenes, dienes, and enynes with **3** in THF led to the formation of acyclic and cyclic coupling products in moderate to high yields after quenching with Br_2, D_2O or H_2O (Table 1). For 1-octene, different solvents such as toluene, 1,2-dichloroethane, 1,4-dioxane, *N*-methylmorpholine, and 10% oxetane/THF were tested, but THF was found to be superior. In the conversion of 1,7-octadiene, additives such as PPh_3, $AsPh_3$, and $P(OPh)_3$ also failed to improve cyclization yields. Only products derived from coupling at the internal alkene positions could be observed for substrates **4**, **6**, and **8** (entries 1–3). *cis*-Cyclohexane **11** was formed exclusively in the coupling of α,ω-diene **10** after quenching with Br_2 (entry 4). Homoallylic diamine **12** provide the tetrasubstituted cyclohexyl diamine **13** as a single stereoisomer (entry 5), in contrast to a recent literature protocol for the formation of this compound.[13] Interestingly, *trans*-alkene **16** showed a higher diastereoselectivity in the coupling reaction than the corresponding *cis*-alkene **18** (6:1 vs 1.7:1), but the yield was considerably higher for the *cis*-substrate (entries 7 and 8). The reason for the differential stereoselectivity is not yet clear, but it is possible that the slower reacting **16** experiences more severe steric interactions in the transition state of the process. In general, intramolecular coupling reactions, which were carried out under moderate dilution conditions, required longer reaction times, and in the case of enynes, slight heating was necessary to effect reasonable turnover. Yields are based on reactants, and since one full equivalent of alkene is used for zirconocene generation (vide infra), they are based on a maximum conversion of 50%.[14] Significant amounts of reduced compounds were indeed isolated from all reaction mixtures.

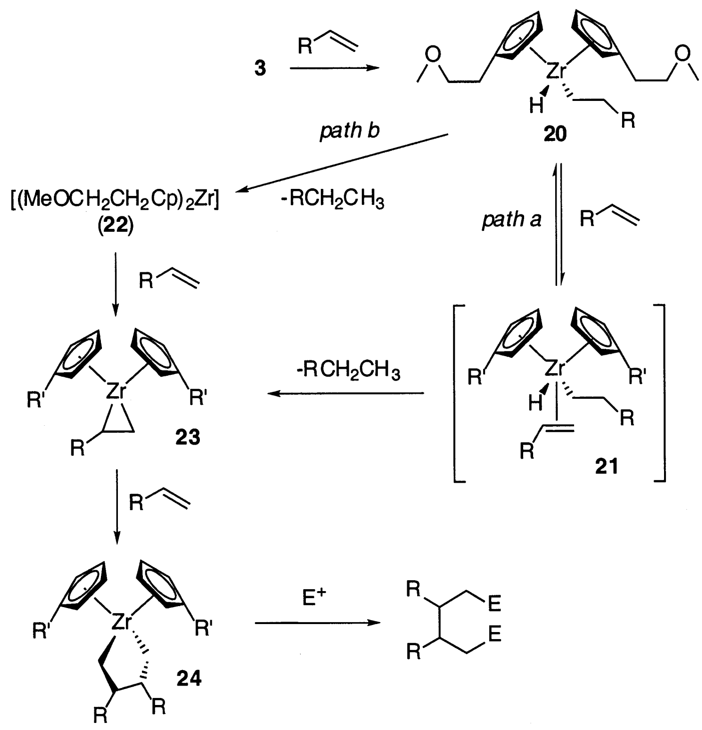
A possible mechanism for these novel coupling reactions is shown in Scheme 2. Based in part on analogies to Bercaw's studies,[16] we propose that the THF-soluble zirconocene dihydride **3** adds to alkene to produce the alkyl hydride complex **20** via hydrozirconation.[17] Subsequently, this complex reacts with another alkene to give the transient complex **21**. Reductive elimination of RCH_2CH_3 from **21** produces zirconacyclopropane **23**, which ring expands to zirconacyclopentane **24** in the presence of another olefin. Metallacycle **23** could also be formed via zirconocene **22** by reductive elimination of RCH_2CH_3 from **20**, followed by insertion into an alkene. Zirconacyclopentane **24** is quenched with suitable electrophiles to give the final isolated products. Both pathways are possible according to our experimental results.

Table 1
Coupling of unsaturated substrates with dihydride 3[15]

entry	reactant	product[a]	t [h]	T [°C]	yield [%][e]
1	 **4**	 **5**	4	r.t.	82%
2	 **6**	 **7**	8	r.t.	36%
3	 **8**	 **9**	8	r.t	30%
4	 **10**	 **11**	5	r.t.	33%
5	 **12**	 **13**	20	r.t.	42%
6	 **14**	 **15**	26	45-50	82%[b]
7	 **16**[c]	 **17**[d]	24	45-50	28%[b]
8	 **18**[c]	 **19**[d]	24	45-50	78%[b]

[a] In a typical protocol, reactants (0.6 mmol for entries 1-3, 0.3 mmol for entries 4-8) were added to a solution of **3** (0.3 mmol) in THF (1.5 mL for entries 1-3, 3 mL for entries 4-8). After stirring at r.t. or slightly elevated temperatures for 5-24 h, the reaction mixture was quenched with Br_2 at 0 °C (entries 1 and 4), D_2O at room temperature (entries 2 and 3), or H_2O at room temperature (entries 5-8). [b] Yield was determined by GC-MS analysis. [c] Ratio of *cis*:*trans*-isomers (determined by ^{13}C NMR integration): for **16**, 1:9; for **18**, 4.6:1. [d] Ratio of diastereomers (determined by ^{13}C NMR integration): for **17**, 6:1; for **19**, 1.7:1. [e] Based on a maximum of 50% conversion of reactants.

Treatment of Cp_2ZrCl_2 with two equivalents of ^{n}BuLi generates a 'Cp_2Zr' equivalent that is particularly useful for cyclization of enynes and α,ω-dienes.[9] However, substrates containing terminal alkynes cannot be used in this protocol, presumably due to the ready oxidative addition of the electron-rich metallocene into the acidic acetylenic carbon–hydrogen bond.[18] Barluenga et al. used a β-hydrogen activation process, followed by insertion of unactivated unsaturated molecules for the intramolecular coupling of terminal alkynes.[19] In the latter method, two equivalents of ^{t}BuLi were used to remove the acidic acetylene hydrogen before the coupling reaction. However, in our protocal, terminal α,ω-enynes can be used directly to give cyclic products. Disubstituted alkenes lead to a moderate level of diasteroselectivity even with remote



Scheme 2. Proposed mechanism for the activation of **3** and reductive coupling reactions

1,6-stereoinduction, whereas excellent stereocontrol can be achieved with homoallylic substitution. Intermolecular reductive alkene–alkene couplings proceed in an analogous fashion. In conclusion, the introduction of ether side chains on the Cp ligands of zirconocene dihydride **3** led to a THF-soluble early transition metal complex that displayed a novel reactivity pattern.[20] Monoenes, dienes, and enynes with terminal alkynes and internal alkenes can be reductively coupled with **3** in moderate to good yields. A plausible mechanism involves the formation of a 14-electron zirconium(II) species and zirconacyclopentane **24** that is trapped by electrophiles to give functionalized derivatives.

Acknowledgements

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12. Wailes, P. C.; Weigold, H. *J. Organomet. Chem.* **1970**, *24*, 405. **Bis(1-(2-methoxy-ethyl)-cyclopentadienyl)zirconium dihydride** (**3**). To a solution of **2** (1.14 g, 1.50 mmol) in THF (10 mL) was added dropwise at room temperature a solution of $LiAlH_4$ (1.0 M in Et_2O, 1.50 mL, 1.50 mmol). The resulting mixture was stirred overnight. After removing solvents in vacuo, dry toluene (20 mL) was added. The filtrate was dried in vacuo to yield **3** as a pink solid (1.05 g, quant.): IR (mineral oil) 3063, 1579, 1216, 1186, 1165 cm^{-1}; ^1H NMR (C_6D_6) δ 6.10–5.33 (m, 8H), 4.07 (bs, 1H), 3.52–3.38 (m, 4H), 3.15 (s, 6H), 2.87–2.80 (m, 4H), −2.86 (bs, 1H); ^{13}C NMR (C_6D_6) δ 122.1, 104.6, 102.8, 99.2, 74.3, 58.1, 31.6.
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15. All new compounds were fully characterized by ^1H NMR, ^{13}C NMR, HRMS and IR. **7,8-Bis-bromomethyl-tetradecane** (**5**). To a solution of **3** (170 mg, 0.500 mmol) in THF (2.5 mL) was added dropwise at room temperature 1-octene (112 mg, 157 μL, 1.00 mmol). After stirring for 4 h, the reaction mixture was cooled to 0°C and Br_2 (80 μL, 1.60 mmol) was added. The resulting mixture was stirred at 0°C for a further hour, diluted with Et_2O and H_2O, and extracted with Et_2O. The combined organic layers were washed with $Na_2S_2O_3$ (10% aqueous solution) and brine, dried ($MgSO_4$), and concentrated. The residue was purified by chromatography on SiO_2 (hexanes) to yield colorless oily **5** (79.4 mg, 82%): IR (neat) 2956, 2926, 1465, 1378, 1259, 1235, 1153 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.61–3.48 (m, 4H), 1.79–1.77 (m, 2H), 1.46–1.30 (m, 20H), 0.90 (t, 6H, $J=6.5$ Hz); ^{13}C NMR ($CDCl_3$) δ 41.0, 37.0, 31.8, 29.4, 29.1, 27.4, 22.7, 14.2; HRMS (EI) m/e calculated for $C_{16}H_{32}{}^{79}Br_2$: 382.0871, found: 382.0858.
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