Carbometalation of α,ω-Dienes and Olefins Catalyzed by Zirconocenes

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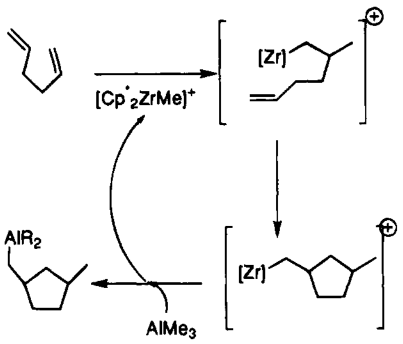
Ziegler–Natta catalysts rival enzymes in activity and stereospecificity for the formation of carbon–carbon bonds. The advent of stereoselective homogeneous Ziegler–Natta catalysts has stimulated renewed interest in exploiting these remarkable systems for fine chemical synthesis.[1-5] The key carbon–carbon bond-forming step in olefin polymerization is the carbometalation of an olefin with a transition metal alkyl. While catalytic carbometalation of alkynes has proven a useful synthetic method,[6,7] the development of efficient carbometalation reactions of olefins has proven more challenging.[8-13] In this contribution, we report the efficient carbometalation of olefins and cyclocarbometalation of diolefins with trimethylaluminum in the presence of cationic metallocene catalysts.

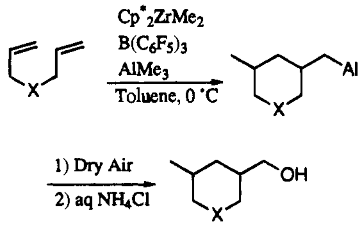
Cyclization of dienes, enynes, and diynes catalyzed by organometallic species is an important entry into useful carbo- and heterocyclic structures.[14] Our interest in the cyclopolymerization of α,ω-dienes with group 4 metallocene catalysts[15] led us to explore these systems for the synthesis of monocyclic products through use of $\mathrm{AlMe_3}$ as a chain transfer agent.[16] Heterogeneous Ziegler–Natta type systems have long been used for the cyclopolymerization of α,ω-dienes,[17] but attempts to synthesize monocyclic products did not appear until recently.[13,18,19] Stoichiometric systems using intramolecular insertion of ω-alkenyltitanium species[20,21] first showed the feasibility of this type of reaction and its potential for high diastereoselectivity. Catalytic cyclization of dienes to cycloalkanes has been reported by Bercaw using an organoscandium catalyst,[18] Molander using an organoyttrium catalyst,[19] and Negishi using a titanium alkoxide catalyst.[13]

Scheme 1



Catalytic cycloalkylation of 1,5-hexadiene was carried out in the presence of $\mathrm{Cp^*_2ZrMe_2}$[22] /$\mathrm{B(C_6F_5)_3/AlMe_3}$ (Scheme 1).[23] Under the optimal conditions (0 °C, 5 mol % Zr, 2 equiv of $\mathrm{AlMe_3}$), 1,5-hexadiene was completely consumed, and 1,3-dimethylcyclopentane was produced in 74% yield, upon hydrolysis, in <2 h.[24,25] The reaction temperature proved to be a critical parameter in optimizing the selectivity for monocyclic products: the selectivity for cyclization was lower at both 25 and −15 °C.

A variety of 1,5-, 1,6-, and 1,7-dienes were cyclized and oxidized with dry air to give alcohols in good yields (eq 1, Table 1). Yields for the oxidation step were typically 85–90% as judged by GC. Attempts to cyclize 1,8-nonadiene, 1,9-decadiene, or 1,4-pentadiene gave only oligomeric products which could not be fully characterized. Alcohols protected by the TBS group can be cyclized at a rate similar to that for the unsubstituted diene (Table 1, entry 5), while the TMS-protected analog gave slow conversion to uncharacterizable oligomeric products.[26] An entry into the piperidine ring structure was provided by cyclization of phenyldiallylamine, but reaction times were on the order of days rather than hours (Table 1, entry 4).



(1)

The diastereoselectivities for the cyclocarbometalation are moderate to high (60–100%). Cyclization of the unsubstituted 1,5-, 1,6-, and 1,7-dienes affords the 5-, 6-, and 7-membered *cis*-carbocycles with diastereoselectivities of 70, 60, and 65%, respectively (Table 1, entries 1a–c).[27] These results are similar to those observed in the cyclopolymerization of these substrates with similar catalysts.[28,29] The 2-methyl- and 2-ethyl-1,5-

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(22) Cp* = 1,2,3,4,5-pentamethylcyclopentadienyl.

(23) Attempted cyclization of 1,5-hexadiene in the presence of triethylaluminum or triisobutylaluminum was unsuccessful.

(24) Changing the Al/olefin ratio from 1 to 3 did not appear to affect the yield or rate of the reaction.

(25) General procedure: in a drybox, $\mathrm{Cp^*_2ZrMe_2}$ (0.13 mmol) and $\mathrm{B(C_6F_5)_3}$ (0.13 mmol) were dissolved in 5 mL of toluene, and trimethylaluminum (5.2 mmol) added. The olefin (2.6 mmol) was dissolved in 25 mL of toluene and added slowly over 2 h to a cooled (0 °C) catalyst solution. Upon consumption of olefin, dry air was bubbled through the reaction mixture for 1 h. Workup gave crude alcohols which were purified by column chromatography.

(26) TBS = *tert*-Butyldimethylsilyl; TMS = trimethylsilyl.

(27) The cycloalkane diastereomers were assigned by GC by comparison to authentic samples (Wiley).

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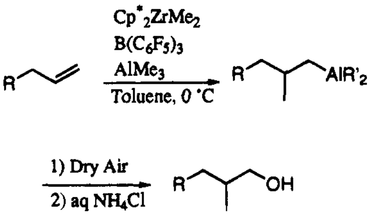
hexadienes yielded single isomers which have been tentatively assigned as the *trans* isomers.[30] For the heptadiene derivatives, substitution of the central CH_2 for a heteroatom (N or Si) appears to improve the diastereoselectivity in the formation of the 6-membered ring (entries 3, 4, Table 1). Cyclization of the protected 1,6-heptadien-4-ol **9** yielded a 46:43:11 ratio of **10a/b/c**.[31] This mixture of diastereomers apparently results from a nonstereoselective initial insertion (see **15**, below), followed by a diastereoselective cyclization step.[32]

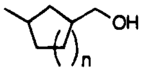
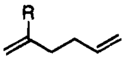
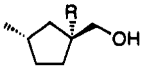
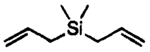
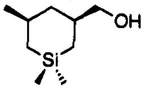
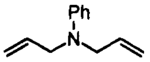
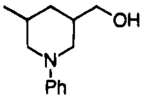
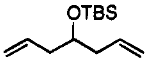
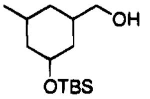
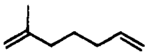
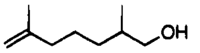
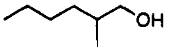
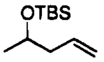
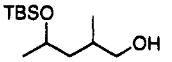
This catalyst system is also capable of the direct carbometalation of unactivated alkenes (eq 2, Table 1, entries 6–8). We



(2)

are aware of only two other systems which will catalyze the carbometalation of olefins with organoalanes or organomagnesium reagents.[8–12] Attempts to cyclize 2-methyl-1,6-heptadiene yielded the linear product **12** resulting from simple carbometalation of the unhindered olefin. In contrast, cyclization of the hexadiene analog **3a** gave only the cyclic product. Presumably, transmetalation to $AlMe_3$ is faster than cyclization for the substituted heptadiene derivative. Carbometalation of 1-hexene (**13**) and homoallylic silyl ether (**15**) proceeded in yields of 75 and 82%, respectively. The carbometalation of **15** was essentially nonstereoselective, affording a 55:45 mixture of diastereomers.

Table 1. Carbometalation of Olefins and Dienes in the Presence of Cationic Zirconocenes

entry	olefin	time (h)	product	(%) Yield[a]	diastero-selectivity[b]
1					
	1a, $n = 1$	2	**2a**, $n = 1$	70	70% *cis*
	1b, $n = 2$	3	**2b**, $n = 2$	60	60% *cis*
	1c, $n = 3$	3	**2c**, $n = 3$	67	65% *cis*
2					
	3a, R = Me	2	**4a**, R = Me	88	100% *trans*
	3b, R = Et	2	**4b**, R = Et	70	100% *trans*
3					
	5	3	**6**	61	100% *cis*
4					
	7	48	**8**	51	70% *cis*
5					
	9	3	**10a–c**	65	46:43:11 **10a/b/c**[c]
6					
	11	2	**12**	71	
7					
	13	2	**14**	75	
8					
	15	4	**16**	82	55:45 dr

[a] Yields are for isolated products. All compounds are fully characterized (^1H NMR, ^{13}C NMR, FTIR, HRMS, elemental analysis). [b] Diastereoselectivity ratios (dr) determined by GC of hydrolized reaction mixture or by ^1H NMR. Major diastereomers were determined as described in text. [c] See ref 29 for isomer designations.

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Supplementary Material Available: Experimental procedures and product characterization (6 pages). This material is contained in many librairies on microfiche, immediately follows this in article in the microfiche version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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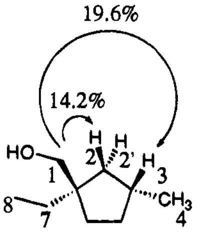
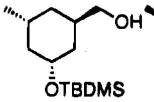
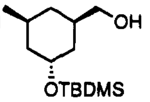
(30) The structure of **4b** was determined using NOE difference NMR. Upon irradiation of proton 1, protons 2 and 3 exhibited enhancements of 14.2 and 19.6%, respectively. No enhancement was observed between proton 1 and protons 2' or 4. **4a** was assumed similarly to be the *trans* isomer.



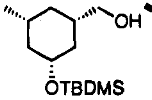
(31) The possible structures are



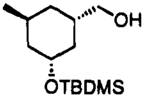
10a



10b



10c



10d

(32) The structures of **10a–c** were assigned as follows. The hydrolysis product from the cyclization of **9** was compared to the three diastereomers of an authentic sample of 1-TBSO-3,5-dimethylcyclohexane. The diastereomers of the model compound were assigned on the basis of the CH-OTBS proton. **9** gave products corresponding to **10a** or **10d** (enantiomers) and **10b**. A third minor isomer observed only in the GC was assigned to the product corresponding to **10c**. **10a** was determined to be the major isomer by assuming that the initial insertion is stereorandom, as seen with **15**. The second insertion is stereoregular, resulting in the CH_2OH being *trans* in both the major products (**10a** and **10b**).