Ersch. in: Inorganica Chimica Acta ; 280 (1998), 1-2. - S. 189-192

http://dx.doi.org/10.1016/S0020-1693(98)00065-6

Cyclomagnesation of dienes catalyzed by a chiral ansa-zirconocene [1]

Sandra Martín [2], Hans-Herbert Brintzinger *

Fakultät für Chemie, Universität Konstanz, D-78457 Konstanz, Germany

Dedicated to the memory of Professor Mark E. Vol'pin

Abstract

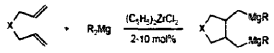
The biphenyl-bridged, chiral zirconocene complex rac-2,2′-biphenyl-bis(3,4-dimethylcyclopentadienyl)zirconium dichloride catalyzes the reaction of 1,6- and 1,7-dienes with excess dibutyl magnesium to bis(butyl-magnesio-methyl)-substituted cycloalkane derivatives. Analogous reactions occur with butyl magnesium chloride and with heteroatom-containing dienes. The preference of 1,6-dienes for *trans*-fused cyclization products and that of 1,7-dienes for *cis*-fusion at ambient and for *trans*-fusion at elevated temperatures is similar to that observed before for unsubstituted zirconocene complexes. The *R*-enantiomer of the biphenyl-bridged zirconocene complex gives *trans*-fused cyclization products with an optical purity of only 15 ± 1% ee. The stereochemistry of these cyclomagnesation reactions is explained in terms of the relative rates of mutually competing cyclization and transmetalation steps.

Keywords: Ansa-zirconocene; Catalysis; Diene cyclomagnesation

1. Introduction

Since the discovery by Vol'pin and coworkers that metallacyclic compounds are formed from low-valent group IV metallocenes with unsaturated substrate molecules [1], the formation of metallacyclic intermediates by reductive coupling reactions has become an effective tool for the construction of carbo- and heterocyclic ring structures [2–6]. Early studies concerned primarily the stoichiometric cyclization of enynes and dienes [7–15]. Molecular mechanics and density functional methods were used by Taber and coworkers [16] to predict the relative stabilities of alternative zirconacyclic products and to rationalize the stereoselectivity of the cyclization step.

More recently, zirconocene dichloride was found to catalyze the cyclization of non-conjugated dienes in the presence of dialkyl magnesium, i.e. their conversion to cycloalkanes with two alkyl-magnesium-methyl substituents (Eq. (1)) [17–19]. On the basis of the corresponding stoichiometric reactions [11–16], a mechanism for this catalytic cycle was proposed, which involves the formation of zirconacyclic intermediates and their transmetalation with excess alkyl magnesium reagent [20].



(1)

Depending on the diene and alkyl magnesium reagents and on the reaction conditions, these cyclizations occur with different stereochemistry: the $(C_5H_5)_2ZrCl_2$-catalyzed cyclomagnesation of 1,6-heptadiene with dibutyl magnesium gave predominantly the *trans*-fused diastereomer [19,20], while 1,7-octadiene was cyclized either to the *cis* or the *trans* product, depending on the reaction conditions. These observations were explained by Waymouth and coworkers on the basis of kinetic and thermodynamic preferences arising from different rates of the zirconacycle formation and transmetalation steps [20]. The relative rates of transmetalation for alternative intermediates were also considered to be crucial for the enantioselectivity of asymmetric cyclomagnesations with the chiral ethylene-bridged bis(tetrahydroindenyl)zirconium complex en(thind)$_2$ZrCl$_2$ [21].

We have tried to obtain further clues to the factors which control the diastereoselectivity and enantioselectivity in zirconium-catalyzed cyclomagnesations of non-conjugated dienes by investigating the reactions of 1,6- and 1,7-dienes with n-Bu$_2$Mg or n-BuMgCl in the presence of catalytic

* Corresponding author. Tel.: +49-7531-882 629; fax: +49-7531-883 137.

[1] ansa-Metallocene derivatives part XLII. For part XLI see: H.R.H. Damrau, M.H. Prosenc, U. Rief, F. Schaper, H.H. Brintzinger, J. Organomet. Chem., in press.

[2] Present address: Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Ciudad Universitaria CC 61, SUC. 16, 5016 Córdoba, Argentina.

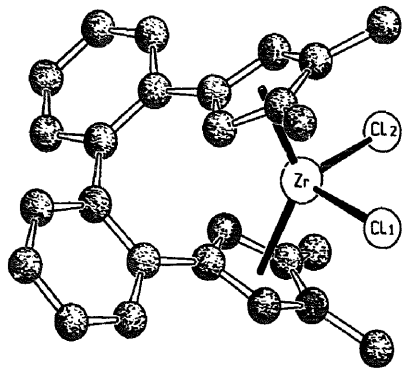


Fig. 1. Structure of 2,2'-biphenyl-bis(3,4-dimethylcyclopentadienyl)zirconium dichloride (**1**), as determined by X-ray diffraction [22]; the *R*-enantiomer is represented; hydrogen atoms are omitted for clarity.

amounts of the chiral biphenyl-bridged zirconocene biph($C_5H_2Me_2$)$ZrCl_2$ (**1**) [22], the geometry of which is less affected by conformational fluctuations than that of ethylene-bridged zirconocene derivatives [23,24] and hence more suited for stereochemical model considerations (Fig. 1).

2. Experimental

All work involving air- or moisture-sensitive compounds was carried out under an atmosphere of Ar or N_2, using standard Schlenk or glovebox techniques. NMR spectra were recorded on Bruker AC 250 MHz, WM 250 MHz or DRX 600 MHz spectrometers. Chemical shifts are reported in ppm with the solvent as the internal standard. Gas chromatographic (GC) analyses were performed on a Perkin-Elmer 8320 GC with a FID detector using a Machery and Nagel SE capillary column (25 m, 0.25 mm ID) and a 25 m capillary column with heptakis(6-*O*-methyl-2,3-di-*O*-pentyl)-β-cyclodextrin as a stationary phase for enantiomer analyses. Under N_2 atmosphere, diethyl ether was distilled from Na metal/benzophenone, toluene from Na metal. 1,7-Octadiene, 1,6-heptadiene and diallyl-dimethylsilan were purchased from Adrich; 9,9-diallylfluorene [20], 4-tert-butyldimethylsiloxy-1,6-heptadiene [25] and *N*-tert-butyldiallylamine [26] were prepared as described in the literature.

2.1. Zirconium-catalyzed cyclomagnesation (representative procedure)

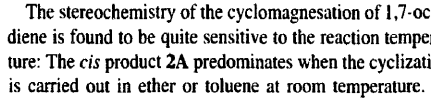
In a glovebox, 60 mg (0.12 mmol) of complex **1** [22], placed in a 50 ml Schlenk tube, was suspended in 13 ml diethyl ether. After addition of 2.25 ml (3 equiv., 4.5 mmol) of a 2 M solution of n-BuMgCl in ether, the reaction mixture was stirred for 5 min. Then 0.58 ml (1.50 mmol) of 1,7-octadiene was added. The solution was stirred for 48 h, and then quenched with a saturated aqueous solution of NH_4Cl. The organic layer was separated and the water layer washed three times with 20 ml portions of ether. The combined organic layers were washed with saturated solutions of $NaHCO_3$ and NaCl and dried over anhydrous $MgSO_4$. Yields and isomer ratios were determined by gas chromatography (GC), using toluene as internal standard. The identity of each product was confirmed by GC co-injection with an authentic sample and by the following ^{13}C NMR data (all in $CDCl_3$). *cis*-1,2-Dimethylcyclohexane (**2A**) [27], δ 15.95, 23.58, 31.32, 34.24; *trans*-1,2-dimethylcyclohexane (**2B**) [27], δ 20.37, 26.93, 35.89, 39.38; *trans*-1,2-dimethylcyclopentane (**3B**) [28], δ 18.89, 23.40, 35.03, 42.67; *trans*-1,2-dimethyl-3-*O*-TBDMS-cyclopentane (**4B**) [19], δ 18.10, 20.56, 22.38, 26.35, 35.48, 66.82; *N*-tert-butyl-*trans*-3,4-dimethylpyrrolidine (**5B**) (cf. Ref. [29]), δ 19.06, 20.56, 42.12, 59.42, 62.45; 1,1-dimethyl-*trans*-3,4-dimethyl-1-silacyclopentane (**6B**) [30], δ −1.11, −3.52, 21.89, 18.58; spiro[(*trans*-3,4-dimethylcyclopentane)-1,9'-fluorene] (**7B**) [20], δ 17.87, 43.82, 49.26, 55.18, 119.62, 122.76, 126.64, 127.5, 138.89, 156.01.

2.2. Asymmetric cyclizations

The *R*-enantiomer of **1** was obtained by an asymmetric transformation procedure [31]; an optical purity of >95% ee was determined by ^1H NMR analysis of its (*S*)-1-phenyl-1-propanol derivative. With this catalyst, cyclomagnesations of 1,6-heptadiene and 1,7-octadiene were conducted and the products collected as described above. The enantiomeric excess of the *trans* isomer was determined by GC with the capillary cyclodextrin column mentioned above.

3. Results and discussion

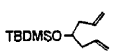
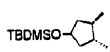
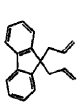
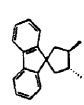
Treatment of 1,7-octadiene with n-Bu_2Mg (1.5 equiv.) or with n-BuMgCl (3 equiv.) in the presence of complex **1** (8 mol.%) in ether at room temperature yields, after hydrolysis, mostly *cis*-1,2-dimethylcyclohexane (**2A**), together with 10–20% of the *trans* isomer **2B** (Eq. (2), Table 1). Deuterolysis of the cyclization products with DCl/D_2O affords 1,2-bis(deuteriomethyl)cyclohexane in 92% yield. This documents the complete formation of dimagnesated reaction products, i.e. of useful synthons for a wide range of further functionalization reactions.



(2)

The stereochemistry of the cyclomagnesation of 1,7-octadiene is found to be quite sensitive to the reaction temperature: The *cis* product **2A** predominates when the cyclization is carried out in ether or toluene at room temperature. At 100°C in toluene, however, the *trans* diastereomer **2B** is the dominant product. Cyclization of 1,6-heptadienes, on the

Table 1
Zirconium-catalyzed cyclomagnesation of 1,6- and 1,7-dienes [a]

Substrate	Alkyl-magnesium	Solvent	Temperature (°C)	Product [b]		Yield (%)	*Cis:trans* ratio [c]
	n-BuMgCl	Et_2O	25		**2A**	94	90:10
	n-Bu_2Mg	Et_2O	25		**2A**	89	80:20
	n-BuMgCl	toluene	100		**2B**	91	9:91
	n-BuMgCl	Et_2O	25		**3B**	91	9:91
	n-Bu_2Mg	Et_2O	25		**3B**	85	12:88
	n-BuMgCl	Et_2O	25		**4B**	80	20:80
	n-BuMgCl	Et_2O	25		**5B**	85	30:70
	n-BuMgCl	Et_2O	25		**6B**	86	14:86
	n-BuMgCl	Et_2O	25		**7B**	87	8:92

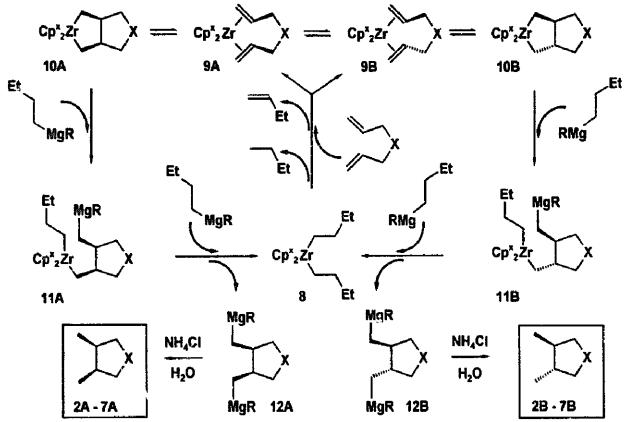
[a] Reactions with 8 mol.% of **1** and 1.5 equiv. n-Bu_2Mg or 3 equiv. n-BuMgCl.
[b] Workup with NH_4Cl/H_2O.
[c] By GC.

other hand, yields predominantly the *trans* products **3B–7B** even at room temperature. The stereochemistry of all of these reactions is similar to that observed before for reactions catalyzed by unsubstituted $(C_5H_5)_2ZrCl_2$ [17–20]. Like other zirconocene complexes, complex **1** is also able to cyclomagnesate heptadiene substrates containing different heteroatoms, as shown in entries 6–8 of Table 1.

We have further tested the enantioselectivity of the reaction of 1,6-heptadiene with n-BuMgCl in the presence of 8 mol.% of enantiopure (*R*)-**1** [31] in ether. After hydrolysis, a 91% yield of *trans*-1,2-dimethylcyclopentane was obtained with an optical purity of only 14% ee. The cyclization of 1,7-octadiene with n-BuMgCl and with (*R*)-**1** as a catalyst in toluene at 100°C, followed by hydrolysis, afforded a 91% yield of *trans*-1,2-dimethylcyclohexane with a similarly low ee of 16%.

Our experimental results can be incorporated into the mechanistic analysis proposed by Waymouth and coworkers [20], which involves the formation of dibutylzirconocene (**8**) from the zirconocene dichloride and n-BuMgR (R = Cl, n-butyl), its decomposition [32] under formation of alternative diene chelates (**9A** and **9B**), their reversible cyclization to *cis*- or *trans*-fused metallacycles (**10A** and **10B**) and relatively slow transmetalations with n-BuMgX, the second of which frees the respective cyclomagnesation products from the Zr center and completes the catalytic cycle by regenerating the instable dibutylzirconocene species **8** (Scheme 1). Previous observations on stoichiometric reaction systems [10–16] as well as the effects of changing reaction temperatures and reagent concentrations on the observed diastereoselectivities [20] indicate that for 1,6-dienes *trans*-fusion is favored in kinetic as well as thermodynamic terms while for 1,7-dienes *cis*-fusion is faster, but *trans*-fusion still favored thermodynamically.

Our observation that very similar product distributions arise with the chirally substituted, biphenyl-bridged complex **1** as with unsubstituted $(C_5H_5)_2ZrCl_2$ shows that the stereochemical course of the cyclization catalysis — including the relative rate of the transmetalation steps — is hardly affected by the ligand geometry of the zirconocene complex. Interactions within the alternative bicyclic zirconium diolefin chelates **9A** and **9B** and their respective *cis*- and *trans*-fused metallacyclic products **10A** and **10B** thus appear to dominate over any interactions involving the ligand framework with



Scheme 1. Alternative catalytic cycl s leading to *cis*-fused and *trans*-fused cyclomagnesation products **12A** and **12B**, respectively.

regard to the stereochemical course of the cyclization reaction.

Entirely in line with this lack of influence of the ligand framework on the stereochemical course of the diolefin cyclization is the very low enantiomer excess obtained from cyclomagnesations catalyzed by the enantiopure complex *R*-**1**. Our results thus support the notion [20,21] that the metallacyclic intermediates **10A** and **10B** are in a relatively fast, reversible equilibrium with each other, which is only minimally affected by the zirconocene structure. Useful enantioselectivities, as observed by Mori and coworkers [21], are thus to be expected only if the transmetalation step is stereoselectively accelerated by interactions of additional substituents at the zirconacycle with the chiral ligand framework.

Further studies are aimed at a more detailed molecular mechanics analysis of crucial steric interactions in these reaction systems and at an exploration of the possibility to improve enantioselectivities for this type of catalysis by engineering the rate-limiting transmetalation step in such a way that one of the product enantiomers is released from the Zr reaction center faster than its counterpart.

Acknowledgements

Financial support of this work by a DAAD stipend is gratefully acknowledged.

References

[1] M.E. Vol'pin, V.A. Dubovitski, O.V. Nogina, D.N. Kursanov, Dokl. Akad. Nauk. SSSR 151 (1963) 1100.
[2] S.L. Buchwald, R.B. Nielsen, Chem. Rev. 88 (1988) 1047.
[3] P.A. Wender, F.E. McDonald, J. Am. Chem. Soc. 112 (1990) 4956.
[4] G. Angel, E. Negishi, J. Am. Chem. Soc. 113 (1991) 7424.
[5] M. Akita, H. Yasuda, H. Yamamoto, A. Nakamura, Polyhedron 10 (1991) 1.
[6] M. Mori, N. Uesaka, F. Saitoh, M. Shibasaki, J. Org. Chem. 59 (1994) 5643.
[7] E. Negishi, T. Takahashi, Acc. Chem. Res. 27 (1994) 124.
[8] E. Negishi, S.J. Holmes, J.M. Tour, J.A. Miller, J. Am. Chem. Soc. 107 (1985) 2568.
[9] E. Negishi, F.E. Cederbaum, T. Takahashi, Tetrahedron Lett. 27 (1986) 2829.
[10] E. Negishi, S.J. Holmes, J.M. Tour, J.A. Miller, F.E. Cederbaum, D.R. Swanson, T. Takahashi, J. Am. Chem. Soc. 111 (1989) 3336.
[11] D.R. Swanson, C.J. Rousset, E. Negishi, T. Takahashi, T. Seki, M. Saburi, Y. Uchida, J. Org. Chem. 54 (1989) 3521.
[12] W.A. Nugent, D.L. Thorn, R.L. Harlow, J. Am. Chem. Soc. 109 (1987) 2788.
[13] T.V. RajanBabu, W.A. Nugent, D.F. Taber, P.J. Fagan, J. Am. Chem. Soc. 110 (1988) 7128.
[14] W.A. Nugent, D.F. Taber, J. Am. Chem. Soc. 111 (1989) 6435.
[15] C.J. Rousset, D.R. Swanson, F. Lamaty, E. Negishi, Tetrahedron Lett. 30 (1989) 5105.
[16] D.F. Taber, J.P. Louey, Y. Wang, W.A. Nugent, D.A. Dixon, R.L. Harlow, J. Am. Chem. Soc. 116 (1994) 9457.
[17] K.S. Knight, R.M. Waymouth, J. Am. Chem. Soc. 113 (1991) 6268; Organometallics 13 (1994) 2575.
[18] D.B. Millward, R.M. Waymouth, Organometallics 16 (1997) 1153.
[19] U. Wischmeyer, K.S. Knight, R.M. Waymouth, Tetrahedron Lett. 33 (1992) 7735.
[20] K.S. Knight, D. Wang, R.M. Waymouth, J. Ziller, J. Am. Chem. Soc. 116 (1994) 1845.
[21] Y. Yamaura, M. Hyakutake, M. Mori, J. Am. Chem. Soc. 119 (1997) 7615.
[22] M.E. Huttenloch, J. Diebold, U. Rief, H.H. Brintzinger, Organometallics 11 (1992) 3600.
[23] A. Schäfer, E. Karl, L. Zsolnai, G. Huttner, H.H. Brintzinger, J. Organomet. Chem. 328 (1987) 87.
[24] F. Piemontesi, I. Camurati, L. Resconi, D. Balboni, A. Sironi, M. Moret, R. Zeigler, N. Piccolrovazzi, Organometallics 4 (1995) 1256.
[25] S.K. Chaudhary, O. Hernandez, Tetrahedron Lett. (1979) 99.
[26] Y. Negi, S. Harada, O. Ishizuka, J. Polym. Sci., Part A 5 (1967) 1951.
[27] T. Müller, J. Chem. Phys. 37 (1962) 1167.
[28] B. William, T. Nurmi, P. Jeffrey, W. Wei, J. Am. Chem. Soc. 10 (1987) 2442.
[29] G. Pandey, G. Reddy, G. Kumaraswamy, Tetrahedron 50 (1994) 8185.
[30] J.-L. Boucher, S. Vadon, A. Tomas, B. Viossat, D. Mansuy, Tetrahedron Lett. 37 (1996) 3113.
[31] M. Ringwald, H.H. Brintzinger, manuscript in preparation.
[32] V.K. Dioumaev, J.F. Harrod, Organometallics 16 (1997) 1452.