Octahedral Grignard Reagents Can Be Chiral at Magnesium**

Marcus Vestergren, Björn Gustafsson,
Öjvind Davidsson, and Mikael Håkansson*

The typical Grignard reagent is four-coordinate in the solid state.[1–6] That [$CH_3MgBr(thf)_3$] is five-coordinate[7] can be rationalized by the small size of the methyl group.[8–10] Higher coordination numbers in RMgX and MgR_2 reagents normally require R groups with substituents that can form intramolecular coordinate bonds.[2, 3] We were thus surprised to find that *trans*-[Mg(thienyl)$_2$(thf)$_4$] (**1**) is six-coordinate in the solid state (Figure 1). The possibility of preparing octahedral Grignard reagents with stereogenic magnesium by using bidentate neutral ligands now seemed worth investigating. Since it is advantageous if the ligands can be identical to the solvent, dimethoxyethane (DME) was the obvious first ligand/solvent choice, and we prepared and structurally characterized the octahedral enantiomers Δ- and Λ-*cis*-[(thienyl)MgBr(dme)$_2$] (**2**; Figure 2) as well as Δ- and Λ-*cis*-[(vinyl)MgBr(dme)$_2$] (**3**; Figure 3). Both complexes were prepared and crystallized from neat DME.

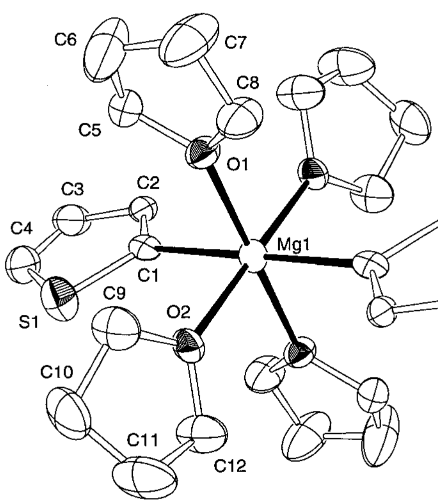

Figure 1. Magnesium is six-coordinate in *trans*-[Mg(thienyl)$_2$(thf)$_4$] (**1**). Selected bond lengths [Å] and angles [°]: Mg1-O1 2.228(4), Mg1-O2 2.178(4), Mg1-C1 2.290(6), S1-C1 1.695(5), S1-C4 1.705(7), C1-C2 1.364(8), C2-C3 1.469(8), C3-C4 1.329(9); O1-Mg1-C1 89.90(17), O2-Mg1-C1 90.99(17), O2-Mg1-O1 89.53(14), C1-S1-C4 93.7(3).

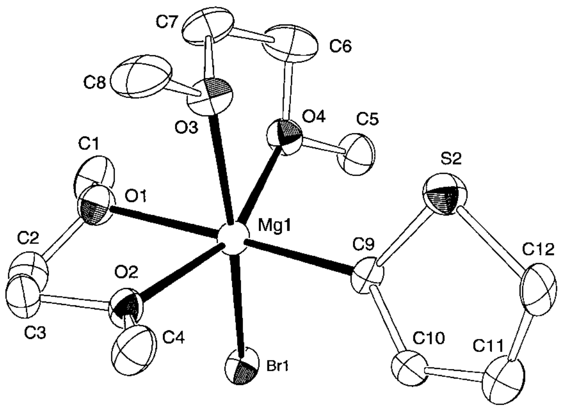

Figure 2. Molecular structure of Δ-**2**. Both enantiomers of the *cis* isomer are present in crystals of **2**. Selected bond lengths [Å] and angles [°]: Mg1-Br1 2.634(2), Mg1-O1 2.218(5), Mg1-O2 2.107(5), Mg1-O3 2.244(5), Mg1-O4 2.132(5), Mg1-C9 2.171(7), C9-C10 1.376(8), C9-S2 1.728(6), C10-C11 1.419(9), C11-C12 1.334(10), C12-S2 1.734(8); O1-Mg1-Br1 86.80(14), O2-Mg1-Br1 95.50(14), O3-Mg1-Br1 167.39(15), O4-Mg1-Br1 96.59(14), C9-Mg1-Br1 97.52(19), C9-Mg1-O1 172.0(2), C9-Mg1-O2 98.1(2), C9-Mg1-O3 93.1(2), C9-Mg1-O4 100.7(2), O2-Mg1-O4 156.09(19), O2-Mg1-O1 74.68(18), O4-Mg1-O1 85.48(18), O2-Mg1-O3 89.65(18), O4-Mg1-O3 74.71(17), O1-Mg1-O3 83.47(18).

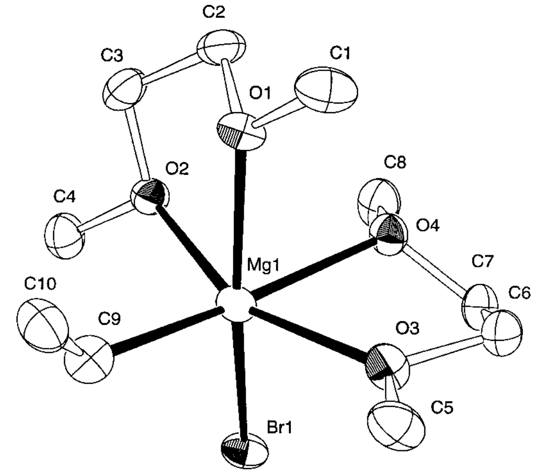

Figure 3. The Λ-enantiomer of **3**. The *cis* geometry is clearly preferred. Selected bond lengths [Å] and angles [°]: Br1-Mg1 2.6479(16), Mg1-O1 2.221(3), Mg1-O2 2.151(3), Mg1-O3 2.137(3), Mg1-O4 2.271(3), Mg1-C9 2.125(11), C9-C10 1.32(2); O1-Mg1-Br1 163.49(10), O2-Mg1-Br1 93.48(9), O3-Mg1-Br1 95.82(10), O4-Mg1-Br1 86.85(9), C9-Mg1-Br1 103.8(6), C9-Mg1-O1 89.6(6), C9-Mg1-O2 99.5(6), C9-Mg1-O3 99.8(6), C9-Mg1-O4 168.1(6), O3-Mg1-O2 155.88(13), O3-Mg1-O1 91.25(12), O2-Mg1-O1 74.56(11), O3-Mg1-O4 73.52(12), O2-Mg1-O4 84.86(12), O1-Mg1-O4 80.86(12), Mg1-C9-C10 132.0(12).

Octahedral RMgX and MgR_2 reagents are attractive, since they can be made configurationally chiral by simple solvation if the solvent is bidentate, such as DME. They are also likely to retain their solid-state structure in DME or THF solutions, since extended X-ray absorption fine structure spectroscopic (EXAFS) and large-angle X-ray scattering (LAXS) measurements[11–15] have shown that octahedral monomers, at least when the R group is vinyl, dominate in THF. Indeed, ^{1}H NMR data show that *cis*-octahedral **2** seems to retain its solid-state structure in toluene solution[16] (Figure 4). From +50 °C to

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[*] Dr. M. Håkansson, M. Vestergren, B. Gustafsson
Department of Inorganic Chemistry
Chalmers University of Technology
41296 Göteborg (Sweden)
Fax: (+46) 31-772-2846
E-mail: hson@inoc.chalmers.se

Dr. Ö. Davidsson
Organic Chemistry
Department of Chemistry
Göteborg University
41296 Göteborg (Sweden)

[**] This work was supported by the Swedish Natural Science Research Council (NFR). We thank Karin Bengtsson, Fredrik Blomgren, Henrik Glänneskog, and Dan Lundberg for preparative assistance.

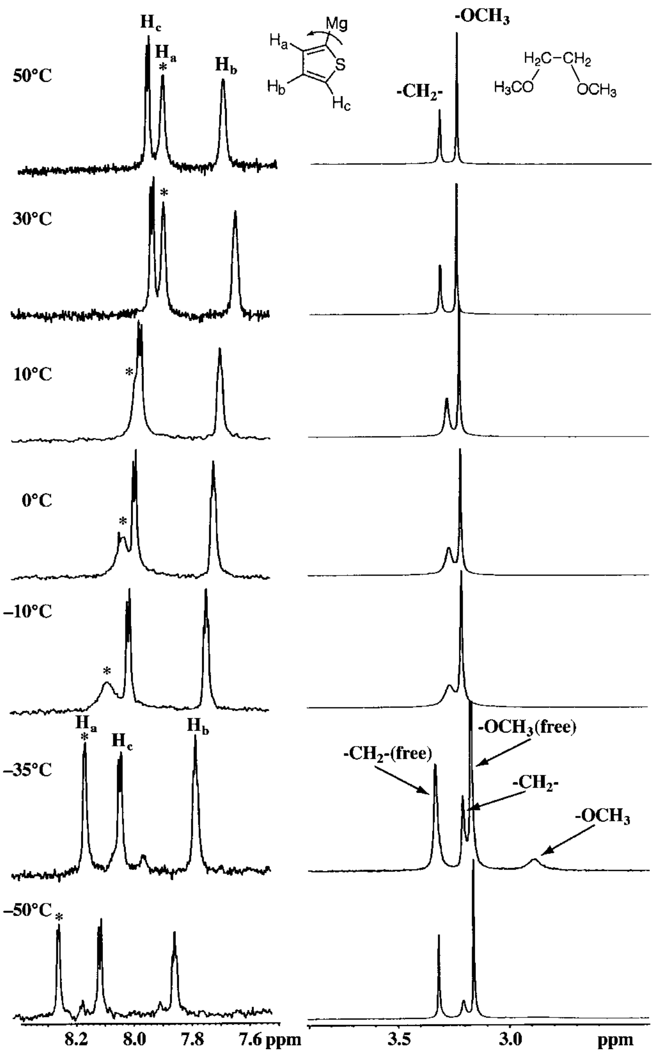

Figure 4. ^1H NMR spectra of **2** in [D$_8$]toluene at selected temperatures with extracts between $\delta = 7.5$ to 8.4 (the chemical shift region for the thienyl protons) and between $\delta = 3.0$ to 3.5 (DME protons). The thienyl proton H_a (marked with an asterisk) shows chemical shift and lineshape changes due to restricted rotation around the Mg1-C9 bond. An additional set of DME proton signals appear at low temperatures due to freezing of the exchange between free and coordinated DME.

−50 °C, there is only one set of thienyl proton resonances, which makes it unlikely that the octahedral *trans* isomer is present in appreciable concentration. The thienyl proton closest to the magnesium atom, H_a, exhibits a broadening that can be explained by hindered rotation of the thienyl group around the Mg–C bond rather than inter- or intramolecular exchange. At −20 °C, the broadening effect vanishes, which indicates that the thienyl group is locked into the solid-state position, where S–Br interactions are minimized (Figure 2). At −35 °C, the CH_2 and CH_3 resonances from complexed DME appear upfield from the free DME signal and indicates that exchange processes with uncomplexed DME now are slow on the NMR time scale. Integrated proton intensities at −35 °C show that the stoichiometry thienyl:DME is 1:2, which rules out both the presence of [Mg(thienyl)$_2$] complexes (from the Schlenk equilibrium) and tetrahedral complexes that would result from loss of one DME ligand.[17] The formation of soluble larger aggregates with this stoichiometry is also unlikely.

The crystal structure of **1** (Figure 1) exhibits magnesium in an octahedral geometry with thienyl groups in the *trans* positions. Octahedral *trans* coordination has previously been reported[18–20] in the *N*,*N*,*N*′,*N*′-tetramethyl-1,2-ethanediamine (TMEDA) complexes of bis(phenylethynyl)magnesium and bis(*tert*-butylethynyl)magnesium, which led to the assumption that sp-hybridization is necessary for sixfold coordination.[3] The crystal structures of **2** and **3** (Figures 2 and 3) show that they are both octahedral *cis* isomers and, thus, chiral. This geometry has also been found in *cis*-[MgCl$_2$(dme)$_2$].[21] The Mg–C distances in **1** (2.29 Å) are long, which could indicate a larger polarization of the Mg–C bond as a result of the coordination of the four Lewis basic THF ligands. The Mg–C distances in **2** (2.17 Å) and **3** (2.13 Å) are normal, despite the high coordination number, while the Mg–Br distances of 2.65 and 2.64 Å are significantly longer than the typical (2.4–2.5 Å) values for four-coordinate RMgBr complexes.[3] Judging from the angles O-Mg-C9 (mean in **2**: 97°; in **3**: 96°) and O-Mg-Br (mean in **2**: 93°; in **3**: 92°), it seems as if the steric requirements are larger for both the thienyl and the vinyl group as compared to the bromide. It is noteworthy that the Br-Mg-C9$_{\text{vinyl}}$ angle in **3** is significantly larger (104°) than the Br-Mg-C9$_{\text{thienyl}}$ angle (98°) in **2**. Although there are short intermolecular C-H-Br′ contacts in both **2** (2.64 Å) and **3** (2.74 Å), they can hardly be considered as classical hydrogen bonds.

Crystals of **2** and **3** are racemic. If octahedral Grignard reagents are to be useful in stereoselective synthesis, the Δ- and Λ-enantiomers have to be resolved. In some cases, spontaneous resolution may occur directly at crystallization[22] but conventional resolution methods can, of course, also be utilized. We are presently trying to predetermine[23] the chirality by the use of chiral ligands. For [RMgX(LL)$_2$] species, introduction of chirality into one or both of the bidentate neutral ligands (LL) is the apparent choice but using chiral anions is also viable.

In conclusion, and contrary to previous belief, six-coordinate Grignard reagents can be easily prepared in high yield by using appropriate R groups and bidentate neutral ligands. Such octahedral Grignard reagents have been found to be configurationally chiral and stereochemically rigid in toluene solution. Grignard reagents, which are chiral at the magnesium atom, should give strong asymmetric induction and if their chirality can be controlled or predetermined, they have a promising potential in stereoselective syntheses.

Experimental Section

All operations were carried out under argon using Schlenk, glove box, or low temperature[24] techniques.

[Mg(thienyl)$_2$(thf)$_4$] (**1**): Magnesium turnings (0.270 g, 11.1 mmol) and 2-bromothiophene (1.00 mL, 10.3 mmol) were stirred for 1 h at 50 °C in THF (10 mL). Dioxane (3.0 mL, 35.4 mmol) was added and the resulting suspension was centrifuged and the clear brown solution was transferred by syringe to another Schlenk vessel. The solution was evaporated to dryness in order to remove residual dioxane, and THF (10 mL) was added. After 12 h at −80 °C, colorless crystals of **1**, which lose THF rapidly when isolated at ambient temperature, had formed. Approximate yield: 1.0 g, 20 %. Crystal structure data for $MgS_2O_4C_{24}H_{38}$ (**1**): crystal size 0.25 × 0.20 × 0.15 mm, monoclinic, space group $P2_1/c$ (no. 14), $a = 8.508(4)$, $b = 13.892(4)$, $c = 10.900(4)$ Å, $\beta = 92.70(3)°$, $V = 1286.9(8)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.236$ g cm^{-3}, $2\theta_{max} = 50.0°$, $Mo_{K\alpha}$ radiation, $\omega/2\theta$ scan mode, $T = -120$ °C, psi-scan corrections (abs. range 0.936 – 0999), $\mu = 0.258$ mm^{-1}. Refinement on F^2 for 2256 reflections and 142 parameters gave $R1 = 0.057$ and $wR2 = 0.137$ for $I > 2\sigma(I)$. Residual electron density $-0.29 < \Delta\rho < 0.36$ e Å^{-3}. Mg, S, O, and C atoms were refined anisotropically and the H atoms with a riding model.

[(thienyl)MgBr(dme)$_2$] (**2**): Magnesium turnings (0.360 g, 14.8 mmol) and 2-bromothiophene (1.00 mL, 10.3 mmol) were stirred for 1 h at 50 °C in DME (20 mL). The reaction mixture was allowed to settle (by centrifugation, if necessary) and the clear brown solution was transferred by syringe to another Schlenk vessel. After a few hours at ambient temperature, large amounts of light brown crystals of **1** had formed. After recrystallization from DME, the crystals were washed with cold DME (2 × 2 mL) and dried briefly under vacuum. When treated in this way, solid **2** does not lose any DME. Yield: 1.80 g, 95 %. Solubility: 0.01 M in DME at 20 °C (2 M at 50 °C); sparingly in toluene. IR (Nujol, Fluorolube): $\tilde{\nu} =$ 3072 m, 3046 m, 3013 m, 2934 s, 2883 s, 2854 s, 2833 s, 2804 m, 2764 m, 2058 w, 1964 w, 1927 w, 1851 w, 1808 w, 1738 w, 1627 m, 1462 s, 1408 m, 1378 s, 1299 m, 1285 m, 1275 m, 1249 m, 1192 m, 1114 m, 1081 m, 1029 m, 982 m, 942 m, 866 m, 836 m, 820 m, 771 m, 712 m cm^{-1}. Crystal structure data for $MgBrSO_4C_{12}H_{23}$ (**2**): crystal size 0.20 × 0.15 × 0.15 mm, monoclinic, space group $P2_1/c$ (no. 14), $a = 7.417(4)$, $b = 17.528(3)$, $c = 13.062(15)$ Å, $\beta = 95.85(3)°$, $V = 1689.3(11)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.445$ g cm^{-3}, $2\theta_{max} = 50.0°$, $Mo_{K\alpha}$ radiation, $\omega/2\theta$ scan mode, $T = -120$ °C, psi-scan corrections (abs. range 0.971 – 0995), $\mu = 2600$ mm^{-1}. Refinement on F^2 for 2965 reflections and 264 parameters gave $R1 = 0.040$ and $wR2 = 0.068$ for $I > 2\sigma(I)$. Residual electron density $-0.66 < \Delta\rho < 0.46$ e Å^{-3}. Mg, Br, S, O, and C atoms were refined with anisotropic thermal displacement parameters and the H atoms with isotropic parameters.

[(vinyl)MgBr(dme)$_2$] (**3**): The solvent was evaporated from a commercial solution of vinylmagnesium bromide in THF (10 mL, 10 mmol). The oily solids were dried briefly under vacuum and redissolved in DME (10 mL). From the resulting dark red solution, light brown crystals of **3** formed after a few hours at ambient temperature. Yield (not optimized): 1.07 g, 34 %. IR (Nujol, Fluorolube): $\tilde{\nu} =$ 3072 m, 3046 m, 3013 m, 2934 s, 2883 s, 2854 s, 2833 s, 2804 m, 2764 m, 2061 w, 1965 w, 1920 w, 1620 w, 1464 s, 1377 s, 1365 s, 1294 m, 1277 m, 1243 m, 1212 w, 1190 m, 1114 m, 1098 m, 1052 m, 1025 m, 867 m, 833 m, 771 w, 722 m cm^{-1}. Crystal structure data for $MgBrO_4C_{10}H_{23}$ (**3**): crystal size 0.30 × 0.20 × 0.10 mm, monoclinic, space group $P2_1/n$ (No. 14), $a = 7.3311(18)$, $b = 15.353(2)$, $c = 12.9726(19)$ Å, $\beta = 90.986(17)°$, $V = 1459.9(5)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.417$ g cm^{-3}, $2\theta_{max} = 50.0°$, $Mo_{K\alpha}$ radiation, $\omega/2\theta$ scan mode, $T = -120$ °C, psi-scan corrections (abs. range 0.666 – 0999), $\mu = 2856$ mm^{-1}. Refinement on F^2 for 2564 reflections and 255 parameters gave $R1 = 0.033$ and $wR2 = 0.066$ for $I > 2\sigma(I)$. Residual electron density $-0.37 < \Delta\rho < 0.33$ e Å^{-3}. Mg, Br, O, and C atoms were refined with anisotropic thermal displacement parameters and the H atoms with isotropic parameters. The vinyl groups and bromide atoms are all disordered on double sites, to the effect that the ligands are interchanged. The site occupancy factor for the atoms shown in Figure 3, refined to 0.904.

All three structures were solved and refined using SHELX-97.[25] Figures 1 – 3 were represented using ORTEP3.[26] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-140697, CCDC-140698, and CCDC-140699. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Received: March 23, 2000
Revised: July 4, 2000 [Z14888]

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[16] A small amount of extra DME was added (free:complexed = 60:40) during dissolution of **2** in toluene.

[17] Above −30 °C it is no longer possible to estimate the thienyl:DME ratio due to signal coalescense and one referee correctly pointed out that the possibility of tetrahedral species at ambient temperature has to be considered. The existence of two complexes (octahedral and tetrahedral) but only one set of thienyl signals could then be explained by assuming an equilibrium that is strongly shifted towards an octahedral complex at −50 °C and towards a tetrahedral complex at 50 °C. The broadening of the H_a signal would be interpreted as coalescence of resonances from tetra- and octahedral complexes, instead of restricted rotation around the Mg–C bond. The fact that there is no coalescence for the H_b and H_c resonances has to be explained by chemical shift equivalency. In our opinion, this is unlikely since the electronic effects in the thienyl group should be considerable on going from four- to six-fold coordination.

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