metal complex inside their tunnels, which makes these materials a good point of departure for designing new catalysts; a stable framework after removal of the transition metal complex; and large distances between the active metal centers, which allows unhindered access of reactants to these centers through uniformly sized 8Rc channels.

## *Experimental Section*

X-ray structure analysis of ICMM-2Cu, ICMM-2Ag, and ICMM-2H: Orthorhombic, space group *Pnna*, $Mo_{K\alpha}$, dimensions of crystals: $0.2\times0.1\times0.05$, $0.02\times0.08\times0.2$, and $0.04\times0.16\times0.2$ mm, respectively; see Table 1 for the cell parameters. Data were collected in a Siemens SMART-CCD diffractometer using $\omega$ scans over the range $3<\theta<26°$. Of 4663, 5159, and 3518 reflections, 1301, 1651, and 1187 were independent for Cu, Ag and H compounds, respectively. The structures were solved by direct methods. In the Cu and Ag compounds, all the hydrogen atoms were located in difference Fourier maps and those of the $NH_4$ cation refined with a model of disorder due to the special position of this N atom. Refinement was by full-matrix least-squares analysis with anisotropic thermal parameters for all non-hydrogen atoms and isotropic thermal parameters for hydrogen atoms.[27] Further details on the crystal structure investigation may be obtained from the Fachinformationszentrum Karlsruhe, D-76344 Eggenstein-Leopoldshafen, Germany (fax: (+49)7247-808-666; e-mail: crysdata@fiz-karlsruhe.de), on quoting the depository numbers CSD-410751 (ICMM-2Cu), -410752 (ICMM-2Ag), and -410753 (ICMM-2H).

Cyclopropanation reactions: The sample of ICMM-2Cu was previously dried at 100 °C. Ethyl diazoacetate (4.11 mmol) was added dropwise over a period of 2 h in a $N_2$ atmosphere at 50 °C to a stirred mixture of styrene (3 mmol) and the catalyst (0.04 mmol). After the $N_2$ evolution had ceased, the chemical yields were determined by gas chromatography.

CAS-registry no. for ICMM-2: 9900953.

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# Donor/Acceptor Metallocenes: A New Structure Principle in Catalyst Design[**]

K. Aleksander Ostoja Starzewski,[*] W. Mark Kelly, Andreas Stumpf, and Dieter Freitag

*Dedicated to Dr. Pol Bamelis*
*on the occasion of his 60th birthday*

Soon after their discovery and structure elucidation[1] metallocenes were being applied as well-defined organometallic species in transition metal catalyzed polymerization with alkylaluminum halide cocatalysts.[2] However, it was only after spectacular work by Sinn, Kaminsky, Brintzinger, Ewen, and others on the increase in catalyst activity in olefin polymerization by aluminoxanes[3] and on the realization of stereospecificity in propene polymerization with homogeneous stereorigid $C_2$-symmetric *ansa*-metallocenes[4] that the new era of worldwide polyolefin catalyst research began. The results have an impact on a current world market of more than 170 million tonnes of polymers, of which almost half are polyolefins.[5]

The metallocene catalysts developed up to now can be divided into two large classes: 1) unbridged and 2) covalently bridged sandwich compounds.[6]

The catalysts of the first group are highly active in the polymerization of the small ethylene molecule.[7a] A limited

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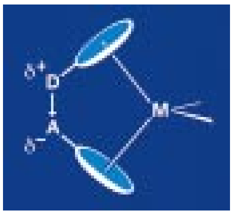
incorporation of $\alpha$-olefins (propene, butene, hexene) in the production of short-chain branched low-pressure polyethylene (LLDPE) is possible.[7d–g] Homopolymerization of $\alpha$-olefins with three or more C atoms proceeds with much lower activity and predominantly results in products of low molecular weight.[7a,c] Possibilities for stereocontrol in this group are insufficient.[7b]

The catalysts of the second group force and define a smaller centroid-metal-centroid angle through covalent bridging of the two rings, so that sterically demanding monomers can also be readily linked.[6] In the copolymerization, a high incorporation of comonomer is achieved with a statistical distribution (very-low-density-polyethylene (VLDPE), cycloolefin-olefin-copolymers (COC), ethene-propene-ethylidene-norbornene (EPDM)).[6c, 7d,g] Such catalysts are particularly suitable for the homopolymerization of propene, but also of higher $\alpha$-olefins. Structure-optimized *ansa* compounds of specific symmetry ($C_2$, $C_s$) allow near perfect stereocontrol for isotactic and syndiotactic polypropylene (iPP and sPP, respectively).[8]



Scheme 1. Donor/acceptor metallocenes.

In a continuation of our investigations on ylide–nickel polymerization catalysts for linear and branched polyethylene[11b–g] we report herein on a new class of metallocene catalysts: the donor/acceptor (D/A) metallocenes (Scheme 1). In these metallocenes one π ligand of the sandwich complex bears a donor substituent with a lone pair of electrons and the other π ligand an acceptor substituent with an electron pair vacancy. In this way a strongly polarized coordinative $D^+ \rightarrow A^-$ bonding interaction results spontaneously between the two π ligands.

The rotation of the rings with respect to each other is effectively hindered and at the same time the aperture angle of the metallocene is influenced. This new structure concept in metallocene catalysis offers a wide range of additional control instruments. Thus, different donor atoms (e.g. O, N, P), different acceptor atoms (e.g. B, Al), and their respective substituents can be enlisted to optimize the catalytic behavior.

The present case is concerned with the first zirconocene with a strong coordinative P → B interaction (**1**). The stepwise reaction of zirconium tetrachloride with the silylated donor ligand $Me_2P(Cp)SiMe_3$ ($Cp = C_5H_4$) gives the donor half-sandwich complex $[Me_2P(Cp)ZrCl_3]$ and subsequent reaction with the silylated acceptor ligand $Cl_2B(Cp)SiMe_3$[9] gives the D/A metallocene $[\{Me_2P(Cp)\}\{Cl_2B(Cp)\}ZrCl_2]$ (**1**).

Compound **1** can be obtained in the form of needlelike crystals by recrystallization from toluene. The molecular structure in the crystal (Figure 1)[10] shows a bis(cyclopentadienyl)zirconocene, whose rings are bridged by a $Me_2P \rightarrow BCl_2$ interaction. The P–B bond length is 198 pm and the centroid-metal-centroid angle is 127.9°. The structure has no mirror plane; it is $C_1$-symmetric. The molecule is chiral in the crystalline state and exists as a pair of enantiomers.

Multinuclear NMR investigations confirm the presence of the D/A bridge also in solution. The $^1$H NMR spectrum at room temperature shows a mirror symmetrical structure as the dynamic average on the NMR time scale, that is only two signals are observed for each Cp ring and only one signal for the P-bound methyl groups. In the $^{13}$C{$^1$H} NMR spectrum, the signal of the $\alpha$-ring carbon atom adjacent to the four-coordinate P atom occurs at higher field ($\delta = +104$), which is in agreement with a phosphonium cyclopentadienylide ligand. For a comparison with NMR data of free and complexed ylide ligands see references [11a, b, d]. The ring-bridging dative P → B interaction is directly visible in the $^{11}$B NMR spectrum through a well-resolved $^{31}$P-$^{11}$B coupling of 120 Hz. The low field shift of the $^{31}$P NMR signal compared to that of the silylated donor (D) ligands and the high field shift of the $^{11}$B NMR signal relative to that of the silylated acceptor (A) ligands of about 50 ppm is in agreement with a lower electron density at the phosphorus atom and a higher electron density at the boron atom. The polar D–A bridge in the present case is thermally very stable; thus, even at 100 °C the $^1$H NMR spectrum in dideuterotetrachloroethane remains unchanged with regard to the previously described qualitative appearance and the size of the $^{31}$P-$^1$H coupling.

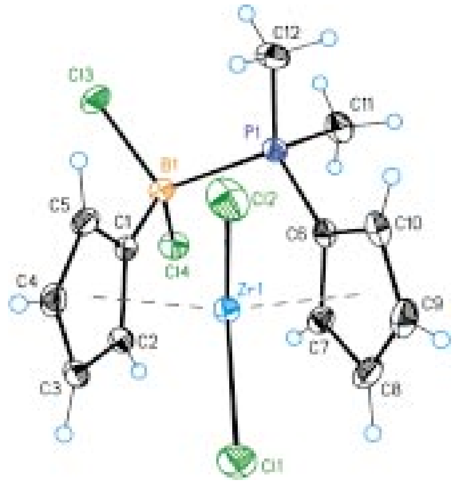


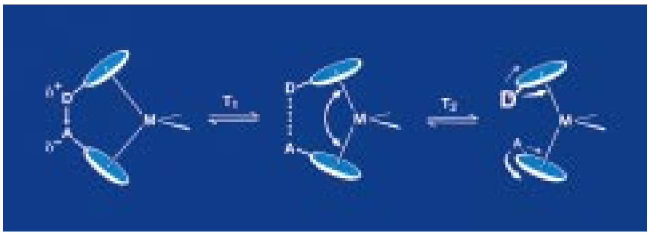
Figure 1. Molecular structure of **1** in the crystal.

The D/A metallocene **1** is under methylaluminoxane (MAO) activation a highly effective and thermally robust catalyst for ethene polymerization. For example, at a polymerization temperature of 100 °C and an ethene pressure of 10 bar it catalyzes the formation of high molecular weight polyethylene (PE) with a catalyst activity of about 118 tonnes PE per mol catalyst per hour.

The development potential of the class of catalysts presented here is illustrated for the polymerization of isotactic polypropylene (iPP). Whereas the production of high-melting iPP of high tacticity and high molecular mass with the existing metallocene catalysts can only be achieved if these contain synthetically demanding substitution patterns,[6, 7a, 8a,b] this goal can be readily reached with a simple bis(indenyl)zirconocene, in which the *rac* ligand arrangement is fixed by D/A interaction and remains intact under the action of the cocatalyst in the catalytic cycle: by applying *rac*-$[\{Et_2P(2\text{-}Me\text{-}ind)\}\{Cl_2B(2\text{-}Me\text{-}ind)\}ZrCl_2]$ (**2**), which had been activated with triisobutylaluminum/dimethylanilinium-tetrakis(pentafluorophenyl)borate, at room temperature under 2 bar propene in toluene a highly isotactic polypropylene is obtained with an isotacticity index of 97 %, isotactic *mmmm*-pentads of 92 % (misinsertions not detected), a melting temperature $T_m$ of 161/158 °C (1st and 2nd, heating cycle, respectively) determined by differential scanning calorimetry (DSC), and an average, molecular mass $M_v$ of 422 000 g mol$^{-1}$ determined by viscosimetry. For a direct comparison with other metallocene catalysts see references [7a, 8a]. For a corresponding polymerization in bulk, that is without solvent, the analytical data of the polymer increase: isotacticity index 98 %, *mmmm*-pentad probability 94 %, $T_m = 165/158$ °C and $M_v = 2.0 \times 10^6$ g mol$^{-1}$ (!). By raising the polymerization temperature to about 50 °C, the molecular mass drops to about $M_v = 434\,000$ g mol$^{-1}$, the isotacticity index to 92 %, and the *mmmm*-pentad probability to 82 %. Since the melting temperature $T_m$ (158/154 °C), however, remains high,[8a] this is an indication for the formation of atactic propylene sequences alongside long isotactic ones. Also in this case there is no evidence for misinsertions by 2,1- or 1,3-insertion.

The diverse electronic and steric possibilities of the donor and acceptor building blocks and the adjustable D → A bond strengths offer fascinating possibilites to model the architecture and property profile of the catalysts. Thus the length of the $P^+ \rightarrow B^-$ bridge of the D/A compound **1** is 198 pm and the length of the $N^+ \rightarrow B^-$ bridge in the D/A titanocene [{Me$_2$N(Cp)}{Me$_2$B(Cp)}TiCl$_2$] (**3**) is 174 pm.

The catalysts presented here are prototypes of the new class of D/A metallocene catalysts. Specifically optimized substitution patterns give excellent properties for the synthesis of high melting, highly crystalline thermoplastic materials, amorphous thermoplastic materials with high glass transition temperature as well as polyolefin elastomers with low glass $T_g$. Thus, the statisical copolymerization of ethene and propene can be achieved in every desired composition as can the insertion of bulky cycloolefins such as in ethene–propene–ethylidene–norbornene (EPDM rubbers) or in amorphous cycloolefin–olefin–copolymers (COCs).[12b–d] Furthermore, sequence polymers such as (EPDM-PE)$_n$ are accessible, whose formation can be explained with temperature-dependent equilibria (Scheme 2). The patent for this class of catalysts has been registered worldwide.[12a]



Scheme 2. Equilibria between donor/acceptor metallocenes with bridged and unbridged structure.

## *Experimental Section*

All reactions were carried out under strict anaerobic conditions and by using Schlenk or high-vacuum techniques. The solvents used were dry and saturated with argon. Chemical shifts $\delta$ are given relative to the relevant standard ($^1$H: tetramethylsilane, $^{11}$B: boron trifluoride etherate, $^{13}$C: tetramethylsilane, $^{31}$P: 85 % phosphoric acid). Negative signs mean a shift to higher field.

**1:** In a Schlenk flask trimethylsilylcyclopentadiene (0.1 mol; Fluka) was diluted with dry diethyl ether (700 mL) and cooled to −20 °C. Butyllithium (0.1 mol of a 2.5 M solution in hexane) was added dropwise to this solution and the resulting suspension was stirred at room temperature for 2 h. Subsequently, dimethylchlorophosphane (0.1 mol) in diethyl ether (50 mL) was added dropwise at 0 °C and the reaction mixture was stirred at room temperature for about 14 h, the solvent was removed under vacuum, and then the residue was taken up in hexane (200 mL). After filtration the solvent was removed under vacuum and the silylated donor ligand Me$_2$P(Cp)SiMe$_3$ was purified by trap-to-trap distillation at $10^{-2}$ Torr.

A solution of the silylated donor ligand (0.07 mol) in toluene (100 mL) was added dropwise over about 3 h to a suspension of zirconium tetrachloride (0.07 mol) in toluene (200 mL) cooled to 0 °C, and the resulting yellow suspension was stirred for about 14 h at room temperature. The sparingly soluble, yellow donor half-sandwich complex was filtered off, washed with toluene, dried under vacuum ($10^{-3}$ Torr), and treated with silylated acceptor ligands to give the D/A metallocene. For this the donor half-sandwich complex (0.01 mol) was suspended in toluene (200 mL) and Cl$_2$B(Cp)SiMe$_3$[9] (0.01 mol) in toluene (40 mL) was slowly added dropwise at 0 °C. After the reaction had been allowed to proceed at room temperature (ca. 14 h), the mixture was filtered, the filtrate was concentrated under vacuum until the solution became turbid and then crystallized in a freezer. The D/A metallocene was obtained in the form of fine needles, which were suitable for X-ray structure analysis, by recrystallization from toluene.

X-ray structure analysis of **1**: $d$(P–B) = 198.25(13) pm, $d$(centroid-(Cp$_P$)–Zr) = 221.5 pm; $d$(Zr–centroid(Cp$_B$)) = 219.2 pm; angle (centroid-Zr-centroid) = 127.9°; angle (Cl-Zr-Cl) = 96.562(12)°; $^{31}$P{$^1$H} NMR (162 MHz, CD$_2$Cl$_2$): $\delta = -7.7$ (m); $^{11}$B{$^1$H} NMR (128 MHz, CD$_2$Cl$_2$): $\delta = -0.1$ (d, $^1J(^{31}P,^{11}B) = 120$ Hz); $^{13}$C{$^1$H} NMR (101 MHz, CD$_2$Cl$_2$): $\delta = +8.7$ (d, $^1J(^{31}P,^{13}C) = 41$ Hz, CH$_3$), +104.1 (d, $^1J(^{31}P,^{13}C) = 66$ Hz, Cp$_P$-$\alpha$-C), +119.4 (s, Cp$_B$-$\beta$-C), +120.2 (d, $^2J(^{31}P,^{13}C) = 8$ Hz, Cp$_P$-$\beta$-C), +123.2 (d, $^3J(^{31}P,^{13}C) = 7$ Hz, Cp$_P$-$\gamma$-C), +125.7 (s, Cp$_B$-$\gamma$-C); $^1$H NMR (400 MHz, CD$_2$Cl$_2$): $\delta = +1.94$ (d, $^2J(^{31}P,^1H) = 12.0$ Hz, CH$_3$), +6.56 (m, Cp$_B$-$\beta$-H), +6.74 (pseudo-q, 3 Hz, Cp$_P$-$\gamma$-H), +6.79 (pseudo-t, 3 Hz, Cp$_B$-$\gamma$-H), +7.01 (pseudo-q, 3 Hz, Cp$_P$-$\beta$-H). The assignment was based on $^1$H-NOESY, $^1$H-$^{13}$C-HMQC, and $^1$H-$^{13}$C-HMBC-2D-NMR spectra.

**2:** At 0 °C a solution of *n*-butyllithium (59 mL of a 2.5 M solution in hexane) was added dropwise to a solution of 2-methylindene (0.147 mol) in diethyl ether (350 mL). The solution was allowed to warm to room temperature and stirred for 1 h. Then diethylchlorophosphane (0.147 mol) was added dropwise at 0 °C, and the bright yellow suspension was stirred at room temperature for a further 1 h. After renewed cooling to 0 °C, additional *n*-butyllithium solution (59 mL) was added dropwise, and the mixture was stirred at room temperature for about 1 h, before tributylchlorostannane (0.148 mol) was added dropwise at 0 °C. After the mixture had been stirred for about 1.5 h, the volatile components were removed under vacuum, the residue was taken up in hexane (100 mL), and precipitated lithium chloride was filtered off. After removal of the solvent, the stannylated donor ligand tributylstannyldiethylphosphanyl-2-methylindene remained as a yellow oil (yield about 80 %, $^{31}$P NMR (CD$_2$Cl$_2$): $\delta = -36.0$). This was added to an equivalent amount of zirconium tetrachloride in dichloromethane at −30 °C, and after this mixture had been stirred for 5 h at 25 °C the insoluble donor half-sandwich complex **2** was obtained as a yellow powder, which was purified by Soxhlet extraction with dichloromethane. Yield 78 %.

In analogy to the D/A metallocene **1** the silylated acceptor ligand trimethylsilyldichloroboranyl-2-methylindene (0.019 mol) in toluene (50 mL) was added to a suspension of the donor half-sandwich complex diethylphosphanyl-2-methylindenezirconium trichloride in toluene (350 mL). The reaction mixture was heated to 80 °C and stirred for 24 h. After cooling and filtration, hexane (300 mL) was added to the clear, orange solution. A clear yellow solution, which was decanted off from an orange-colored oil that deposited on the glass wall, was concentrated and cooled to about −25 °C. The *rac* compound **2** formed as a bright yellow powder. $^{31}$P{$^1$H} NMR (162 MHz, CD$_2$Cl$_2$): $\delta = +21.4$; $^{11}$B{$^1$H} NMR (128 MHz, CD$_2$Cl$_2$): $\delta = +3.7$ (d, $^1J(^{31}P,^{11}B) = 108$ Hz); $^1$H NMR (400 MHz, CD$_2$Cl$_2$): $\delta = +8.14$ (d, $J = 8.6$ Hz, 1 H), +7.96 (d, $J = 8.9$ Hz, 1 H), +7.47 to 7.05 (various overlapping multiplets, 6 H), +6.53 (d, $J = 1.9$ Hz, 1 H), +6.47 (s, 1 H), +3.0 to 2.55 (various overlapping multiplets, 4 H), +2.21 (s, 3 H), +2.08 (s, 3 H), +1.44 (m, 3 H), +1.07 (m, 3 H).

Trimethylsilyldichloroboranyl-2-methylindene: Hexane (500 mL) and butyllithium (70 mL of a 2.5 M solution in hexane) were placed in a 1000-mL flask, and 2-methylindene (0.175 mol) was added dropwise at room temperature; the mixture was stirred for about 14 h. Then trimethylsilyl chloride (0.18 mol) was added dropwise at room temperature and the mixture was stirred for a further 8 h. LiCl was filtered off, and butyllithium (70 mL of a 2.5 M solution in hexane) was added to the clear filtrate. After this mixture had been stirred for a furhter 14 h, trimethylsilyl chloride (0.18 mol) was added, and the resulting mixture was stirred for a further 8 h. LiCl was filtered off and the solvent was removed under vacuum. Bis(trimethylsilyl)2-methylindene remained as a colorless oil. Yield: 85%. $^1$H NMR (400 MHz, $CD_2Cl_2$): $\delta = +7.51$ (1 H, d, $J = 7.7$ Hz), $+7.38$ (d, $J = 7.5$ Hz, 1 H), $+7.19$ (t, $J = 7.4$ Hz, 1 H), $+7.08$ (t, $J = 7.3$ Hz, 1 H), $+3.54$ (s, 1 H), $+2.32$ (s, 3 H), $+0.41$ (s, 9 H), 0.0 (s, 9 H). Bis(trimethylsilyl)-2-methylindene (0.096 mol) was placed in a 250-mL Schlenk flask that was fitted with a dry ice condenser. Boron trichloride (0.096 mol) was added, and the mixture was stirred for 3 h at room temperature and a further 6 h at 55 °C. The trimethylchlorosilane formed in the reaction was removed under vacuum, leaving the crude product as a brown oil. Trap-to-trap distillation under an oil pump vacuum delivered the silylated acceptor ligand as a colorless, sticky solid. Yield about 75%. $^{11}$B{$^1$H} NMR (128 MHz, $CD_2Cl_2$): $\delta = +50.0$; $^1$H NMR (400 MHz, $CD_2Cl_2$): $\delta = +8.09$ (d, $J = 7.9$ Hz, 1 H), $+7.37$ (d, $J = 7.6$ Hz, 1 H), $+7.26$ (t, $J = 7.5$ Hz, 1 H), $+3.89$ (s, 1 H), $+2.61$ (s, 3 H), 0.0 (s, 9 H).

**3:** A solution of dimethylboranylcyclopentadienyltitanium trichloride[9b] (0.18 g, 0.7 mmol) in toluene (10 mL) was added at $-20$ °C over 10 min to a suspension of *N*,*N*-dimethylaminocyclopentadienyllithium[9c] (0.081 g, 0.7 mmol) in toluene (10 mL), resulting in a deep red solution. After the solution had been allowed to warm to room temperature over 2 h, it was filtered and the solvent was removed under vacuum. After the resulting red powder had been redissolved in warm toluene (10 mL) and insoluble material had been separated by filtration, the solution was placed in a refrigerator for about 14 h, during which time red needles formed (0.1 g) (43% yield). $^{11}$B{$^1$H} NMR (128 MHz, $CD_2Cl_2$): $\delta = +20.3$ (br.); $^1$H NMR (400 MHz, $CD_2Cl_2$): $\delta = +7.00$ (t, $J = 2.3$ Hz, 2 H), $+6.47$ (t, $J = 2.3$ Hz, 2 H), $+6.41$ (t, $J = 2.8$ Hz, 2 H), $+6.26$ (t, $J = 2.8$ Hz, 2 H), $+2.97$ (s, 6 H), $+0.42$ (s, 6 H); $^1$H NMR (400 MHz, $C_6D_6$): $\delta = +6.85$ (t, $J = 2.3$ Hz, 2 H), $+6.15$ (t, $J = 2.3$ Hz, 2 H), $+6.10$ (t, $J = 2.8$ Hz, 2 H), $+5.57$ (t, $J = 2.8$ Hz, 2 H), $+1.98$ (s, 6 H), $+0.35$ (s, 6 H).

Ethene polymerization: Anhydrous, argon-saturated toluene (100 mL) was placed in a vacuum-dried, oxygen-free, 300-mL-V4A steel autoclave fitted with a magnetic stirrer. The autoclave was heated to 100 °C, the catalyst was injected, and the ethylene pressure was set to 10 bar. Compound **1** (0.1 μmol), which had been pretreated with MAO (1.0 mmol) in toluene (0.66 mL) for 1 h, was used as catalyst. The temperature inside the autoclave rose under air cooling from 100 to 105 °C. After 30 min the polymerization was stopped. After the pressure had been released from the autoclave, the reaction mixture was added to ethanol (450 mL) and concentrated aqueous HCl (50 mL) and stirred for about 14 h, the polymer was filtered off, washed thoroughly with ethanol, and dried at 100 °C in the vacuum drying cabinet until the weight remained constant. The PE yield was 5.9 g, which corresponds to a catalyst activity of about 118 tonnes of polymer per mol zirconocene per hour. The intrinsic viscosity [$\eta$] (in *ortho*-dichlorobenzene at 140 °C) was 1.64 dL g$^{-1}$ which corresponds to an average molecular mass $M_v$ of 106 kg mol$^{-1}$. The melting maximum determined by DSC was 136 °C in the 2nd heating cycle.

Propene polymerization: Anhydrous, argon-saturated toluene (100 mL) and a 1 M triisobutylaluminum/toluene solution (0.5 mL) were placed in a vacuum-dried, oxygen-free, 300-mL-V4A steel autoclave fitted with a magnetic stirrer. Subsequently, **2** (1 μmol), which had been pretreated with triisobutylaluminum (0.1 mmol of a 1 M solution in toluene) for 30 min, and dimethylanilinium tetrakis(pentafluorophenyl)borate (4 μmol) in chlorobenzene (1 mL) were injected, and the polymerization was carried out at room temperature under 2 bar propene pressure. After 30 min, the polymerization was stopped. The contents of the autoclave were placed in ethanol (450 mL) and concentrated HCl (50 mL) and the mixture was stirred for 2 h. The white polypropylene was filtered off, washed thoroughly with ethanol, and dried in the vacuum drying cabinet at about 110 °C until the weight remained constant. The iPP yield was 3.5 g, which corresponds to a catalyst activity of about 7 t polymer per mol zirconocene per hour. The intrinsic viscosity [$\eta$] (in *ortho*-dichlorobenzene at 140 °C) was 2.30 dL g$^{-1}$, which, according to the [$\eta$]/$M$ relationship for isotactic polypropylene,[9d] corresponds to an average molecular mass $M_v$ of 422 kg mol$^{-1}$. The thermoanalytical investigations (DSC) were carried out in two successive measurements in the temperature range $-30$ °C to $+200$ °C. For this the sample was heated at a rate of 20 K min$^{-1}$, then quenched at 320 K min$^{-1}$ to the starting temperature of the 2nd heating cycle, and then renewed at 20 K min$^{-1}$. The melting maxima of the 1st and 2nd heating cycles lie at 161 and 158 °C, respectively, the melting enthalpies at 108 and 90 J g$^{-1}$, respectively. The $^{13}$C NMR spectroscopic investigation of the microstructure gave an isotacticity index of 97.2% as well as a share of isotactic *mm*-triads of 95.6%, of atactic *mr/rm* triads of 3.2%, and of syndiotactic *rr*-triads of 1.2%. The share of isotactic *mmmm*-pentads was 92.2%. The statistics from the pentad analysis confirm that the polymerization is enantiomorphic site controlled.

The $^{13}$C NMR measurements of polypropylene at 100 °C in dideuterotetrachloroethane were recorded on a Bruker-DRX-400 spectrometer with a 5-mm-QNP-probe head with the solvent as reference ($\delta = 73.88$).

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[10] Crystal structure analysis of **1**: Bruker-Smart-CCD area detector system, $Mo_{K\alpha}$ irradiation, graphite monochromator, Rigaku rotating-anode M18HF (operating at 50 kV, 100 mA). The reflections were recorded at 153 K on a shock-cooled crystal with the dimensions $0.4 \times 0.3 \times 0.3$ mm$^3$ under an inert oil (RS3000; Riedel-de Haen) up to $2\theta_{max} = 61°$. The data were processed with the programs SAINT (data reduction, SAINT-NT V5.0) and SADABS (absorption correction). The structure solution and refinement were carried out with SHELXTL (NT-Version V5.1). $C_{12}H_{16}B_1Cl_4P_1Zr_1$, $M_r = 433.03$, monoclinic, space group $P2_1/c$, $a = 14.6429(5)$, $b = 8.3296(3)$, $c = 13.3791(5)$ Å, $\beta = 103.6560(10)°$, $V = 1585.71(10)$ Å$^3$, $\rho_{calcd} = 1.814$ Mg m$^{-3}$, $\mu = 1.449$ mm$^{-1}$, 17987 measured reflections, 4834 independent ($R_{int} = 0.0264$), and 4245 observed ($F_o > 4\sigma(F_o)$). The hydrogen atoms were refined with isotropic temperature factors, all other atoms with anisotropic ones. $R1 = 0.0171$, $wR2 = 0.0436$ (all data), GOF = 1.020 for 228 parameters. Max./min. residual electron density $0.436/-0.305$ e Å$^3$. 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- CCDC-118714. 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).

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# Macrolide Analogues of the Novel Immunosuppressant Sanglifehrin: New Application of the Ring-Closing Metathesis Reaction[**]

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More than two decades ago, the discovery of cyclosporin A (CsA) allowed a spectacular progress in the field of organ transplantation.[1] Since then, the number of transplanted organs has grown continuously, and the search for novel immunosuppressants has been intensified.[2] Besides its important therapeutic use, CsA has also proven to be a powerful tool for dissecting signal transduction pathways at the molecular level.[3] It has been shown that the biological activity of CsA is mediated by an intracellular binding protein called cyclophilin (CyP). However, although CyP binding is required, it is not sufficient for the immunosuppressive activity of this drug. Full biological activity is obtained only once the CyP–CsA complex binds to and inhibits the serine/threonine phosphatase activity of calcineurin, thereby blocking the production of cytokines including interleukin-2.[4]

We wondered whether other ligands for cyclophilin might exist which would interfere with signaling pathways not involving calcineurin. The screening of microbial broth extracts for CyP-binding substances led to the isolation from *Streptomyces flaveolus* of a new class of compounds named sanglifehrins.[5a] Among the 20 different sanglifehrins isolated so far from this strain, sanglifehrin A (SFA, Figure 1) is the most abundant component. The affinity of SFA for cyclophilin is remarkably high ($IC_{50} = 2-4$ nM),[6] approximately 20-fold higher than that of CsA ($K_i = 82$ nM). Sanglifehrin A displays potent immunosuppressive activity in the mixed lymphocyte reaction ($IC_{50} = 170$ nM), an in vitro immune response assay.[5a] However, SFA does not affect T-cell receptor-mediated cytokine production, indicating a mode of action different from that of CsA. Moreover, in contrast to the T-cell-selective drug CsA, SFA inhibits mitogen-induced B-cell proliferation ($IC_{50} = 90$ nM). These data clearly indicate that the immunosuppressant SFA acts by a new mode of action. However, the details of the mechanism by which this compound exerts its immunosuppressive activity at the molecular level are unknown.

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