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Stereoselective synthesis of functionalized hexene oligomers catalyzed by chiral *ansa*-zirconocene in the presence of Al- and B-containing activators

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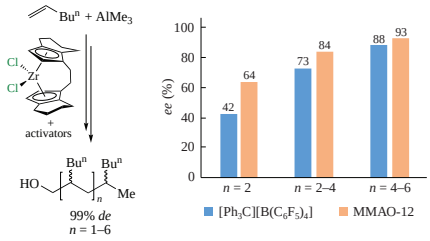
Enantiomerically enriched (38–93% *ee*) diastereomerically pure (99% *dr*) functionally substituted dimers and oligomers with the starting Me-group were obtained by the reaction of 1-hexene with $AlMe_3$ in the presence of enantiomerically pure dichloro[(*R*,*R*)-ethylenebis(4,5,6,7-tetrahydroinden-1-yl)]-zirconium(IV). Modified methylaluminoxane MMAO-12 as the activator was somewhat superior to boron-containing compound $[Ph_3C][B(C_6F_5)_4]$.



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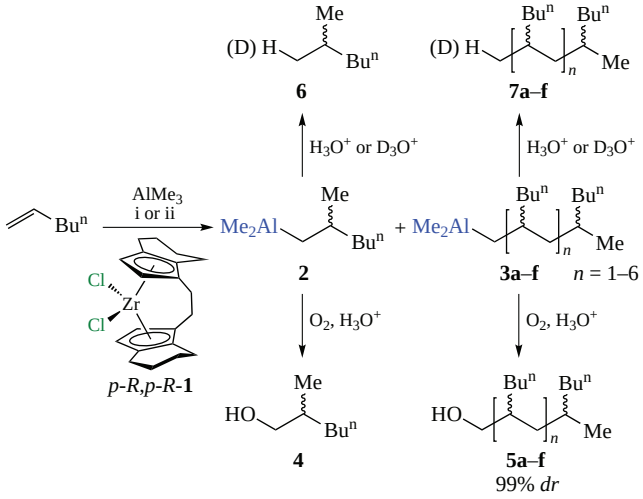
The growing interest in dimers and oligomers of terminal alkenes is due to their potential application as comonomers in the ethylene polymerization, raw materials for the production of adhesives, surfactants, flavors, synthetic lubricants for fuel, *etc*.[1–4] Stereomerically pure oligomeric fragments can also be components of pheromones,[5] glycolipids,[6] and some alkaloids.[7] Synthesis of stereomerically pure fragments typically involves gradual addition of monomeric units, and each iteration occurs through several stages.[8,9] The multi-stage process within a single iteration, along with an increase in the number of iterations depending on the sum of units in the oligomer, ultimately leads to a significant reduction in the yield of the target product, especially in the case of an enantioselective synthesis. To overcome this problem, a reaction of the alkene transformation catalyzed by metallocenes producing oligomers with high yield, chemo-, regio-, and stereoselectivity, can be applied.[10–17] This approach provides the way to the one-pot synthesis of structural blocks of practically significant molecules.

This work aimed at the study of the reaction of 1-hexene with $AlMe_3$ catalyzed by enantiomerically pure complex, dichloro[(*R*,*R*)-ethylenebis(4,5,6,7-tetrahydro-1-indenyl)]-zirconium(IV) (*p*-*R*,*p*-*R*-**1**) in the presence of activators MMAO-12 (modified methylalumoxane) and $[Ph_3C][B(C_6F_5)_4]$ and the development of a stereoselective one-pot method for the synthesis of functionally substituted alkene oligomers.

We found that the reaction of 1-hexene with $AlMe_3$ in the presence of complex *p*-*R*,*p*-*R*-**1** and activators (MMAO-12, $[Ph_3C][B(C_6F_5)_4]$) at specific ratios of reagents provided organometallic products **2** and **3** with a methyl starting group (Scheme 1). Their further oxidation and hydrolysis yielded alcohols **4** and **5**. Apparently, oligomers **3** are formed as a result of the sequential insertion of alkene molecules into the carbometalation product, which was formed at the initial stages of the reaction. The conversion of the substrate exceeds 97% within 72 h under the reaction conditions (Table 1). For monitoring the reaction course, the intermediate organoaluminium species **2** and **3** were subjected to hydrolysis or deuterolysis to give the corresponding hydrocarbons **6** and **7** which could be analyzed by GC-MS.

The composition of the reaction products significantly depended on the type of activator. For example, in the case of MMAO-12, the fraction of oligomers (**3**, $n = 2–6$) reached 63–81%, while the content of low-molecular-weight carboalumination product **2** remained at 18–34% (see Table 1, entries 1, 3). The use of $[Ph_3C][B(C_6F_5)_4]$ as an activator led to an increase in the fraction of oligomers to 94–98% (entries 2, 4). Hydroxy-substituted oligomers **5** obtained after oxidation and hydrolysis of the reaction mixture represented an enantiomerically enriched diastereomerically pure product (99% *dr*).



Scheme 1 *Reagents and conditions*: i, [Zr]/$AlMe_3$/MMAO-12/hexene ratio is 1 : 200 : 50 : (250–500); ii, [Zr]/$AlMe_3$/$[Ph_3C][B(C_6F_5)_4]$/hexene ratio is 1 : 200 : 0.6 : (250–500).

Table 1 Catalytic activity and chemoselectivity of systems based on *p-R,p-R*-**1** and activators (MAO-12 and $[Ph_3C][B(C_6F_5)_4]$) in the reaction of 1-hexene with $AlMe_3$ (toluene, 20 °C, 72 h).

Entry	Activator	Molar ratio [Zr]:$AlMe_3$: activator:alkene	Alkene conversion (%)	Composition of the reaction products (%)[a,b]						
				6	**7a** (*n* = 1)	**7b** (*n* = 2)	**7c** (*n* = 3)	**7d** (*n* = 4)	**7e** (*n* = 5)	**7f** (*n* = 6)
1	MMAO-12	1:200:50:250	>99	18	21	17	13	12	10	8
2	$[Ph_3C][B(C_6F_5)_4]$	1:200:0.6:250	>99	<1	23	18	18	16	14	9
3	MMAO-12	1:200:50:500	>99	34	19	22	12	12	–	–
4	$[Ph_3C][B(C_6F_5)_4]$	1:200:0.6:500	97	5	15	19	18	16	13	10

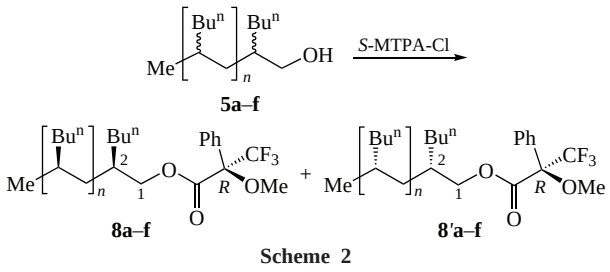
[a] Determined by GC-MS for the deuterolysis or hydrolysis products of the corresponding organoaluminium precursors **2** and **3a–f** (whose contents were considered close to those of the detected hydrocarbons **6** and **7a–f**, respectively). [b] Content of vinylidene products (2-methyl-1-hexene, dimers, and oligomers) and hydroalumination products (hexane) did not exceed 1% in all experiments.

Table 2 Enantioselectivity of the reaction of 1-hexene with $AlMe_3$ in the presence of *p-R,p-R*-**1** and activators.

Entry	Molar ratio [Zr]:$AlMe_3$: activator:alkene	Activator	*ee* (%) ($[\alpha]_D^{25}$, *c*/mg ml^{-1})		
			5a (*n* = 1)	**5b–d** (*n* = 2–4)	**5e,f** (*n* = 5, 6)
1	1:200:0.6:500	$[Ph_3C][B(C_6F_5)_4]$	38–42 (+6.9, 0.4)	68–73 (–1.7, 0.5)	75–88 (–5.6, 3.2)
2	1:200:50:500	MMAO-12	60–64 (+8.8, 0.7)	78–84 (–3.2, 0.16)	88–93 (–9.8, 0.6)

To determine the enantiomeric purity of oligomeric products, Mosher's reagent (MTPA)[18,19] was used as a derivatization agent. The enantiomeric purity of alcohols **5a–f** was assessed using ^{1}H and ^{19}F NMR spectroscopy of their MTPA esters **8a–f** and **8′a–f** (Scheme 2). In the ^{1}H NMR spectra of **8a–f/8′a–f** mixture, diastereomeric splitting for the proton signals at the C^1 atom was observed at 3.9–4.3 ppm (Figure 1). The ^{19}F NMR spectra exhibited double signals for the CF_3 groups in the range of –71.3 to –71.5 ppm.

An increase in the number of monomeric units in oligomers is accompanied by an increase in enantioselectivity in all experiments, regardless of the activator structure. However, the type of activator used in the reaction affects the enantioselectivity of alkene oligomerization (Table 2). For example, the reaction of alkenes with $AlMe_3$ in the presence of MMAO-12 proceeds with relatively low enantioselectivity at the level of 60–64% *ee* for oligomers **3** containing two monomeric units, and at the level of 78–84% *ee* for oligomeric products with *n* = 2–4 (see Table 2). The enantioselectivity of the reaction reaches 93% *ee* in oligomers with *n* = 5, 6. Replacement of MMAO-12 by $[Ph_3C][B(C_6F_5)_4]$ provides a decrease in enantioselectivity to 42, 73 and 88% *ee* for oligomers **3** with *n* = 1, *n* = 2–4 and *n* = 5, 6, respectively. Consequently, the use of a boron-containing activator $[Ph_3C][B(C_6F_5)_4]$ is accompanied by a loss of reaction enantioselectivity, averaging around 10–20% *ee*. The amount of substrate involved in the reaction does not significantly affect the enantiomeric excess of reaction products.



Scheme 2

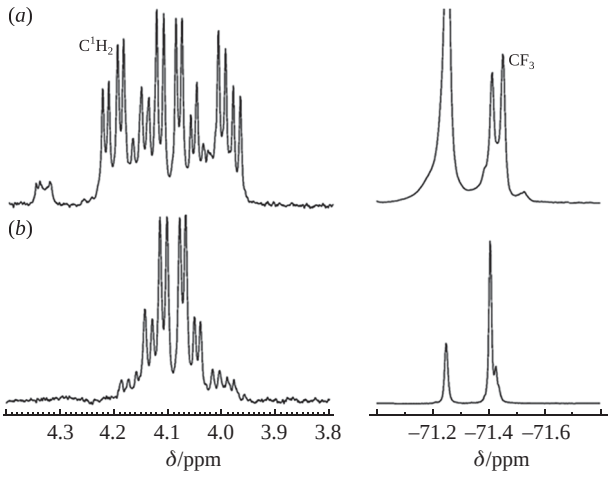


Figure 1 ^{1}H NMR (left) and ^{19}F NMR (right) spectra of MTPA esters **8b** and **8′b** containing two monomeric units obtained in the reaction of 1-hexene with $AlMe_3$ in the presence of (*a*) racemic *rac*-**1** and MMAO-12 and (*b*) enantiomerically pure *p-R,p-R*-**1** and MMAO-12.

As follows from the experimental data, the stereoselectivity of the oligomerization process in the studied catalytic systems is controlled by both the alkene coordination site and the growing chain, which aligns with the Corradini's model.[20] The data obtained also indicate the importance of considering the counterion in the stage of alkene insertion into catalytically active centers of the type $[L_2Zr^+Alk\cdots SLA]$ (SLA is strong Lewis acid). In the presence of the activator $[Ph_3C][B(C_6F_5)_4]$, the content of oligomeric products increases, indicating a potential acceleration of the reaction rate due to better separation of ion pairs. However, in this case, a reduction in enantioselectivity occurs, which can also be controlled through the counterion generated with the participation of the cocatalyst.[21]

In summary, a one-pot method has been developed for the chemo- and stereoselective synthesis of functionally substituted oligomers of 1-hexene with the Me-starting group. This strategy can be utilized for direct synthesis of structural units, *e.g.*, stereomerically pure fragments of biologically active compounds.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2024.01.018.

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