

# Zirconium-Catalyzed Enantioselective Alkylaluminum of Monosubstituted Alkenes Proceeding via Noncyclic Mechanism

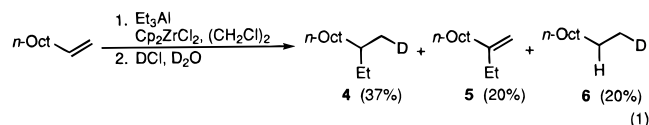
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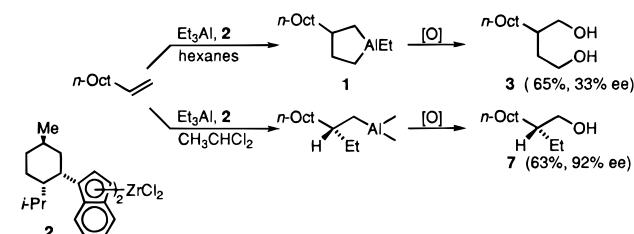
We recently reported a Zr-catalyzed enantioselective methylaluminum of monosubstituted alkenes.<sup>1</sup> In contrast, the initial outlook for achieving a similar Zr-catalyzed enantioselective alkylmetalation with ethyl-, propyl-, and higher alkylmetals was not promising. The reaction of monosubstituted alkenes with EtMgX, where X = Cl or Br, in the presence of a catalytic amount of Cp<sub>2</sub>ZrCl<sub>2</sub> was known to give (2-ethylalkyl)magnesium halides.<sup>2</sup> The reaction was later shown to proceed via a cyclic mechanism,<sup>3,4</sup> and its successful application to the development of a cyclic enantioselective carbometalation–elimination tandem reaction involving cyclic, allylic ethers and amines has been recently reported.<sup>5</sup> However, attempts to develop Zr-catalyzed enantioselective conversion of monosubstituted alkenes into (2-ethylalkyl)magnesium halides have led only to very disappointing results. Also known was the reaction of monosubstituted alkenes with Et<sub>3</sub>Al, catalyzed by Cp<sub>2</sub>ZrCl<sub>2</sub>, producing aluminacyclopentanes, *e.g.*, **1**,<sup>6</sup> but the reaction of 1-decene with 1 equiv of Et<sub>3</sub>Al in the presence of 8 mol % of dichlorobis(neomenthylindenyl)zirconium (**2**)<sup>7</sup> in hexanes produced, after oxidation, a 65% yield of 2-(*n*-octyl)-1,4-butanediol (**3**) in only 33% ee (Scheme 1).

Interestingly, the reaction of 1-decene with 1 equiv of Et<sub>3</sub>Al in the presence of 8 mol % of Cp<sub>2</sub>ZrCl<sub>2</sub> in (CH<sub>2</sub>Cl)<sub>2</sub> in place of hexanes produced, after deuteration, a 37% yield of 3-(deuteriomethyl)undecane (**4**), which contained D in the C-1 position only to the extent of 9%. The extent of D incorporation in the deuteriomethyl group was >90%. 2-Ethyl-1-decene (**5**) and 1-deuteriododecane (**6**) were also obtained in 20% yield each<sup>8</sup> (eq 1). Although synthetically unattractive, these results clearly



indicated that, in polar solvents, *e.g.*, (CH<sub>2</sub>Cl)<sub>2</sub>, noncyclic ethylaluminum similar to methylaluminum,<sup>1</sup> partially accompanied by competitive hydroalumination involving a (2-ethyldecyl)alane, can take place in preference to the previously reported cyclic carbometalation processes.<sup>2–6</sup> Following this intriguing lead, we treated 1-decene with Et<sub>3</sub>Al in (CH<sub>2</sub>Cl)<sub>2</sub> at 25 °C using 8 mol % of **2** as a catalyst and obtained, after oxidation with O<sub>2</sub>, a 65% yield of (*R*)-2-ethyl-1-decanol (**7**) in

Scheme 1



68% ee. In view of the dramatic solvent effects discussed above, various halogenated solvents were screened, and it was found that the use of CH<sub>3</sub>CHCl<sub>2</sub> or CH<sub>2</sub>Cl<sub>2</sub> in place of (CH<sub>2</sub>Cl)<sub>2</sub> boosted the % ee figures to the 80s, and they were further increased to the 90–95% range for various monosubstituted alkenes by merely lowering the reaction temperature to 0 °C. Some representative results are summarized in Table 1. The % ee figures were determined from the <sup>1</sup>H NMR spectra of the (+)- and (–)-MTPA esters. In most cases, the CH<sub>2</sub> group directly bonded to OH showed distinct signals for the two diastereomers. In the cases of (*R*)-2-ethyl-1-hexanol and (*R*)-2-ethyl-1-decanol, the CH<sub>3</sub> signals for the ethyl substituent were used for this purpose. As in the methylaluminum with Me<sub>3</sub>Al and **2**, alkylmetalation takes place selectively and uniformly on the re face of alkenes.<sup>9</sup> The optimized % ee figures range from 90 to 96% except for one case involving (*n*-Oct)<sub>3</sub>Al, where the product was 85% ee. Here again, the presence of remote hydroxy and amino groups may not significantly affect the course of reaction, and diallyldimethylsilane underwent an inter–intra tandem carbometalation exhibiting >92% de and 96% ee stereoselectivity figures. On the other hand, ethylaluminum of styrene gave an intractable product, and that of cyclohexylethene did not proceed over 12 h at 25 °C.

The highly favorable results observed in ethylaluminum in CH<sub>3</sub>CHCl<sub>2</sub> prompted us to reexamine the previously reported methylaluminum<sup>1</sup> in this solvent. Under otherwise the same conditions, the reaction of 1-octene with Me<sub>3</sub>Al in the presence of 8 mol % of **2** at 25 °C in CH<sub>3</sub>CHCl<sub>2</sub> gave, after oxidation, an 83% yield of (*R*)-2-methyl-1-octanol in 81% ee, corresponding to an increase by roughly 10% in % ee.<sup>1</sup> Evidently, % ee figures for ethylaluminum are 10–15% higher than the corresponding figures for methylaluminum under comparable conditions. On the other hand, the yields of ethylaluminum are slightly but unmistakably lower than those of methylaluminum. A detailed analysis of the products of the above reaction indicated the presence of 3-methylundecane (17%), decane (2%), and the unreacted 1-decene (2%). No more than traces, if any, of 2-ethyl-1-decene and dimeric products were present. Clearly, the lower yield is not due to competitive hydrometalation. Since the results of deuteration with DCl–D<sub>2</sub>O closely parallel those of oxidation, the origin of 3-methylundecane does not appear to be due to incomplete oxidation. It must have been formed during the carboalumination itself. The use of (CH<sub>2</sub>Cl)<sub>2</sub> and CH<sub>2</sub>Cl<sub>2</sub> led to its formation in 12 and 11%, respectively. The fact that the reaction run in CD<sub>2</sub>Cl<sub>2</sub> followed by protonolysis with 3 N HCl does not incorporate D suggests that the solvents

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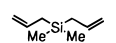
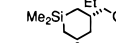
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(8) The amounts of possible dimeric products, such as 2-(*n*-octyl)-dodecane and 2-(*n*-octyl)-1-dodecene, were ≤1–2%, if any.

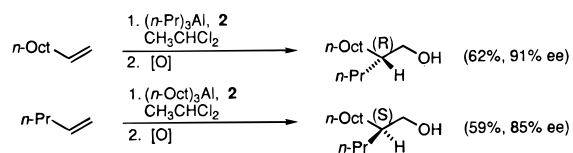
(9) The absolute configurations of (*R*)-2-ethyl-1-hexanol (Barth, S.; Effenberger, F. *Tetrahedron Asymmetry* **1993**, *4*, 823), (*R*)-5-methyl-1-octanol (Sonnet, P. E.; Gazzillo, J. A.; Dudley, R. L.; Boswell, R. T. *Chem. Phys. Lipids* **1990**, *54*, 205), and (*R*)-5-methyl-1-heptanol (Chattopadhyay, S.; Mamdapur, V. R.; Chadha, M. S. *Synth. Commun.* **1990**, *20*, 825) were assigned by comparing the observed optical rotation signs and magnitudes with those reported in the literature. The other assignments are more tentative and are based, in part, on empirical predictions [(a) Brewster, J. H. *J. Am. Chem. Soc.* **1959**, *81*, 5475. (b) Marker, R. E. *J. Am. Chem. Soc.* **1936**, *58*, 976]] and experimental observation of optical rotation signs and, in part, on an assumption that the uniform sign of the observed optical rotation is an indication that the face selection remains the same for all cases herein reported.

**Table 1.** Zirconium-Catalyzed Alkylaluminumation of Monosubstituted Alkenes<sup>a</sup>

| substrate                                                                         | R of R <sub>3</sub> Al    | solvent                                                                           | temp °C | time h | quenching agent | product                                                                           | yield <sup>b</sup> % | %ee |
|-----------------------------------------------------------------------------------|---------------------------|-----------------------------------------------------------------------------------|---------|--------|-----------------|-----------------------------------------------------------------------------------|----------------------|-----|
| <i>n</i> -Bu                                                                      | Et                        | (CH <sub>2</sub> Cl) <sub>2</sub>                                                 | 25      | 4      | O <sub>2</sub>  | <i>n</i> -Bu-CH(OH)-Et                                                            | 65                   | 68  |
| <i>n</i> -Bu                                                                      | Et                        |  | 25      | 4      | O <sub>2</sub>  | <i>n</i> -Bu-CH(OH)-Et                                                            | 70                   | 68  |
| <i>n</i> -Bu                                                                      | Et                        |  | 25      | 4      | O <sub>2</sub>  | <i>n</i> -Bu-CH(OH)-Et                                                            | 72                   | 67  |
| <i>n</i> -Bu                                                                      | Et                        | CH <sub>2</sub> Cl <sub>2</sub>                                                   | 25      | 6      | O <sub>2</sub>  | <i>n</i> -Bu-CH(OH)-Et                                                            | 57                   | 81  |
| <i>n</i> -Bu                                                                      | Et                        | CH <sub>2</sub> Cl <sub>2</sub>                                                   | 0       | 6      | O <sub>2</sub>  | <i>n</i> -Bu-CH(OH)-Et                                                            | 63                   | 92  |
| <i>n</i> -Bu                                                                      | Et                        | CH <sub>2</sub> Cl <sub>2</sub>                                                   | -25     | 6      | O <sub>2</sub>  | <i>n</i> -Bu-CH(OH)-Et                                                            | 60                   | 94  |
| <i>n</i> -Bu                                                                      | Et                        | CH <sub>3</sub> CHCl <sub>2</sub>                                                 | 25      | 6      | O <sub>2</sub>  | <i>n</i> -Bu-CH(OH)-Et                                                            | 70                   | 86  |
| <i>n</i> -Bu                                                                      | Et                        | CH <sub>3</sub> CHCl <sub>2</sub>                                                 | 0       | 24     | O <sub>2</sub>  | <i>n</i> -Bu-CH(OH)-Et                                                            | 74                   | 93  |
| <i>n</i> -Oct                                                                     | Et                        | CH <sub>3</sub> CHCl <sub>2</sub>                                                 | 0       | 12     | O <sub>2</sub>  | <i>n</i> -Oct-CH(OH)-Et                                                           | 64                   | 92  |
| <i>i</i> -Bu                                                                      | Et                        | CH <sub>3</sub> CHCl <sub>2</sub>                                                 | 0       | 24     | O <sub>2</sub>  | <i>i</i> -Bu-CH(OH)-Et                                                            | 77                   | 90  |
| Ph                                                                                | Et                        | CH <sub>3</sub> CHCl <sub>2</sub>                                                 | 0       | 24     | O <sub>2</sub>  | Ph-CH(OH)-Et                                                                      | 69                   | 93  |
| HO(CH <sub>2</sub> ) <sub>4</sub>                                                 | Et <sup>c</sup>           | CH <sub>3</sub> CHCl <sub>2</sub>                                                 | 10      | 24     | HCl             | HO(CH <sub>2</sub> ) <sub>4</sub> -CH(OH)-Et                                      | 88                   | 90  |
| Et <sub>2</sub> N(CH <sub>2</sub> ) <sub>3</sub>                                  | Et <sup>d</sup>           | CH <sub>3</sub> CHCl <sub>2</sub>                                                 | 25      | 72     | O <sub>2</sub>  | Et <sub>2</sub> N(CH <sub>2</sub> ) <sub>3</sub> -CH(OH)-Et                       | 56                   | 95  |
|  | Et                        | CH <sub>3</sub> CHCl <sub>2</sub>                                                 | 0       | 24     | O <sub>2</sub>  |  | 66                   | 96  |
| HO(CH <sub>2</sub> ) <sub>4</sub>                                                 | <i>n</i> -Pr <sup>c</sup> | CH <sub>3</sub> CHCl <sub>2</sub>                                                 | 10      | 24     | HCl             | HO(CH <sub>2</sub> ) <sub>4</sub> -CH(OH)- <i>n</i> -Pr                           | 90                   | 91  |
| <i>n</i> -Oct                                                                     | <i>n</i> -Pr              | CH <sub>3</sub> CHCl <sub>2</sub>                                                 | 0       | 12     | O <sub>2</sub>  | <i>n</i> -Oct-CH(OH)- <i>n</i> -Pr                                                | 62                   | 91  |
| <i>n</i> -Pr                                                                      | <i>n</i> -Oct             | CH <sub>3</sub> CHCl <sub>2</sub>                                                 | 0       | 12     | O <sub>2</sub>  | <i>n</i> -Pr-CH(OH)- <i>n</i> -Oct                                                | 59                   | 85  |

<sup>a</sup> The reactions were run using 8 mol % of **2** and 1 equiv of R<sub>3</sub>Al, unless otherwise stated. <sup>b</sup> Isolated yields. <sup>c</sup> Three-fold excess of R<sub>3</sub>Al was used. <sup>d</sup> Two-fold excess of R<sub>3</sub>Al was used.

are not likely to be the sources of hydrogen. One likely process that might be responsible for the formation of 3-methylundecane is M–H exchange via  $\sigma$ -bond metathesis,<sup>10</sup> although this point needs to be further clarified.

**Scheme 2**

As expected, the scope of this reaction is not restricted to ethylaluminumation. Thus, the reaction of 5-hexen-1-ol with 3 equiv of (*n*-Pr)<sub>3</sub>Al in CH<sub>3</sub>CHCl<sub>2</sub> in the presence of 8 mol % of **2** at 10 °C for 24 h provided, after protonolysis, a 90% yield of (*R*)-5-methyl-1-octanol<sup>11</sup> in 91% ee. It is worth noting that the *n*-Pr group of (*n*-Pr)<sub>3</sub>Al is incorporated as such. Any cyclic processes involving alkene–zirconocene derivatives would incorporate the same group as an *i*-Pr group.<sup>5,12</sup> Both *R* and *S* isomers of 2-(*n*-propyl)-1-decanol can be prepared by *n*-propylaluminumation of 1-decene and *n*-octylaluminumation of 1-pentene, respectively, using the same catalyst **2** (Scheme 2).

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**Supporting Information Available:** Representative procedure for the synthesis of (*R*)-2-ethyl-1-hexanol; spectral data as well as optical rotation and % ee figures for all isolated products listed in Table 1; and representative <sup>1</sup>H NMR spectra for several compounds (29 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm 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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