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Zirconium-Catalyzed Enantioselective Methylalumination of Monosubstituted Alkenes

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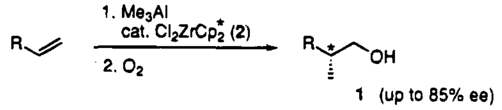
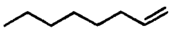
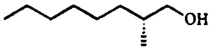
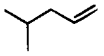
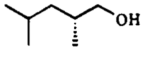
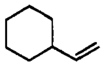
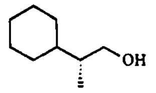
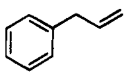
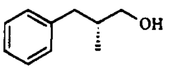
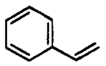
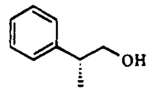
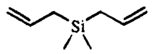
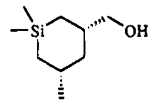
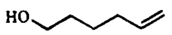
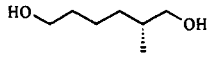
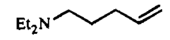
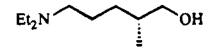
Catalytic enantioselective carbon−carbon bond formation involving simple alkenes without heteroatom functional groups represents a highly desirable but formidable synthetic task.[1] Aside from the long-known asymmetric cyclopropanation catalyzed by various late transition metal complexes,[2] the currently known reactions of this class, including asymmetric carbonyl ene reaction,[3] asymmetric hydroformylation,[4] and asymmetric hydrocyanation,[5] have been reported only within the last several years. It should also be noted that the scope of the carbonyl ene reaction is essentially limited to 1,1-dialkyl-substituted alkenes, and that of the latter two appears to be limited to vinylarenes.

We now report that the reaction of various monosubstituted alkenes containing hydrocarbon substituents as well as those containing heteroatom substituents with Me_3Al and a catalytic amount of a chiral zirconocene derivative provides, after oxidation with O_2, 2-methyl-1-alkanols **1** in generally high yields with up to 85% ee (typically 70−75% ee) (eq 1).[6]



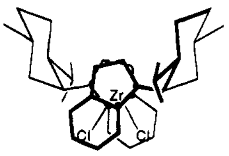
(1)

Table 1. Zirconium-Catalyzed Methylalumination of Monosubstituted Alkenes^a

substrate	time, h	product	yield,^{b} %	ee, %
	12		88	72
	12		92	74
	12		80	65
	24		77	70
	528		30	85
	12		81	74
	12^c		79	75
	96^d		68	71

^{a} The reactions were run using 8 mol % of **2** and 1 equiv of Me_3Al in 1,2-dichloroethane at 22 °C. ^{b} Isolated yields. ^{c} Three-fold excess of Me_3Al was used. ^{d} Two-fold excess of Me_3Al was used.

Typically, 1-octene was treated with 1 molar equiv of Me_3Al in 1,2-dichloroethane and dichlorobis(1-neomenthylindenyl)-zirconium (**2**)[7] (8 mol %) at 22 °C for 12 h under 1 atm of Ar.



2

Oxygen was then bubbled through the reaction mixture (30 min, 0 °C), and the resultant mixture was further stirred for 6 h under oxygen. After treatment with 15% aqueous NaOH, the usual extractive workup and Kugelrohr distillation provided (2*R*)-2-methyl-1-octanol[8] (88% yield) in 72% ee as determined from the ^1H and ^{13}C NMR spectra of the ester derived from (+)- and (−)-MTPA, *i.e.*, α-methoxy-α-(trifluoromethyl)phenylacetic acid, using the standard procedure.[9,10] The experimental results obtained with **2** used as a catalyst are summarized in Table 1. The observed success critically hinges on a series of highly unexpected and fortunate circumstances. We earlier reported the Zr-catalyzed methylalumination of alkynes,[11] which was shown to proceed via direct addition of the Me−Al bond assisted by a Zr catalyst.[12] We then found that the corresponding reaction of monosubstituted alkenes with $Me_3Al-Cl_2ZrCp_2$ did not give the expected methylaluminated products in detectable yields. It should be noted along this line that $i\text{-}Bu_3Al-Cl_2ZrCp_2$ is a convenient reagent system for hydroalumination, rather than carboalumination, of monosubstituted alkenes,[13] for which the mechanism shown in Scheme 1 appears to be plausible. Although not definitively established, a six-centered transition state represented by **3** may be proposed. Reinvestigation of the reaction of 1-octene with Me_3Al (1 molar equiv) and Cl_2ZrCp_2 (8 mol %) has now revealed that the products obtained after protonolysis consist of 2-(*n*-hexyl)-1-decene (**4**), which accounts for 59% of 1-octene and 2-methyl-1-octene (18%), the yield of the desired 2-methyloctane being <2%.

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(10) $[\alpha]^{20}_D$ +7.4° (*c* 15.9, CH_2Cl_2) [lit.[8a] $[\alpha]^{20}_D$ +11.17° (*c* 4.7, CH_2Cl_2)].

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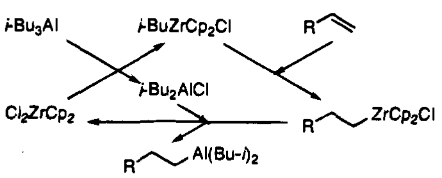
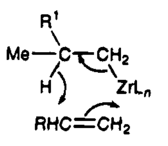
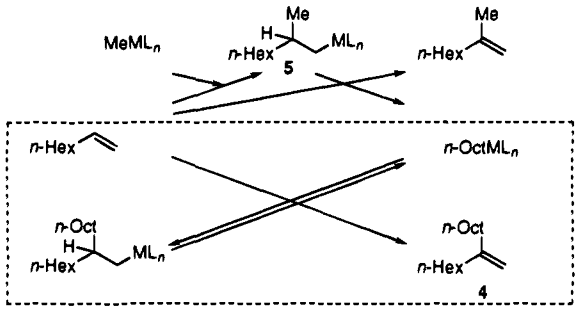
Scheme 1





3

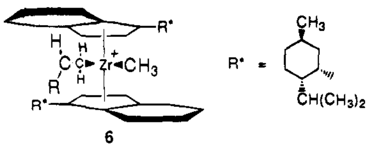
Scheme 2



MLₙ = Zr and/or Al group

Evidently, the initially formed 2-methyloctylmetal (**5**) containing Al and/or Zr readily reacts with 1-octene to induce hydrometalation similar to that shown in Scheme 1, to give 2-methyl-1-octene and an *n*-octylmetal derivative. The latter undergoes carbometalation with 1-octene to give a 2-(*n*-hexyl)-1-decylmetal derivative, which then undergoes hydrometalation with 1-octene to complete a catalytic cycle producing **4** (Scheme 2).

On the basis of the above mechanistic interpretation, it appears likely that the hydride transfer process between the initially formed methylmetalated product **5** and the starting 1-alkene must be blocked in order to obtain **5** in high yield. For yet unclear reasons, the bulky chiral ligands, *e.g.*, **2**, must be effective for this purpose. It is likely that, by virtue of their large steric requirements, they effectively block the six-centered interaction depicted in **3**. The observed high ee figures are also difficult to explain in terms of direct addition of the Me−Al bond assisted by zirconocene derivatives observed in the Zr-catalyzed methylalumination of alkynes.[12,14] On the other hand, the results appear to be more consistent with direct Me−Zr bond addition promoted by organoaluminium species, in line with the widely believed mechanism for the homogeneous Ziegler−Natta-type reactions.[15] In the light of the X-ray structure of **2**,[7a] the uniformly observed *R* configuration of 2-methyl-1-alkanols **1** in cases where **2** was the catalyst not only is consistent with the four-centered *syn* Me−Zr addition, as depicted in **6**, but also lends further support for the direct Me−Zr bond addition mechanisms. The X-ray structure of **2** indicates that the four octants on the back side are not available for chemical transformations. In the transition state model **6**, both Zr−CH_3 σ orbital and empty orbitals are on the front side. The upper right and lower left octants are more open than the other two and hence accommodate the R group of a monosubstituted alkene, leading to Zr−alkene interaction on the *Re* face of the alkene and subsequent formation of a (2*R*)-2-methyl-1-alkanol. Yet another fortunate aspect critical to the development of the reaction shown in eq 1 is that methylalanes can undergo Zr-catalyzed methylalumination with alkenes, which is totally discrete from the known reaction of ethylalanes producing 3-alkylaluminacyclopentanes via cyclic carbozirconation.[16] In fact, the reaction of 1-octene with Et_3Al (1 molar equiv) and **2** (8 mol %) in hexanes gave, after oxidation, a 69% yield of 2-(*n*-hexyl)-1,4-butanediol in only 36% ee.[17]



6

As indicated in Table 1, the methylalumination of monosubstituted alkenes with Me_3Al and a catalytic amount of **2** promises to be reasonably general with respect to the substituent in the starting alkenes. Thus, those containing *n*-Hex, *i*-Bu, cyclohexyl, and benzyl were converted to the corresponding (2*R*)-2-methyl-1-alkanols of 65−75% ee in 77−92% yields. Styrene was converted to (2*R*)-2-phenyl-1-propanol of 85% ee albeit in low yield (30%). Particularly encouraging are the results observed with heteroatom-containing 1-alkenes. Both 5-hexen-1-ol and 4-pentenyldiethylamine proceeded normally and satisfactorily to give the corresponding 2-methyl-1-alkanols of 75 and 71% ee, respectively, while diallyldimethylsilane provided (3,3,5-trimethyl-3-silacyclohexyl)methanol,[18] which was >95% *cis* and 74% ee, in 81% yield. Only 3,3-dimethyl-1-butene has thus far failed to undergo this reaction.

Although our search for more satisfactory chiral catalysts is ongoing, the other chiral catalysts tested thus far in this study have been less satisfactory. Specifically, the reaction of 1-octene with Me_3Al (1 molar equiv) in the presence of 8 mol % of bis(1-neoisomenthylindenyl)zirconium dichloride,[7a] bis(1-neoisomentyl-4,5,6,7-tetrahydroindenyl)zirconium dichloride,[7a] (*R,R*)-ethylenebis(4,5,6,7-tetrahydro-1-indenyl)zirconium dichloride,[19] and (*R,R*)-ethylenebis(4,5,6,7-tetrahydro-1-indenyl)zirconium (*R*)-1′,1″-bi-2-naphtholate[19] gave 2-methyl-1-octanol of 50% ee (*S*, 67%), 6% ee (*S*, 60%), 8% ee (*R*, 45%), and 6% ee (*R*, 53%), respectively, in the yields shown in parentheses.

In view of a large number of natural products that are either represented by or accessible via 2-methyl-1-alkanols, the potential synthetic significance of this reaction is evident. Futher improvement of the procedure and exploration of the scope are currently underway.

Acknowledgment. We thank the National Science Foundation (CHE-9402288) for support of this research.

Supporting Information Available: Representative experimental procedure and characterization data for the alcohols described herein (3 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be obtained 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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(14) We believe that the mechanism of the Zr-catalyzed methylalumination reaction of alkenes and alkynes must be mutually distinct, although this point is under further investigation.

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