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The Cp_2ZrCl_2-catalyzed cycloalumination of functionally substituted olefins with triethylaluminum

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Reactions of functionally substituted olefins (allylamines, sulfides and ethers, homoallylic alcohols and amines, as well as vinyl ethers) with Et_3Al in the presence of Cp_2ZrCl_2 as a catalyst were studied. Cycloalumination of allylamines occurs with high regioselectivity to furnish after subsequent deuterolysis 4-deutero-2-(deuteromethyl)butyl-substituted amines. Cycloalumination of alkyl allyl sulfide is accompanied by a side process of the C—S bond cleavage. In the case of allyl and vinyl ethers, no cycloalumination products are formed under the reaction conditions. However, the reactions with homoallylic alcohol and amine after deuterolysis gave the corresponding dideutero-containing compounds in good yields.

Key words: cycloalumination, functionally substituted olefins, aluminacyclopentanes.

Reactions of α-olefins and acetylenes with Et_3Al catalyzed with Cp_2ZrCl_2 and known as a cycloalumination reaction is a unique method for the synthesis of aluminacyclopentanes and aluminacyclopentenes.[1,2] Zirconium chiral complexes $Cp(NMI)ZrCl_2$ (NMI is the 1-neomenthylindenyl) and $[ETBHI]ZrCl_2$ (ETBHI is the (*R*,*R*)-ethylene-1,2-bis(η^5-4,5,6,7-tetrahydro-1-indenyl)) catalyze reactions of Et_3Al with allyl phenyl sulfide and 2,5-dihydrofuran.[3] However, there are still absent the data concerning cycloalumination of vinyl, allyl, and homoallylic alcohols and amines, whose transformation would have allowed one to develop new one-pot methods for the synthesis of functionally substituted cyclobutanes, cyclopentanols, and tetrahydrothiophenes.[4] Earlier,[5] we have studied a Cp_2ZrCl_2-catalyzed reaction of acetylene alcohols and propargylamines with Et_3Al. It was found that the presence of a hydroxy or amine function in the molecule of acetylene compound does not interfere cycloalumination and formation of 2,3-disubstituted aluminacyclopent-2-enes. In this connection and in order to develop an efficient method for the synthesis of functionally substituted aluminacyclopentanes, we studied the reaction of vinyl, allyl, and homoallylic compounds with Et_3Al in the presence of Cp_2ZrCl_2 in catalytic amounts.

It was found that the reaction of allylamines (*N*-allylcyclohexylamine, *N*-allyl-*tert*-octylamine, *N*-allylpiperidine) with 1 equiv. of Et_3Al in the presence of Cp_2ZrCl_2 (10 mol.%) in hexane for 8 h at 40 °C after subsequent deuterolysis leads to the corresponding 4-deutero-2-(deuteromethyl)butyl-substituted amines **1a—c** in 64—83% yields (Scheme 1). Cycloalumination of the unsaturated bond proceeds regioselectively. The structures of the deuterolysis products were established by one- and two-dimensional NMR spectroscopy. The ^{13}C NMR spectrum of compound **1a** exhibits two triplets for the deutero-substituted carbon atoms at δ 11.00 ($^1J_{C,D}$ = 19 Hz) and 17.45 ($^1J_{C,D}$ = 19 Hz). Two multiplets for the diastereotopic hydrogen atoms of the methylene group at the nitrogen atom have a cross-peak with the hydrogen atom on the tertiary carbon atom at the CH_2D group in the COSY spectrum. In the HMBC spectrum, the multiplets mentioned have cross-peaks with the signal for the tertiary carbon atom of the cyclohexane ring, the methylene carbon atom of the 2-deuteroethyl fragment, the tertiary carbon atom at the CH_2D group, as well as with the triplet signal for the CH_2D group at δ 17.45. Compounds **1b**,**c** were identified similarly. The numeration of the carbon atoms used in the description of the NMR spectra of deuterolysis products **1a—c** is shown in Fig. 1.

It is interesting to note that allylphenylamine and diallylphenylamine showed no activity in the reaction under study. Unsubstituted diallylamine gave cycloalumination product straight at the two double bonds. After deuterolysis of the reaction mixture, the tetradeutero-substituted amine **2** was isolated in 69% yield. However, the reaction with diallyl(*tert*-octyl)amine involves only one double bond to yield after deuterolysis a dideutero-containing unsaturated amine **3** (see Scheme 1).

Catalytic cycloalumination of allyl heptyl sulfide gives lower yields (Scheme 2). After deuterolysis of the reaction mixture, d_1-heptanethiol **5** was found in the mixture (the yield was 28%) together with dideuterated derivative **4** (the yield was 53%). The ^{13}C NMR spectrum of com-

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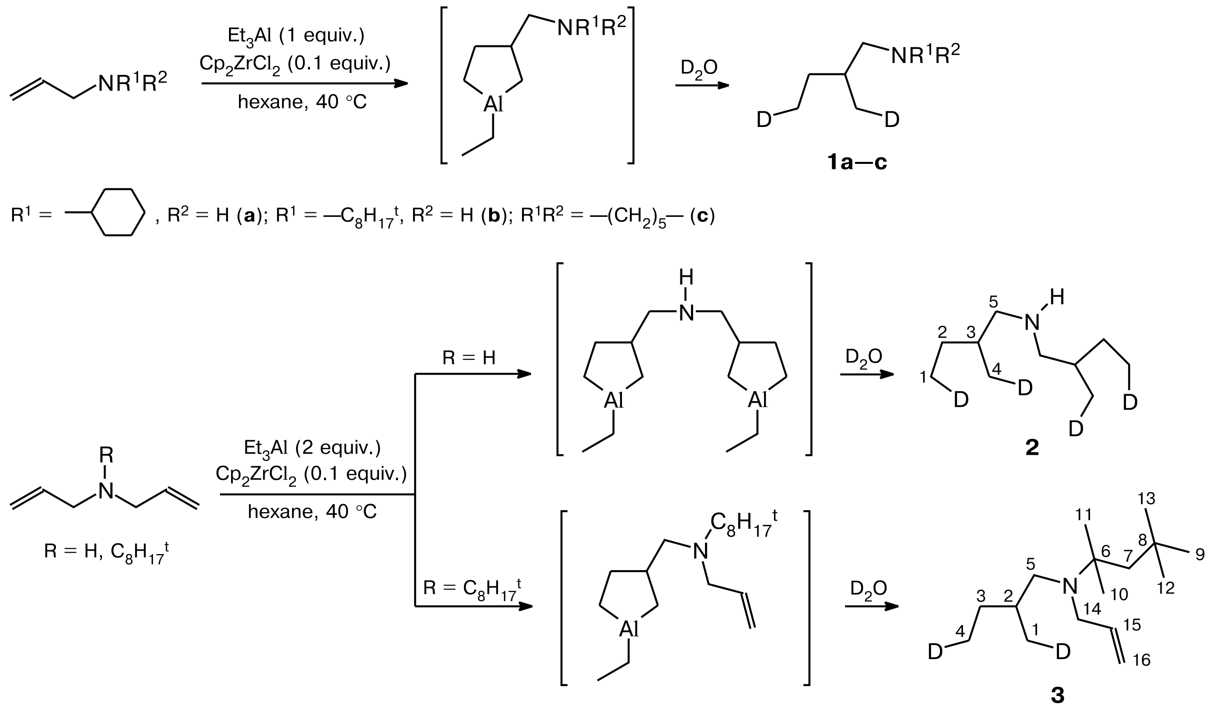
Scheme 1



pound **4** exhibits two triplets for the CH_2D group at δ 11.01 ($^1J_{C,D}$ = 19 Hz) and 18.66 ($^1J_{C,D}$ = 19 Hz).

According to the mechanism of the cycloalumination reaction suggested earlier,[1,6] one of the steps consists in the formation of zirconocene-ethylene complex **A** (Scheme 3), which by the reaction with allyl sulfide is converted either to zirconacyclopropane **B**, or to zirconacyclopentane **C**. Apparently, heptanethiol is formed by β-elimination of a sulfide group from the intermediate **B**. Such a phenomenon has been observed earlier[7] in the reaction of Negishi reagent with allyl ethers, therefore, we assume that cleavage of the carbon—oxygen bond will occur in the case of allyl and vinyl ethers under condition of the studied by us reaction. In fact, because of higher disposition of an alkoxy group to elimination, we failed to involve alkyl allyl and alkyl vinyl ethers into the cycloalumination reaction. In the reaction of allyl *n*-undecyl ether with Et_3Al in the presence of a catalytic amount of Cp_2ZrCl_2 under conditions indicated above after subsequent hydrolysis of the reaction mixture, undecyl alcohol was obtained in quantitative yield, whereas butyl vinyl ether in the reaction under study after hydrolysis gave *n*-butyl alcohol.

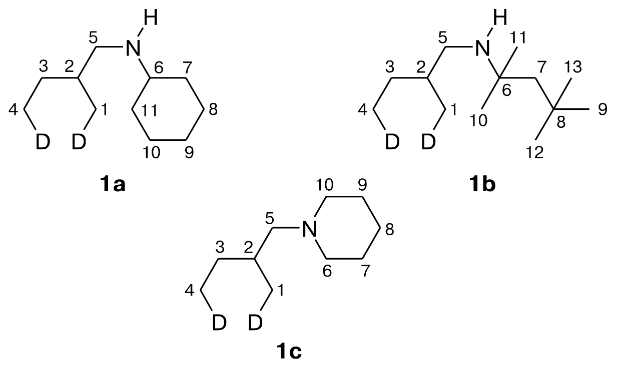


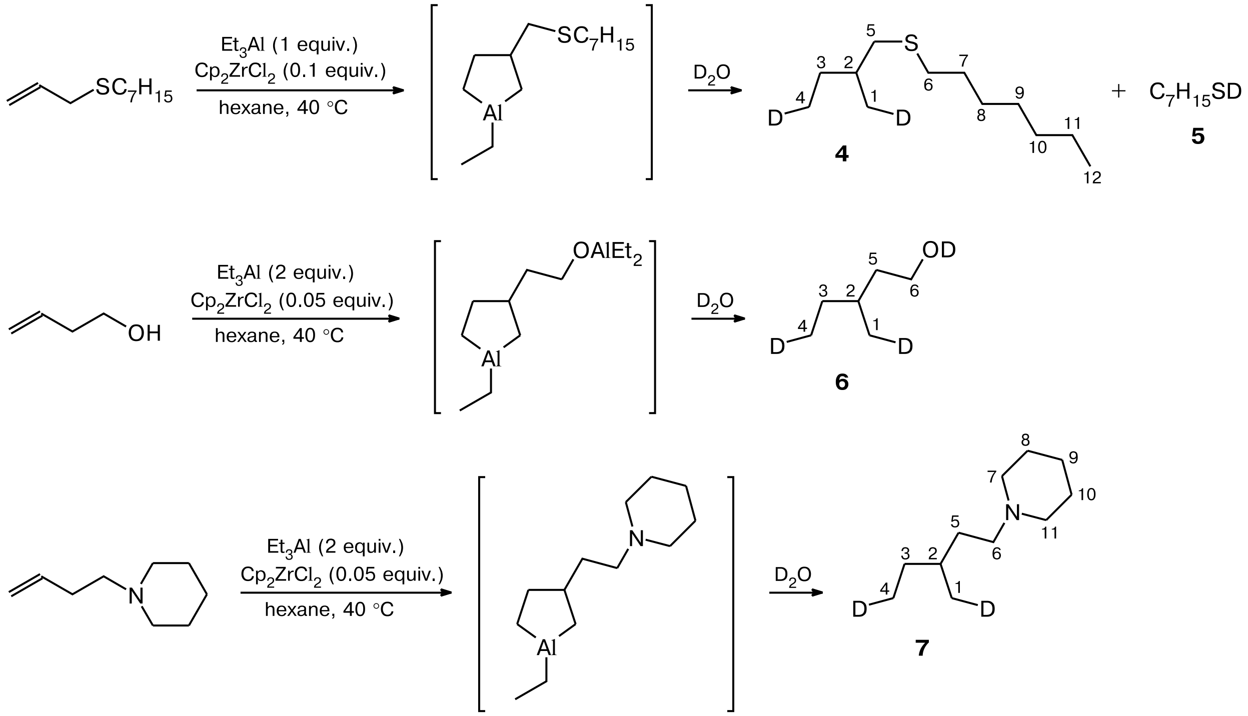
Fig. 1. The numeration of carbon atoms used in the description of the NMR spectra of the deuterolysis products **1a**—**c**.

However, when homoallylic alcohol (3-buten-1-ol) was involved into the reaction with subsequent deuterolysis of the reaction mixture, a deutero-containing alcohol **6** was obtained in 79% yield (see Scheme 2). Thus, when two methylene units are present between a double bond and a hydroxy group, cycloalumination is not accompanied by a side elimination reaction. Substituted homoallylic amine (1-(3-butenyl)piperidine) behaves similarly in the cycloalumination reaction. After deuterolysis, a dideutero-containing amine **7** was isolated in good yield (85%).

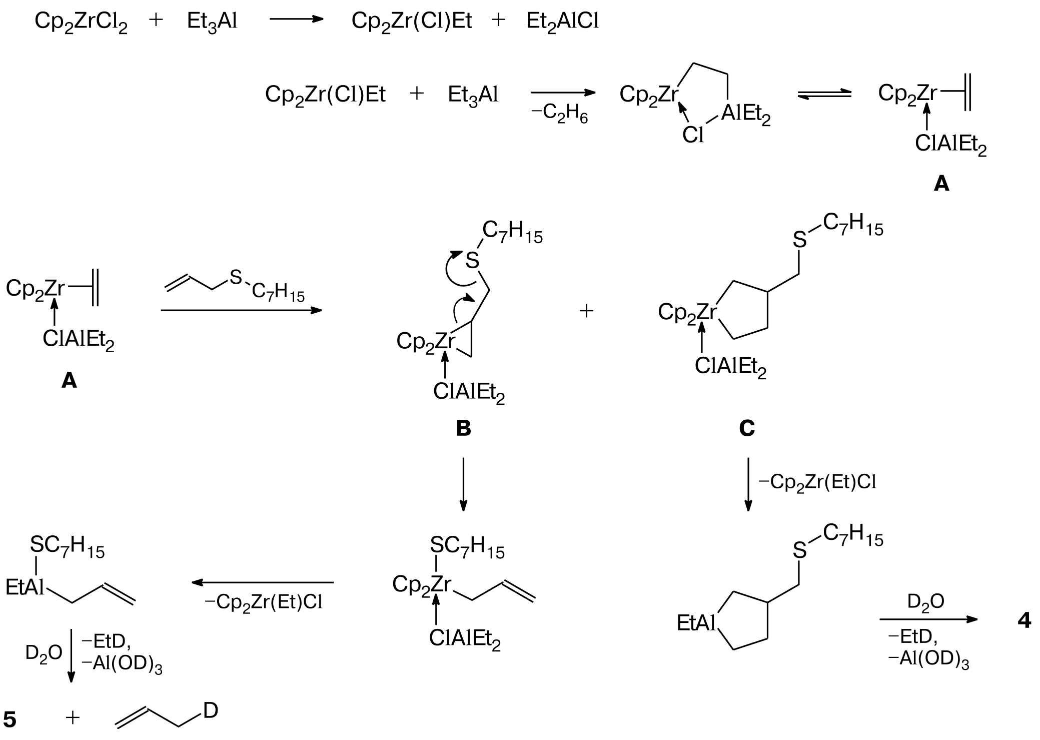
Experimental

Commercially available reactants were used in this work. Reactions with organoaluminum compounds were carried out under dry argon. Hexane was distilled over Bu^i_3Al. Mono- and diallylamines were obtained by the reaction of allyl bromide with secondary and primary amines upon the action of NaH.[8] Allyl heptyl sulfide was synthesized by allylation of heptanethiol.[9] 1-(3-Butenyl)piperidine was obtained by aminomethylation of allyl bromide.[10] Reaction products were analyzed on a Carlo Erba chromatograph (using a 25 m × 0.2 mm Ultra-1 glass

Scheme 2



Scheme 3



capillary column (Hewlett Packard), flame-ionizing detector, operating temperature of 50—170 °C, and helium as a carrier gas). Mass spectra were measured on a Finnigan 4021 instrument (70 eV), the temperature of injector was 200 °C. Elemental analysis was performed on a Carlo Erba model 1106 elemental analyser. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 spectrometer (400.13 and 100.62 MHz, respectively), using $SiMe_4$ and $CDCl_3$, respectively, as internal standards. The product yields were determined by GLC using undecane or hexadecane as internal standards.

Cycloalumination of *N*-allylamines, *N*,*N*-diallylamines, and allyl heptyl sulfide (general procedure). Allylic compound (1 mmol), Cp_2ZrCl_2 (0.029 g, 0.1 mmol), hexane (3 mL), and Et_3Al (1 mmol, or 2 mmol in the case of *N*,*N*-diallylamines) were sequentially placed under argon into a 50-mL glass reactor equipped with a magnetic stirrer and heated using a water bath to 40 °C, and the mixture was stirred for 8 h at 40 °C.

Deuterolysis of aluminacyclopentanes (general procedure). Hexane (5 mL) was added to the reaction mixture obtained by the procedure described above, followed by a dropwise addition of D_2O (3 mL) with cooling of the reactor in an ice bath. A precipitate that formed was filtered off using a paper filter. The aqueous layer was extracted with diethyl ether, the extract was combined with the organic layer, dried with anhydrous $CaCl_2$, and concentrated *in vacuo*. Individual compounds **1a**—**c** and **2**—**5** were isolated by distillation at reduced pressure.

1-[4-Deutero-2-(deuteromethyl)butyl]cyclohexylamine (1a). Clear oily liquid. The yield was 64%, b.p. 93—95 °C (10 Torr). Found (%): C, 75.93; N, 8.01. $C_{11}H_{21}D_2N$. Calculated (%): C, 77.12; N, 8.18. ^{1}H NMR, δ: 0.85—0.95 (m, 4 H, C(1)H_2D, C(4)H_2D); 1.00—1.35 (m, 6 H, C(3)H_a, C(7)H_a—C(11)H_a); 1.35—1.45 (m, 1 H, C(3)H_b); 1.45—1.55 (m, 1 H, C(2)H); 1.60—1.65 (m, 1 H, C(9)H_b); 1.70—1.80 (m, 2 H, C(8)H_b, C(10)H_b); 1.85—1.95 (m, 2 H, C(7)H_b, C(11)H_b); 2.35—2.45 (m, 2 H, C(5)H_a, C(6)H); 2.50—2.60 (m, 1 H, C(5)H_b). ^{13}C NMR, δ: 11.00 (t, C(1), $^1J_{C,D}$ = 19 Hz); 17.45 (t, C(4), $^1J_{C,D}$ = 19 Hz); 25.14 (2 C, C(8), C(10)); 26.24 (C(9)); 27.49 (C(3)); 33.67, 33.76 (2 C, C(7), C(11)); 34.93 (C(2)); 53.19 (C(5)); 56.99 (C(6)). MS, *m/z*: 172 $[M + 1]^+$ (2), 171 $[M]^+$ (6), 170 $[M - 1]^+$ (2), 141 $[M - Et]^+$ (1), 128 (18), 127 (6), 113 (10), 112 (100) [*cyclo*-$C_6H_{11}NHCH_2]^+$.

1-[4-Deutero-2-(deuteromethyl)butyl]-*tert*-octylamine (1b). Clear oily liquid. The yield was 79%, b.p. 59—61 °C (1 Torr). Found (%): C, 76.21; N, 6.17. $C_{13}H_{27}D_2N$. Calculated (%): C, 77.53; N, 6.96. ^{1}H NMR, δ: 0.85—0.95 (m, 4 H, C(1)H_2D, C(4)H_2D); 1.02 (s, 9 H, C(9)H_3, C(12)H_3, C(13)H_3); 1.13 (s, 6 H, C(10)H_3, C(11)H_3); 1.10—1.20 (m, 1 H, C(3)H_a); 1.43 (s, 2 H, C(7)H_2); 1.40—1.50 (m, 2 H, C(2)H, C(3)H_b); 2.25—2.60 (m, 2 H, C(5)H_2). ^{13}C NMR, δ: 11.06 (t, C(4), $^1J_{C,D}$ = 19 Hz); 17.62 (C(1)); 27.68 (C(3)); 28.84, 28.95 (2 C, C(10), C(11)); 31.80 (3 C, C(9), C(12), C(13)); 35.84 (C(2)); 48.01 (C(5)); 53.59 (C(7)); 53.94 (C(6)).

1-[4-Deutero-2-(deuteromethyl)butyl]piperidine (1c). Clear oily liquid. The yield was 83%, b.p. 65—67 °C (10 Torr). Found (%): C, 76.04; N, 8.99. $C_{10}H_{19}D_2N$. Calculated (%): C, 76.36; N, 8.90. ^{1}H NMR, δ: 0.80—0.90 (m, 4 H, C(1)H_2D, C(4)H_2D); 1.00—1.15 (m, 2 H, C(3)H_2); 1.35—1.50 (m, 3 H, C(2)H, C(8)H_2); 1.50—1.65 (m, 4 H, C(7)H_2, C(8)H_2); 1.95—2.15 (m, 2 H, C(5)H_2); 2.20—2.40 (m, 4 H, C(6)H_2, C(10)H_2). ^{13}C NMR, δ: 11.11 (t, C(4), $^1J_{C,D}$ = = 19 Hz); 17.66 (t, C(1), $^1J_{C,D}$ = 19 Hz); 24.65 (C(8)); 26.08 (2 C, C(7), C(9)); 27.82 (C(3)); 31.88 (C(2)); 66.38 (C(5)).

Bis[4-deutero-2-(deuteromethyl)butyl]amine (2). Clear oily liquid. The yield was 69%, b.p. 78—80 °C (15 Torr). Found (%): C, 73.93; N, 8.51. $C_{10}H_{19}D_4N$. Calculated (%): C, 74.45; N, 8.68. ^{1}H NMR, δ: 0.85—0.95 (m, 8 H, C(1)H_2D, C(4)H_2D); 1.10—1.20 (m, 2 H, C(3)H_a); 1.35—1.50 (m, 2 H, C(3)H_b); 1.50—1.60 (m, 2 H, C(2)H); 2.30—2.45 (m, 2 H, C(5)H_a); 2.45—2.60 (m, 2 H, C(5)H_b). ^{13}C NMR, δ: 11.02 (t, 2 C(4), $^1J_{C,D}$ = 19 Hz); 17.34 (t, 2 C(1), $^1J_{C,D}$ = 19 Hz); 27.49 (2 C(3)); 34.75 (2 C(2)); 56.32 (2 C(5)).

***N*-Allyl-*N*-[4-deutero-2-(deuteromethyl)butyl]-*tert*-octylamine (3).** Clear oily liquid. The yield was 80%, b.p. 101—103 °C (1 Torr). Found (%): C, 79.14; N, 5.71. $C_{16}H_{31}D_2N$. Calculated (%): C, 79.59; N, 5.80. ^{1}H NMR, δ: 0.80—0.90 (m, 4 H, C(1)H_2D, C(4)H_2D); 1.01 (s, 9 H, C(12)H_3, C(15)H_3, C(16)H_3); 1.15 (s, 6 H, C(13)H_3, C(14)H_3); 1.10—1.20 (m, 1 H, C(3)H_a); 1.44 (s, 2 H, C(10)H_2); 1.35—1.60 (m, 2 H, C(2)H, C(3)H_b); 2.20—2.30 (m, 1 H, C(5)H_a); 2.30—2.40 (m, 1 H, C(5)H_b); 4.90—5.00 (m, 1 H, C(8)H_a); 5.05—5.15 (m, 1 H, C(8)H_b); 5.85—6.00 (m, 1 H, C(7)H). ^{13}C NMR, δ: 11.04 (t, C(4), $^1J_{C,D}$ = 19 Hz); 17.12 (t, C(1), $^1J_{C,D}$ = 19 Hz); 27.42 (C(3)); 28.05, 28.18 (C(13), C(14)); 34.59 (C(2)); 49.52 (C(5)); 53.96 (C(10)); 56.98 (C(6)); 113.50 (C(8)); 141.21 (C7)). MS, *m/z*: 241 $[M]^+$ (1), 226 $[M - CH_3]^+$ (9), 182 $[C_8H_{17}{}^tN(All)CH_2]^+$ (6), 171 (12), 170 (92), 169 (12).

4-Deutero-2-(deuteromethyl)butyl heptyl sulfide (4). Clear oily liquid. The yield was 53%, b.p. 97—101 °C (5 Torr). Found (%): C, 69.11. $C_{12}H_{24}D_2S$. Calculated (%): C, 70.51. ^{1}H NMR, δ: 0.80—0.90 (m, 5 H, C(4)H_2D, C(12)H_3); 0.90—1.00 (m, 2 H, C(1)H_2D); 1.15—1.40 (m, 9 H, C(3)H_a, C(8)H_2—C(11)H_2); 1.40—1.50 (m, 1 H, C(3)H_b); 1.50—1.65 (m, 3 H, C(2)H, C(7)H_2); 2.30—2.40 (m, 1 H, C(5)H_a); 2.48 (t, 2 H, C(6)H_2, *J* = 7.6 Hz); 2.45—2.55 (m, 1 H, C(5)H_b). ^{13}C NMR, δ: 11.00 (t, C(4), $^1J_{C,D}$ = 19 Hz); 14.04 (C(12)); 18.20 (t, C(1), $^1J_{C,D}$ = = 19 Hz); 22.60 (C(11)); 28.69 (C(3)); 28.90, 28.92 (C(8), C(9)); 29.79 (C(7)); 31.74 (C(10)); 32.84 (C(6)); 34.84 (C(2)); 39.83 (C(5)).

d_1-Heptanethiol (5). Clear oily liquid. The yield was 28%, b.p. 41—45 °C (5 Torr). ^{1}H and ^{13}C NMR spectral characteristics are identical to those described earlier[11] (with allowance for the absence of signals for SH group in the ^{1}H NMR spectrum).

Cycloalumination of 3-buten-1-ol and 1-(3-butenyl)piperidine (general procedure). A homoallylic compound (1 mmol), Cp_2ZrCl_2 (0.015 g, 0.05 mmol), hexane (3 mL), and Et_3Al (2 mmol) were sequentially placed under argon into a 50-mL glass reactor equipped with a magnetic stirrer and heated using a water bath to 40 °C, and the mixture was stirred for 6 h at 40 °C. Deutero-containing compounds were obtained according to the procedure described above for the deuterolysis of aluminacyclopentanes.

5-Deutero-3-(deuteromethyl)-1-deuteroxypentane (6). Clear oily liquid. The yield was 79%, b.p. 63—65 °C (20 Torr). Found (%): C, 67.82. $C_6H_{11}D_3O$. Calculated (%): C, 68.51. ^{1}H NMR, δ: 0.60—1.00 (m, 4 H, C(1)H_2D, C(4)H_2D); 1.00—1.80 (m, 5 H, C(3)H_2, C(5)H_2, C(2)H); 3.63 (t, 2 H, C(6)H_2, *J* = 5.6 Hz). ^{13}C NMR, δ: 10.84 (t, C(4), $^1J_{C,D}$ = 19 Hz); 18.72 (t, C(1), $^1J_{C,D}$ = = 19 Hz); 29.40 (C(3)); 30.96 (C(2)); 39.43 (C(5)); 60.98 (C(6)).

1-[5-Deutero-3-(deuteromethyl)pentyl]piperidine (7). Clear oily liquid. The yield was 85%, b.p. 70—74 °C (5 Torr). Found (%): C, 77.51; N, 8.08. $C_{11}H_{21}D_2N$. Calculated (%): C, 77.12; N, 8.18. ^{1}H NMR, δ: 0.80—0.95 (m, 4 H, C(1)H_2D, C(4)H_2D); 1.10—1.50 (m, 7 H, C(2)H, C(3)H_2, C(5)H_2, C(9)H_2); 1.55—1.65 (m, 4 H, C(8)H_2, C(10)H_2); 2.25—2.35 (m, 2 H, C(6)H_2); 2.35—2.45 (m, 4 H, C(7)H_2, C(11)H_2). ^{13}C NMR, δ: 11.01 (t, C(4), $^1J_{C,D}$ =

= 19 Hz); 19.05 (t, C(1), $^1J_{\mathrm{C,D}}$ = 19 Hz); 24.55 (C(9)); 26.03 (2 C, C(8), C(10)); 29.56 (C(3)); 33.21, 33.60 (C(5), C(6)); 54.78 (2 C, C(7), C(11)); 57.81 (C(6)).

Reaction of allyl *n*-undecyl and butyl vinyl ethers with Et_3Al catalyzed with Zr (general procedure). *n*-Hexadecane (0.5 mmol), allyl *n*-undecyl or butyl vinyl ethers (1 mmol), Cp_2ZrCl_2 (0.029 g, 0.1 mmol), hexane (3 mL), and Et_3Al (1 mmol) were sequentially placed under argon into a 50-mL glass reactor equipped with a magnetic stirrer and heated using a water bath to 40 °C, and the mixture was stirred for 8 h at 40 °C. Hexane (5 mL) was added to the reaction mixture, followed by a dropwise addition of H_2O (3 mL) cooling the reactor in an ice bath. A precipitate formed was filtered off on a paper filter. The aqueous layer was extracted with diethyl ether, the extract was combined with the organic layer, dried with anhydrous $CaCl_2$, and concentrated *in vacuo*. Individual compounds (*n*-butanol in the case of butyl vinyl ether and *n*-undecanol in the case of allyl *n*-undecyl ether) were isolated by distillation and identified by comparison of their ^{1}H and ^{13}C NMR spectra with the reported data.[11] The reaction product yields were determined by GLC using *n*-hexadecane as an internal standard.

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