Hydrozirconation of Oleyl Alcohol

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Hydrozirconation of oleyl alcohol gave a mixture of the ω- and γ-zirconium-stearyl alcohols. The zirconium alkyl bonds were cleaved by reaction with D_2O, Br_2 or CO-Br_2-2-methoxyethanol. 18-Bromo-stearyl alcohol (X) and 3-bromo-stearyl alcohol (IX) were isolated after bromination and 2-methoxyethyl 19-hydroxynonadecanoate (XII) and dihydro-3-pentadecyl-2(3H)-furanone (XIII) after carbonylation.

During recent years we have studied hydrozirconation-isomerization (1,2) of olefins, and especially the influence of various functional groups on the reaction (3-6). With a better understanding of the factors that govern the outcome of the reactions, we hope to be able to overcome some of the severe problems that we have observed to be associated with the hydrozirconation of functionalized olefins. Our objective is to develop synthetically useful methods, based on the hydrozirconation reaction, either by taking advantage of the zirconium-functional group interaction or by suppressing the latter. Initially, we have focused our attention on long-chain compounds, which can be derived from oleic acid. In our investigation of the reactions of oleyl ethers (3), long-chain oxazolines (4) and dialkyl oleylamines (5), we observed that the zirconium moiety migrated towards both the functional group and the chain terminus.

Migration towards the functional group, in the case of oleyl ethers, caused loss of the ether functionality via a β-elimination process (3), resulting in an alkene that was subsequently hydrozirconated by excess reagent to provide the α-deuterated alkane after deuterolysis. In addition, ω-deuterated ether was obtained.

Hydrozirconation of unsaturated amines and oxazolines, followed by deuterolysis, gave, in addition to the ω-deuterated derivatives, α- and β-deuterated saturated amines (5) and oxazolines (4), respectively. In the case of amines, the proportions of α- and β-deuteration depended on the nature of the dialkylamino group. Furthermore, it was observed that the direction of migration was influenced by the solvent. Thus, migration towards the terminal position was more pronounced in dioxane than in toluene when N,N-dimethyl 9-Z-octadecenylamine was subjected to the reaction conditions. The oleic acid oxazoline gave a somewhat different distribution than the amines, and also in this case, the outcome was dependent on the solvent (4).

In an extension of our studies on the influences of different functional groups on the hydrozirconation reaction, we have now investigated the reaction of oleyl alcohol, or rather the alcoholate, formed when the alcohol is reacted with $Cp_2Zr(H)Cl$. One drawback is, of course, that a large amount of zirconium hydride is needed, as one equivalent is consumed in the formation of the alcoholate. Therefore, we have also investigated the reaction of the lithium alcoholate of oleyl alcohol.

EXPERIMENTAL PROCEDURES

Materials. Oleyl alcohol (99%; Sigma), stearyl alcohol (Sigma), *tris*(2,2,6,6-tetramethyl-3,5-heptanedionato)-europium ($Eu(thd)_3$; Aldrich), deuterium oxide (99.8% D; Norsk Hydro), butyl lithium (1.418 M in hexane; Chemetall AG), 2-methoxyethanol (Fluka), *bis*(cyclopentadienyl)-zirconium dichloride (Aldrich) and carbon monoxide (Alfax) were used as received from the commercial sources indicated.

General. Melting points are uncorrected. ^1H NMR, ^{13}C NMR and ^2H NMR spectra were recorded on a Varian XL-300 MHz spectrometer at 299.943 MHz, 75.429 M H_3 and 46.004 MHz, respectively. The ^1H NMR shifts and ^{13}C NMR shifts are given relative to TMS in $CDCl_3$, and ^2H NMR shifts relative to TMS-d_{12} in $CHCl_3$. The relative yields (Table 1) of deuterated alcohols were determined using a calibrated capillary tube containing $CDCl_3$ in benzene. Gas chromatographic analyses were performed on a Varian 1400 or a Varian 3300 gas chromatograph equipped with (i) a 2 m glass column containing 3% of Carbowax 20M on Supelcoport 100/120 for deutero- and bromo-stearyl alcohols, or (ii) a 2 m glass column containing 5% of OV17 on Cromosorb W 80/100 for carbonylated stearyl alcohols. Pentadecane was used as an internal standard for quantitative GLC analyses. Flash chromatography (7) was carried out on Silica gel 60 (0.040-0.063 mm) (Merck), using an eluent consisting of pentane (Labscan) and ethyl acetate (Labscan); the proportions were 7:3 for deuterated and brominated stearyl alcohol, and 85:15 for carbonylated stearyl alcohol. Elemental analyses were performed at the Analytical Department at the Chemical Center, Lund.

General procedures. All the hydrozirconation reactions were carried out in an atmosphere of dry nitrogen or argon. Solvents (toluene [Merck] and 1,4-dioxane [BDH]) were dried by refluxing over sodium wire, and distilled under nitrogen prior to use. Carbon tetrachloride (Riedel de Haen) was dried over 4 Å molecular sieves. Solid transfers to thoroughly dried glassware were performed under nitrogen in a Dry-box. Liquid transfers were performed with a syringe or with nitrogen pressure using the septum technique. Red-Al ($NaAlH_2(OCH_2CH_2OCH_3)_2$; Aldrich) was diluted in anhydrous toluene, giving a 1.50 M solution. Bromine (BDH) was diluted in dry carbon tetrachloride, giving a 3.0 M solution.

Deuteration. The hydrozirconation reagent (2, 3 or 5 eq, see Table 2) was generated *in situ* in 25 ml of dry solvent, from Cp_2ZrCl_2 and a 1.50 M solution of Red-Al. After stirring for 2-3 hr, oleyl alcohol and internal standard (see General), dissolved in 5-7 ml solvent, were added (N_2 pressure). The reaction was stirred at the temperature stated. In all reactions, a GLC sample was withdrawn before hydrolysis, and hydrolyzed in water-diethyl ether. Reactions 1 and 2 were quenched with 5 ml of D_2O (added via a dry, N_2-flushed syringe) after 20 hr. The reactions (also valid for those referred to below) were stirred for an additional 2 hr after the addition of D_2O. Reactions 3, 4 and 5 were allowed to react for 24 hr. Then freshly generated $Cp_2Zr(H)Cl$ (1 or 2 eq, see Table 2) was

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added (N_2 pressure), and the reaction continued. Syntheses 3 and 5 were quenched with D_2O at the end of the total time stated, whereas new hydrozirconation reagent (1 eq) was added to reaction 4, and the reaction resumed. After completed hydrolysis, the suspension was filtered through a 3-4 cm column of neutral alumina, using 300 ml of pentane-ethyl acetate (7:3) as eluent. The eluate was concentrated *in vacuo* and subjected to flash chromatography (see General). Analysis (of the product mixture): ^1H NMR: δ 5.38 (m, vinyl); δ 3.64 (t, J = 6.6 Hz, $C\underline{H}_2$-OH); δ 2.00–1.94 (m, allyl); δ 1.62–1.52 (distorted quin, $C\underline{H}_2$-CH_2-OH); δ 1.46–1.23 (br. m, alkyl chain, OH); δ 0.88 (t, J = 6.7 Hz, CH_3). ^2H NMR: δ 1.33 (s, CHD-CH_2-CH_2-OH); δ 0.88 (s, CDH_2-chain).

Deuteration of lithium alcoholate. The hydrozirconation reagent (2 eq) was generated (see Deuteration) in 15 ml of dioxane. A solution of oleyl alcohol in 15 ml of dioxane was cooled on an ice-water bath until the liquid became viscous, and then reacted with 2.89 ml (4.10 mmol) 1.418 M butyl lithium in hexane. The lithium alcoholate solution was stirred for 1 hr, whereupon the zirconium hydride solution was added (N_2 pressure). The reaction was stirred at 40°C for 24 hr, whereupon freshly generated $Cp_2Zr(H)Cl$ (2 eq) was added (N_2 pressure), and the reaction continued. After a total time of 47 hr, the reaction was hydrolyzed with 5 ml of D_2O, filtered, and subjected to flash chromatography (see Deuteration).

Determination of deuterium substitution in stearyl alcohols by means of Eu-shift reagent (8). Initially, the spectrum of a mixture of 16.9 mg stearyl alcohol (**IV**) and 21.5 mg $Eu(thd)_3$ in $CDCl_3$ was analyzed. The proton groups attached to C_1, C_2, C_3, C_4 and C_5 could be separated with baseline separation, and the groups at C_6 and C_7 were slightly separated from the rest of the octadecanoyl protons. The cutting and weighing of the peaks gave an average weight (the order of dimensions being: $C_5 > C_3 > C_4 > C_2 > C_1$), with a maximum divergence of 4% for the individual peaks. Thus, this method could be used for establishing which of the carbons lacked protons, and therefore were substituted with a deuterium atom.

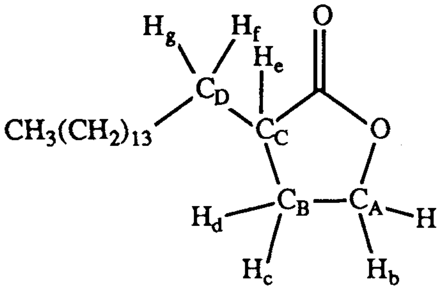
The product obtained from the experiment depicted in Entry 3 in Tables 1 and 2 (14.84 mg), $Eu(thd)_3$ (31.33 mg) and two drops of $CDCl_3$ were mixed in CCl_4. (The product primarily contained deuterated stearyl alcohol (**II** and **III**), but also smaller amounts of non-deuterated stearyl alcohol (**IV**) and *trans*-unsaturated alcohol (**V**). The proton groups attached to C_1–C_7 could be separated with baseline separation and the groups at C_8 and C_9 were slightly separated. Cutting and weighing gave the following results: 1) The proton group at C_1 diverged 8% from the saverage weight, or 11% from the average for the groups attached to C_2, C_4 and C_5. 2) The proton group at C_3 diverged 6% from the average weight, or 9% from the average for the groups attached to C_2, C_4 and C_5.

The divergence for the group attached to C_1 is an artifact caused by the broadening of the peak that occurs when it has been shifted by the europium reagent. The ^2H NMR spectrum of the mixture showed only two signals, of which one originated from the ω-deuterium atom, and the other (6.96 ppm downfield to the signal originating from the ω-deuterium atom) corresponded to the group of protons at C_3 in the europium-shifted proton spectrum.

Bromination. The above description for deuteration in syntheses 3 and 5 was followed. After the stated reaction time was attained, instead of quenching with D_2O, the suspension was transferred (Ar pressure) into two centrifuge tubes (N_2-flushed and sealed with septum), and centrifuged. The supernatant liquid was transferred to a dry flask (N_2 pressure). The liquid was cooled on an ice-water bath until the liquid became viscous. Via a syringe 1.1–4.0 eq (see Table 4) Br_2 (3M solution in dry CCl_4) was added, and the synthesis was stirred for 2 hr (protected against light with aluminum foil), and filtered through neutral alumina (see Deuteration), concentrated *in vacuo,* and subjected to flash chromatography (see General). HPLC separation of ω- and γ-bromo-stearyl alcohol (obtained according to Entry 9) was performed on a 50 × 10 cm (i.d.) Polygosil C_{18} column with methanol-H_2O (95:5) as eluent, using a RI detector. Analysis: 3-Bromo-stearyl alcohol (**IX**): ^1H NMR: δ 4.26–4.17 (m, 1H, $C\underline{H}$-Br); δ 3.89–3.83 (br. t, 2H, $C\underline{H}_2$-OH); δ 2.15–1.92 (m, 2H, $C\underline{H}_2$-CH_2-OH); δ 1.89–1.75 (m, 2H, chain-$C\underline{H}_2$-CHBr); δ 1.62–1.39 (m, 2H, chain-$C\underline{H}_2$-CH_2-CHBr); δ 1.33–1.15 (br. m, alkyl chain, OH, 25H); δ 0.88 (t, 3H, J = 6.7 Hz, CH_3). Elemental analysis: calcd.: C: 61.9; H: 10.7 found: C: 61.1; H: 10.6. Melting point: 39–40°C. 18-Bromo-stearyl alcohol (**X**): ^1H NMR: δ 3.64 (t, 2H, J = 6.9 Hz, $C\underline{H}_2$-OH); δ 3.41 (t, 2H, J = 6.9 Hz, $C\underline{H}_2$-Br); δ 1.85 (quin, 2H, J = 6.9 Hz, $C\underline{H}_2$-CH_2-Br); δ 1.56 (quin, 2H, J = 6.9 Hz, $C\underline{H}_2$-CH_2-OH); δ 1.45–1.22 (br. m, alkyl chain, 29H). Elemental analysis: calcd.: C: 61.9; H: 10.7 found: C: 60.4; H: 10.5. Melting point: 60–61°C.

Determination of product distribution in the bromination reactions using ^1H NMR. The amounts of the various products were determined by comparison of integrals for appropriate peaks (see below) with that for the sum of all protons α to an alcohol functionality (at 3.64 and 3.85 ppm). The following signals were used in the quantitative analysis: 3.86 ppm [γ-bromo-stearyl alcohol **IX**, $C\underline{H}_2$-OH]; 3.41 ppm [ω-bromo-stearyl alcohol **X**, CH_2-Br]; 5.38 ppm [*trans*-unsaturated alcohol **V**, vinylic protons]; and 4.2 ppm [dibrominated compound **XI**, $C\underline{H}$-Br]. As the signal from the protons attached to the dibrominated compound coincides with the signal from the protons α to the bromine atom in γ-bromo-stearyl alcohol, the fraction derived from γ-bromo-stearyl alcohol had to first be subtracted.

Carbonylation. The description above for deuteration of syntheses 3 and 5 was followed. After the stated reaction time had been reached, instead of quenching with D_2O, the suspension was transferred (Ar pressure) into two centrifuge tubes (N_2-flushed and sealed with septum), and centrifuged. The supernatant liquid was transferred to a dry Parr flask (N_2 pressure). The flask was placed in a Parr apparatus, a 4 atm. pressure of carbon monoxide was applied and the flask was shaken overnight. After the completed reaction, the solution was transferred to a single-necked flask (N_2 pressure). The liquid was cooled on an ice-water bath until it became viscous. Via a syringe 1.9 ml (5.7 mmol) of Br_2 (3M solution in dry CCl_4) was added, and the synthesis was stirred for 2 hr (protected against light with aluminum foil). Finally, 0.5 ml (6.3 mmol) of 2-methoxyethanol was added via a syringe, and stirring was continued for 2 hr. The reaction mixture was filtered through neutral alumina (see Deuteration), concentrated *in vacuo,* and subjected to flash chromatography (see General). In this way, pure **XI** was obtained. HPLC purification of the substance remaining after flash chromatography was performed on a 25 × 10.0 cm (i.d.) Nucleosil-OH column with heptane-ethyl acetate (95:5) as eluent, using a RI detector, yielding pure **XIII**. Analysis: 2-Methoxyethyl 19-hydroxynonadecanoate (**XII**): ^{1}H NMR: δ 4.22 (distorted t, $J = 4.7$ Hz, 2H, $C\underline{H}_2$-O-CO); δ 3.67–3.56 (m, 4H, $C\underline{H}_2$-OH and CH_3-O-$C\underline{H}_2$, $J = 4.7$ Hz); δ 3.39 (s, 3H, $C\underline{H}_3$-O); δ 2.34 (t, 2H, $J = 7.6$ Hz, $C\underline{H}_2$-CO-O); δ 1.67–1.51 (m, 5H, CO-CH_2-$C\underline{H}_2$, $C\underline{H}_2$-CH_2-OH and OH); δ 1.35–1.51 (br. m, alkyl chain, 28H). Elemental analysis: calcd.: C: 70.9; H: 11.9; O: 17.2 found: C: 71.7; H: 12.2; O: 16.6. Melting point: 59.5–60.5°C. Dihydro-3-pentadecyl-2(3H)-furanone (**XIII**): ^{1}H NMR: δ 4.34 (dt, 1H, H_a, $J_{a,b} = 9.3$ Hz, $J_{a,c} = 8.3$ Hz, $J_{a,d} = 3.0$ Hz); δ 4.19 (dt, 1H, H_b, $J_{b,a} = 9.3$ Hz, $J_{b,c} = 6.7$ Hz, $J_{b,d} = 9.3$ Hz); δ 2.57–2.45 (m, 1H, H_e); δ 2.44–2.33 (m, 1H, H_c); δ 2.00–1.85 (m, 2H, H_d [the part near 2.00 ppm] and H_f [the part near 1.85 ppm]); δ 1.61–1.19 (br. m., 27H, chain and H_g [around 1.45 ppm]); δ 0.88 (t, 3H, $J = 6.7$ Hz, CH_3). ^{13}C-^{1}H HETCOR: C_A (66.5 ppm) couples with H_a and H_b; C_B (28.7 ppm) couples with H_c and H_d; C_C (39.2 ppm) couples with H_e; C_D (30.35 ppm) couples with H_f and H_g. Furthermore, a ^{13}C signal at 14.1 ppm couples with the CH_3 protons, and the other ^{13}C signals (at 31.95, 29.8–29.3, 27.3, and 22.7 ppm) couples with the protons in the alkyl chain. Elemental analysis: calcd.: C: 77.0; H: 12.2; O: 10.8 found: C: 77.0; H: 12.2; O: 10.8. Melting point: 53–55°C.



XIII

RESULTS AND DISCUSSION

Deuteration reaction. In connection with our investigation of the reaction of oleyl ethers (3), we observed that a minimum of 3 equivalents of zirconium hydride was needed to achieve reasonable migration along the entire carbon skeleton. As for oleyl alcohol, more reagent is needed, since the alcohol functionality consumes one equivalent of the hydride. We found that 3 equivalents of $Cp_2Zr(H)Cl$ gave an incomplete reaction (Table 2), while 5 equivalents of zirconium hydride gave a satisfactory conversion, particularly when the synthesis was allowed to run for two days and the reagent was added in two portions. A reaction time of three days and addition of the reagent in three portions gave no major improvement. 1,4-Dioxane was found to be a better solvent than toluene (Table 2), which is in good agreement with earlier observations (3–5).

Hydrozirconation of oleyl alcohol in 1,4-dioxane for 46–68 hr at 40–45°C gave, after deuterolysis, 28–30% of ω-deuterio-stearyl alcohol **III** and 14–17% of γ-deuterio-stearyl alcohol **II**, in addition to 8–13% of undeuterated stearyl alcohol **IV** and 4–6% of *trans*-unsaturated alcohol **V** (Scheme 1, Tables 1 and 2).

TABLE 1

Analysis of Deuterium Content

Entry	Yield (%)[a,b] II	III	IV	Deuterium content (%)	γ:ω ratio
3	14	30	8	85	0.32:0.68
4	17	28	13	76	0.38:0.62

[a] We were not able to separate unsaturated alcohol, deuterated, nor non-deuterated stearyl alcohol from each other, neither by GLC nor flash chromatography. Thus, compounds **II**, **III**, **IV** and **V** were isolated as a mixture, and the yields calculated on this mixture. The amount of unsaturated alcohol in the product mixture was determined via comparison of the integrals of the vinylic protons and the protons α to the alcohol functional group. The deuterium content was determined by ^{2}H NMR using a calibrated capillary tube; see Experimental Procedures.

[b] The γ:ω ratio was calculated on the basis of the integrals in the ^{2}H NMR spectrum.

TABLE 2

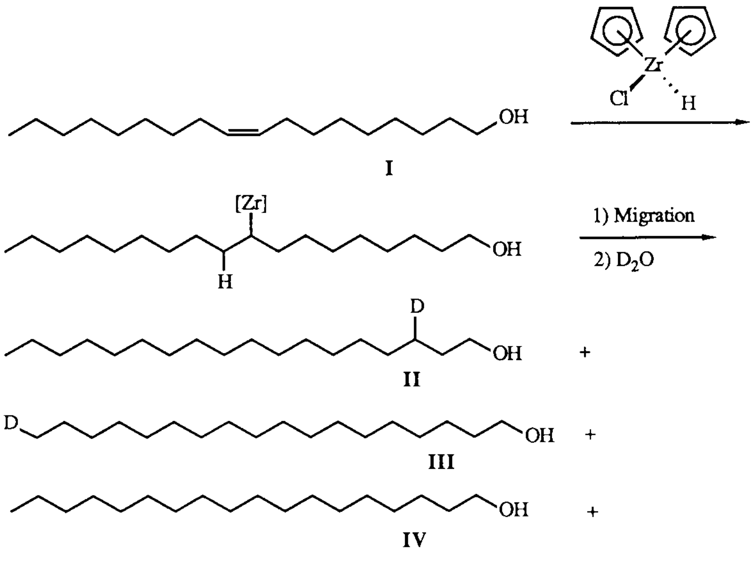
Analysis of Products Obtained After Hydrozirconation-Deuteration of Oleyl Alcohol

Entry	Eq. $Cp_2Zr(H)Cl$	Temp. (°C)	Time (hr)	Solvent	Yield (%)[a] II+III+IV	V	Octadecane[b]
1[c]	3	35–44	20	1,4-Dioxane	44	21	4
2[c]	5	35–44	20	1,4-Dioxane	41	11	6
3	3+2	40	46	1,4-Dioxane	52	6	6
4	2+1+1	40–45	68	1,4-Dioxane	58	4	6
5[c]	3+2	40–45	46	Toluene	10	23	2

[a] We were not able to separate unsaturated alcohol, deuterated, nor non-deuterated stearyl alcohol from each other, neither by GLC nor flash chromatography. Thus, compounds **II**, **III**, **IV** and **V** were isolated as a mixture, and the yields calculated on this mixture. The amount of unsaturated alcohol in the product mixture was determined via comparison of the integrals of the vinylic protons and the protons α to the alcohol functional group. The deuterium content was determined by ^{2}H NMR using a calibrated capillary tube; see Experimental Procedures.

[b] GLC yield.

[c] Deuterium analysis was not performed as the reaction was incomplete.



trans-unsaturated C_{18}-alcohol V

SCHEME 1

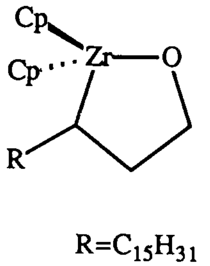


FIG. 1

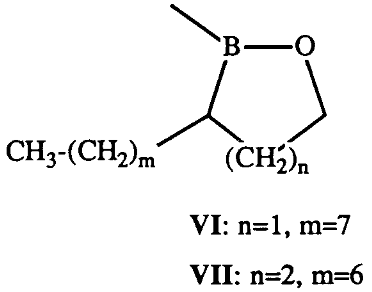
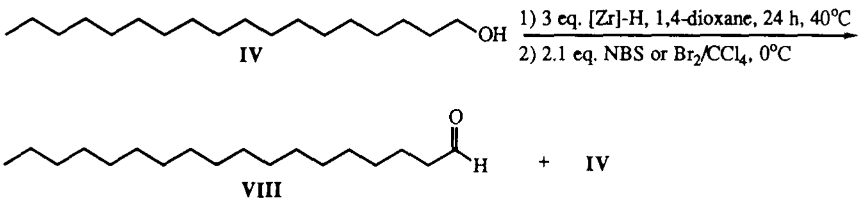


FIG. 2

That the γ-isomer was formed was proven by Eu-shifted (8) ^1H and ^2H NMR (see Experimental Procedures). We believe that the high selectivity for γ-substitution in the case of oleyl alcohol originates from a cyclic intermediate (probably dimeric), in which the zirconium moiety is trapped on the γ-carbon (Fig. 1). A related dimeric zirconacycle (R = Me) has been isolated (9). The formation of a stable intermediate similar to that depicted in Figure 1 could explain why, in contrast to oleyl ethers, the β-elimination was almost completely suppressed. (Less than 6% octadecane was formed in the hydrozirconation of oleyl alcoholate (Table 2). The zirconium moiety is less prone to migrate to the β-position, which is required for elimination.

These results may be compared with previous findings regarding hydroboration-isomerization of the internal double bond of oleyl alcohol (10). A lower yield of 1,18-isomer was obtained than those found in hydrozirconation. Interestingly, no 1,3-substituted product was found, but instead 1,4-diol, with minor amounts of 1,5-diol was produced. Sisido (11) *et al.* obtained 1,3- and 1,4-product, with 1,4-product as the dominant component, after hydroboration-isomerization-oxidation of 3-, 6- and 10-undecen-1-ol. The formation of the 1,3- and 1,4-isomers was explained as the result of the intermediacy of oxaborolanes **VI** or oxaborinanes **VII** (Fig. 2). They found, in analogy to our results (3), that no such trapping existed in the hydroboration-isomerization-oxidation of methyl-3-undecenyl ether and methyl-10-undecenyl ether. Similar cyclic intermediates have been utilized to explain why the addition of $HAl(i\text{-}C_4H_9)_2$ to *n*-hexenols does not give equal amounts of the two conceivable bifunctionalized products (12). Both 5- and 6-membered rings were considered as intermediates, the 5-membered ring being somewhat favored.

It is of interest to minimize the amount of Schwartz reagent that has to be used. Therefore we decided to try to hydrozirconate the lithium alcoholate of oleyl alcohol. Thus, hydrozirconation of the lithium alcoholate of oleyl alcohol in 1,4-dioxane for 47 hr at 40°C using 2 + 2 equivalents of zirconium hydride gave, after deuterolysis, 28% of ω-deuterio-stearyl alcohol **III** and 14% of γ-deuterio-stearyl alcohol **II**, in addition to 10% of undeuterated stearyl alcohol **IV** and 7% of *trans*-unsaturated alcohol **V**. A comparison with Entry 3 in Tables 1 and 2 reveals that the amount of zirconium hydride can be reduced if the lithium alcoholate is used instead of the alcohol.



SCHEME 2

TABLE 3

Oxidation of Zirconium Alcoholate of Stearyl Alcohol with NBS or Br_2/CCl_4

Reagent	Yield (%)[a] IV	Yield (%)[a] VIII
NBS	29	42
Br_2/CCl_4	55	8

[a]Determined via GLC analysis with internal standard.

Bromination reaction. Zr(IV)-alkyl compounds can be cleaved in a variety of ways, apart from hydrogenolysis/deuterolysis, yielding different types of functionalized alkanes (1,2,13-15). We have previously investigated the bromination of zirconium alkyl compounds, obtained after hydrozirconation of oxazolines, derived from *cis*-4-octenoic, oleic, elaidic and erucic acid (4). The ω-bromo fatty acid oxazolines were obtained in 22-35% yield after reaction with Br_2, which compares favorably with the yields obtained via the Hunsdiecker reaction. Also α,β-unsaturated fatty acid oxazolines were obtained in 9-13% yield, stemming from the α- or β-bromo derivatives. We have now studied the bromination of hydrozirconated oleyl alcoholate with N-bromosuccinimide (16) or Br_2 (17) as electrophiles in order to obtain compounds of synthetic interest.

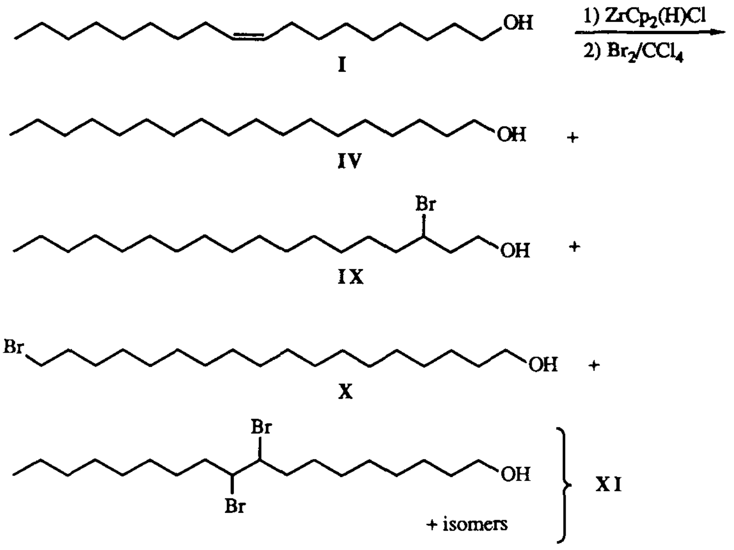
Initially, we did not obtain the expected products when we reacted the zirconium alkyls with these electrophilic reagents. Instead, the zirconium alcoholate of stearyl alcohol was oxidized to the aldehyde with NBS or Br_2/CCl_4, the former being the most powerful oxidant (Scheme 2, Table 3). NBS also partially oxidized the lithium alcoholate of stearyl alcohol in 1,4-dioxane, while stearyl alcohol itself was unaffected. That primary alcohols are resistant to oxidation by NBS has been observed previously (18). Usually, the more powerful reagent NCS is used for oxidations of alcohols. To our knowledge, there are no examples of oxidations of primary alcoholates with NBS, as an alternative to oxidize alcohols with NCS, although the anionic character of the oxygen atom obviously facilitates the reaction. We chose to use Br_2 for bromination of the hydrozirconated intermediate, as it showed a smaller tendency to oxidze the alcoholate. The amount of added Br_2 does not affect the yield of aldehyde to any great extent. In the syntheses where bromination was attempted, 1.0-4.0 eq. Br_2 was used.

Hydrozirconation of oleyl alcohol in 1,4-dioxane for 48 hr at 36-50°C, followed by bromination with Br_2/CCl_4 after removal of the precipitate by centrifugation, gave a mixture of ω-bromo-stearyl alcohol **X** and γ-bromo-stearyl alcohol **IX** in 21.2-42.9% combined isolated yield (Scheme 3, Table 4). Also some di-brominated **XI** and non-brominated **IV** compounds were formed. We were unable to separate the products from each other by flash chromatography. Using HPLC (see Experimental Procedures), we were able to isolate the pure ω- and γ-bromo-stearyl alcohols (white crystalline compounds) from the mixture obtained after bromination according to Entry 9. We were not able to establish any GLC yields, as these bromo compounds decompose on the columns used for GLC analysis. The proportions of the different stearyl alcohol derivatives were determined on the mixture obtained after flash chromatography, via ^1H NMR investigations (see Experimental Procedures).

Reaction of the precipitate with D_2O showed that it also contained small amounts of hydrozirconated product, in which the γ:ω ratio was different from the proportions in the supernatant liquid, as measured by bromination, but similar to that previously obtained by deuteration.

Carbonylation reaction. Insertion of carbon monoxide into a carbon zirconium bond is yet another useful method for functionalization, ultimately yielding aldehydes and carboxylic acid derivatives (1,2,13). Esters can be obtained by treating the acylzirconium (IV) species with NBS (giving the intermediary acyl halide) and an alcohol. Alternatively, Br_2 can be used instead of NBS. Butenolides can be obtained from propargylic alcohols via hydrozirconation-carbonylation-halogenation (19). As mentioned before, NBS may give side reactions, and as it turned out, NBS/2-methoxyethanol was an inferior reagent compared with Br_2/2-methoxyethanol. The reason for using 2-methoxyethanol was that we in some preliminary experiments found that the acylzirconium species, formed after hydrozirconation-carbonylation of 1-decene, gave a mixture of the methyl and methoxyethyl ester of undecanoic acid when treated with NBS/methanol. The 2-methoxyethanol originates from Red-Al, used for the *in situ* generation of $Cp_2Zr(H)Cl$ (see Experimental Procedures).

Hydrozirconation of oleyl alcohol in 1,4-dioxane for 48 hr at 40-43°C, followed by insertion of carbon monoxide and treatment of the acylzirconium compound with Br_2 and 2-methoxyethanol, gave a mixture of 2-methoxyethyl 19-hydroxynonadecanoate **XII** (45%) and dihydro-3-pentadecyl-2(3H)-furanone **XIII** (20%) (yields according to GLC analysis) (Scheme 4). The ester was obtained in 15% isolated yield after flash chromatography. The lactone was purified by HPLC, and its structure proven by ^{13}C-^1H HETCOR analysis (see Experimental Procedures).



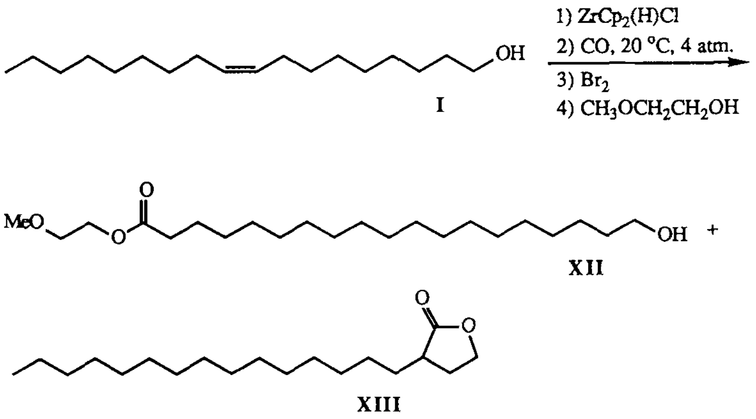
SCHEME 3

TABLE 4

Hydrozirconation of Oleyl Alcohol with 3+2 Eq. $ZrCp_2(H)Cl$ in 1,4-Dioxane, 48 Hours, Followed by Centrifugation-Bromination with Br_2/CCl_4

Entry	Temp. (°C)	Eq. Br_2	Yield (%) I	IV	IX	X	XI	Octadecane[a]
6	36-40	1.1	3.4	4.3	21.7	16.4	2.4	6
7	37-50	1.3	1.5	—	22.8	20.1	3.0	3
8	43-50	4.0	1.0	—	10.8	10.4	1.8	6
9	30-44	4.0	—	—	13.4	13.3	3.0	—

[a]Determined via GLC analysis with internal standard on an aliquot withdrawn before bromination and hydrolyzed in water-diethyl ether.



SCHEME 4

ACKNOWLEDGMENT

Grants from the Swedish Natural Science Research Council are gratefully acknowledged.

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[Received November 28, 1988; accepted September 13, 1989]
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