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Reactivity of Organocerium Compounds with Allyl Alcohols

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We were recently interested in the reactivity of electrophiles with organocerium reagents:[1] inexpensive, nontoxic, and nonbasic organometallic reagents introduced in the 1980s.[2] These reagents show low basicity and high nucleophilicity as opposed to organolithium and Grignard reagents;[2b] therefore, they can be used with enolizable substrates (e.g., benzyl ketones,[2a] phosphinoyl ketones,[1c] enaminones[1e,g]). However, they have never been tested with substrates generally inert toward nucleophilic attack such as carbon−carbon double bonds in allyl alcohols.

The observation that organometallic compounds can add to allyl alcohols dates back many years ago,[3] but this interesting reaction has not found general synthetic applicability. In fact, only primary alkyllithiums are reported to react with allyl alcohol in the presence of TMEDA under mild conditions, leading to alcohols in which the alkyl group binds to the double bond carbon atom nearer to the hydroxy function.[4] On the other hand, secondary or tertiary alkyllithiums react under drastic reaction conditions (97 °C in sealed tubes).[5] Reactive (allyl and benzyl) Grignard reagents have been shown to add to allylic alcohols in refluxing ether in a time range of 50−96 h.[6] The presence of catalytic amounts of chelating phosphine−nickel and phosphine−palladium complexes ensures the addition of Grignard reagents to allyl alcohols in milder conditions, but with poor regioselectivity.[7]

Table 1. Reactions of Oct-1-en-3-ol 1a with Preformed Butylcerium Derivatives with Various Substrate−Cerium(III) Chloride−Butyllithium Ratios at − 78 °C in THF

entry	substrate−$CeCl_3$−BuLi	method[a]	recvd start. mater (%)	6-dodecene (%)
1	1:1:1	A	83	15
2	1:4:4	A	0	22[c]
3	1:4:4[b]	A	0	75[c]
4	1:1:4	A	0	78[c]
5	1:1:3	B	0	92
6	1:1:1	B	58	35

[a] Method A: adding oct-1-en-3-ol to the stirred suspension of BuLi−$CeCl_3$. Method B: adding a THF solution of lithium oct-1-en-3-olate to the stirred suspension of BuLi−$CeCl_3$. [b] Reaction carried out in DME. [c] No other characterizable products were recovered.

Therefore, we have investigated the reactivity of organocerium compounds with allyl alcohols. In this paper, we report results about an efficient and mild reaction to give alkyl-substituted alkenes.

In preliminary investigations (Table 1) oct-1-en-3-ol **1a** (method A) and oct-1-en-3-olate **2a** (method B) were added to a stirred suspension of BuLi−$CeCl_3$ (**3**). Various relative amounts of the reactants (entries 1, 2, 4−6) were tested in THF, and a run was carried out in DME (entry 3). Most of the starting material is recovered with equimolecular amounts of $CeCl_3$, BuLi, and **1a** (entry 1). However, adventitious water[8] seems to have no influence in the reaction because even with a 1:1 cerium−alkyllithium ratio the reaction occurs if the alcohol is 1:4 with respect to the organometallic reagent (entries 2, 3). An excess of cerium trichloride is not necessary to allow its addition to the substrate (entries 4−6). On the other hand, as in the reaction of epoxides with cerium reagents,[9] higher yields are obtained with a large excess of the lithium derivative with respect to both the cerium trichloride and the substrate. In fact, the reaction requires a 4-fold excess of lithium reagent starting from the alcohol (entry 4), or a 3-fold excess starting from the alcoholate (entry 5).[10] The latter methodology gives the product in higher yields.

These findings strongly support alcoholate **2** as the key intermediate of the reaction. Moreover, allyl ethers do not react with organocerium reagents, and starting material is recovered at the end of the reaction.

On the basis of the above-reported results, the reaction was carried out as follows and extended to various

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[10] The reported excesses are presumably enough to allow the reaction to occur. Actually a further 10% of reagent is added, since currently no methods to exactly evaluate organocerium concentration are known.

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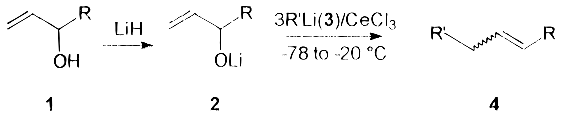
Table 2. Reaction of Allyl Alcoholates and Organoceriums at −78 °C (see method B, Table 1) Followed by Acidic Quenching



entry	R in **2**	R′ in **3**	product	reaction time (h)	yield (%)	*cis*:*trans* ratio
1	C_5H_{11}	Me	**4a**	24	67	1:3
2	C_5H_{11}	Bu	**4b**	2	92	1:3
3	C_5H_{11}	s-Bu	**4c**	3	79	2:3
4	C_5H_{11}	t-Bu	**4d**	24	79	1:2
5	C_5H_{11}	C_6H_{13}	**4e**	3	94	1:3
6	C_5H_{11}	Ph	**4f**	24	76	1:5
7	C_5H_{11}	Me[a]	**4a**	72	36[b]	1:3
8	H	C_6H_{13}	**4g**	3	70	−
9	H	Ph	**4h**	18	64	−
10	Ph	Bu	**4i**	18	70	1:1

[a] Grignard reagent used instead of organolithium. [b] 63% starting material recovered.

lithium derivatives and alcohols. The allyllithium alcoholate **2** was preformed from equimolecular amounts of alcohol and lithium hydride at 0 °C. The organocerium reagent **3** was prepared from a 3-fold excess of lithium reagent with respect to “anhydrous” cerium trichloride (1.2 equiv per equiv of allyl alcohol) at −78 °C. Then **2** was added to **3.** During the reaction time, the temperature was allowed to rise to −20 °C, the mixture was quenched with 4% aqueous HCl, and usual workup afforded the corresponding olefin **4**. The reaction always occurs in very good yields (Table 2): long, secondary, and tertiary alkyl chains and aromatic groups can be introduced under mild conditions, with very good regioselectivity at the farthest carbon atom in contrast to simple alkyllithiums.[3−7]

The low stereoselectivity of the reaction leads to the more stable *E*-olefin only with a slight excess. When the cerium reagent is prepared from cerium trichloride and 4 mol equiv of a Grignard reagent instead of alkyllithium, the reaction proceeds more slowly and less efficiently (Table 2, entry 7).

In conclusion a mild general method to add organometallic reagents to the double bond of allyl alcohols is now available. This methodology overcomes most of the drawbacks of the previously reported reactions[3−7] such as long reaction times, high temperatures, and simple reduction of the double bond via hydride transfer from the reagent. Studies are in progress to understand the influence on the addition of substituents on the double bond and the mechanistic pathway followed.

Experimental Section

THF was dried by refluxing over sodium wire until the blue color of benzophenone ketyl persisted and then distilling into a dry receiver under nitrogen atmosphere. DME was dried by refluxing over sodium wires and then over lithium aluminum hydride.

Preparation of the Organocerium Reagent. Commercial cerium(III) chloride heptahydrate (6 mmol) was placed in a flask with a stirring bar. The flask was heated in vacuo in an oil bath to 140 °C/0.2 mmHg for 2 h. Nitrogen was introduced while the flask was still hot. The flask was cooled in an ice bath, and dry THF was introduced from a syringe. The suspension was stirred overnight at room temperature. The resulting white slurry was then cooled at −78 °C, and the titrated commercial organolithium reagent (17.5 mmol) was added dropwise from a syringe.

Reaction of Oct-1-en-3-ol with Butylcerium Chloride. Method A. Butyllithium and anhydrous cerium trichloride were mixed in the ratios reported in Table 1 in THF or DME, and the mixture was allowed to stand at −78 °C for 2 h under a nitrogen atmosphere. Then oct-1-en-3-ol was (5 mmol) added into the organocerium reagent with stirring at −78 °C.

Method B. Lithium hydride (5.5 mmol) was poured into a THF solution of allyl alcohol (5 mmol) with stirring at 0 °C under a nitrogen atmosphere. After 1 h the mixture was syringed into the organocerium reagent prepared as above with stirring at −78 °C under a nitrogen atmosphere.

After 2 h, the temperature was allowed to rise to −20 °C. The mixture was then quenched with 4% HCl solution, extracted with diethyl ether, and washed with water. The dried (Na_2SO_4) extracts were concentrated under reduced pressure and purified by flash chromatography on a silica gel column (light petroleum ether (40−60 °C):diethyl ether, 9:1 as eluant). Yields of the recovered 6-dodecene are listed in Table 1. 6-Dodecene was recognized by comparison of its physical data with those in the literature.[11]

General Procedure. Lithium hydride (5.5 mmol) was poured into a THF solution of allyl alcohol (5 mmol) with stirring at 0 °C under a nitrogen atmosphere. After 1 h the mixture was syringed into the organocerium reagent (prepared from 5.5 mmol of cerium trichloride and 16.5 mmol of alkyllithium) with stirring at −78 °C under a nitrogen atmosphere. During the reaction time (Table 2), the temperature was allowed to rise to −20 °C. The mixture was then quenched with 4% HCl solution, extracted with diethyl ether, and washed with water. The dried (Na_2SO_4) extracts were concentrated under reduced pressure and purified by flash chromatography on a silica gel column (light petroleum ether (40−60 °C):diethyl ether, 9:1 as eluant). Yields of the recovered products are listed in Table 2. All compounds were fully characterized by NMR, IR, and mass spectra. 2,2-Dimethyl-4-decene (**4d**),[12] 6-tetradecene (**4e**),[13] 1-phenyl-2-octene (**4f**),[14] and 1-phenyl-1-heptene (**4i**)[15] had physical data identical to that reported in the literature. 3-Nonene (**4a**), 1-nonene (**4g**), and allylbenzene (**4h**) were recognized by comparison with commercial samples (Aldrich).

3-Methyl-5-undecene (**4c**): *cis:trans* mixture. ^{1}H NMR ($CDCl_3$) δ 0.75−0.95 (m, 9H); 1.20−1.50 (m, 9H); 1.70−1.90 (m, 4H, cis-isomer); 1.90−2.05 (m, 4H, trans-isomer); 5.30−5.40 (m, 2H). Relevant ^{13}C NMR ($CDCl_3$) δ 128.42 (CH═ *cis*), 128.79 (CH═*trans*), 130.60 (CH═ *cis*), 131.57 (CH═ *trans*). MS *m*/*z* 168 (M^+), 139, 112, 97, 83, 70 (100), 69, 57, 55, 41. Anal. Calcd for $C_{12}H_{24}$ (168.32): C, 85.63; H, 14.37. Found: C, 85.60; H, 14.40.

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