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ETHER FORMATION FROM ALLYLIC ALCOHOLS CATALYZED BY SAMARIUM TRICHLORIDE

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Abstract - The behaviour of various allylic alcohols in the presence of catalytic amounts of $SmCl_3$ (by heating in 1,2-dichloroethane) has been studied. Diallyl ethers are obtained in many cases in good yields. Mixed allyl alkyl ethers are also prepared if 2-5 equivalents of an aliphatic alcohol is present. The reactions are interpreted as proceeding through a pseudo allylic carbonium intermediate initiated by a preliminary complexation of the allyl hydroxyl to the samarium ion.

Introduction

Allylic substitution is an important process allowing many synthetic operations (see ref. 1 for a review). Classically it involves an allylic leaving group (halide, tosylate, mesylate,...) and a nucleophile taken generally as an anion. Mechanism and stereochemistry of these reactions were widely studied[1]. Acetates in an allylic position are good leaving groups in palladium or nickel-catalyzed reactions involving various types of nucleophiles[2-5]. Allylic alcohols can be also directly used in some allylic substitutions, but examples are quite rare and mainly involved organometallic reactions catalyzed by transition metal complexes[4-7]. We wish to report that samarium trichloride is a convenient catalyst for allylic substitution on some allylic alcohols, allowing C-O bond formation.

We have investigated for several years the use of lanthanide derivatives in organic synthesis[8-12]. Many trivalent salts are easily available and have found various uses, presumably because of a mild Lewis acidity[13-17]. We incidently discovered that allylic alcohols cleanly give the symmetrical diallyl ether when heated in presence of a catalytic amount of $SmCl_3$. A modification of the procedure also allows to prepare mixed ethers.

Synthesis of ethers from allylic alcohols

The general procedure involves refluxing an allylic alcohol with 0.1 equivalent of $SmCl_3$ in 1,2-dichloroethane for a few hours. Yields of isolated diallyl ethers can be very good and are indicated in Table 1.

We found that saturated alcohols (e.g. methanol, cyclohexanol), benzyl alcohol or propargylic alcohol do not give rise to ether formation under the above experimental conditions. This observation led us to an interesting development : the synthesis of mixed ethers containing only one allyl radical. The reaction occurs on heating the allylic alcohol in the presence of a few equivalents of another alcohol and catalytic amounts of $SmCl_3$. The results are listed in Table 1.

Thiophenol can replace in some cases the alcohols, giving rise to allylic thioethers. Geraniol and 3 mol eq. of thiophenol gave a 56 % yield in 5 (only one regioisomer).

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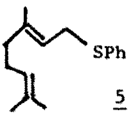

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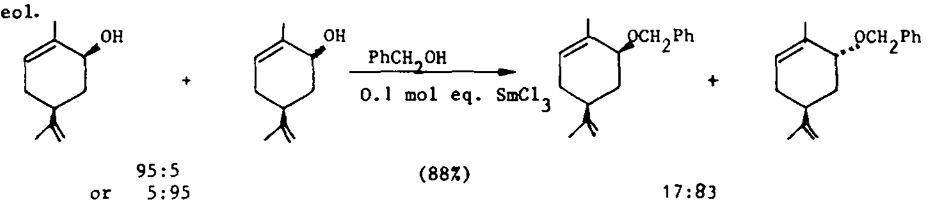
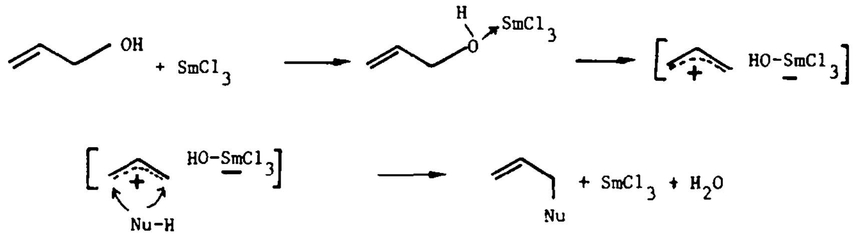
Discussion

All the previous results are consistent with the intervention of a protic nucleophile (an alcohol) attacking an electrophilic allylic moiety derived from the allylic alcohol. The interest of the reaction lies in the possibility to use a hydroxyl group directly as a leaving group and to avoid the classical Williamson reaction. Water is formed and does not deactivate the catalyst, making unnecessary its removal. Most of the allylic alcohols which were investigated are cyclic compounds. Acyclic primary allylic alcohols such as 2-butenol, 2-hexenol or geraniol gave poor yields of ethers. However, secondary alcohols with internal double bond produce mixed ethers (see Table 1). To gain some informations on the mechanism of the reaction we considered reactions of cis and trans-carveol.



Scheme 1

Benzyl alcohol was selected as nucleophile. The substitution product was obtained as a racemate, with the same trans/cis ratio (83/17), independently of the initial stereochemistry of the carveol. This result gives some support to the formation of a kind of allylic cation with loss of the initial stereochemistry, and subsequent nucleophilic attack at the less hindered side. The samarium center should activate the allylic C-OH bond through strong coordination. This catalytic process related to metal-assisted solvolysis[18] is roughly described in the Scheme 2.



Scheme 2

A similar system was recently found where catalytic $RuCl_3$ in methanol acts as a Lewis acid to cleave the carbon-oxygen bond of allylic alcohols[20], allowing the formation of various methyl allylic ethers. The nature of the intermediate (allylic carbonium ion or Ru-π-allyl complex) was not established.

A nickel catalyst ($Ni(Acac)_2$-$\underline{n}Bu_3P$-$NaBH_4$) selectively converts allyl alcohol into diallyl ether at 40°C but isomerizes it into propanal at higher temperature[5,20]. It also allows S-allylation of $CH_3(CH_2)_7SH$ and N-allylation of pyrrolidine by allyl alcohol. These reactions were considered by the authors to proceed through π-allyl intermediates. Since 4f orbitals of lanthanides show quite small involvment in bonding[21] the allylic intermediate of the scheme should be much closer to an allylic cation than to a π-allyl system. It is interesting to make some comparisons between our lanthanide-catalyzed reaction and alkylations performed by alcohols in presence of classical Lewis or protic acids. Frequently BF_3, $AlCl_3$ or $SnCl_4$ give with allylic alcohols side products derived from intramolecular dehydration or cyclization. Recently ZnI_2 was described as a superior catalyst for sulfide formation from benzylic or allylic alcohols[22]. Thus 0.2 to 0.5 mol equivalent of ZnI_2 allows the formation of diphenylthioether from benzyl alcohol and thiophenol at room temperature. The reaction is believed to be a $S_{N}1$-like process since racemisation occurs in the sulfide formation from optically active 1-phenyl ethanol.

Our reactions seem related to the one induced by ZnI_2 but we have not made detailed experiments in order to compare the both systems.

In the allylic substitutions catalyzed by lanthanide salts we checked the effect of a limited number of catalysts in a comparative way (3h reflux in $ClCH_2CH_2Cl$, 0.1 mol eq. of catalyst) in the symmetrical ether formation from 2-cyclohexenol. $La(OAc)_3(H_2O)_{3/2}$, Ln_2O_3 and $Sm(fod)_3$ are completely inactive, $La(NO_3)_3(H_2O)_6$ gives a small amount of products ; $LaCl_3\ (H_2O)_7$, $La(OCOCF_3)_3(H_2O)_3$, $SmCl_3(H_2O)_{11/2}$, $EuCl_3\ (H_2O)_6$ give similar yields of diallylic ether.

We selected $SmCl_3\ (H_2O)_{11/2}$ or anhydrous $SmCl_3$ as the catalyst, because of the ready availability of the salt. Methanol is not suitable as a solvent for the synthesis of mixed ethers, presumably because of the saturation of coordination sites on the metal leading to a deactivation of the catalyst.

We are currently investigating the scope of various lanthanide catalysts with Lewis acid properties[23] for the allylic substitution on allylic alcohols, with special emphasis on C–C bond formation.

Acknowledgements

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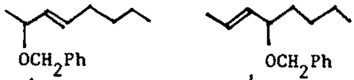
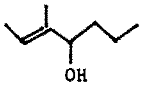
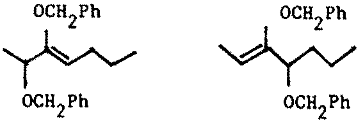
TABLE 1

Synthesis of ethers and thioethers from allylic alcohols

Allylic alcohol[a]	Second alcohol (or thiol) (mol eq.)	Products (isolated yield %)[c]
2-Cyclopenten-1-ol 1	1[b]	bis(2-cyclopentenyl) oxide (69)
2-Cyclohexen-1-ol 2	2[b]	bis(2-cyclohexenyl) oxide (80)
2-Cyclohepten-1-ol 3	3[b]	bis(2-cycloheptenyl oxide (20), 3 (50)
2-Cyclohexen-1-ol 2	Methanol (5)	(2-cyclohexenyl) methyl oxide (48)[d]
2-Cyclohexen-1-ol 2	Benzyl alcohol (2)	(2-cyclohexenyl) benzyl oxide (74)[d]
2-Cyclohexen-1-ol 2	Propargyl alcohol (2)	(2-cyclohexenyl) propargyl oxide (73)[d]
2-Cyclohexen-1-ol 2	Thiophenol (2)	(2-cyclohexenyl) phenyl sulfide 4 (95)
Geraniol	Thiophenol (3)	geranyl phenyl sulfide 5 (56)
Carveol[e]	Benzyl alcohol (3)	(carveyl) benzyl oxide (88)[d]
2-Octen-4-ol 6	Benzyl alcohol (3)	 (76) (2:1)
	Benzyl alcohol (3)	 (80)[d] (1.5:1)

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[a] In $ClCH_2CH_2Cl$ (5 mmol allylic alcohol in 20 ml), 12h at reflux $[SmCl_3]$ / [allylic alcohol] = 0.1. Catalyst remains insoluble.

[b] The total amount of allylic alcohol is the quantity given in note a.

[c] Isolation by column chromatography. The starting allylic alcohol accounts for the material balance.

[d] No diallylic ether could be detected.

[e] The reaction was performed on (-)cis or (-)trans carveol (cis/trans = 0.5:5 or 5:0.5). The trans benzyl ether was formed (see Scheme 1).

Experimental Section

Apparatus

Proton magnetic resonance spectra (^1H NMR) were recorded with a Perkin-Elmer Model R 32 spectrometer at 90 MHz, except for the mixture of isomers obtained from alcohols 6 and 7 which were recorded at 400 MHz. Chemical shifts in $CDCl_3$ are reported in parts per million from Me_4Si as an internal standard. Mass spectra were obtained on a GC-MS Ribermag R 10-10 instrument. Gas chromatographic analyses were carried out on a Carlo Erba Fractovap 2101 chromatograph. Peak area integration was performed with a Delsi Icap 5 calculator. Flash chromatography was performed on silica gel (Merck, 230-240 mesh ; 0.040-0.063 mm).

Reagents

Anhydrous $SmCl_3$ was purchased from Strem.
Trans carveol 5 was obtained from cis carveol via trans carveol benzoate with the method described by Mitsonobu (26).
3-Methyl-2 hepten-4-ol 7 was synthetized by reaction of Z,2 buten-2-yl lithium with butanal.
All other reagents were commercial samples purified by distillation.

General procedure

For symmetric ethers, the allylic alcohol (5 mmol) was dissolved in 20 ml 1,2-dichloroethane and refluxed with samarium trichloride (0.5 mmol) for 12 h. After filtration of samarium salts and evaporation of solvent the crude product was purified by flash chromatography. For mixed ethers the same procedure was followed, using a mixture of allylic alcohol (5 mmol) and methanol (25 mmol) or propargyl alcohol (10 mmol) or benzyl alcohol (15 mmol). Thioethers were obtained with the same procedure but the excess of thiophenol was distilled before flash chromatography.

(2-Cyclohexenyl)propargyl oxide

NMR δ : 1.8 (m, 6H) ; 2.4 (t, 1H, J=3Hz) ; 4.1 (m, 1H) ; 4.19 (d, 2H, J=3Hz) ; 5.82 (s, 2H).
Mass spectrum : (70 e.v.) m/e (relative intensity) 136 (1.4, M+) ; 135 (13.0, M-H) ; 108 (35.8) ; 107 (55.1).

Carveyl benzyl oxide

Ratio of trans and cis isomers were determined by GLC by comparison with authentic samples of trans carveyl benzyl oxide and cis carveyl benzyl oxide of known stereochemistry synthetized independently (27).
NMR δ: 1.73 (s, 6H) ; 2.15 (m, 5H) ; 3.72 (m, 1H) ; 4.58 (q, 2H) ; 4.75 (s, 2H) ; 5.60 (m, 1H) ; 7.32 (m, 5H).
Mass spectrum : (70 e.v.) m/e (relative intensity) : trans isomer 242 (0.4, M^+) ; 151 (22.2, $M-CH_2Ph$) ; 134 (3.0) ; 91 (100).
cis isomer 242 (0.3 M^+) ; 151 (13), $M-CH_2Ph$) ; 134 (12.9) ; 91 (100).

(3-Octen-2-yl) benzyl oxide

NMR δ : 0.89 (t, 3H) ; 1.24 (d, J=7Hz, 3H) ; 1.32 (m, 2H) ; 2.04 (q, 1H) ; 3.85 (m, 1H) 4.34 (d, J=13Hz, 1H) ; 4.57 (d, J=13Hz , 1H) ; 5.37 (m, 1H) ; 5.6 (m, 1H) ; 7.32 (m, 5H).
Mass spectrum (70 e.v.) m/e (relative intensity) 203 (1.1, $M-CH_3$) ; 127 (2.6, $M-CH_2Ph$) ; 112 (35.6) ; 91(100).

(2-Octen-4-yl) benzyl oxide

NMR δ : 0.89 (t, 3H) ; 1.32 (m, 4H) ; 1.72 (d of d, 3H) ; 3.64 (q, 1H) ; 4.31 (d, 1H, J=13 Hz) ; 4.57 (d, J=13Hz, 1H) ; 5.37 (m, 1H) ; 5.6 (m, 1H) ; 7.32 (m, 5H).
Mass spectrum (70 e.v.) m/e (relative intensity) : 218 (0.2, M+) ; 176 (2.1) ; 175 (17.1) 112 (5.5) ; 91 (100).

(3-Methyl-3-hepten-2 yl) benzyl oxide

NMR δ : 0.84 (t, 3H) ; 1.18 (d, J=6Hz , 3H) ; 1.32 (m, 2H ; 1.52 (s, 3H) ; 1.95 (m, 2H) 3.76 (q, 1H) ; 4.14 (d, J=12Hz , 1H) ; 4.35 (d, J=12Hz , 1H) ; 5.27 (m, 1H) ; 7.22 (m, 5H).
Mass spectrum : (70 e.v.) m/e (relative intensity) 203 (1.1, $M-CH_3$) ; 127 (2.6, $M-CH_2Ph$) ; 112 (35.6) ; 92 (15.8); 91 (100).

(3-Methyl-2 hepten-4 yl) benzyl oxide

NMR δ : 0.79 (t, 3H) ; 1.32 (m, 4H) ; 1.50 (s, 3H) ; 1.57 (d, J=6Hz , 3H) ; 3.54 (t, 1H) 4.14 (d, J=12Hz , 1H) ; 4.35 (d, J=12Hz , 1H) ; 5.27 (m, 1H) ; 7.22 (m, 5H)

Mass spectrum : (70 e.v.) m/e (relative intensity) 218 (0.2, M+) ; 175 (17.1 ; $M-C_3H_7$) ; 127 (0.3 ; $M-CH_2Ph$) ; 112 (5.5) ; 92 (8.3) ; 91 (100).

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