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Clay Catalyzed Highly Selective O-Alkylation of Primary Alcohols with Orthoesters[†]

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Abstract: Montmorillonite KSF catalyzes the selective O-alkylation of various primary allylic and benzylic alcohols when reacted with different orthoesters at room temperature to afford ethers in moderate to high yields. © 1997 Published by Elsevier Science Ltd.

Conversion of alcohols to the corresponding ethers is an important functional group transformation in organic synthesis. The common methods for this O-alkylation reaction are based on the reaction of metal salts of alcohols with different alkylating agents with or without phase transfer catalysts.[1] Condensation of alcohols and their salts with alkyloxides, aldehydes, olefins and dialkyl phosphites are also reported to be useful methods for this transformation.[2] However such reactions employ highly acidic or basic conditions. Montmorillonite has been successfully used for the O-alkylation of alcohols in presence of pyranulose acetate and olefins like isobutene and dihydropyran.[3] Recently application of cerium (IV) for selective alcoholysis of allylic and tertiary benzylic alcohols has been reported.[4] Herein we demonstrate that orthoesters can be used for a highly selective O-alkylation of primary alcohols under mild conditions.

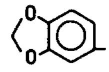
$$\underset{(1a\text{-}j)}{\text{R-OH}} \xrightarrow[\text{r.t, 8-12 h}]{\text{R'C (OR")}_3\text{, Montmorillonite KSF}} \underset{(2a\text{-}j)}{\text{R-O-R" (51-93\%)}}$$

R = allylic, benzylic,
R' = H, CH_3,
R" = CH_3, C_2H_5, n-C_3H_7

Scheme

Primary allylic and benzylic alcohols undergo selective O-alkylation when they are reacted with different orthoesters in presence of Montmorillonite KSF catalyst at room temperature. The reactions were carried

Table. Montmorillonite Catalysed Selective O-Alkylation of Alcohols with Orthoesters.

Entry	Alcohol (1)	Reaction Conditions[a]	Product (2)	Yield[b] (%)
a.	C_6H_5-CH=CH-CH_2OH	2eq.TMOA, 8h	methyl ether	93
b.	"	2eq.TEOA, 8h	ethyl ether	90
c.	"	2eq.TEOF, 12h	ethyl ether	72
d.	"	2eq.TPOF, 12h	propyl ether	51
e.	CH_2=CH-CH_2OH	2eq.TMOA, 8h	methyl ether	86[c]
f.	$(CH_3)_2$C=CH-CH_2OH	2eq.TMOA, 10h	"	81[c]
g.	$C_6H_5CH_2$OCH=CH-CH_2OH	2eq.TMOA, 8h	"	62
h.	$C_6H_5CH_2$OH	2eq.TMOA, 12h	"	83
i.	 CH_2OH	2eq.TMOA, 12h	"	92
j.	 CH_2OH	2eq.TMOA, 12h	"	84

a. All reactions are carried out at room temperature, b.Yields of isolated products, c. Based on GC analysis of the reaction mixture

out by stirring various primary alcohols (1a-j) with 2 equivalents of orthoesters in presence of Montmorillonite KSF (30% w/w of alcohol). The progress of the reaction could be monitored by TLC and the ethers were isolated by simple work up of filtration and evoporation of volatiles in vaccuo. The recovered catalyst could be readily regenerated for further use without any loss of activity. Different orthoesters like trimethylorthoacetate (TMOA), triethylorthoacetate (TEOA), triethylorthoformate (TEOF) and tripropylorthoformate (TPOF) were studied and corresponding ethers were obtained in moderate to high yields. All the products (2a-j) gave satisfactory IR, ^{1}HNMR & mass spectra and the physical constants of known compounds were in good agreement with the reported data in literature. TEOF & TPOF were found to be comparetively less reactive than TEOA and TMOA. Saturated primary alcohols (eg. n-hexanol) and secondary allylic alcohols (eg. C_6H_5CHOHCH=CHC_6H_5) did not undergo O-alkylation under these experimental conditions, which confirms the highly selective nature of this transformation. Further no traces of ethers were obtainable through direct alcoholysis of allylic or benzylic alcohols with methanol in presence of montmorillonite KSF at room temperature. Alcohol and ester derived from orthoester were isolated as byproducts in these reactions (eg. MeOH & CH_3CO_3Me in case of TMOA).

Use of orthoesters for the O-alkylation of various substrates is well documented in literature. Orthoesters were used as alkylating agents to convert several carboxylic, sulfonic and phosphinic acids to their corresponding esters.[5] Neutral substrates like aldehydes and ketones were readily converted into acetals by orthoesters in presence of external acidic catalysts such as $FeCl_3$, amberlyst-15, PTSA and montmorillonite.[6] Just et al[7] and Gopalan et al[5a] proposed O-alkylation mechanisms involving a cationic intermediate formed by the action of acid on orthoester. Based on these precedents, it is likely that O-alkylation of allylic & benzylic alcohols by orthoesters may also follow as similar mechanism involving a cationic intermediate of type, $R\text{-}C(OR'')={}^{+}OR''$, generated by the action of acidic montmorillonite KSF on orthoesters. Selective alkylation through stablization of such cationic species in the interlamellar space of smectite clay can not be ruled out.[8]

In conclusion, considering the merits like high selectivity, good yields, mild reaction conditions, easy experimental & work up procedures and use of inexpensive catalyst that can be conveniently reused, presently described O-alkylation of allylic and benzylic alcohols may find use in organic synthesis.

Experimental Section: In a typical experiment, mixture of cinnamyl alcohol (6.42g, 0.05 mol) trimethylorthoacetate (12.01g, 0.1 mol) and montmorillonite KSF (2g, 30% w/w), was stirred vigorously under anhydrous condition. The reaction was followed by TLC and after completion of reaction (8h), the reaction mixture was filtered and catalyst washed with dichloromethane (10ml). The combined filtrate was concentrated in vacuo and the product was purified by flash chromatography on silica gel (hexane, ethylacetate 4:1) to afford cinnamyl methyl ether (6.88 g, 93%) as a colourless oil.; IR(Neat, cm^{-1}), 960, 1150, 2800-3080. ^1H NMR ($CDCl_3$, δ) 3.3 (s, 3H), 4.0 (d, 2H), 6.1-6.3 (m, 1H), 6.55 (d, 1H), 7.1-7.4 (m, 5H). Mass m/z(%) : 148 (M^+, 66), 117(52), 115(54), 105(27), 77(28).

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