



Montmorillonite clay catalyzed in situ Prins-type cyclisation reaction[†]

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Received 16 June 2000; revised 13 October 2000; accepted 26 October 2000

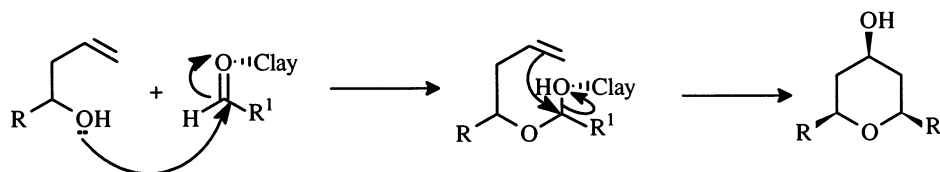
Abstract—Homoallylic alcohols smoothly undergo cross-coupling reactions with aldehydes on the surface of montmorillonite clay to generate 4-hydroxy-2,6-disubstituted tetrahydropyrans in high yields with high diastereoselectivity. © 2000 Elsevier Science Ltd. All rights reserved.

The acid catalyzed condensation of olefins with carbonyl compounds, known as the Prins reaction, is an important reaction for carbon–carbon bond formation.¹ The tetrahydropyran ring is part of the backbone of various important carbohydrates and natural products.² Furthermore, tetrahydropyrans hydroxylated at the 4-position are found in a number of natural products³ such as avermectins, aplysiatoxin, oscillatoxins, latrunculins, talaromycins and acutiphycins. The synthesis of halogenated tetrahydropyrans is reported using conventional Lewis acids⁴ which often generate mixtures of products. Recently $\text{Sc}(\text{OTf})_3$ has been employed for Prins type cyclisations,⁵ which afford a mixture of tetrahydropyranyl ethers and tetrahydropyranol.

In recent years, the use of solid acidic catalysts⁶ such as clays and zeolites has received considerable attention in different areas of organic synthesis because of their environmental compatibility, reusability, high selectivity, operational simplicity, non-corrosiveness, low cost and ease of isolation of the products. In particular, clay

catalysts⁷ make reaction processes convenient, more economic, environmentally benign and act as both Bronsted and Lewis acids in their natural and ion-exchanged forms, enabling them to function as efficient catalysts for various organic transformations. Although, the construction of the six-membered tetrahydropyran ring is an important process in the synthesis of natural products, the use of strongly acidic conditions, expensive reagents and the formation of mixtures of products illustrates the need for efficient, inexpensive and environmentally acceptable catalysts which can effect the transformation under mild conditions.

In continuation of our interest on the applications of solid acid catalysts (KSF) for various transformations⁸ herein we report a new and highly efficient procedure for the synthesis of tetrahydropyranol using montmorillonite KSF as the catalyst. 4-Hydroxy-2,6-disubstituted tetrahydropyran derivatives were formed in high yields when homoallyl alcohols were treated with aldehydes in the presence of KSF clay.⁹ For example,



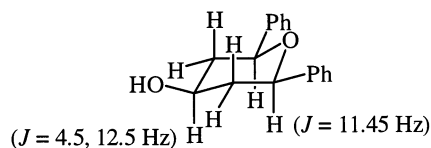
Scheme 1.

Keywords: montmorillonite KSF; homoallylic alcohols; Prins cyclisation; tetrahydropyrans.

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[†] IICT Communication No.4565.

the reaction of benzaldehyde with 1-phenyl-3-buten-1-ol on the surface of montmorillonite in refluxing dichloromethane leads to the formation of 2,6-diphenyl-4-hydroxytetrahydropyran in 90% yield with high diastereoselectivity. The coupling constants of the benzylic hydrogens ($J = 11.45$ Hz) in the ^1H NMR spectrum of the products as well as the hydrogen on the carbon bearing the hydroxyl group ($J = 4.5$ and 12.5 Hz) showed a structure consistent with the two phenyl groups and the hydroxyl group being in the *cis*-orientation and equatorial. The predominant formation of a single stereoisomer is probably due to thermodynamic factors.



The formation of the tetrahydropyranol may be explained by hemi-acetal formation and subsequent Prins-type cyclisation (Scheme 1).

The reaction of aromatic aldehydes with the corresponding homoallylic alcohols in the presence of KSF clay generated symmetric 2,6-disubstituted 4-hydroxytetra-

Table 1. Montmorillonite KSF catalysed synthesis of tetrahydropyrans^a

$ \begin{array}{c} \text{OH} \\ \\ \text{R}-\text{CH}-\text{CH}=\text{CH}_2 \end{array} + \begin{array}{c} \text{O} \\ \\ \text{R}^1-\text{CH} \end{array} \xrightarrow[\Delta, \text{CH}_2\text{Cl}_2]{\text{KSF}} \begin{array}{c} \text{OH} \\ \\ \text{R}-\text{CH}-\text{CH}-\text{CH}-\text{R}^1 \\ \\ \text{O} \end{array} $				
Entry	Homoallyl alcohol	Aldehyde	Reaction time (h)	Yield (%) ^b
a)			3	90
b)			5	87
c)			3.5	70
d)			4	92
e)			5	75
f)			4.5	86
g)			5	90
h)			7	73
i)			3.5	78
j)			5	84
k)			4	87
l)			3.5	90
m)			3	92
n)			4	85
o)			3.5	78
p)			3	90

a) All products were characterised by ^1H , ^{13}C NMR, IR and mass spectra

b) Isolated yields after purification.

hydropyrans in high yields. Similarly, the Prins cyclisation between aliphatic aldehydes and the corresponding homoallylic alcohols gave the symmetric 2,6-disubstituted 4-hydroxytetrahydropyrans with high stereoselectivity. Moreover, the cross-coupling between aromatic homoallylic alcohols and aliphatic aldehydes or the cross-coupling between aliphatic homoallylic alcohols and aromatic aldehydes gave the corresponding unsymmetric tetrahydropyrans in good yields. The results summarized in Table 1 indicate the scope and generality of the reaction with respect to various aldehydes and homoallylic alcohols. The nature of the substituents on the aromatic rings of the reagent shows some effect on this conversion. It is of interest to note that aliphatic, simple aromatic and moderately activated aromatic aldehydes like chloro-, bromo-, meta-phenoxy- and meta-methoxy-benzaldehyde gave high yields of products compared to strongly activated or deactivated nitro or cyano substituted aldehydes. The use of the solid acid catalyst offers high yields of products with high stereoselectivity. The clay catalyst was recovered by filtration, washed with methanol and reused, after activation, for three cycles without significant loss of activity.

In summary, we have described a new and highly efficient procedure for the synthesis of tetrahydropyrans using an environmentally acceptable montmorillonite KSF clay. The catalyst is inexpensive, non-toxic and reusable which makes the process convenient, more economic and environmentally benign.

Acknowledgements

BVS, GMK and CVSR thank CSIR New Delhi for the award of fellowships

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- Typical procedure:** A mixture of 1-phenyl-3-buten-1-ol (5 mmol), benzaldehyde (5 mmol) and KSF clay (1.5 g) in dichloromethane (20 ml) was refluxed for 3 h. On completion, as indicated by TLC, the catalyst was filtered and washed with dichloromethane (2×15 ml). The combined organic layers were washed with water, brine, dried over anhydrous Na₂SO₄ and concentrated in vacuo. The resulting reaction mass was purified by column chromatography on silica gel (Merk, 100–200 mesh, ethyl acetate–hexane, 2:8) to afford 2,6-diphenyl-4-hydroxytetrahydropyran as a white solid (mp 101–102°C). ¹H NMR (CDCl₃): δ 1.50 (brs, OH), 1.60 (dd, 2H, *J* = 12.5 and 11.4 Hz), 2.35 (dd, 2H, *J* = 12.5 and 4.5 Hz), 4.18 (m, 1H), 4.60 (d, 2H, *J* = 11.4 Hz), 7.23–7.30 (m, 10 H, Ar-H). ¹³C NMR (proton decoupled): δ 43.0 (CH₂), 68.5 (CH), 78.5 (CH), 126.0, 127.8, 128.5, 142.0 (aromatic). EIMS: *m/z* (%): 254 M⁺ (15), 236 (40), 136 (60), 104 (100), 77 (35).