Asian Journal of Chemistry; Vol. 24, No. 9 (2012), 3876-3878

ASIAN JOURNAL OF CHEMISTRY

www.asianjournalofchemistry.co.in

Simple and Efficient Method for Tetrahydropyranylation of Alcohols and Phenols by Using Silica Supported Sodium Hydrogen Sulphate as a Catalyst

K. RAVI KUMAR[1], P.V.V. SATYANARAYANA[2,*] and B. SRINIVASA REDDY[1]

[1]RA Chem Pharma Limited, Research and Development Division, Prasanth Nagar, Hyderabad-500 072, India
[2]Department of Chemistry, Acharya Nagarjuna University, Nagarjuna Nagar, Guntur-522 510, India

*Corresponding author: E-mail: chemperuri@yahoo.co.in

(*Received*: 28 September 2011; *Accepted*: 15 April 2012) AJC-11259

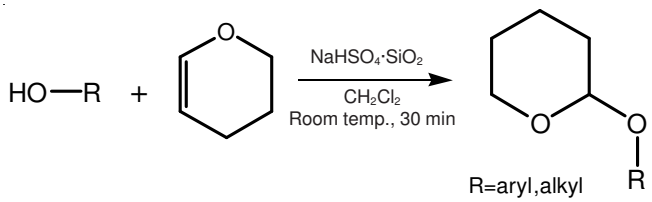
A Simple and efficient process for tetrahydropyranylation of alcohols and phenols has been developed by reacting with dihydropyran at room temperature in presence of catalytic amount of silica supported sodium hydrogen sulphate.

Key Words: Alcohol and phenols, Tetrahydropyranylation, Silica supported sodium hydrogen sulphate, Dichloromethane.

INTRODUCTION

Tetrahydropyranylation is a versatile method for protection of hydroxyl groups[1]. Due to the stability of the tetrahydropyranyl ethers under different conditions such as alkaline media, reactions involving Grignard reagents, lithium alkyls, alkylting, acylating reagents and oxidation and reduction by inorganic hydrides. Tetrahydropyranylation is a general process to protect hydroxyl groups in multistep organic transformations[2]. Tetrahydropyranyl (THP) derivatives can be prepared by using a variety of reagents such as protic acids[3a], Lewis acids[3b], ion-exchange resins[3c], alumina impregnated with $ZnCl_2$[3d], silica chloride[3e], sulfuric acid on silica gel[3f], heteropolyacids[3g], dialkylimidazolium tetrachloroaluminates[3h], K-10 clay[3i] and I_2[3j], polystyrene supported aluminum chloride[3k], $PdCl_2(CH_3CN)_2$,[3l] and tetrabutylammonium bromide[3m]. Although these methods are suitable for many synthetic conditions, many of these are associated with several drawbacks, which include long reaction times, reflux conditions, the use of catalysts which may effect other functionalities present, harsh and acidic conditions, poor selectivity, formation of polymeric byproducts of the dihydropyran and isomerization. In addition, some of these catalysts are not recyclable and require work-up of the reaction mixture. Thus, there is still need for mild selective methods for this purpose.

In recent years, heterogeneous catalysts have gained imp-ortance in several organic transformations due to their inte-resting reactivity as well as for economic and environmental reasons. Recent works[4] and their applications for this heterogeneous catalysts observed that silica supported sodium hydrogen sulphate is highly efficient catalyst for tetrahydropyranylation and this was a good reusable catalyst.



Scheme-I

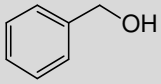
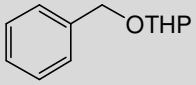
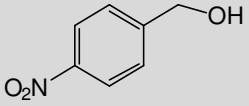
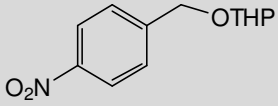
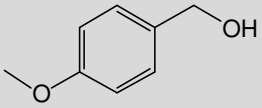
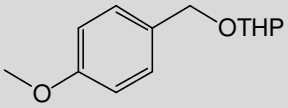
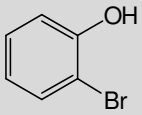
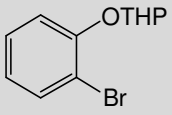
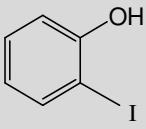
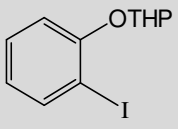
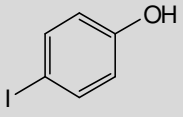
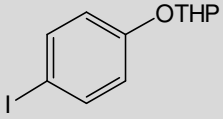
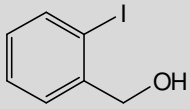
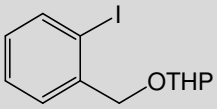
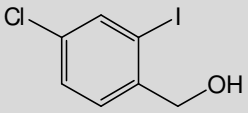
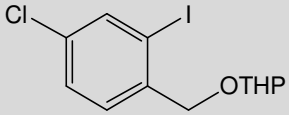
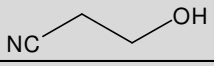
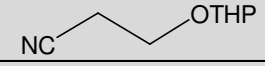
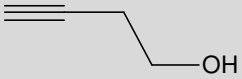
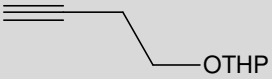
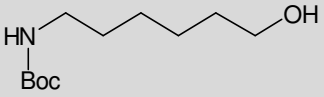
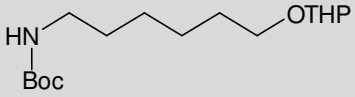
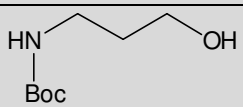
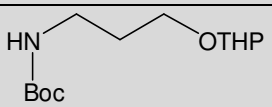
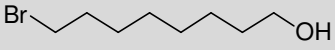
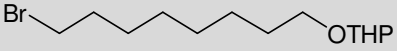
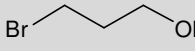
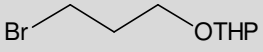
Alcohols and phenols are treated with 3,4-dihydro-2*H*-pyran in dichloromethane at room temperature in presence of the above mentioned catalyst produced the corresponding tetrahydropyranyl (THP) ethers in high yields (**Scheme-I**, Table-1). The conversion proceeded within a short time (30-40 min) and with a small quantity of catalyst. The catalyst can easily be prepared[5] from the readily available $NaHSO_4$ and silica gel (230-40 mesh) and these are inexpensive and non-toxic as the reaction is heterogeneous in nature, so the catalyst can easily be removed by simple filtration. The filtered catalyst was dried and again reused for protection.

EXPERIMENTAL

$NaHSO_4$ was obtained from Finar chemicals Ltd. Distilled CH_2Cl_2 was used for all experiments. 100-200 mesh silica gel was employed for column purification. Tetrahydropyranyl (THP) ethers were characterized by ^1H NMR (400 MHz).

To a stirred solution of 4-nitro benzyl alcohol (153 mg, 1 mmol) and 3,4-dihydro-2*H*-pyran (101 mg, 1.2 mmol) in distilled dichloromethane (10 mL) was added activated (while hot) $NaHSO_4$-SiO_2 (10 mg) at room temperature (the catalyst

TABLE-1
TETRAHYDROPYRANYLATION (THP) OF ALCOHOLS AND PHENOLS BY USING $NaHSO_4$-SiO_2[a]

Entry	Substrate	Product	Time (min)	Yield (%)
a			30	97
b			30	97
c			30	96
d			35	92
e			35	93
f			40	93
g			30	94
h			30	90
i			30	92
j			30	91
k			40	88
l			40	87
m			30	91
n			30	90

[a]Structures of the products were characterized by their spectral (^{1}H NMR) data

was kept in an oven at 120 ºC for 48 h before using it). After completion of the reaction (monitored by TLC) the catalyst was filtered and washed with dichloromethane (5 mL), the filtrate and washings were combined and the solvents were removed under vaccum. The residue was purified by column chromatography using hexane:EtOAc (4:1) over silica gel to afford the tetrahydropyranyl ether of 4-nitro benzyl alcohol (230 mg, 97 % yield).

Conclusion

A simple and efficient process is developed for tetrahydropyranylation of alcohols and phenols using $NaHSO_4$-SiO_2 catalyst at room temperature. The mild reaction condition, high yield, fast reaction time, less expensive and readily available reagents and easy experimental procedure are the advantages of the present method. We believe the present process will find applications as a useful synthetic methodology.

ACKNOWLEDGEMENTS

The authors sincerely thank the RA Chem. Pharma Ltd. for financial support and encouragement. Support from the analytical department is also acknowledged.

REFERENCES

1. (a) T.W. Greene and P.G.M. Wuts, Protective Groups in Organic Synthesis, John Wiley & Sons, New York, edn. 3, pp. 17-292 (2000).
2. S. Hoyer and P. Laazol, *Synthesis,* 655 (1986) and reference cited therein.
3. (a) J.H. Van Boom, J.D.M. Herschied and C.B. Reese, *Synthesis*, 169 (1973); M. Miyashita, A. Yoshikoshi and P.A. Grieco, *J. Org. Chem.*, **42**, 3772 (1977); R. Nouquier, *Tetrahedron Lett*., **23**, 2951 (1982); (b) H. Alper, and L. Dinkes, *Synthesis*, 812 (1972); B. Karimi and J. Maleki, *Tetrahedron Lett*., **43**, 5353 (2002); V.V. Namboodiri and R.S. Varma, *Tetrahedron Lett*., **43**, 1143 (2002); (c) A. Bongini, G. Cardillo, M. Orena and S. Sandri, *Synthesis*, 618 (1979); F.M. Menger and C.H. Chu, *J. Org. Chem*., **46**, 5044 (1981); G.A. Olah, A. Husain, B.P. Singh, *Synthesis*, 892 (1983); R.D. Johnston, C.R. Marston, P.E. Krieger and G.L. Goe, *Synthesis,* 393 (1988); (d) B.C. Ranu and M. Saha, *J. Org. Chem*., **59**, 8269 (1994); (e) N. Ravindranath, C. Ramesh and D. Biswanath, *Synlett,* 1777 (2001); (f) F. Chavez and R. Godinez, *Synth. Commun.*, **22**, 159 (1992); (g) A. Molnar and T. Beregsazaszi, *Tetrahedron Lett*., **37**, 8597 (1996); (h) V.V. Namboodiri and R.S. Varma, *Chem. Commun.*, 342 (2002); (i) S. Hoyer and P. Laszlo, *Synthesis,* 655 (1986); (j) N. Deka and J.C. Samara, *J. Org. Chem*., **66**, 1947 (2001); (k) B. Tamami and K.P. Borujeny, *Tetrahedron Lett.*, **45**, 715 (2004); (l) Y.G. Wang, X.X. Wu and Z.Y. Jiang, *Tetrahedron Lett*., **45**, 2973 (2004); (m) S. Naik, R. Gopinath and B.K. Patel, *Tetrahedron Lett*., **42**, 7679 (2001).
4. (a) B. Das, B. Venkataiah and P. Madhusudan, *Synlett.,* 59 (2000); (b) B. Das and P. Madhusudan, *Synth. Commun.*, 1671 (2000); (c) B. Das, R. Ramu, B. Ravikanth and K.R. Reddy, *Tetrahedron Lett.*, **47**, 779 (2006); (d) C. Ramesh, N. Ravindranath and B. Das, *J. Org. Chem*., **68**, 7101 (2003); (e) K.V.N. Srinivas and B. Das, *J. Org. Chem*., **68**, 1165 (2003).
5. G.W. Breton, *J. Org. Chem*., **62**, 8952 (1997).