Simple, Facile and Highly Selective Tetrahydropyranylation of Alcohols Using Silica Chloride[1]

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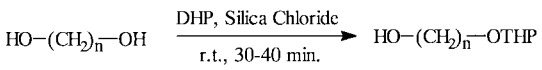
Abstract: A simple and efficient process for tetrahydropyranylation of alcohols has been developed by reacting with dihydropyran at room temperature in presence of catalytic amount of silica chloride. The process is highly selective for monoprotection of the hydroxyl groups of symmetric diols.

Key words: alcohols, tetrahydropyranylation, silica chloride, symmetric diols, monoprotection

Tetrahydropyranylation is a versatile method for protection of hydroxyl groups.[2] Due to the stability of the tetrahydropyranyl ethers under different conditions such as alkaline media, reactions involving Grignard reagents and lithium alkyls, oxidative reagents, metal hydrides and alkylating and acylating reagents tetrahydropyranylation is a general process to protect hydroxy groups in multistep organic transformations.[3] Tetrahydropyranyl derivatives can be prepared by using a variety of reagents such as protic (HCl, *p*-toluenesulfonic acid) and Lewis acids ($BF_3{\cdot}OEt_2$, $Al_2(SO_4)_3$ on silica gel, $ZnCl_2$ on alumina),[2,4] clay materials,[3] ion exchange resins[5] and DDQ.[6] However, several reported methods are associated with certain drawbacks which include long reaction time, refluxing condition and the uses of reagents which may effect the other functionalities. They have also limitation in selectivity of monoprotection of the hydroxyl groups of symmetric diols. Thus there is a need for suitable mild and selective method for this purpose.



Scheme

In continuation of our recent work[7] on solid supported reactions we have observed that silica chloride is a convenient and efficient catalyst for tetrahydropyranylation of alcohols. These compounds when treated with 3,4-dihydro-2H-pyran at room temperature in presence of the above mentioned catalyst produced the corresponding tetrahydropyranyl ethers in high yields (Scheme, Table). The process was found to be highly selective for monotetrahydropyranylation of symmetric diols. The conversion proceeded within a short time (30–40 min) and with a small quantity of catalyst. The catalyst can easily be prepared[8] from the readily available reagents, thionyl chloride and silica gel. When the reaction was carried out with only thionyl chloride in absence of silica gel the yields and the selectivity were diminished. The experimental procedure is easy. After the reaction was complete the product was isolated by simple elution of the solid mass with CH_2Cl_2. The structures of all the products were established from their spectral and analytical data.

In conclusion, we have developed a simple, efficient and highly selective process for tetrahydropyranylation of alcohols using combination of the solid surface of silica gel and thionyl chloride. 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.

Typical experimental procedure:
To a solution of hexane-1,6-diol (118 mg, 1 mmol) and 3,4-dihydro-2*H*-pyran (84 mg, 1 mmol) in CH_2Cl_2 (10 mL), silica chloride (10 mg) was added. The reaction was stirred at room temperature and was monitored by TLC. After 30 min the mixture was filtered and the filtrate was concentrated and purified by column chromatography over silica gel to afford monotetrahydropyranyl ether of hexane-1,6-diol (180 mg, 90%).

Acknowledgement

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References and Notes

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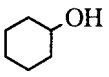
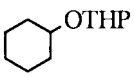
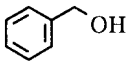
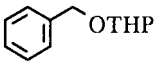
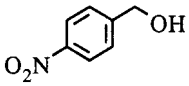
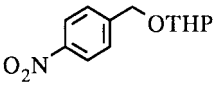
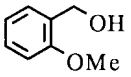
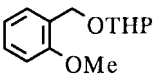
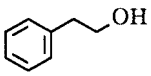
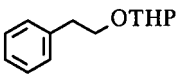
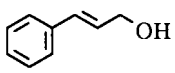
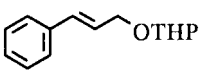
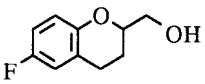
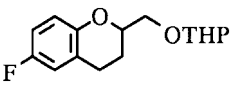
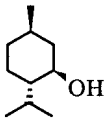
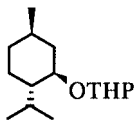
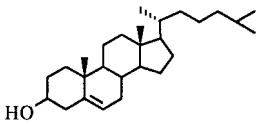
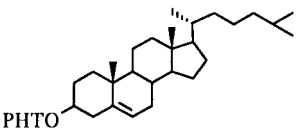
Table Tetrahydropyranylation of Alcohols using Silica Chloride

Entry	Alcohol	Product	Time (min.)	Isolated Yield (%)
1	H_3C-$(CH_2)_{11}$-OH	H_3C-$(CH_2)_{11}$-OTHP	15	82
2	HO-CH_2-CH_2-OH	HO-CH_2-CH_2-OTHP	30	82
3	HO-$(CH_2)_3$-OH	HO-$(CH_2)_3$-OTHP	35	84
4	HO-$(CH_2)_4$-OH	HO-$(CH_2)_4$-OTHP	30	88
5	HO-$(CH_2)_6$-OH	HO-$(CH_2)_6$-OTHP	30	91
6	HO-$(CH_2)_8$-OH	HO-$(CH_2)_8$-OTHP	30	86
7	HO-$(CH_2)_{10}$-OH	HO-$(CH_2)_{10}$-OTHP	40	89
8			15	85
9			10	93
10			15	92
11			10	86
12			10	91
13			15	88
14			15	86
15			20	85
16			25	84

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