

## Mild and Efficient Tetrahydropyranylation of Alcohols-Catalysis by Lithium Perchlorate in Diethyl Ether.

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**Abstract**: Treatment of 3,4-dihydro-2*H*-pyran 1 with various alcohols 2 - 10 furnished the tetrahydropyranyl ethers 11 - 19 in the presence of 5M lithium perchlorate in diethyl ether (5M LPDE), which is essentially a neutral medium. © 1998 Elsevier Science Ltd. All rights reserved.

keywords : dihydropyran, alcohols protection, lithium perchlorate in diethylether, Lewis acid.

Protection of alcohols, a recurring event in organic synthesis, continues to receive wide attention. In particular, protection as a tetrahydropyranyl (THP) ether is often sought after as THP ethers are stable under basic conditions. In addition to the well known protic and Lewis acids,<sup>1</sup> other reagents and catalysts such as iodotrimethylsilane,<sup>2</sup> triphenylphosphine hydrobromide,<sup>3</sup> montmorillonite (an acidic clay),<sup>4</sup> and of late, heteropoly acids,<sup>5</sup> have been used to effect the tetrahydropyranylation of alcohols.

In recent years, lithium perchlorate in diethyl ether (LPDE) has gained importance as a versatile reaction medium for effecting various organic transformations such as, 1,3-Claisen rearrangements,<sup>6</sup> glycoside synthesis,<sup>7</sup> ring-opening reactions of oxiranes,<sup>8</sup> selective carbonyl protection as dithioacetal,<sup>9</sup> *etc.* Herein, we report a mild and efficient catalyst, *viz.* 5M LPDE, which is essentially a neutral medium, for the tetrahydropyranylation of alcohols.

Treatment of 3,4-dihydro-2*H*-pyran 1 with benzyl alcohol 5 in 5*M* LPDE for 12 hours at 25-30°C afforded the 2-benzyl tetrahydropyranyl ether 13 in 86% yield. The reaction was extended to a variety of alcohols 2-9 (primary, secondary, tertiary, allylic, propargylic, benzylic) which also underwent facile tetrahydropyranylation in 5*M* LPDE at ambient temperature, affording the corresponding tetrahydropyranyl ethers 10-17. Even the otherwise less reactive *t*-butanol 9 afforded the corresponding acetal 17, in moderate yield.



Alcohol (ROH)	)	Product (Time, yield) <sup>#</sup>	Alcohol (ROH)	Product (Time, yield) <sup>#</sup>
СН3(СН2)6СН2ОН	2	10 (8h, 92%)	ОН 6	14 (11h, 80%)
скорон	3	11 (8h, 74%)	<del>ОН</del> 7	15 (8h, 90%)
OH	4	12 (9h, 83%)	ОН 8	16 (12h, 80%)
ОН	5	13 (12h, 86%)	у но	17 (17h, 56%)

**Table 1.** 5M LPDE mediated tetrahydropyranylation of alcohols.

<sup>#</sup> Isolated yields of pure products with compatible <sup>1</sup>H and <sup>13</sup>C NMR spectral data

In summary, we have observed 5M LPDE to be an excellent medium for the protection of alcohols as tetrahydropyranyl ethers essentially under neutral and mild conditions, besides enabling an easy work up.

Typically, 3,4-dihydro-2*H*-pyran 1 (5 mmol) is treated with an alcohol (5 mmol), in 5*M* lithium perchlorate in diethyl ether (1 ml) at ambient temperature. After completion (tlc), the reaction mixture was quenched by addition of water (25 ml) and extracted with dichloromethane (3 x 25 ml), which was dried, filtered and purified by flash column chromatography on silica gel.

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