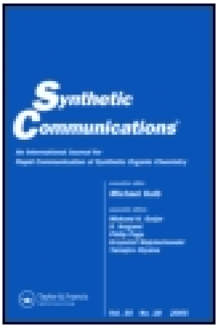

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Alpo$_4$ and Alpo$_4$-Al$_2$O$_3$ as New Heterogeneous Catalysts for the Solvent-Free Tetrahydropyranylation of Alcohols and Phenols

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$AlPO_4$ AND $AlPO_4$-Al_2O_3 AS NEW HETEROGENEOUS CATALYSTS FOR THE SOLVENT-FREE TETRAHYDROPYRANYLATION OF ALCOHOLS AND PHENOLS

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ABSTRACT: OH-protection of alcohols and phenols by heating the hydroxylated compound with 3,4-dihydro-2H-pyrane in the presence of an $AlPO_4$ or $AlPO_4$-Al_2O_3 heterogeneous acid catalyst is described. Isolated yields, not optimized, were in the range 50-99%.

3,4-Dihydro-2H-pyrane it is one of the most generally useful protecting groups for hydroxyl functions. The tetrahydropyranyl (THP) ethers thus formed are stable under a variety of reaction conditions such as basic media, reduction with hydrides, and contact with Grignard, oxidative, alkylating and acylating reagents.[1-5] The reaction is carried out under acid-catalysed conditions either with mineral acids or in the presence of catalysts such as toluene-p-sulphonic acid, pyridinium p-toluensulphonate or trifluoroacetic acid. However, for better isolation of the reaction products, in the last years heterogeneous acid

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catalysts, such as ion-exchange resins,[6-8] acidic clays[9] and aluminum sulfate supported on silica gel,[10] have been used. In this sense, the use of inorganic solids such as silica, alumina or zeolites provide opportunities for catalysis and control of organic reactions.[11,12] Besides, yields are often higher and work-up procedures easier than for the corresponding homogeneous reactions, and it may be possible to improve isomer selectivity.

The surface acid-base character of $AlPO_4$ and $AlPO_4$-Al_2O_3 catalysts enable them to be used for a number of organocationic reactions in gas phase[13,14] or in the field of selective synthetic chemistry which involves acid- and basic-catalysed reactions. Thus, we have reported previously their use as catalysts for base catalysed condensations, in liquid-phase[15] or in a dry medium.[16] Here we explored the application of these heterogeneous catalysts for acid reactions in liquid-phase.

Thus, we now wish to report a simple and mild approach to the tetrahydropyranylation of alcohols and phenols which involves the reaction of alcohol or phenol with 3,4-dihydro-2H-pyrane, under heterogeneous liquid-solid catalysis, on $AlPO_4$ and $AlPO_4$-Al_2O_3 catalysts and in the absence of solvent. Our results are summarized in the Table I. Isolated yields were not optimized and the results obtained after 15 min were used for evaluation.

Several effects are evident from the results in Table I. First of all, it is clear that the protection of OH group occurred with all catalysts although $AlPO_4$ was extremely able to catalyse the tetrahydropyranylation of alcohols and phenols. Furthermore, methyl groups in ortho-position on the aromatic ring

TABLE I. SYNTHESES OF THP ETHERS ON $AlPO_4$, $AlPO_4$-Al_2O_3

R-OH	Yield [a] (%)			
	$AlPO_4$	$AlPO_4$-Al_2O_3	Al_2O_3[b]	SiO_2[b]
Phenol	93	93	13	-
2-Methylphenol	85	91		
3-Methylphenol	92	87		
4-Methylphenol	92	89		
2,6-Dimethylphenol	54	41		
Cyclohexanol[c]	97	71		
Phenylmethanol	99	70		

a. Reported yields refer to product purified by vacuum distillation (purity >99% as determined by GLC). Also, all the products showed satisfactory microanalytical values.

b. Catalyst weight: 1 g.

c. Catalyst weight: 50 mg.

of the phenol affected the reaction thus inhibiting the formation of THP ethers, presumably due to steric hindrance. Moreover, $AlPO_4$-Al_2O_3 catalyst afforded, in general, low isolated yields of THP-ethers as a consequence of its higher surface acidity, as compared to $AlPO_4$, by hydrolyzing the THP ether previously formed. Thus, with $AlPO_4$-Al_2O_3 catalysts short reaction times, lower reaction temperatures or smaller catalyst weight are needed to increase conversion to THP-ethers.

TABLE II. SYNTHESES OF THP-ETHERS ON $AlPO_4$, $AlPO_4$-Al_2O_3 UNDER ROOM TEMPERATURE STIRRING OR ULTRASOUND IRRADIATION

R-OH	Catalyst	Cat. weight (mg)		t (min)	Yield (%)
Phenol	$AlPO_4$	50	r.t.-stirr	15	12
		50	r.t.-US(20W)	15	61
		25	reflux	15	93
Cyclohexanol	$AlPO_4$-Al_2O_3	50	r.t.-stirr	30	4
		75	r.t.-US(20W)	30	37
		50	reflux	15	71

Furthermore, Al_2O_3 and SiO_2, under the same conditions, does not afforded any reaction. Besides, Al_2O_3 afforded only 13% of THP-phenol for a catalyst weight forty times higher than $AlPO_4$ or $AlPO_4$-Al_2O_3 catalysts.

On the other hand, we also found that at room temperature the reaction proceeds at a very slow rate under magnetic stirring but ultrasound irradiation (20W) improved THP-ether yields (Table II)

The excellent yields found with $AlPO_4$ demonstrate this catalyst to be superior to other catalysts. For example, THP-cyclohexanol is obtained in short reaction times and/or with smaller amount of catalyst that previously reported for tetrahydropyranylation catalysed by pyridinium p-toluensulphonate[17], ion-exchange resins[7,8] orK-10 clay[9].

So, $AlPO_4$ is an effective yet mild acid catalyst for the tetrahydropyranylation of alcohols and phenols. The reaction, that is carried out in the presence of excess dihydropyran, proceeds selectively under mild conditions in very good yields (not optimized) with short reaction times and without the formation of troublesome oligomeric pyrans. Also, work-up is reduced to a easy separation of THP-ethers by simple filtration and elimination of 3,4-dihydro-2H-pyrane excess, as it is usual whatever heterogeneous catalyst.

EXPERIMENTAL

Cyclohexanol, phenylmethanol, phenol and substituted phenols were commercial p.a. quality chemicals purchased from Aldrich and were purified prior to use. 3,4-Dihydro-2H-pyrane p.a. from Merck was doubly distilled. All reaction products were characterized by their physical and spectral characteristics (b.p., FT-IR, ^1H and ^{13}C-NMR, etc.). NMR spectra ($CDCl_3$/TMS) were recorded on a Bruker AC200 instrument after 200 scans. ^{13}C-NMR DEPT editing technique was used to differentiate carbon spins according to the number of directly bonded protons. The purity of the isolated THP-ethers was checked by GLC. GLC analyses were run on a HP-5890 GC with a FID by using a 15% OV-1/Chromosorb W AW-DMCS 100/120 column (3mm i.d., 0.3 m).

Catalysts

Two catalysts were used: an $AlPO_4$ obtained by precipitation using aqueous ammonia, dried at 390 K and calcined at 923 K for

3 h (surface area 109 m^2 g^{-1}).[13] An $AlPO_4$-Al_2O_3 (75:25 wt%) system obtained in propylene oxide, dried at 390 K and calcined at 923 K for 3 h (surface area 319 m^2 g^{-1}).[14]

General procedure

The synthesis of O-(2-tetrahydropyranyl)-phenylmethanol is representative of the procedure used. $AlPO_4$ catalyst (25 mg), phenylmethanol (25 mmol) and 3,4-dihydro-2H-pyrane (110 mmol) were mixed with stirring and heated under reflux (359 K) for 15 min. After removal of the catalyst by filtration the catalyst was rinsed with THP and then, the excess dihydropyran is removed under reduced pressure on a rotary evaporator yielding the pure O-(2-tetrahydropyranyl)-phenylmethanol: b.p. 105/5 (99%). ^{1}H-NMR ($CDCl_3$/TMS) δ: 7.2-7.3 (m, 5H, Ar-H), 4.7 (t, 1H, O-CH-O), 4.6 (AB, 2H, C_{Ar}-CH_2-O), 3.5-3.8 (m, 2H, O-CH_2-C_{Aliph}), 1.5-1.8 (m, 6H, CH_2 THP); ^{13}C-NMR ($CDCl_3$/TMS) δ: 127-138 (C_{Ar}), 97.3 (O-C-O), 68.4 (Ar-C-O), 61.5 (O-C-Aliph), 19-30 (CH_2 THP).

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