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NATURAL KAOLINITIC CLAY : A MILD AND EFFICIENT CATALYST FOR THE TETRAHYDROPYRANYLATION AND TRIMETHYLSILYLATION OF ALCOHOLS

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Abstract : Natural kaolinitic clay possessing transition metals such as Fe, Ti in its lattice has been found to catalyze efficiently the protection of a variety of alcohols with 2,3-dihydro-4H-pyran (DHP) and hexamethyldisilazane (HMDS) at ambient conditions.

The protection of alcoholic hydroxyl functions has found widespread application especially in the chemistry of steroids, sugars, glycerides and synthesis of natural products. However, a central problem in organic synthesis is to ensure that a specific hydroxyl function in a multifunctional molecule is protected from unwanted reactions altogether or until such time as its intrinsic reactivity is required. The tetrahydropyranylation is one of the methods of choice to protect a hydroxyl

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function in a multi-step organic synthesis due to its remarkable stability toward a variety of conditions such as reactions involving Grignard reagents and lithium alkyls, reduction with hydride etc.¹ A variety of reagents have been developed for the tetrahydropyranylation of alcohols which include mainly protic acids², Lewis acids³, ion-exchange resins⁴, heterogeneous catalysts⁵ and others⁶.

Currently, acid catalysis of organic transformations by clay aluminosilicates is an area of considerable potential and interest due to ease of handling and work-up, low corrossiveness and low cost of clays.⁷ Due to their Bronsted and Lewis acidities, clays, both in their natural and ion-exchanged forms, function as efficient catalysts for a variety of important transformations.⁸ We wish to report that the natural kaolinitic clay⁹ catalyzes very efficiently the protection of a variety of alcohols with DHP (2) or HMDS (4) producing tetrahydropyranyl and trimethylsilyl ethers (3 and 5) respectively (Scheme 1).



The kaolinitic clay was procured from the padappakara mine of Quilon District, Kerala, India and it was subsequently purified, dried, calcined and treated with acid (2M HCl) as reported elsewhere.¹⁰ The clay has been thoroughly characterized¹¹ by XRD, UV, ESR, SEM, EDX and chemical analysis. The composition of the clay has been found : (i) by Electron Dispersive X-ray (EDX) analysis (in %) : SiO₂ = 62.8, Al₂O₃ = 24.92, Fe₂O₃ = 7.5, TiO₂ = 3.79 and K = 0.4; (ii) by chemical analysis (in %) : SiO₂ = 67.45, Al₂O₃ = 22.2, Fe₂O₃ = 6.1, TiO₂ = 3.45, and K = 0.8.

Entry	Substrate	THP ether, 3 (a-j)	TMS ether, 5
	1 (a-j)	Yield (%) ^a	(a-j)
			Yield (%) ^a
а	Cyclohexanol	85	92
b	l-Menthol	82 ^b	94°
с	1,10-Decanediol	81 ^d	
d	10-Bromodecanol	88	
e	Allyl alcohol	85	
ſ	Propargyl alcohol	78	
g	t-Butyl alcohol	83	89
h	Benzyl alcohol	91	90
i	Cinnamyl alcohol	90	85
j	Phenol	0	95

Table 1 :Protection of alcohols with DHP	(2) or HMDS (4) catalyzed b	y clay
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a = Isolated after chromatographic purification, products were thoroughly characterized by IR, ¹H and ¹³C NMR, MS; b = $[\alpha]_D$ -79° (C 3, acetone); c = $[\alpha]_D$ - 76.6° (C 3, acetone); d = *Mono* OTHP (65%), *di* OTHP (35%).

The results of the alcohol protection with DHP and HMDS are summarized in Table 1. As can be seen from the Table 1, the clay catalyzed efficiently the protection of a variety of alcohols. For example, it is remarkable that the acid sensitive alcohols such as t-butanol underwent protection with DHP and HMDS producing their corresponding ethers in a quantitative fashion without undergoing dehydration. In the case of diol, with one mole of DHP, it was possible to achieve to a greater extent a selective protection of alcoholic function (*mono* protection 65%, *di* protection 35%) with the clay catalyst [entry 3c]. Interestingly, the clay has been found to be an excellent catalyst for the protection of phenolic hydroxyl group with HMDS in high yields. Further, functional groups such as Br, C=C, C=C did not interfere during protection (entries 3d-3f) 4,5,6). However, it is to be noted that the protection of alcohol with trimethylsilyl chloride could not be achieved with the clay, nor the phenolic hydroxyl could be protected with DHP under the reaction conditions. Mechanistically, the natural kaolinitic clay having transition metal ions such as Fe, Ti in its lattice possesses disordered structure and hence on acid activation results in the generation of large amounts of relocatable cations (Al³⁺, Fe³⁺) in the interlamellar space producing higher surface area and Bronsted and Lewis acidities which are responsible¹² for catalyzing the protection of alcohols. The clay catalyst was recovered and reused 5 times with virtually no loss of activity and selectivity.

In conclusion, we have shown that the natural kaolinitic clay is an excellent reusable catalyst for the protection of variety of alcohols with DHP and HMDS at ambient conditions.

EXPERIMENTAL SECTION

IR spectra were recorded on a Perkin-Elmer 137-E spectrometer. Column chromatography were performed on silica gel (60-120 mesh). ¹H and ¹³C NMR spectra were recorded on a Brucker FT90 and 200 MHz instruments. The chemical shifts were reported with TMS as internal standard. The mass spectra (MS) were recorded on an automated Finnigan MAT 1020C mass spectrometer using ionization energy of 70 eV.

Typical Reaction Procedure

In a typical reaction procedure, a mixture of alcohol (0.0075 mol),

NATURAL KAOLINITIC CLAY

2,3-dihydro-4H-pyran (0.94 g, 0.012 mol), [or hexamethyldisilazane (0.012 mol) as the case may be] and clay catalyst (100 mg, 10% m/m) in CCl_4 (15 ml) was stirred at RT for 2 h. After the reaction was complete (TLC), the catalyst was filtered off, the product analyzed by GLC capillary column and purified by flash chromatography to afford the THP ether (or TMS ether).

3d : IR (Neat) : 1450, 1350, 1250, 1220, 1150, 1080, 1050, 880, 770 and 550 cm⁻¹; ¹H NMR (90 MHz, CDCl₃) : δ 1.1 - 2.0 (22 H, m, 11 x CH₂), 3.2 - 4.0 (4H, m, 2 x OCH₂), 3.35 (2H, t, J = 8 Hz, CH₂-Br), 4.5 (1H, brs (OCH); ¹³C NMR (50.3 MHz, CDCl₃) : δ 98.8, 67.6, 62.2, 33.7, 32.9, 30.8, 29.8, 29.4, 28.7, 28.2, 26.2, 25.6 and 19.7.

5b : IR (Neat) : 1450, 1375, 1250, 1100, 900, 850, 750, 700, 525 and 400 cm⁻¹; ¹H NMR (200 MHz, CDCl₃) : δ 0.15 (9H, s, SiMe₃), 0.75 (3H, d, J = 6 Hz, CH₃), 0.85 [6H, d, J = 6 Hz, (CH₃)₂], 0.85 - 1.1 (4H, m, 2 x CH₂), 1.4 (1H, m, CH), 1.65 (2H, m, CH₂), 1.9 (1H, br. d, J = 4 Hz, CH), 2.2 (1H, m, CH), 3.45 (1H, dt, J = 6 Hz, and 2 Hz, OCH); MS : m/z (% rel. intensity) 228 (M⁺, 4), 213 (7), 171 (4), 157 (5), 143 (84), 138 (24), 95 (20), 81 (40), 75 (100) and 67 (12).

5i : IR (Neat) : 1400, 1250, 1125, 1075, 975, 900, 850, 750, 700, 425 and 400 cm⁻¹; ¹³C NMR (50.3 MHz, CDCl₃) : δ 0.182, 63.1, 126.8, 127.2, 128.0, 129.7, 129.1 and 137; MS : m/z (% rel. intensity); 206 (M⁺, 82), 191 (51), 135 (18), 117 (100), 115 (51), 91 (20) and 73 (65).

5j : IR (Neat) : 1600, 1490, 1250, 900, 850, 750, 700, 525 and 400 cm⁻¹; ¹H NMR (200 MHz, CDCl₃) : δ 0.35 (9H, s, SiMe₃), 6.85 - 7.1 (3H, m), 7.25 - 7.35 (2H, m); MS : m/z (% rel. intensity) 166 (M⁺, 35), 152 (22), 151 (100), 135 (12), 95 (25), 91 (29), 77 (38), 73 (30) and 65 (25).

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