Bis[trimethylsilyl] Sulfate-Catalyzed Alcohol Protection with Dihydropyran, Deprotection, and Transesterification

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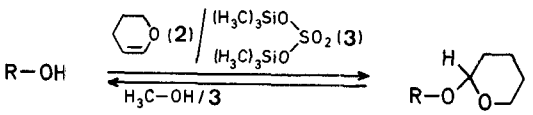
We report that bis[trimethylsilyl] sulfate[1-5] **(3)** is an efficient catalyst both for tetrahydropyranylation of alcohols **(1)** as well as for removal of the protecting group[6,7] from **4** under mild conditions as compared with those of the conventional protic acid catalysis[8]. For example, the tetrahydropyran-2-yl ether **4** of an alcohol **1** is prepared at 0 °C with 1.1 equiv of dihydropyran **(2)** in the presence of 2 mol% of **3** within 1 h. Isolation of the product is effected simply by adding pyridine, concentrating, and column chromatography of the residue, or alternatively by adding potassium carbonate to the reaction mixture and distillation. Deprotection is carried out at room temperature in methanol during ~1 h (Table).



1 4

It is worth pointing out that even tertiary allylic alcohols can be protected without rearrangement or other side reactions

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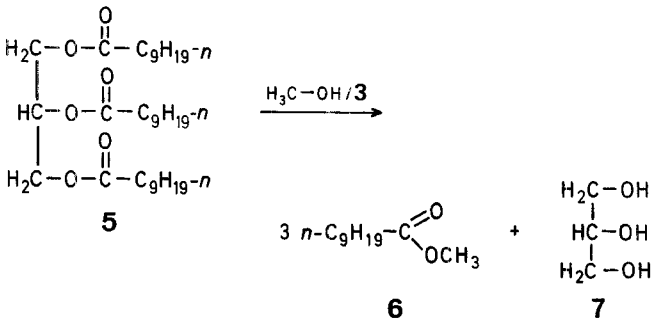
(1g, h). The ether of testosterone **(4i)** was prepared in a quantitative yield in much shorter time as compared with the pyridinium tosylate catalysis[8].

The catalyst **3** is also useful for transesterification[9,10]. For example, when benzyl acetate was heated to reflux in methanol in the presence of **3** (10 mol%) for 2 h, benzyl alcohol was isolated in 89% yield. Particularly this reaction is applicable to the alcoholysis of a glyceride as exemplified by the conversion of 1,2,3-propanetriyl tris[decanoate] **(5)** into methyl decanoate **(6)** and glycerol **(7)**.

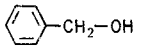
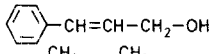
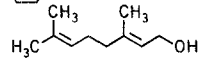
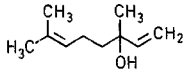
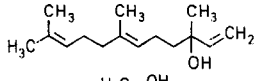
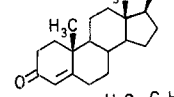
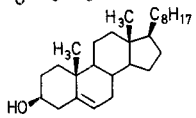


5 **6** **7**

Cinnamyl Tetrahydropyranyl Ether (4c); Typical Tetrahydropyranylation Procedure:

A dichloromethane (20 ml) solution of cinnamyl alcohol (**1c**; 1.00 g, 7.5 mmol), dihydropyran (**2**; 0.72 ml, 7.8 mmol) and **3** (1.0 molar dichloroethane solution, 0.02 ml, 0.02 mmol) is stirred at 0°C. T.L.C. monitoring reveals that the reaction is completed in 10 min. At this point pyridine (~0.1 ml) is added to the reaction mixture and all the volatile material is evaporated under reduced pressure. Column chromatography (silica gel, ~40 g; eluent: 20:1 hexane/ethyl acetate) gives the corresponding ether **4c**; yield: 1.60 g (98%). In another experiment of 1/2 scale, the work-up is effected by the addition of potassium carbonate (~0.1 g) to the reaction mixture. Concentration and distillation over the potassium carbonate gives the product **4c**; yield: 0.70 g (86%); b.p. 125–130°C (bath temperature)/1 torr.

Table. Protection and Deprotection of Alcohols **1** with Bis[trimethylsilyl] Sulfate **(3)**

Alcohol	Protection with Dihydropyran (2)[a]				Deprotection[c]	
	Reaction time	Yield [%][d] of **4**	b.p. [°C]/torr[b] or m.p. [°C]	Molecular formula[e] or Lit. data	Reaction time	Yield [%][d] of **1**
1a n-$C_{12}H_{25}$–OH	10 min	97[f]	95–98°/0.04	$C_{17}H_{34}O_2$ (270.5)	90 min	98
1b 	12 min	97[g]	120–125°/4	105°/4[11]	70 min	95
1c 	10 min	98	125–130°/1	$C_{13}H_{18}O_2$ (206.3)	60 min	100
1d 	15 min	100[f]	78–85°/1	70°/1[11]	—	—
1e t-C_4H_9– 	8 min	93[f]	82–89°/0.04	$C_{15}H_{28}O_2$ (240.4)	50 min	95
1f	15 min	92[f]	65–70°/0.04	$C_{17}H_{32}O_2$ (268.4)	—	—
1g 	10 min	92[h,i]	80–83°/0.04	57–74°/0.01[12]	20 min	94
1h 	40 min	89[i]	112–124°/0.08	98–100°/0.5[11]	10 min	93
1i 	20 min	100[j,k]	101°	98–100°[13]	1 h	95[k]
1j 	20 min	98[j,k]	154°	150°[11]	30 min	98[k,l]

[a] A mixture of an alcohol **1** (1 mmol), dihydropyran (**2**; 1.1 mmol) and **3** (2 mol%) is dissolved in dichloromethane (3 ml) and the whole is stirred at 0°C.

[b] Distillation was effected with Kugelrohr (bath temperature given). Each product was homogeneous on silica gel T.L.C. plate chromatography.

[c] The ether **4** (1 mmol) dissolved in methanol (7 ml) is stirred in the presence of **3** as catalyst (0.02 mmol) at room temperature.

[d] Unless otherwise stated isolation was effected by addition of pyridine (more than one equivalent of **3**) followed by concentration and column chromatography.

[e] Satisfactory microanalyses obtained: C ±0.22, H ±0.23. Products **4c, f** were 100% pure by G.L.C. analysis (silicone SE 30, 5%, 75 cm, 100°C).

[f] The product was isolated by addition of excess pyridine, washing the reaction mixture with aqueous sodium hydrogen carbonate solution, concentration, and column chromatography.

[g] 0.6 mol% **3** used.

[h] 1.5 mol% **2** used.

[i] 2 mmol **2** used.

[j] 1.5 mmol **2** used.

[k] ~5 mol% **3** used.

[l] The reaction was carried out at 55°C as the cholestereol ether was insoluble in methanol at room temperature. A homogeneous solution in ethanol/dichloromethane (1:1) was allowed to react at room temperature for 20 h to produce cholestereol in 97% yield.

Deprotection of 4c; Typical Procedure:
A methanol (5 ml) solution of **4c** (150 mg, 0.69 mmol) and **3** (1.0 molar dichloroethane solution, 0.02 ml, 0.02 mmol) is stirred at room temperature for 1 h. Addition of pyridine (~0.1 ml), concentration in vacuo, and short silica gel column chromatography (eluent: 5 : 1 hexane/ethyl acetate) gives *cinnamyl alcohol* (**1c**); yield: 93 mg (100%).

Transesterification of 1,2,3-Propanetriyl Tris[decanoate] (5):
A mixture of the glycerol triester **5** (15.0 g, 27 mmol), **3** (1.0 molar dichloroethane solution, 1.2 ml, 1.2 mmol) and methanol (25 ml) is heated under reflux for 8.5 h. The catalyst **3** is hydrolyzed by adding water (0.024 ml, 1.3 mmol) and potassium carbonate (0.20 g, 1.4 mmol). Concentration in vacuo results in the separation of two oily products. Distillation of the upper layer gives *methyl decanoate* (**6**); yield: 13.5 g (89%); b.p. 107–108 °C/3 torr.

Distillation of the lower layer gives *glycerol* (**7**); yield: 2.0 g (82%); b.p. 142–153 °C (Kugelrohr, bath temperature)/3 torr.

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