1,8-Diazabicyclo[5.4.0]undec-7-ene. An Effective and Selective Catalyst for the *t*-Butyldimethylsilylation of Alcohols

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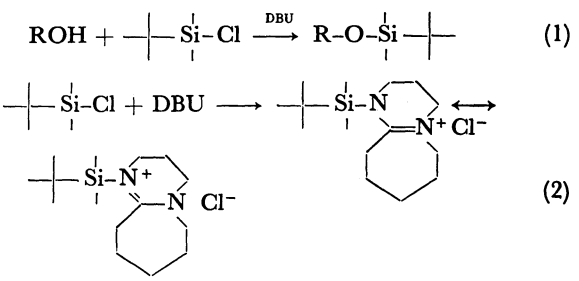
Synopsis. The use of 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) as a catalyst has been found to be very effective and selective in the *t*-butyldimethylsilylation of primary and secondary alcohols.

In view of the great importance of the *t*-butyldimethylsilyl group in the protection of alcohols,[1] various synthetic methods have been reported in the literature after discovery by Corey.[2,3]

We have found that DBU is an effective and selective catalyst for the *t*-butyldimethylsilylation of alcohols (Eq. 1). Under the present reaction conditions, it is assumed that DBU forms a complex with *t*-butyldimethylchlorosilane (TBDCS) which subsequently reacts with alcohols to give *t*-butyldimethylsilyl ethers (Eq. 2). Furthermore, in view of large steric requirements of the complex, it is expected that high selectivity between primary alcohols and secondary

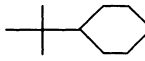


alcohols can be achieved by use of DBU as a catalyst.

Table 1 includes several experimental results and shows the efficiency, the applicability, and the scope of this procedure. When primary alcohols such as phenethyl alcohol and nonyl alcohol were allowed to react with equimolar amounts of TBDCS and DBU in dichloromethane at room temperature, the reaction was complete within 20 min and the *t*-butyldimethylsilyl ethers were obtained in high yields. Application of 0.2 equiv of DBU in the presence of 1 equiv of triethylamine in dichloromethane at room temperature for 4 h resulted in clean silylation of alcohols. Furthermore, the silylation of alcohols using DBU proceeded smoothly in various solvents such as *N,N*-dimethylformamide, acetonitrile, and tetrahydrofuran. Similarly, secondary alcohols were cleanly silylated to the corresponding *t*-butyldimethylsilyl ethers in high yields at room temperature within 4 h. As we expected from large steric requirements of the complex as shown in Eq. 2, this procedure reaches a limit with tertiary alcohols. Thus, the *t*-butyldimethylsilylation of 2-phenyl-2-butanol did not occur to an observable extent, even after prolonged stirring.

TBDCS has been used in the selective protection of primary alcohols in the presence of secondary alcohols due in part to steric bulkiness of *t*-butyldimethylsilyl group.[4] It has been reported that the use of 4-dimethylaminopyridine (DMAP)[5] as a catalyst is very

TABLE 1. PREPARATION OF *t*-BUTYLDIMETHYLSILYL ETHERS AT ROOM TEMPERATURE[a]

No.	Alcohol	Amine[b]	Solvent	Time	Yield/%[c]	Bp θ_b/°C/Torr[d]
		A	CH_2Cl_2	20 min	98	80—82/0.5[3h]
		B	CH_2Cl_2	4 h	96	
1	$C_6H_5CH_2CH_2OH$	C	CH_2Cl_2	20 min	98	
		A	DMF	10 min	95	
		A	CH_3CN	20 min	96	
		A	THF	20 min	98	
2	$C_6H_5CH_2OH$	C	CH_2Cl_2	20 min	90	64—67/0.5[3g]
3	$C_6H_5CH{=}CHCH_2OH$	B	CH_2Cl_2	5 h	93	93—96/0.5[3c]
4	$CH_3(CH_2)_7CH_2OH$	A	CH_2Cl_2	20 min	90	106—110/1.7[3c]
5	$C_6H_5CH(OH)CH_3$	A	CH_2Cl2	4 h	98	58—61/0.5
6		B	DMF	20 min	95	88—90/1.0[3b]
		C	CH_2Cl_2	1 h	89	
7	$C_6H_5C(CH_3)C_2H_5$ (OH)	A	DMF	24 h	0	
		A	CH_2Cl_2	24 h	0	
8	$CH_3(CH_2)_2CH(OH)CHCH_2OH$ (C_2H_5)	A	CH_2Cl_2	30 min	89 (99:1:0)	
		B	CH_2Cl_2	2 h	94 (99:1:0)	
9	$C_6H_5CH(OH)CH_2OH$	B	CH_2Cl_2	4 h	95 (97:1:2)	
10	$CH_3CHCH_2CH_2OH$ (OH)	A	CH_2Cl_2	20 min	92 (97:3:0)	
		B	CH_2Cl_2	1 h	93 (98:2:0)	

a) For selective silylation of selected diols, 1.0 equiv of TBDCS was used, Otherwise, 1.1 equiv of TBDCS was employed. b) A: 1.1 equiv DBU, B: 0.2 equiv DBU/1 equiv Et_3N, C: 1.1 equiv DBN. c) The numbers in parentheses indicate the ratio of the primary silyl ether, the secondary silyl ether, and the bissilyl ether, respectively. The product ratios were determined by GLC analysis. d) Spectral data of silyl ethers were in satisfactory agreement with reported or expected values. 1 Torr=133.322 Pa.

effective in the selective *t*-butyldimethylsilylation of primary alcohols in the presence of secondary alcohols, whereas the use of imidazole does not give satisfactory results.[3b] We have found that DBU can be utilized for the selective silylation of primary alcohols in the presence of secondary alcohols. For example, reaction of 2-ethyl-1,3-hexane-diol with 1 equiv of TBDCS and 1.1 equiv of DBU gave almost exclusively the primary silyl ether with a trace amount (<1%) of the secondary silyl ether, whereas it is known that the use of imidazole gives a mixture of all the possible isomers without high selectivity. Similar results were obtained with 1,3-butanediol and 1-phenyl-1,2-ethanediol. The selectivity achieved with DBU as a catalyst is superior to imidazole and is comparable to DMAP as a catalyst in the selective silylation of primary alcohols.[3b]

It is noteworthy that 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) was also found to be effective in the *t*-butyldimethylsilylation of alcohols.

In conclusion, the present procedure offers the advantages of the ready availability of DBU, the rapidity of the reaction, the wide choice of solvents, and the high selectivity between primary alcohols and secondary alcohols.

Experimental

^{1}H-NMR spectra were recorded with a Varian T-60A spectrometer and infrared spectra were recorded on a Perkin-Elmer 267. GLC analysis was performed on a Varian 2800 gas chromatograph using FID detector. All analyses were carried out on 10 ft×0.125 in. 10% Carbowax 20 M. Reported boiling points are those observed during distillation with a Kugelrohr apparatus and are uncorrected.

Since the reaction were performed are all similar in many respects, typical reactions will be described as specific examples.

t-Butyldimethylsilylation of Cinnamyl Alcohol. To a solution of cinnamyl alcohol (270 mg, 2.0 mmol), DBU (60 mg, 0.4 mmol), and triethylamine (205 mg, 2.0 mmol) in dichloromethane (5 ml) at room temperature was added *t*-butyldimethylchlorosilane (335 mg, 2.2 mmol). The reaction mixture was stirred at room temperature for 5 h, diluted with dichloromethane (40 ml), and washed with cold 5% HCl solution (20 ml), saturated $NaHCO_3$ solution (20 ml), and brine (20 ml). The organic layer was dried over anhydrous $MgSO_4$ and evaporated to dryness. The residue was distilled *in vacuo* to give *t*-butyldimethylsilyl cinnamyl ether (465 mg, 93%). Bp 93—96 °C/0.5 Torr (lit,[3c] bp 90—92 °C/0.3 Torr). ^{1}H-NMR (CCl_4) δ=0.10 (s, 6H), 1.0 (s, 9H), 4.35 (d, 2H, J=6), 6.20—6.80 (m, 2H), 7.25 (s, 5H).

Selective t-Butyldimethylsilylation of 2-Ethyl-1,3-hexanediol. To a solution of 2-ethyl-1,3-hexanediol (290 mg, 2.0 mmol), DBU (58 mg, 0.4 mmol), and triethylamine (210 mg, 2.0 mmol) in dichloromethane (6 ml) at room temperature was added *t*-butyldimethylchlorosilane (298 mg, 2.0 mmol). The reaction mixture was stirred at room temperature for 2 h, diluted with dichloromethane (30 ml), and washed with cold 5% HCl solution (20 ml), saturated $NaHCO_3$ solution (20 ml), and brine (20 ml). The organic layer was dried over anhydrous $MgSO_4$ and evaporated to dryness to afford the primary silyl ether (486 mg) in 94% yield. The product was subjected to GLC analysis, which showed 99% of the primary silyl ether and <1% of the secondary silyl ether without any contamination of the bissilyl ether. For the characterization of the products, a mixture of all the possible isomers was prepared by the known procedure, while the primary silyl ether was also prepared by use of DMAP–Et_3N.[3b]

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