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1,8-DIAZABICYCLO[5.4.0]UNDEC-7-ENE (DBU): AN EFFECTIVE BASE FOR THE INTRODUCTION OF ^{t}BUTYLDIMETHYLSILYL GROUP IN ORGANIC COMPOUNDS[1].

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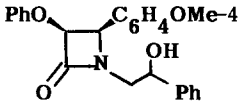
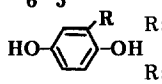
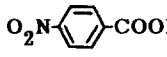
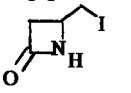
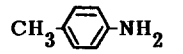
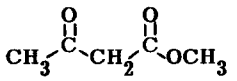
Summary: Reaction of alcohols, thiols, amines, carboxylic acids, phenols, hydroquinones, ketoesters and amides with equimolecular amounts of t-butyldimethylchlorosilane and DBU, even in solvents other than dimethylformamide affords the corresponding t-butyldimethylsilyl derivatives in high yield.

The t-butyldimethylsilyl group became significant during recent years in Organic Synthesis[2]. Among several functions liable to t-butyldimethylsilylation, only the hydroxy group has received more attention in the lastdecade. The conventional procedure for the preparation of TBDMS ethers[3] involves reaction of an alcohol with t-butyldimethylchlorosilane (TBDMSC) in the presence of imidazole (Im) in dimethylformamide (DMF) as solvent; other solvents were found to be unsuitable for this transformation[3]. In view of the great importance of the TBDMS group for the protection of alcohols, various methods have been recently reported[4,5] for the preparation of TBDMS ethers. In this note we wish to report a very effective procedure for the introduction of TBDMS group in a wide variety of substrates by using the readily available t-butyl_ dimethylchlorosilane and DBU as base. The general procedure can be considered as follows: to a solution of TBDMSC (0.333g, 2.22mmol) and DBU (0.366g, 2.40mmol) in dichloromethane , benzene or acetonitrile (4.0 ml) the substrate (2.00 mmol) was added, and the mixture was stirred at room temperature or gently refluxed (see Table) until completion of the reaction. The progress of the reaction was conveniently monitored by tlc or nmr analysis of the reaction crude mixture. When the reaction was carried out in benzene, DBU.HCl precipitation was observed. Products were isolated by simply washing the reaction mixture with cold water, 0.1N hydrochloric acid solution , and $NaHCO_3$ saturated solution. Evaporation of the solvent yields crude t-butyldimethylsilyl compound , which is purified by reduced pressure distillation. A number of representative examples is presented in the Table. Examination of the table shows that the preparation of TBDMS derivatives of alcohols, thiols, carboxylic acids, phenols, hydroquinones, ketoesters, amines and amides is exceptionally practical and simple in a variety of solvents. It should be noted that whereas TBDMSC/Im/DMF method did not exhibit any reaction with thiols, gave poor yields with amines, and variable results with carboxylic acids, our procedure gives high yields for aliphatic and aromatic thiols, carboxylic acids including a sterically hindered one, and for primary and secondary amines[6a]. A further utility of our procedure is that good chemoselectivity was observed when a mixture of alcohols was t-butyldimethylsilylated. Thus, following the general procedure, we have found great preference in the formation of secondary silyl ethers over the tertiary ones, and the primary silyl ethers over the secondary ones.[7] On the other hand, strong base-sensitive structures, such as beta-lactam ring (entries 3 and 10) are unaffected under the described conditions. In summary, our procedure seems to be very efficient for the introduction of TBDMS group in a wide variety of substrates, even in solvents other than dimethylformamide and avoids the use of sophisticated or sensitive reagents, such as allyl-t-butyldimethylsilane[5a], t-butyldimethylsilyl enol ethers of pentane-2,4-dione[5b,c], t-butyldimethyliodosilane[5d], N-t-butyldimethylsilyl amides[5e], t-butyldimethylsilyl trifluoromethanesulfonate[5f] and t-butyldimethylsilyl perchlorates[4d]. We are continuing to explore the scope of the method and will report the results in a full paper in due course.

Table. ^{t}Butyldimethylsilylation of Organic Compounds by TBDMSC/DBU system.

	Substrate	solvent	time	%Yield
1	$C_6H_5CH_2OH$	CH_2Cl_2	15m	93
2	$(C_6H_5)_2CHOH$	C_6H_6	3h	98
3		C_6H_6	24h	92
4	C_6H_5OH	C_6H_6	1.5h[a]	92
5	 R:H	CH_2Cl_2	30m	92
	R:Cl	CH_2Cl_2	20m	91
6	C_6H_5SH	CH_3CN	2h[a]	83
7	$CH_3CH_2CH_2SH$	C_6H_6	30m	94
8		CH_2Cl_2	2h	87

	Substrate	solvent	time	%Yield
9	$(CH_3)_3CCOOH$	C_6H_6	10m	96
10		CH_3CN	45m	80
11	$C_6H_5CH_2NH_2$	C_6H_6	1.5h[a]	99[b]
12		C_6H_6	1.5h[a]	97[b]
13		C_6H_6	15m	85[b]
14		C_6H_6	30m	90[b]
15		C_6H_6	2.5h	93

For entries 1-11, the reaction was carried out at room temperature; for entries 12-15, the reaction temperature was 80ºC. Yield of pure isolated TBDMS compounds, characterized by physical and spectroscopic data. a) Reaction time not optimized. b) Water washing was avoided in the purification of the products[6b]; isolation was achieved filtering off the DBU.HCl precipitate and subsequent distillation.

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1.- Considered as Reagents and Synthetic Methods 46. This work was supported by the Hezkuntza Saila of Eusko Jaurlaritza (Basque Government) and Bayer S.A. (Spanish) with gifts of 1,8-diazabicyclo-[5.4.0]-undec-7-ene (DBU). We thank Mikel Oiarbide for his collaboration in this work.

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6.- a) Recently, S.W. Djurić has demonstrated that reaction of secondary amines with TBDMSCl, triethylamine and 4-N,N,-dimethylaminopyridine (cat.) in dimethylformamide as solvent arosed to the formation of N-formyl derivatives instead of the expected aminosilanes. See **J. Org. Chem.**, 49, 1311 (1984). b) TBDMS derivatives of amines are not completely stable to aqueous work-up, see also M.J. Calverley, **Synth. Commun.**, 13, 601 (1983).

7.- For instance, when an equimolecular mixture of cyclohexanol and 1,1-dimethylpropan-1-ol was treated with an equivalent of DBU and TBDMSC for 40min at room temperature, a mixture of 1,1-dimethylpropan-1-ol (100%) and t-butyldimethylsilyloxycyclohexane (85%) was obtained. In the same way, a mixture of 2-phenylethanol and 2-methylcyclohexanol gave a mixture of 3-methylcyclohexanol (90%) and 1-t-butyldimethylsilyloxy-2-phenylethane(80%).

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