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RAPID AND SELECTIVE DETRITYLATION OF PRIMARY ALCOHOLS USING FORMIC ACID

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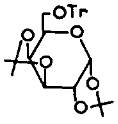
SUMMARY : A facile and chemoselective method of detritylation is described. Several polyfunctionalized examples were tested to emphasize the selectivity of the system over different protecting groups.

Triphenylmethyl ethers have been widely used as a selective protecting group for primary alcohols especially in carbohydrate and nucleoside chemistry[1,2], but procedures for its selective cleavage are scarce. For example, reflux with 80 % acetic acid[3], or treatment with mineral acid in various solvents[4-6], zinc bromide[7], trifluoroacetic acid[8], or hydrogenolysis[9,10], are not selective in the presence of other sensitive protecting groups.

The procedure described now is highly efficient for the detritylation of alcohols in the presence of a variety of protecting groups. Acid sensitive groups such as benzylidene, isopropylidene, t-butyl dimethyl silyl ether survived the conditions of the reaction. Even the highly sensitive tetrahydropyranyl ether was cleaved only to an extent of 40 %. The results are summarized in table I.



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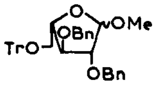

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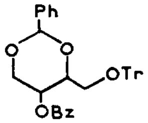

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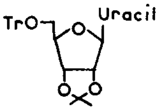

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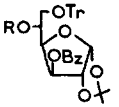

5 R = Ac-
6 R = t-BuMe$_2$Si-
7 R = Thp-

TABLE I

Compound	Acid/ether ratio[11]	Reaction time	Yield[12]
1	2/2	7 min	83 %
2	2/2	7 min	85 %
3	2/3	45 min	88 %
4	3/2	5 min	84 %
5	2/2	15 min	92 %
6	3/2	5 min	88 %
7	2/3	40 min	60 %

A general procedure is as follows : 1 mmol of the trityl ether was dissolved in a mixture of formic acid and diethyl ether, after the end of the reaction the solution was diluted with diethyl ether, washed successively with brine and saturated aqueous sodium hydrogen carbonate until neutral, dried and concentrated. The residue was either cristallized or purified further on flash chromatography to remove the tritanol by-product.

In order to study a possible effect of the solvent on the selectivity the reaction was carried out on 6 using various aprotic solvents. As shown on table II the reaction was activated by acidic solvents, thus the ratio of acid to solvent could be decreased as their acidity increased. Moreover the selectivity remained unchanged.

Table II

	Solvent	Acid/solvent ratio[11]	Reaction time
6	CH_3NO_2	1/4	15 min
	CH_3CN	1/3	20 min
	EtOAc	2/3	10 min

The above results clearly indicate that this method offers the advantage of being compatible with a variety of protecting groups. This will eventually extend the scope of applicability of the trityl group, by obviating the difficulties often encountered in its cleavage.

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11- In ml per mmole of compound. The different ratios were established as a compromise between short reaction time and selectivity.
12- Isolated yields of primary alcohols (OTr ⟶ OH).

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