Tris(2,4,6-trimethoxyphenyl)phosphine (TTMPP): A Novel Catalyst for Selective Deacetylation

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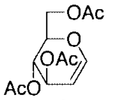
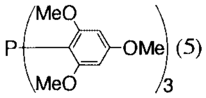
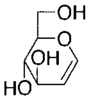
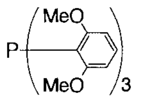
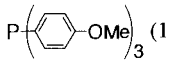
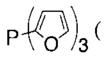
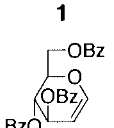
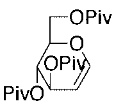
Chemo- and stereoselective deacetylation was achieved by the use of a catalytic amount of tris(2,4,6-trimethoxyphenyl)phosphine (TTMPP).

The acetyl group is one of the most useful protecting groups in organic synthesis. Therefore, many protecting and deprotecting methods have been developed so far.[1] Several reagents have been reported to convert acetylated compounds to the corresponding hydroxy compounds. Among those, hydrolysis and transesterification under basic condition have been often used. On the other hand, in 1984, Wada and Higashizaki reported high basicity of tris(2,4,6-trimethoxyphenyl)phosphine (TTMPP).[2] After that Imamoto and his co-workers reported TTMPP-catalyzed aldol reaction between ketene silyl acetals and aldehydes.[3] Here we would like to report a novel procedure for deacetylation using phosphine-based catalyst.

Table 1. Deacylation of 3,4,6-tri-*O*-acyl-D-glucal[a]

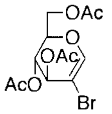
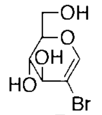
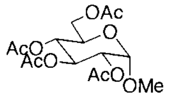
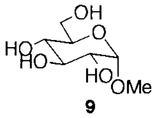
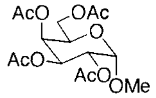
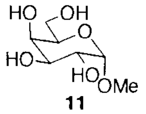
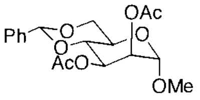
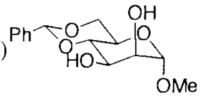
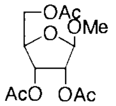
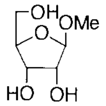
Entry	Substrate	Phosphine-based catalyst (mol%)	Temp/°C (Time/h)	Product	Yield/%[b]
1	 **1**	 (5) TTMPP **2**	22 (5)	 **3**	98
2	**1**	 (10)	22 (5)	**3**	0
3	**1**	 (10)	22 (5)	**3**	0
4	**1**	P(*o*-tol)$_3$ (10)	22 (5)	**3**	0
5	**1**	PPh$_3$ (10)	22 (5)	**3**	0
6	**1**	 (10)	22 (5)	**3**	0
7	**1**	P(*n*-Bu)$_3$ (10)	22 (5)	**3**	0
8	 **4**	**2** (10)	22 (24)	**3**	63
9	 **5**	**2** (10)	22 (72)	**3**	0

[a]All reactions were carried out in methanol. [b]Isolated yield.

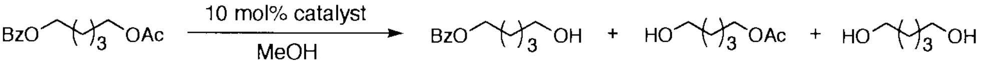
During the course of our study on the synthesis of carbohydrate compounds, we found 3,4,6-tri-*O*-acetyl-D-glucal (**1**) was deacetylated to D-glucal (**3**) by the aid of 5 mol% of tris(2,4,6-trimethoxyphenyl)phosphine (TTMPP) (**2**) in 98% yield (at 22 °C for 5 h in methanol).[4] Other phosphine compounds we examined such as tris(2,6-dimethoxyphenyl)phosphine, tris(4-methoxyphenyl)phosphine, tri-*o*-tolylphosphine, triphenylphosphine, tri-*n*-butylphosphine and tri-2-furylphosphine (10 mol%) in methanol were not effective for deacetylation under the above conditions (Table 1).[5] 3,4,6-Tri-*O*-benzoyl-D-glucal (**4**) was also deprotected, though less reactive (entry 8). The pivaloyl derivative was inert to TTMPP (**2**) (entry 9). As shown in Table 2, other acetylated glycopyranosyl and ribofuranosyl derivatives were also effectively deprotected by the action of 10 mol% of TTMPP (**2**) in methanol under mild conditions.

A variety of acetylated compounds other than carbohydrates were converted into the corresponding hydroxy compounds in high yield. Some of the results obtained are summarized in Table 3. High chemoselectivity between benzoyl and acetyl was observed (eq 1). The discrimination between pival-

Table 2. Deacetylation of carbohydrate compounds[a]

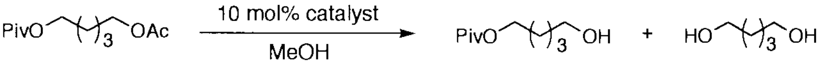
Entry	Substrate	Phosphine-based catalyst (mol%)	Temp/°C (Time/h)	Product	Yield/%[b]
1	 **6**	**2** (10)	20 (7.5)	 **7**	89
2	 **8**	**2** (10)	22 (48)	 **9**	82
3	 **10**	**2** (10)	20 (30)	 **11**	93
4	 **12**	**2** (10)	28 (14)	 **13**	96
5	 **14**	**2** (10)	20 (28)	 **15**	93

[a]All reactions were carried out in methanol. [b]Isolated yield.



TTMPP (**2**) (80 °C, 8 h)	62%	4%	10%
K_2CO_3 (20 °C, 1.5 h)	38%	0%	42%
CH_3ONa (20 °C, 1.5 h)	53%	0%	47%

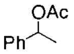
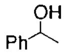
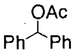
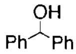
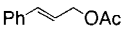
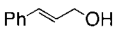
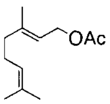
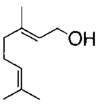
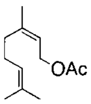
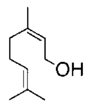
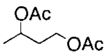
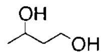
(eq 1)



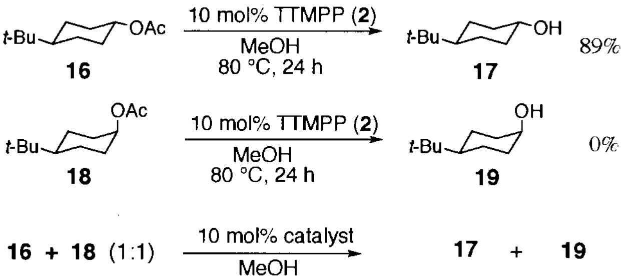
TTMPP (**2**) (80 °C, 8.5 h)	94%	0%
K_2CO_3 (20 °C, 1.5 h)	73%	6%
CH_3ONa (20 °C, 2 h)	86%	5%

(eq 2)

Table 3. Deacetylation of a variety of acetylated compounds[a]

Entry	Substrate	Catalyst (mol%)	Temp/°C (Time/h)	Product	Yield/%[b]
1	Ph-CH_2OAc	TTMPP (5) **2**	50 (3)	Ph-CH_2OH	90
2		**2** (5)	50 (24)		78
3		**2** (5)	50 (8.5)		88
4		**2** (5)	50 (4.5)		99
5		**2** (5)	50 (9)		86
6		**2** (5)	50 (24)		73
7		**2** (10)	50 (5.5)		79

[a]All reactions were carried out in methanol. [b]Isolated yield.



	17	19
TTMPP (**2**) (80 °C, 20 h)	87%	8%
K_2CO_3 (50 °C, 6.5 h)	84%	49%
CH_3ONa (50 °C, 6.5 h)	95%	55%

Scheme 1.

oyl and acetyl was perfect (eq 2). It should be mentioned that the acetate of *trans*-4-*tert*-butylcyclohexanol was deacetylated much faster than the corresponding *cis*-isomer (Scheme 1). In these reactions, the TTMPP-catalyzed reactions exhibited higher selectivity compared with the conventional K_2CO_3- or CH_3ONa-catalyzed deacetylation reactions.[6]

Typical procedure is as follows (entry 4 in Table 3); To a solution of cinnamyl acetate (326 mg, 1.85 mmol) in methanol (1.5 mL) was added TTMPP (**2**) (49 mg, 0.092 mmol). The mixture was stirred at 50 °C for 4.5 h. After confirmation of the completion of the reaction, the mixture was concentrated and the resulting residue was chromatographed on silica-gel to afford cinnamyl alcohol (245 mg, 99%).

The TTMPP catalyst would work as a base in the present deacetylation reactions. The study on the detailed mechanism is now in progress in our laboratory.

References and Notes

1 T. W. Greene and P. G. M. Wuts, "Protective Groups in Organic Synthesis," 3rd ed., John Wiley & Sons, New York (1999), pp 150–160 and references cited therein.

2 M. Wada and S. Higashizaki, *J. Chem. Soc., Chem. Commun.*, **1984**, 482.

3 S. Matsukawa, N. Okano, and T. Imamoto, *Tetrahedron Lett.*, **41**, 103 (2000).

4 The use of methanol was essential for deacetylation using TTMPP system. That is, the deacetylation reaction in ethanol or isopropyl alcohol did not take place.

5 The reactions of **1** with 10 mol% of tris(2,6-dimethoxyphenyl)phosphine even at 80 °C for 24 h afforded **3** only in 8% yield. Starting material **1** was recovered in 65% yield.

6 The yields of competitive reaction in Scheme 1 were estimated by the combined yield of **17** and **19** and the ratio of **17**/**19** determined by ^{1}H NMR analysis.