Tetrahedron Letters, Vol. 34, No. 50, pp. 8071-8074, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

The Efficient Deprotection of Acetals and Tetrahydropyranyl Derivatives of Phenols Using [Ru(CH3CN)3(triphos)](OTf)2 as a Catalyst

Shengming Ma and Luigi M. Venanzi*

Laboratorium für anorganische. Chemie,
ETH-Zentrum, Universitätstr. 6, CH-8092 Zürich, Switzerland

Summary: Acetals and tetrahydropyranyl derivatives of phenols are efficiently and highly chemoselectively deprotected in the presence of catalytic amounts of [Ru(CH_3CN)$_3$(triphos)]-(OTf)$_2$ (triphos = $CH_3C(CH_2PPh_2)_3$), under mild condition, in good to excellent yields.

Deprotection of acetals plays an important role in organic synthesis, and is normally accomplished using protonic or Lewis acids as catalysts.[1] Obviously, these conditions are not suitable for acid-sensitive substrates. Although there are some papers describing deprotection under neutral conditions,[2-6] these methods usually suffer from other disadvantages. Thus, more efficient methods for this conversion under neutral conditions are still actively sought by synthetic chemists.

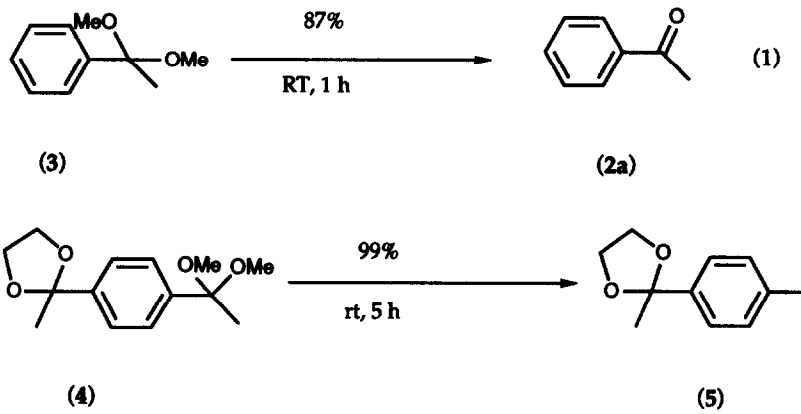
Recently, several transition metal cationic complexes have been shown to be versatile catalytic precursors for the acetalization and transacetalization reactions.[7-11] We report here an efficient method for the deprotection of acetals using [Ru(CH_3CN)$_3$(triphos)](OTf)$_2$ as a catalyst. As transacetalization was found to be milder than acetalization, being usually carried out at rt, the deprotection method described here is based on the former reaction.

Acetone was used both as a reagent and a solvent. A general procedure for the deprotection of acetals is as follows: To a solution of an acetal (10 mmol) and acetone (30 ml for the acetal of a ketone, 50 ml for the acetal of an aldehyde) was added [Ru(CH_3CN)$_3$(triphos)](OTf)$_2$ (1:2000). The reaction was carried out at rt and monitored by GC. When the reaction was complete, the catalyst was removed by filtration through a short column of Al_2O_3. The pure product was usually obtained by the removal of the solvent by rotary evaporation, and where necessary further purified by distillation or chromatography on silica gel.

The results, summarized in **Table 1**, show that (1) both aldehyde and ketone derivatives can be deprotected; (2) no C=C bond migration occurs during this reaction (entries 5 and 6); (3) sterically hindered acetal reacts very slowly (entries 3 and 4).

Acyclic acetals react much faster than 1,3-dioxolanes. Under standard conditions, acetal **3** affords acetophenone (**2a**) in 87% yield within 1 h (eq. 1).

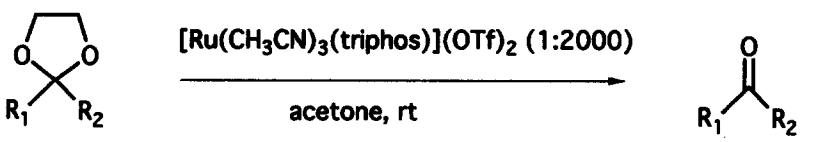
In a molecule with both acyclic acetal and 1,3-dioxolane moieties, i.e., **4**, the acyclic acetal can be



deprotected chemoselectively (eq. 2).

Tetrahydropyranyl derivatives of alcohols are usually unstable under acidic conditions.[1,12]

Table 1. [Ru(CH$_3$CN)$_3$(triphos)](OTf)$_2$-catalyzed Deprotection of 1,3-Dioxolanes.

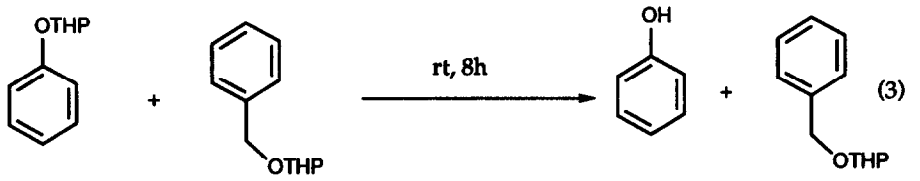


(1) (2)

Entry	Acetal (1) R_1	R_2		Time (h)	Product (2)	Yield of 2(%)[a]
1	Ph	CH_3	(1a)	6	(2a)	90
2	Ph	H	(1b)	6	(2b)	98
3	Ph	Ph	(1c)	24	(2c)	0
4	Ph	Ph	(1c)	48[b]	(2c)	66[c]
5	PhCH=CH(E)	CH_3	(1d)	48	(2d)	100
6	PhCH=CH(E)	H	(1e)	6	(2e)	98
7	-$(CH_2)_5$-		(1f)	4	(2f)	85[c]

a: Isolated yields, unless otherwise stated; b: reflux; c: Yields determined by GC using mesitylene as the internal standard.

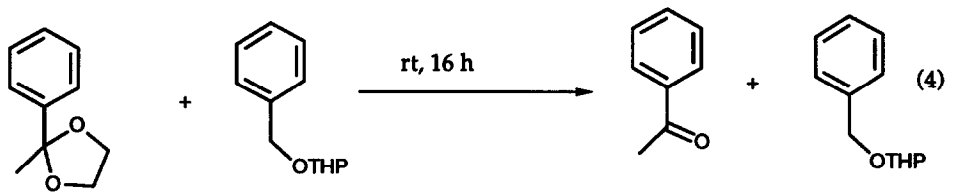
However, under the above conditions, the tetrahydropyranyl derivatives of alphatic alcohols are stable. The deprotection reactions of the tetrahydropyranyl derivatives of benzyl alcohol (6), n-octan-1-ol, cyclohexanol, etc., in the presence of $[Ru(CH_3CN)_3(triphos)](OTf)_2$, in acetone, are very slow. However, the tetrahydropyranyl derivative of phenol (7) can be cleaved to phenol under the present condition in 100% yield.[13] Furthermore, a mixture of tetrahydropyranyl derivatives of phenol (7) and benzyl alcohol (6), in the presence of $[Ru(CH_3CN)_3(triphos)](OTf)_2$, in acetone at rt, afforded phenol chemoselectively in 87% yield, while tetrahydropyranyl derivative of benzyl alcohol (6) was recovered unchanged in 95% yield (eq. 3).[13]



(7) (6) (6)

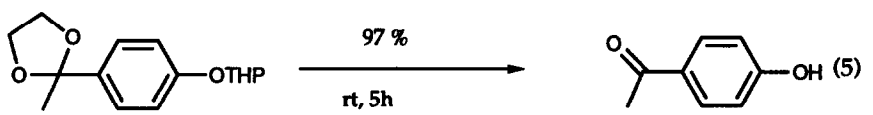
87% 95%

A mixture of 2-methyl-2-phenyl-1,3-dioxolane (**1a**) and the tetrahydropyranyl derivative of benzyl alcohol (6), in the presence of $[Ru(CH_3CN)_3(triphos)](OTf)_2$ in acetone at rt, afforded acetophenone (**2a**) chemoselectively in 83% yield, while 6 was recovered in 93% yield (eq. 4). Furthermore, for substrate (8), the protective group of both the phenolic alcohol and the ketone were removed conveniently to give 4-hydroxyacetophenone (9) in 99% yield in one step (eq. 5).



(1a) (6) (2a) (6)

83% 93%



(8) (9)

Although the above reactions were tested using $[Ru(CH_3CN)_3(triphos)](OTf)_2$, it is likely that the corresponding rhodium(III) complex $[Rh(CH_3CN)_3(triphos)](OTf)_3$[7,15] will also show catalytic activity in the above reactions. It is expected that the above catalysts will find extensive use for the deprotection of acetals and tetrahydropyranyl derivatives of phenols.

References and Notes:

1. Greene, T. W.; Wuts, G. M. *Protective Groups in Organic Synthesis*, 2nd Edn., John Wiley & Son, Inc., New York, **1991** and references cited therein.
2. Jung, M. E.; Andrus, W. A.; Ornstein, P. L. *Tetrahedron Lett.*, **1977**, 4175.
3. Crombie, L.; Fisher, D. *Tetrahedron Lett.*, **1985**, *26*, 2477.
4. Kametani, T.; Kondoh, H.; Honda, T.; Ishizone, H.; Suzuki, Y.; Mori.W. *Chem. Lett.*, **1989**, 901.
5. Tanemura, K.; Suzuki, T.; Horaguchi, T. *J. Chem. Soc. Chem. Commun.*, **1992**, 979.
6. Chang, C.; Chu, K. C.; Yue, S. *Synth. Commun.*, **1992**, *22*, 1217.
7. Ott, J.; Ramos Tombo, G. M.; Schmid, B.; Venanzi, L. M.; Wang, G.; Ward, T. R. *Tetrahedron Lett.*, **1989**, *30*, 6151.
8. Ott, J.; Schmid, B.; Venanzi, L. M., Wang, G.; Ward, T. R. *New J. Chem.*, **1990**, *14*, 495.
9. Gorla, F.; Venanzi, L. M. *Helv. Chim. Acta.*, **1990**, *73*, 690.
10. Ma, S.; Venanzi, L. M. *Synlett*, **in the press.**
11. Venanzi, L. M. et al., to be published.
12. Kim, K. S.; Song, Y. H.; Lee, B. H.; Hahn, C. S. *J. Org. Chem.* **1986**, *51*, 404.
13. In this reaction, the following work-up procedure was used: after the reaction was finished, CH_2Cl_2 (20 mL), water (10 mL) and solid NaOH (5 eq.) were added subsequently. After stirring for several minutes, the aqueous layer was separated and washed with CH_2Cl_2 (2 x 10 mL). The combined organic layer was washed with water (10 mL); then the combined aqueous layer was acidified with HCl, and extracted with CH_2Cl_2 (4 x 10 mL); both the organic layers were dried (Na_2SO_4). After removal of the solvents, the residues were submitted to chromatography on silica gel to afford phenol and $PhCH_2OTHP$ in pure form, respectively.
14. All the acetals[1,7] and tetrahydropyranyl derivatives of alcohols[15] used in this paper were synthesized according to the literature methods. The known products were characterized by comparing their ^1H NMR spectral data and GC retention time with their authenic samples. The new product (5) was characterized by ^1H NMR, ^{13}C NMR, IR, MS and elemental analysis. M.p. 53-55°C(n-hexane); ^1H NMR(250 MHz, $CDCl_3$): 7.90(d, J = 8.0 Hz, 2H), 7.60(d, J = 8.0 Hz, 2H), 4.15-4.00(m, 2H), 3.85-3.70(m, 2H), 2.60(s, 3H), 1.70(s, 3H) ppm; ^{13}C NMR(62.9 MHz, $CDCl_3$): 197.6, 148.5, 136.8, 128.3, 125.5, 108.5, 64.6, 27.4, 26.5 ppm; IR(KBr): 1678, 1602, 1265 cm^{-1}; MS(m/z): 207.0, 206.0(M^+), 192.0, 191.0(100.0), 147.0; Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 70.14; H, 6.91.
15. Ma, S.; Venanzi, L. M. *Tetrahedron Lett.*, **1993**, *34*, 5269.

(Received in Germany 22 September 1993; accepted 3 October 1993)