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2-BENZYLOXY-1-PROPENE: A NOVEL PROTECTIVE REAGENT OF HYDROXYL GROUPS

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Hydroxyl compounds are easily protected on treatment with 2-benzyloxy-1-propene, a novel hydroxyl protective reagent, in the presence of a catalytic amount of dichloro(1,5-cyclooctadiene)-palladium (II). The deprotection to regenerate the parent hydroxyl compounds is also readily carried out by catalytic hydrogenation under neutral conditions.

Recently, synthesis of organic molecules with multiple hydroxyl groups, e.g. carbohydrates and polyoxyantibiotics, has attracted much attention and the protection of hydroxyl groups has become a very important problem in the synthesis of such molecules. A wide variety of methods for the protection of hydroxyl groups has been devised and the protection by the formation of acetal is one of the most commonly employed methods. Usually, formation of acetal and regeneration of alcohol are carried out under acidic conditions, which are imcompatible with other acid-labile functional groups in the molecule, for example, nucleotidic linkage.[1] In this communication, we wish to report on a novel protective reagent of hydroxyl groups, 2-benzyloxy-1-propene (2),[2] with which both protection and regeneration of alcohol under neutral conditions are realized.

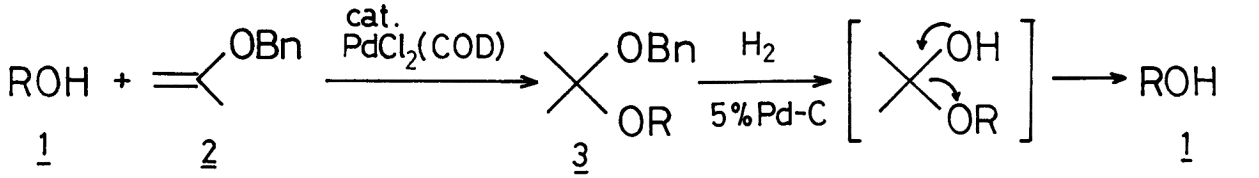
In the first place, an alcohol (1) was treated with 2-benzyloxy-1-propene (2) in the presence of various acidic catalysts or palladium complexes, and it was found that the desired acetal (3), the protected alcohol, was obtained in a high yield by use of a catalytic amount of dichloro(1,5-cyclooctadiene)palladium (II). Next, the regeneration of the parent alcohol (1) from the acetal (3) was examined and it was found that the deprotection is successfully carried out by catalytic hydrogenation in the presence of Pd-C (5%) in EtOH (room temperature, 1 atm, 12 – 24 h) to give 1 in a high yield. The results are summarized in Table 1.

As shown in Entry 5, the diol having both a primary hydroxyl group and a secondary hydroxyl group gave the product in which only the primary hydroxyl group was protected.

The acetal (3) thus formed is not affected by reducing hydride reagents [$LiAlH_4$, i-Bu_2AlH] or organometallics [RLi, R'MgX]. And the acetal (3) is also stable toward alkaline hydrolytic conditions [1 M NaOH-THF (1 : 1)], but is hydrolyzed into the parent alcohol in acidic media [1 M AcOH-THF (1 : 1)].

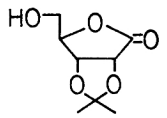
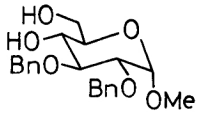
Typical experimental procedure for the protection of alcohols is as follows: Under an argon atmosphere, to a mixture of an alcohol (1, 0.4 mmol) and dichloro-

Table 1.

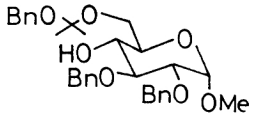


1 2 3 1

Bn= CH_2Ph COD=1,5-cyclooctadiene

Entry	ROH	Protection yield / % of 3	Deprotection yield / % of 1
1	$Ph(CH_2)_3OH$	96 (86)[a]	94
2	$PhCO_2(CH_2)_3OH$	98 (73)[a]	98
3	$CH_3(CH_2)_{17}OH$	85 (61)[a]	92
4		94 (98)[a]	99
5		95[b]	–

a) Yields obtained by use of $POCl_3$ or $TsOH \cdot H_2O$ instead of $PdCl_2(COD)$ as a catalysts.

b) The product is 

(1,5-cyclooctadiene)palladium (II) (0.04 mmol) in benzene (5 ml) was added 2-benzyloxy-1-propene (2, 0.8 mmol) in benzene (2 ml) at room temperature. Stirring was continued for 24 h, and then several drops of pyridine were added to the reaction mixture. The resulting mixture was diluted with ether, and insoluble materials were filtered off. After the solvent was evaporated, the residue was purified by preparative TLC to give the desired acetal (3).

It should be noted that 2-benzyloxy-1-propene (2) is a new and useful protective reagent of hydroxyl groups with the following characteristics; 1) both protection and regeneration of alcohols are carried out under neutral conditions; 2) a primary hydroxyl group is selectively protected; 3) the acetal, the protected alcohol, is stable toward organometallic reagents including reducing hydride reagents and alkaline hydrolytic conditions.

We wish to thank Mr. H. Nagaoka for his experimental assistance.

Refenences

1) S. Chládek and J. Smrt, Chem. Ind. (London), 1964, 1719.

2) 2-Benzyloxy-1-propene was prepared by treatment of 2-benzyloxy-1-chloropropane[3] with t-BuOK in dimethyl sulfoxide at room temperature (82%).

3) K. Steiner, U. Graf, and E. Hardegger, Helv. Chim. Acta, 54, 845 (1971).

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