

THE ALLYLOXYCARBONYL GROUP FOR ALCOHOL PROTECTION : QUANTITATIVE REMOVAL OR
TRANSFORMATION INTO ALLYL PROTECTING GROUP VIA π -ALLYL COMPLEXES OF PALLADIUM

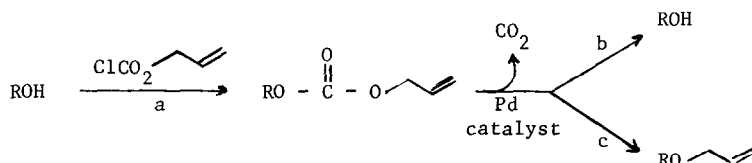
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Summary : In the presence of Pd catalysts and under mild, essentially nonbasic conditions, the allyloxycarbonyl derivatives of alcohols may be either converted into the corresponding allyl ethers or hydrogenolysed (Bu_3SnH) back to the starting alcohol.

The formation of carbonate esters is a useful and widely used method for the protection of the alcoholic function ¹. Besides simple alkoxycarbonyl groups which are usually removed under basic hydrolysis, more sophisticated groups have been designed which are removed under milder and more specific conditions. Such are for example the 2,2,2-trichloro and 2,2,2-tri-bromoethoxycarbonyl groups ^{2,3}, the p-nitrophenoxycarbonyl group ⁴ or the 2-(methylthiomethoxy) ethoxycarbonyl [MTMEC] group ⁵. We wish to propose here a new promising protecting group in that series, namely the allyloxycarbonyl group.

Allyloxycarbonyl derivatives of alcohols are readily prepared from the commercial allyloxycarbonyl chloride. Removal of the allyloxycarbonyl group (reaction b, scheme I) may be achieved in the presence of small amounts of palladium catalysts under various and mild conditions. Furthermore allyloxycarbonyl derivatives of alcohols may also be converted, (reac-

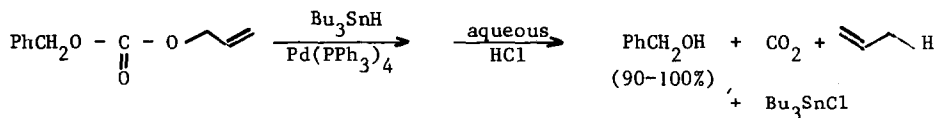


tion c) with the same catalyst and under essentially non basic conditions into the corresponding allyl ether derivatives which constitute another widely used protected form of the alcoholic function ^{1,6}. All those reactions which involve gas evolution are very easily monitored.

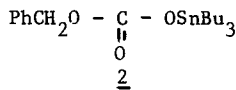
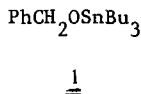
Benzyl allyl carbonate was used as the substrate for preliminary studies. Quantitative conversion to allyl benzyl ether was carried out in benzene or THF solution at 60-70°C in the presence of $2 \cdot 10^{-2}$ equivalent of catalyst - Pd $(\text{PPh}_3)_4$ or Pd $(\text{OAc})_2 + 5 \text{PPh}_3$ - and was found to be complete within 10 min. The reaction occurred also in DMF but at a noticeably slower rate.

Reversal to benzyl alcohol was achieved in various ways ⁷. Hydrogenolysis by Bu_3SnH (1.1 eq.) in the presence of Pd $(\text{PPh}_3)_4$ ($2 \cdot 10^{-2}$ eq.) followed by acidification showed up as a very specific and mild method for deprotection. The reaction was found to be instantaneous in

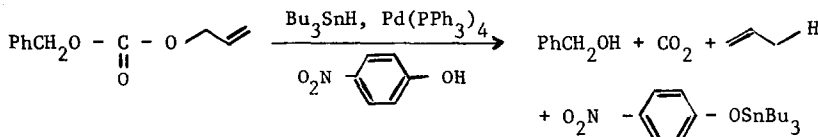
benzene at 5°C and complete within 10 min. in THF at -10°C.



The intermediate obtained before acidification is probably the tributyltin benzyl alkoxide 1; no carbonyl absorption was observed in the 1600 cm^{-1} region of the infrared spectrum which seems to exclude 8 a mixed benzyl tributyltin carbonate structure 2

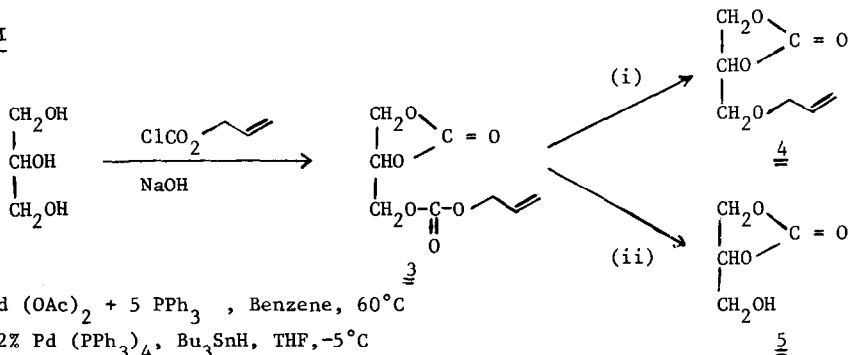


Direct obtention of the alcohol - thus avoiding any accumulation of tin alkoxide which could be undesirable in more complex cases - was found possible by carrying out the hydrogenolysis procedure in THF in the presence of p-nitrophenol as a proton donor ⁹



The reactions outlined in scheme II further illustrate the potentialities of the allyloxycarbonyl protecting group ¹⁰. The racemic mixed cyclic-acyclic carbonate 3 was isolated in 57% yield (bp 146°C/0.05 mm Hg; ir (CHCl₃) ν (CO) 1815 cm^{-1} and 1750 cm^{-1}) ¹¹ from the reaction of racemic glycerol with allyloxycarbonyl chloride under Schotten-Baumann conditions ¹². All subsequent reactions were run under inert atmosphere in deoxygenated solvents

Scheme II



i) 2% Pd(OAc)₂ + 5 PPh₃, Benzene, 60°C

ii) 1) 2% Pd(PPh₃)₄, Bu₃SnH, THF, -5°C

2) HCl

Glycerol 1,2-carbonate 3-allyl ether 4: A solution of 2.5 g (1.23 $\cdot 10^{-2}$ mole) of 3, 58 mg of Pd(OAc)₂ (2.58 $\cdot 10^{-4}$ mole) and 340 mg of PPh₃ (1.3 $\cdot 10^{-3}$ mole) in 7 ml of benzene was heated at 70°C with magnetic stirring. After CO₂ evolution was complete (ca 10-15 min.) the reaction mixture was eluted through a short column of Florisil to eliminate the catalyst and the ether 4 was distilled. Bp: 95°C/0.05 mm Hg; ir (CCl₄) ν (CO) 1820 cm^{-1} . Yield 1.5 g (82%).

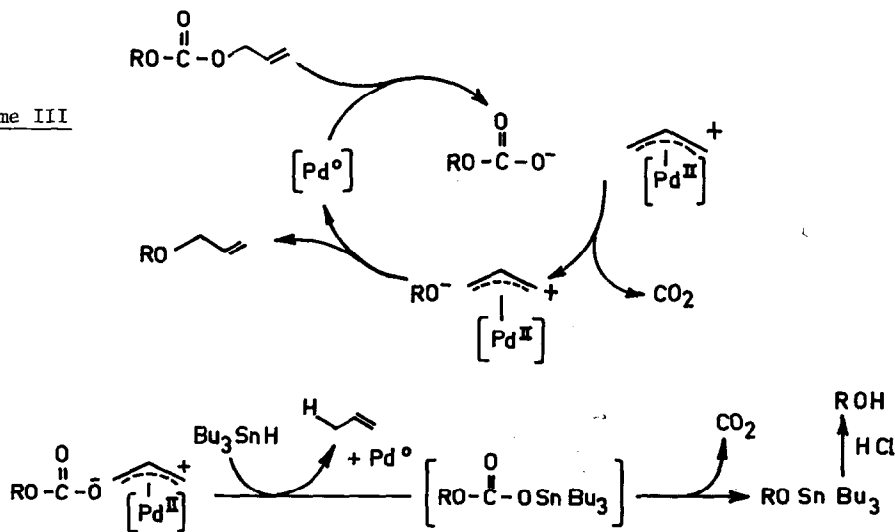
Glycerol 1,2-carbonate 5: To a solution of 3 (5.99g, 2.97 $\cdot 10^{-2}$ mole) in 40ml of THF at -10°C

was added $\text{Pd}(\text{PPh}_3)_4$ (0.68g, 5.9×10^{-4} mole) and then dropwise over a period of 1-2min. Bu_3SnH (10.32g, 3.54×10^{-2} mole). The reaction mixture was further stirred for 10 min., acidified with a small excess of concentrated aqueous HCl and then buffered with sodium hydrogencarbonate. After evaporating THF , hexane and water were added to the residue and the resulting mixture filtrated. The water phase was collected, washed with fresh hexane to completely eliminate tributyltin chloride and evaporated. Acetone was added to the residue and the precipitated inorganic salts filtered off. Distillation gave 5. Bp : $140^\circ\text{C}/0.12\text{mm Hg}$; ir (CH_2Cl_2) $\nu(\text{CO})$ 1810 cm^{-1} , $\nu(\text{OH})$ 3550 cm^{-1} . Yield 3.08g (88%).

The good yields obtained in the formation of 4 as well as 5 show that the conditions of the catalytic reactions are mild enough to be compatible with the presence of the cyclic carbonate function. Allyloxycarbonylation with allyl chloroformate followed by palladium catalyzed decarboxylation of the resulting allyloxycarbonyl derivative (scheme I, reactions a plus c) should therefore constitute a useful way of introducing the allyl ether protecting group into alcalinolabile molecules, particularly into molecules with hydroxyl functions already protected as esters or carbonates.

A likely reaction path for the Pd -mediated transformation of allyloxycarbonyl compounds into allyl ethers is outlined in scheme III¹³. The first step involves the oxidative addition of Pd^0 leading to the π -allyl cation on one hand and the alkoxycarboxylate anion on the other hand. The latter species subsequently loses CO_2 to generate the alkoxy-anion. The third step involves the recombination of the π -allyl cation and the alkoxy-anion to produce the allyl ether and to regenerate the Pd^0 catalyst. According to this assumed mechanism, it may be

Scheme III



seen that the reaction medium remains always very weakly basic since the concentration of the alkoxy species cannot be greater than that of the catalyst. As a matter of fact, if the recombination step is faster than the decarboxylation process as it seems reasonable, its concentration might be much lower. The reaction path leading to alcohol in the presence of tributyltin hydride (hydrogenolysis of the π -allyl species) is also represented on scheme III.

Some other applications of the allyloxycarbonyl group for the protection of alcohol as well as amine functions are currently under investigation in our laboratory.

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Footnotes and References

- 1 C.B. Reese, "Protection of alcoholic hydroxyl groups and glycol systems" chap. 3, p. 95 in J. F. W. Mc Omie, *Protective Groups in Organic Chemistry*, Plenum Press 1973.
- 2 a) T.B. Windholz and D. B. R. Johnston, *Tetrahedron Letters*, 2577 (1967) ; b) F.R. Pfeiffer, C.K. Miao and J. A. Neisbach, *J. Org. Chem.*, 35, 221 (1970).
- 3 A.F. Cook, *J. Org. Chem.*, 33, 3589 (1968).
- 4 R.L. Letsinger and K.K. Ogilvie, *J. Org. Chem.*, 32, 296 (1967).
- 5 S.S. Jones, C.B. Reese and S. Sibana, *Tetrahedron Letters*, 22, 1933 (1981).
- 6 R. Gigg, A.C.S. Symposium, Series n°39, 253 (1977) ; n°77, 44 (1978) ; *J. Chem. Soc. Perkin Trans 1*, 738 (1980).
- 7 Wet THF (10-15% H₂O) 2 10^{-2} eq. of Pd(PPh₃)₄, reflux, 15 min. ; formic acid (4 eq.), 2 10^{-2} eq. of [Pd(OAc)₂ + 5 PPh₃] 85°C, 15 min. ; allyl alcohol as the solvent, 2 10^{-2} eq. of 5% Pd/C, 10⁻¹ eq. of PPh₃, 80°C, 30 min.
- 8 A.J. Bloodworth, A.G. Davies and S.C. Vasishtha, *J. Chem. Soc.*, (C) 1309 (1967).
- 9 Pd(PPh₃)₄ was also found to catalyse the direct reaction between p-nitrophenol and Bu₃SnH. However this reaction is apparently not fast enough to interfere with the unblocking process.
- 10 For an example of use of the somewhat related Cl₃C - CH₂ - OCO - group in glycerol chemistry see ref. 2b.
- 11 In a addition to ir spectroscopy, compound 3 and 4 were also characterized by combustion analysis, NMR and mass spectrometry and compound 5 by NMR and mass spectrometry and through conversion to its trityl derivative (J. Cunningham and R. Gigg, *J. Chem. Soc.*, 1553 (1965).
- 12 The procedure used for the synthesis of the methyl ester analog was followed : C.F. Allpress and W. Maw, *J. Chem. Soc.*, 2259 (1924).
- 13 For a related mechanism in the Pd-mediated conversion of allyl β -ketoesters into C-allylated ketones, see T. Tsuda, Y. Chujo, S.I. Nishi, K. Tawara and T. Saegusa, *J. Am. Chem. Soc.*, 102, 6384 (1980).

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