

Note

Mild, efficient and economical oxidative deprotection of allyl aryl ethers

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An efficient, economical procedure for the cleavage of allyl aryl ethers using a catalytic amount of iodine in dimethyl sulphoxide gives corresponding alcohols or phenols in high yields under mild condition. The reaction can be performed in air without loss of variety of oxidisable functional groups. Allyl ether of phenols is selectively deprotected in preference to alcohols. The reaction is highly regioselective and chemoselective.

Keywords: Allyl aryl ethers, dimethyl sulphoxide, oxidative deprotection

The allyl group has been frequently used in organic synthesis as a protecting group for alcohols^{1a-d}, phenols, acid² and peptides³ due to its stability under basic and acidic condition⁴. Removal of allyl group is usually affected by two step procedures that include isomerization of allyl group to more labile 1-propenyl group with variety of reagents. Strong bases^{5a,b} or transition metal salts^{6a-d} or their expensive complexes^{7a-g} have been used for isomerization purpose followed by acid hydrolysis or oxidation of resulting enol ethers. But this procedure cannot be applied to allyl ethers containing other isomerizable double bonds. Several new methods have been developed using various reagents which includes NBS/hv⁸, CAN⁹, DDQ¹⁰, TBAS¹¹, Pd (PPh₃)/NaBH₄ (Ref 12), *n*-BuLi (Ref 13), Pd/C (Ref 14a,b). These procedures however suffer from the following drawbacks: (i) availability of reagents, (ii) high cost of the reagents, (iii) lengthy procedures, (iv) compatibility of the other functional groups and (v) low yields. Therefore, introduction of an efficient and selective method for the cleavage of allyl ethers to their parent compounds is of practical importance.

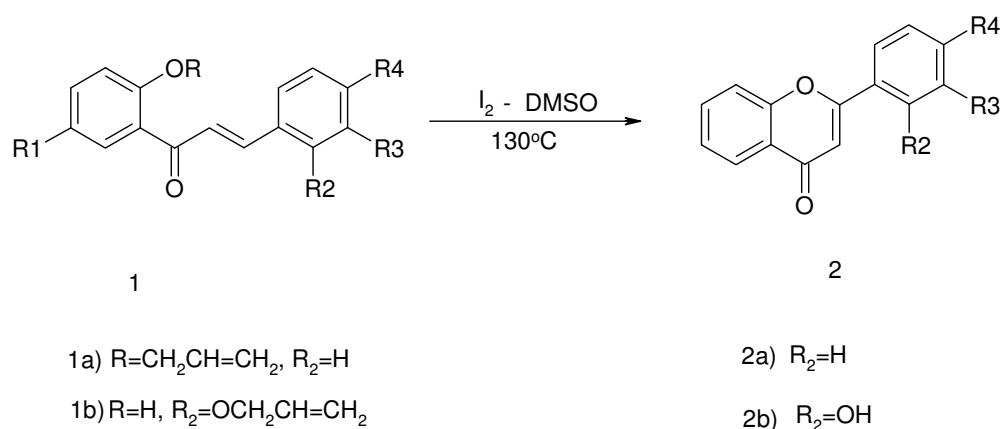
Phenolic hydroxyl groups are ubiquitous in naturally occurring secondary metabolites of plants and animals^{15a,b}. Polyphenols are oxidation prone, sensitive to radicals and possess enhanced nucleophilicity. Therefore, protection of phenolic hydroxyl group in

multistep synthesis of biologically important natural product, flavonoids, including chalcones, flavanones and flavones is of immense importance^{16a}. In the natural product flavones, invariably OH or OMe groups are present as one of the substituents^{16b}. We were interested in the protection of phenolic group in phenols, aldehydes and ketones which were used in the synthesis of chalcones^{16c}. It was observed that these 2'-hydroxychalcones then oxidatively cyclised to naturally occurring hydroxyl flavones. To achieve this aim, iodine in dimethyl sulphoxide seemed to be an appropriate reagent so that deallylation occurs along with oxidative cyclization (**Scheme I**). Very recently we have succeeded in the deallylation of 2'-allyloxychalcone and allyl carboxylic esters^{17a,b}. Earlier, the use of iodine has been reported in allyl deprotection procedures^{18a,b}. This procedure is now extended to allyl phenols containing formyl, ketonic groups and allyl aryl ethers.

Results and Discussion

O-Allyl phenol (entry 1) was selected as a model substrate to optimize the conditions. It was observed that 10 mg of iodine in dimethyl sulphoxide at 120°C effectively cleaved O-allyl bond within 30 min with 92% yield (**Table I**). In the solvents other than dimethyl sulphoxide, methanol, ethanol, dimethylformamide, diethylether, dichloromethane and benzene, the reaction did not proceed at all. The effect of temperature was also examined on the reaction. At 100°C, it was found that there was no deallylation. Reactions initiate at 120°C and complete at 130°C within 30 min. However, at 60°C, with the addition of a drop of sulphuric acid with iodine in DMSO, deallylation occurs smoothly and gives phenol with 85% yield. It is seen that when temperature drops down to 25°C, reaction did not take place. The reaction of 1,3-diallylresorcinol was examined (entry 7). The reaction of O,O'-diallylresorcinol with iodine in DMSO gave the expected mixture of O-allyl phenol and resorcinol at 120°C. On increasing the temperature to 140°C both allyl group cleaved and resorcinol with 78% yield was obtained in 1 hr. It is observed that electron withdrawing groups in phenol slow down the deallylation (**Scheme II**).

Deallylation of 2'-hydroxyacetophenone was carried out. Under the present reaction conditions it was



Scheme I — Oxidative cyclization of allyloxychalcone to flavone

Table I — Cleavage of allyl ethers of phenols with iodine in DMSO

Entry	Substrate R=allyl	Product	Time(hr)	Yield in %
1			0.5	92
2			0.5	85
3			0.5	88
4			0.5	90
5			0.5	86
6			0.5	89
7			1	78
8			1	80

—Contd

Table I— Cleavage of allyl ethers of phenols with iodine in DMSO—*Contd*

Entry	Substrate R=allyl	Product	Time(hr)	Yield in %
9			0.5	88
10			0.5	90
11			0.5	81
12			1	78
13			0.5	93
14			0.5	91
15			0.5	89
16			0.5	90
17			2	79
18			1	78

—*Contd*

Table I— Cleavage of allyl ethers of phenols with iodine in DMSO—*Contd*

Entry	Substrate R=allyl	Product	Time(hr)	Yield in %
19			0.5	89
20			0.5	85
21			0.5	91
22			0.5	93
23			0.5	82

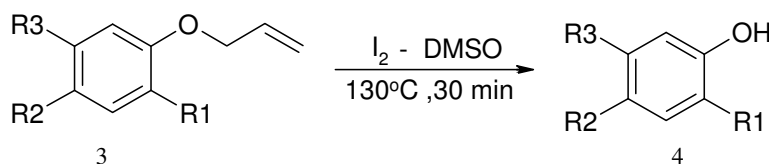
observed that O-allyl acetophenone which has an electron withdrawing or weak electron donation group on the benzene ring was readily deprotected to give corresponding 2'-hydroxyacetophenone in high yields (15-18). In case of 4'-O-benzyloxy-2'-O-allylacetophenone at reflux both groups were cleaved to 2,4-dihydroxyacetophenones. On the other hand, at 120°C only O-allyl group selectively cleaved while benzyl group remained intact (entry 18). Furthermore, yields of cleavages of O-allyloxy acetophenones bearing strong electron donating group such as hydroxyl or methoxyl group were low as compared to those of electron withdrawing groups. The deallylation of 2'-allyloxyacetophenone was faster than the 4'-allyloxyacetophenones. The di-O-allyl ether of 2'-hydroxybenzyl alcohol was deallylated to give 2-hydroxyallyl benzyl ether demonstrating preferential cleavage of phenolic allyl ether (entry 12). 2-Allyloxy methyl salicylate under similar conditions resulted in hydrolysis of acetoxy group along with deallylation (entry 23). However, ester groups of methyl salicylate remain intact at 60°C in presence of H⁺ under reaction to formyl substituted phenols (entries 19-22). The deallylation proceeds smoothly as in case of O-allyloxy vanillin giving a yield of 91% (entry 21). No

other by-products are observed in any of these reactions. This method is found to be compatible with easily oxidizable groups like -CHO, -COCH₃ and polyphenols.

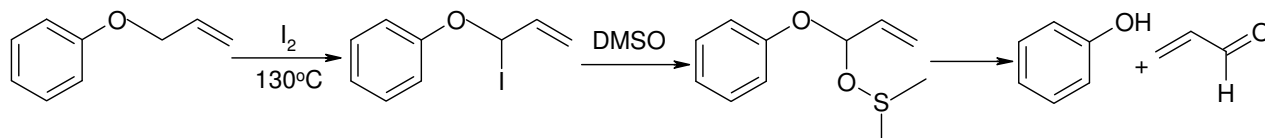
This methodology was applied in the synthesis of 2'-hydroxyflavones. 2'-Hydroxychalcones **1b** were treated with catalytic amount of iodine in DMSO and heated at 130°C to give corresponding 2'-hydroxyflavones **2b** in moderate yields. While no mechanistic study has been undertaken, it is assumed that the reaction proceeds *via* oxidative mechanism (**Scheme III**). The oxidative cleavage of allyl ethers appear to proceed *via* formation of allyl iodides¹⁹ which was further substituted by dimethyl sulphoxide, which is finally cleaved to get phenol, under hydrolytic condition.

Experimental Section

To a solution of compound **3a** (0.1 mmol) in dimethyl sulphoxide (3 mL) was added a catalytic amount of iodine (0.06 mmol). The reddish solution was heated for 60 min. The reaction mixture was diluted with dilute hydrochloric acid and extracted with ether. The excess of iodine was destroyed by addition of sodium thiosulphate solution and then



Scheme II — Deallylation of aryl allyl ethers



Scheme III — A possible reaction mechanism

washed with water followed by brine solution. All the reactions were monitored by TLC on precoated silica gel plates (254 μm). The crude mixture was purified by column chromatography over silica gel (100–200 mesh) to afford the product. All melting points were determined by open capillary method and are uncorrected. ^1H NMR spectra were recorded on Varian 300 spectrometer with TMS as internal standard. All solvents were distilled directly prior to use. All starting allyl ethers were prepared under the usual allylation conditions.

Conclusion

Our method is mild and simple to perform and can be applied to system with a variety of functional groups. It can tolerate moisture and oxygen from the reaction system. Thus, the present work provides an efficient and inexpensive deallylation procedure for a variety of aryl allyl ethers. The ease of handling, short reaction time, and availability of the reagent are added advantages of this procedure. This method was found to be compatible with easily oxidizable groups like CHO, $-\text{COCH}_3$ and polyphenols. Thus it will be further extended to the synthesis of flavonoids.

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