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COMMUNICATION

Rapid and selective deallylation of allyl ethers and esters using iodine in polyethylene glycol-400†

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A simple and selective deallylation of allyl ethers and esters using iodine (10 mol%) in polyethylene glycol-400 as a green reaction solvent is described. The reaction was performed at room temperature with various aryl/alkyl allyl ethers and esters in good to excellent yields. The present methodology includes inexpensive catalyst, easy work-up, benign reaction conditions and high selectivity.

Introduction

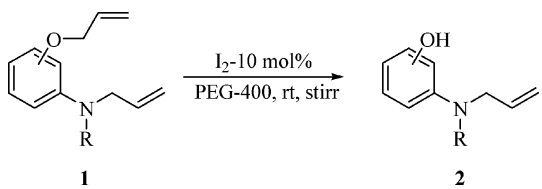
Protection and deprotection of organic functional groups is of great importance in organic synthesis.[1] Allyl groups are widely used in organic synthesis as versatile protecting groups of alcohols, amines, and acids due to their availability and to the stability of the corresponding allyl derivatives. Allyl protecting groups were also found to be very useful in both carbohydrates[2] and peptide synthesis.[3,4] The deprotection of allyl ethers using transition metal catalysts such as palladium,[5] ruthenium(II),[6] iridium(I),[7] titanium[8] and zirconium[9] are reported. The reported procedures have limited scope, are expensive and difficult to loading of catalyst. Development of deprotection methods under mild condition with high selectivity is desired.

Recently, polyethylene glycol (PEG) has been found to be an interesting green solvent system.[10] the use of PEG as an environmentally benign protocol has proved to have many applications[11] particularly, in substitution, oxidation and reduction reactions. A number of recent reviews have also covered PEG chemistry and its applications in biotechnology and medicine.[12,13] The use of molecular iodine in organic synthesis has been explored. In recent years, molecular iodine has received considerable attention as an inexpensive, non-toxic, readily available catalyst for various organic transformations under mild and convenient conditions to afford the corresponding products in excellent yields with selectivity.[14]

Previously, we reported the deprotection of 2′-allyloxy chalcones to flavones[15a] using iodine–DMSO at 130 °C in excellent yields. The deprotection products were not isolated, since the compounds were immediately oxidised to flavones. The deprotection of allyl carboxylic esters to corresponding acids[15b] under similar conditions is reported. The use of DMSO at higher temperature during reaction, get decomposed and some other functional groups are oxidized. To avoid the requirement of higher temperatures, herein we wish to report a selective deallylation of aryl/alkyl allyl ethers in presence of *N*-allyl ethers using iodine (10 mol%) in polyethylene glycol (PEG-400) as the green reaction solvent.

Results and discussion

Our initial studies started with deallylation of aryl allyl ether **1a** (entry 1, Table 1) using 10 mol% of iodine and polyethylene glycol-400 as the reaction solvent at room temperature (Scheme 1, Table 1). The reaction was completed within 20 min as confirmed by TLC. The reaction mixture was poured into a beaker containing sodium thiosulphate solution and extracted with ethyl acetate. The corresponding deallylated product was obtained in 94% yield. The *N*-allyl protecting groups remain constant in the product.



1 **2**

Scheme 1 Selective deallylation of aryl allyl ethers.

In order to establish the best reaction medium, we performed the reaction using substrate **1a** as the model reaction with various solvents such as MeOH, DCM, DMF, DMSO, ethylene glycol and PEG-400 at room temperature; the results are summarized in Table 2. Using ethylene glycol as the solvent gave very low yield (28%) of product after 16 h (Table 2, entry 5). No other solvent effect was observed on the deallylation process. By this result, we established the polyethylene glycol-400 is a best reaction solvent for this condition. To understand the role of PEG as a reaction medium, we also performed the deallylation of same substrate in EG, TEG and other glycols such as PEG-600, PEG-4000, PEG-6000 and PEG-8000 (Table 2). In ethylene glycol and triethylne glycol, the product was observed in low yield (28 and 24%).

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† Electronic supplementary information (ESI) available: Characterization data of deallylated compounds. See DOI: 10.1039/c1gc15153c

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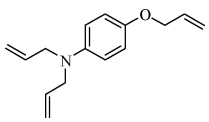
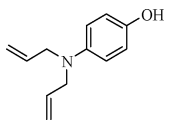
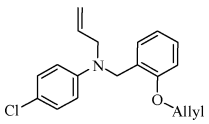
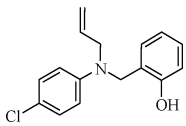
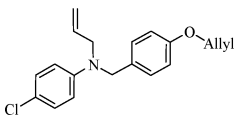
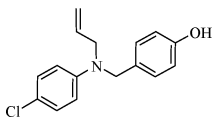
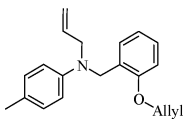
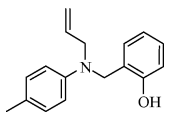
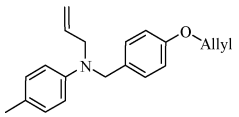
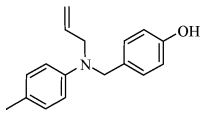
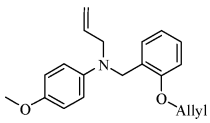
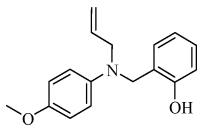
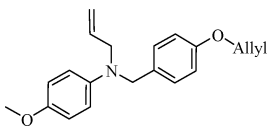
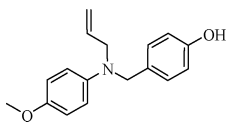
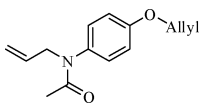
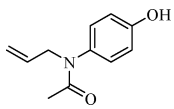
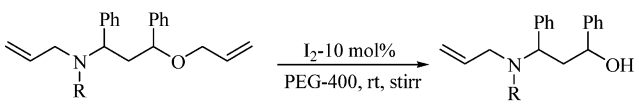
Table 1 Deallylation of aryl allyl ethers using iodine (10 mol%) in PEG-400 at room temperature

Entry	Substrate (1a–h)	Product (2a–h)	Time (min)	Yield (%)[a,b]
1			20	94
2			15	92
3			18	90
4			20	88
5			15	90
6			16	90
7			18	89
8			15	92

[a] Isolated yields of the products. [b] Products are characterized by spectral analysis.

However, as the molecular weight of PEGs increases (Table 2, entries-9–11), the viscosity increases. Because of this reason we raised the temperature up to 70 °C to liquefy the PEG. Even so, no other co-solvents are used.

Next, we investigated the amount of iodine required to catalyze the dellylation of substrate **1a** (entry 1, Table 1). Decreasing the catalyst to 5 mol% of iodine afforded the product in 52% after 5 h with regeneration of substrate. When increased to 20 mol% of iodine, the product yield was slightly improved to 96% after 20 min at same reaction conditions. We then used 30 mol% of iodine to catalyze the reaction, but no significant change in yield and reaction time was observed. Therefore, the best results were obtained with the use of 10 mol% of iodine. With this result, we next turned to a variety of aryl allyl ether substituents (Table 1), which were successfully deallylated with variety of functionalities including benzyl, PMB, methoxy and acetyl groups at room temperature in good to excellent yields. We next examined the deprotection of alkyl allyl ethers in the presence of *N*-allyl protection (Scheme 2) under similar conditions, where the reactions take 45–55 min for completion (Table 3). As additional mol% of iodine was increased, a change in reaction time or yields of the products was not observed.



3 **4**

Scheme 2 Selective deallylation of alkyl allyl ethers.

In order to evaluate the possibility of applying this methodology on a large scale, we carried out the deallyllation of 10 mmol

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Table 2 Effect of solvents on the deallylation of **1a** with 10 mol% of iodine as the catalyst at room temperature

Entry	Solvent	Time (hr)	Yield (%)[a]
1	MeOH	24	—
2	DCM	24	—
3	DMF	24	—
4	DMSO	24	—
5	Ethylene glycol	16	28
6	Triethylene glycol	12	24
7	PEG-400	0.20	94
8	PEG-600	0.25	94
9	PEG-4000	0.40	86
10	PEG-6000	0.40	85
11	PEG-8000	0.35	86

[a] Isolated yield.

of substrate **1a** with 10 mole% of iodine in polyethylene glycol-400 (100 mL) at room temperature. The yield of corresponding deallylated product was almost the same as that obtained in the small scale (~94%).

To determine the reusability of the solvent, the reaction mixture was extracted with ethyl acetate. The combined organic layer was dried over anhydrous sodium sulphate and solvent was evaporated. The remaining mother liquor was subjected to vacuum distillation to remove water leaving PEG behind in the container. The recovered PEG was subjected to charge same substrate for several times (five times) without loss of its activity (Table 4).

The role of PEG is possibly to form a complex with the cation, much like crown ether, and these complexes cause the anion to be activated.[16] In addition, no need of any external Phase Transfer Catalyst (PTC) or acidic medium to activate the oxygen atom of ally ether. Initially, we assumed that the deallylation mechanism is based on the iodine cation, which is stabilized by interaction with PEG oxygen. However, when potassium iodide or sodium iodide was employed in the reaction, the deallylation product

Table 4 Recycling of PEG-400 on deallylation of **1a** with 10 mol% of iodine as catalyst at room temperature

Run	1	2	3	4	5
Yield (%)[a,b]	92	90	90	88	85

[a] All reactions were carried out with 1 mmol of substrate. [b] Isolated yield.

was not observed. Similarly, tetraalkylammonium iodide did not give the expected product. On the basis of results and literatures,[17] a tentative mechanism for deallylation is proposed (Fig. 1). As soon as iodine was added, which activates the C=C bond and forms a three membered iodonium intermediate, it is stabilized by interaction with oxygen atom of PEG. The color of the solution remains unchanged, which supports the regeneration iodine. The formation of allyl alcohol could not be traced in the reaction. Finally, we thought that PEG is not only acting as an efficient solvent system but also acting as PTC; cause the anion to be activated.

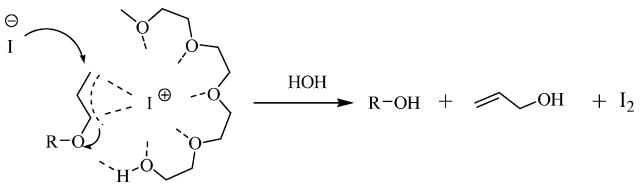
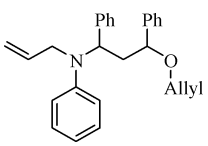
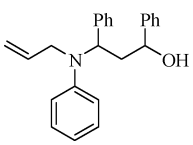
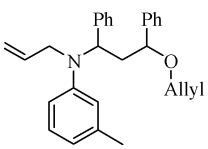
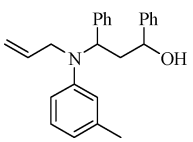
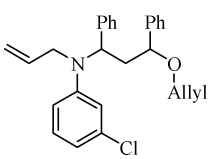
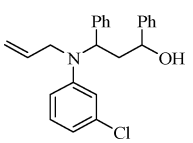


Fig. 1 A proposed mechanism for deallylation of allyl ether using iodine in PEG.

Further, we extended our study towards the selective deallylation of aryl/alkyl esters at room temperature. The corresponding deallylated products were obtained in good yields (75–82%) using 10 mol% of iodine in PEG-400 as reaction solvent (Scheme 3). With this chemoselective deallylation of *N*-allyl protected allyl carboxylic esters, we generalized with various aliphatic and aromatic substrates. The results are summarized in Table 5.

Table 3 Deallylation of alkyl allyl ethers using iodine (10 mol%) in PEG-400 at room temperature

Entry	Substrate (3a–c)	Product (4a–c)	Time (min)	Yield (%)[a,b]
1			50	78
2			55	72
3			45	76

[a] Isolated yields of the products. [b] Products are characterized by spectral analysis.

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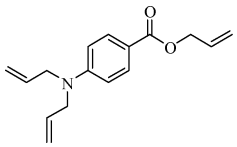
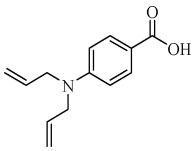
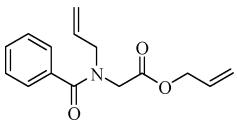
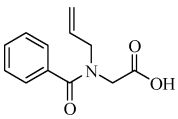
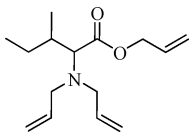
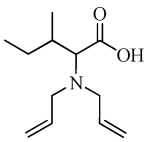
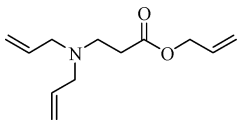
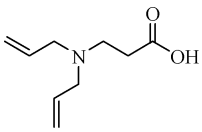
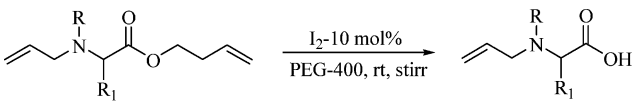
Table 5 Deallylation of aryl/alkyl allyl esters using iodine (10 mol%) in PEG-400 at room temperature

Entry	Substrate (5a–d)	Product (6a–d)	Time (min)	Yield (%)[a,b]
1			25	82
2			35	80
3			40	76
4			35	78

[a] Isolated yields of the products. [b] Products are characterized by spectral analysis.



5 6

Scheme 3 Selective deallylation of aryl/alkyl allyl esters.

Conclusion

In summary, we have demonstrated a simple and selective deallylation of aryl/alkyl allyl ethers and esters using 10 mol% of iodine in polyethylene glycol-400 as a green reaction solvent at room temperature. The present methodology is applied to substrates having benzyl, PMB, methoxy and acetyl groups. Highly selective deallylation of *O*-aryl/alkyl allyl ethers and esters was observed in presence of *N*-allyl protection. Advantages of this protocol include easy of work-up, readily available and inexpensive catalyst, high yields and benign reaction conditions.

Experimental

Merck, pre-coated silica gel 60 F_{254} (Aluminum sheets) plates were used for analytical TLC. IR spectra were recorded (in KBr pallets) on Shimadzu spectrophotometer. ^{1}H NMR spectra were recorded (in $CDCl_3$) on Varian Mercury 300 MHz spectrometer using TMS as an internal standard. The mass spectra were recorded on Shimazdu- QP 5050 GC-MS spectrometer.

General experimental procedure for deallylation

Allylic substrates were prepared by the conventional method (allyl bromide, K_2CO_3, DMF) To a solution of allyl ethers or esters (1 mmol) in polyethylene glycol-400 (10 mL) was added iodine (10 mol%) and the reaction mixture was stirred at room temperature for time period as shown in mentioned in the corresponding Table. After completion of the reaction (monitored by TLC), the reaction mixture was poured into a beaker containing aqueous sodium thiosulphate solution and extracted with ethyl acetate. The corresponding deallylated product was obtained in good to excellent yield.

To reuse the solvent, the reaction mixture was extracted with ethyl acetate. The combined organic layer was dried over anhydrous sodium sulphate and the solvent was evaporated. The remaining mother liquor was subjected to vacuum distillation to remove water leaving PEG in the bottom part of the container. The recovered PEG was subjected to charge the same substrate for five times without loss of its activity.

Spectral data of selected deallylated compounds

2-{(*N*-Allyl-4-chlorophenyl amino) methyl)} phenol (2b). IR (KBr): 3212, 3056: ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.65 (m, 2H), δ 5.26 (m, 1H), δ 5.31 (s, 2H, CH_2), δ 5.94 (m, 1H), δ 6.15 (m, 1H), δ 6.61–7.28 (m, 8H, Ar-H), δ 9.81 (s, 1H, OH); ^{13}H CMR (300 MHz, $CDCl_3$): 50, 58, 115 (2 × C), 117, 119, 121, 123, 127, 128, 129 (2 × C), 130,135, 147, 158; MS(*m*/*z*): 273 (M^+ ion), 275 (M+2); Anal. calcd for $C_{16}H_{16}NOCl$: C, 70.21; H, 5.89; N, 5.12%. Found: C, 70.12; H, 5.96; N, 5.18%

3-(*N*-Allyl-*N*-*m*-tolylamino)-1,3-diphenyl propan-1-ol (4b). IR (KBr): 3198; 3072: ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.24 (s, 3H, CH_3), δ 3.48 (m, 1H), δ 4.13 (m, 1H), δ 4.21 (s, 1H, OH), δ 4.56 (m, 2H), δ 5.01 (m, 1H), δ 5.26 (m, 1H), δ 5.94 (m, 1H), δ 6.41 (m, 1H), δ 6.86–7.41 (m, 14H, Ar-H); MS(*m*/*z*): 357 (M^+

ion); Anal. calcd for $C_{25}H_{27}NO$: C, 83.98; H, 7.61; N, 3.92%. Found: C, 83.87; H, 7.66; N, 3.98%

4-(Diallyamino)benzoic acid (5a). IR (KBr): 3456; 1725: ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.62 (m, 4H), δ 5.22 (m, 2H), δ 5.36 (m, 2H), δ 6.05 (m, 2H), δ 7.14 (d, 2H, J = 8.7 Hz), δ 7.28 (d, 2H, J = 8.7 Hz), 13.22 (bs, 1H, -COOH); ^{13}H CMR (300 MHz, $CDCl_3$):52 (2 × C), 112 (2 × C), 117 (2 × C), 119, 132 (2 × C), 135 (2 × C), 152, 169; MS(m/z): 217 (M^+ ion); Anal. calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45%. Found: C, 71.76; H, 6.91; N, 6.52%

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