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A NEW NOVEL AND PRACTICAL ONE POT METHODOLOGY FOR CONVERSION OF ALCOHOLS TO AMINES

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Abstract: A convenient and efficient one pot sequence has been developed for the transformation of alcohols to amines using Sodium azide, triphenylphosphine in CCl_4-DMF.

Amines are a versatile class of compounds used frequently in organic synthesis, especially in the construction of heterocyclic compounds[1]. Therefore, transformation of alcohols to amines is an important reaction for the synthesis of a variety of organic compounds. The most common approach for their preparation involves a three step protocol viz., a) conversion of alcohols to corresponding halides or sulfonates, b) nucleophilic substitution by azide anion[2] and c) reduction of azide to amine by using various reagents[3]. Alternatively they can be prepared by a two step methodology viz., a) Conversion of alcohol to azide by Mitsunobu reaction using hydrazoicacid,

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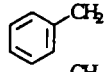
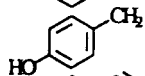
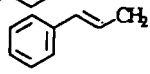
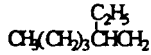
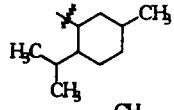
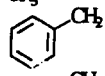
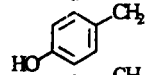
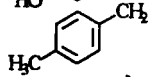
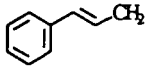
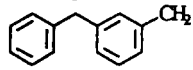
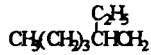
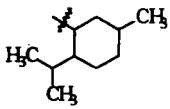
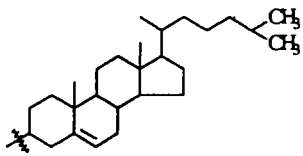
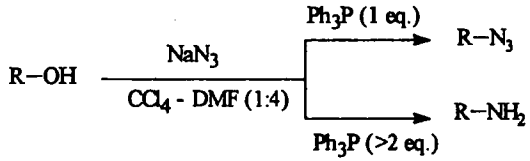
triphenylphosphine and diethylazodicarboxylate (DEAD)[4], b) reduction of azide to amine. Although these methods works well, extra time is required to isolate intermediate products and leading to low overall yields, and involves the risk of handling explosive azides. In view of this, there is a need to develop one pot sequence. Although there is a report of one pot method[5] involving the combination of Mitsunobu and Staudinger reactions, it is less attractive as it involves the usage of toxic and expensive reagents like HN_3 and DIAD respectively. Herein, we report a novel, facile one-pot protocol for the conversion of alcohols to azides/amines using NaN_3 and PPh_3 in CCl_4-DMF (1:4).

Treatment of alcohols with NaN_3 and two equivalents of PPh_3 in CCl_4-DMF (1:4) at 90°C afforded amines in an excellent yields (85-95%) (Scheme-1, Table-1, entry 7-16). Formation of amines may be visualized as the initial azide formed would react with second equivalent of Ph_3P giving the iminophosphorane which in turn converted to the amine upon treatment with water. Treatment of alcohols with one molar equivalent of Ph_3P afforded azides exclusively in good yields (Table-1, entry 1-6) confirming the azide intermediacy. This reaction has general applicability, the results obtained with various primary and secondary alcohols are summarized in Table-1. The reaction of primary alcohols was completed within 4-6 hrs., whereas secondary alcohols required longer times (8-10 hrs.). All the compounds were characterised by ^1H NMR, IR and mass spectral data and found to be in accordance with authentic samples.

Table-1 : Conversion of alcohols to azides/amines

Entry	R	Reaction time (h)	Yield (%)
1		1	95
2		1	94
3		2	92
4	$CH_3(CH_2)_6CH_2$	1	96
5		2	93
6		2	94
7		4	96
8		5	95
9		5	96
10		4	96
11		5	92
12	$CH_3(CH_2)_{10}CH_2$	5	91
13	$CH_3(CH_2)_6CH_2$	4	90
14		5	92
15		7	88
16		7	85



Scheme-1

Typical procedure: A mixture of alcohol (2 mmol), sodium azide (2.4 mmol) and PPh_3 (4.2 mmol) in 10 ml of CCl_4-DMF (1:4) was warmed at 90°C with stirring. After total disappearance of starting material (monitored by TLC), reaction mixture was brought to room temperature and quenched by adding 5 ml of water. After stirring for 10 min., reaction mixture was diluted with ether (25 ml) and washed thoroughly with water. By trituration of ether fraction at 0°C, triphenylphosphineoxide was crystallized out and ether was filtered off. Dried over anhydrous Na_2SO_4, filtration and concentration of solvent afforded amines almost in pure form, which were passed through a short pad of silica gel to give pure amines.

In summary, we developed a facile and efficient one pot methodolgy for the conversion of alcohols to azides/amines by using readily available, cheap reagents. The major advantages of the present work are neutral reaction conditions and can be used for acid and base sensitive substrates, avoids multisteps and hazardous reagents, and offers a practical alternative to the earlier methodologies.

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