novabiochem
innovations 3/03

Oxidation of alcohols using resin-bound IBX

IBX-polystyrene

Hypervalent iodine reagents have been used extensively in organic chemistry as oxidants owing to their low toxicity, ready availability and ease of handling [1]. One of the most widely used of these is the Dess-Martin periodinane [2], which is the tris acetyl derivative of the poorly soluble iodoxybenzoic acid (IBX) [3]. These reagents cleanly and efficiently oxidize benzylic, allylic and aliphatic alcohols to carbonyl compounds in high yields [2,4]. However, the removal of excess reagents and its by-products usually requires basic aqueous extraction, which is not always appropriate for automated parallel synthesis or when the substrate contains acidic functionalities. To overcome these limitations, Sorg, et al. [5] have recently introduced a polymer-supported version of 2-iodoxybenzoic acid (IBX), which offers the additional benefits of being environmentally safe and recyclable (Figure 1). IBX immobilized on silica has been described by Mülbaier and Giannis [6].

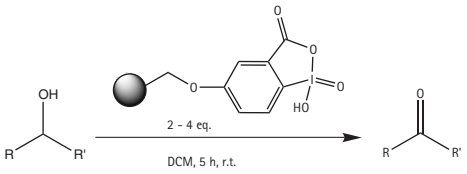

Figure 1: Oxidation of primary and secondary alcohols with IBX-PS.

For most alcohols the reactions are carried out at room temperature in DCM. As can be seen from Figure 2, oxidation is most efficient when an excess of supported IBX is employed. Products are isolated simply by removing the resin by filtration and evaporation of the solvent.

Benzylic and allylic alcohols are most readily oxidized, and this may be exploited to effect selective oxidation in polyhydroxylic compounds. The reagent is also compatible with a wide-range of non-hydroxylic functionalities such as ethers, thioethers, and secondary amides, and has been used to convert protected α-amino alcohols to the corresponding aldehydes.

01-64-0445 **IBX-polystyrene** 1 g
5 g
25 g

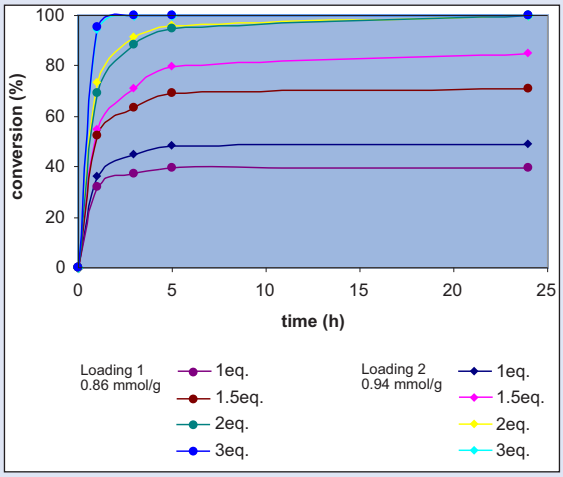

Figure 2: Conversion of 4-bromobenzylalcohol to 4-bromo-benzaldehyde, as determined by HPLC.

Applications

The utility of IBX-polystyrene was demonstrated by the oxidation of a range of primary and secondary alcohols (Table 1, Figures 3-6), according to Method 1.

Method 1: Oxidation of alcohols with IBX-polystyrene

1. Swell the resin (2-4eq. relative to alcohol to be oxidized) in DCM for 15 min.
2. Add the alcohol in DCM.
3. Agitate and follow the reaction by HPLC.
4. Remove the resin by filtration, wash with DCM and evaporate the combined filtrate to dryness.

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Alcohol	% Conversion to aldehyde or ketone		
	2 eq. (IBX-PS)	3 eq. (IBX-PS)	4 eq. (IBX-PS)
4-Bromobenzyl alcohol	100	-	-
Cinnamyl alcohol	98.6	99.2	-
2-Phenylethanol	-	77	80
1-Phenylethanol	98.8	-	-
2-Phenyl-1-propanol	-	90	95
3-Phenyl-1-propanol	-	70	-
5-Phenyl-1-propanol	-	68	71

Table 1: Conversion yields of aldehydes and ketones prepared using IBX-polystyrene. Values were determined by HPLC using Purosphere STAR column; gradient: 35%-70%B in 10 min, 1ml/min; A: 100% water; B: 100% acetonitrile).

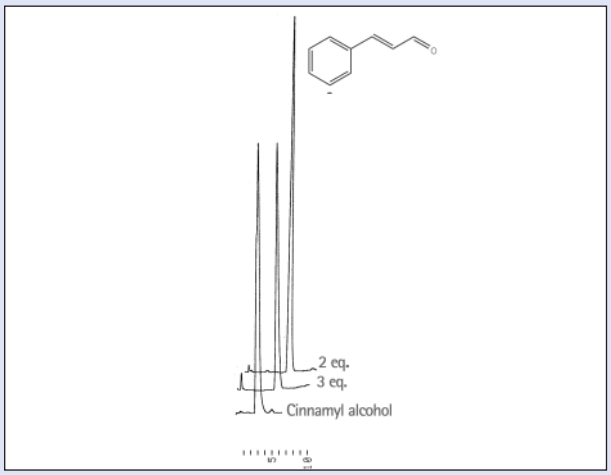

Figure 3: HPLC profiles showing the oxidation of cinnamyl alcohol to cinnamaldehyde with IBX-polystyrene.

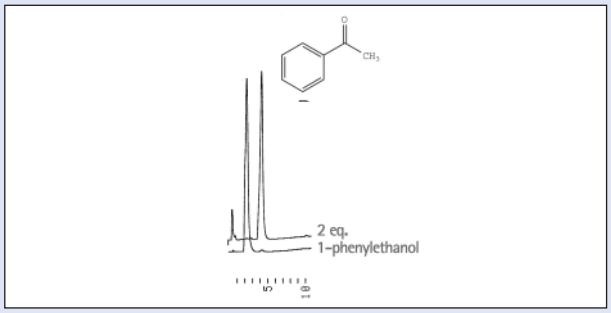

Figure 4: HPLC profiles showing the oxidation of 1-phenylethanol to acetophenone with IBX-polystyrene.

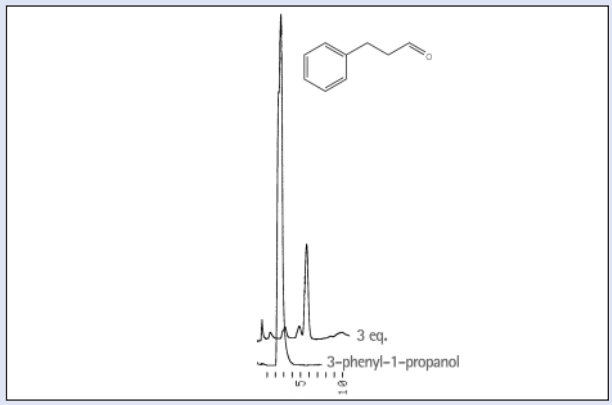

Figure 5: HPLC profiles showing the oxidation of 3-phenyl-1-propanol to 3-phenyl propanal with IBX-polystyrene.

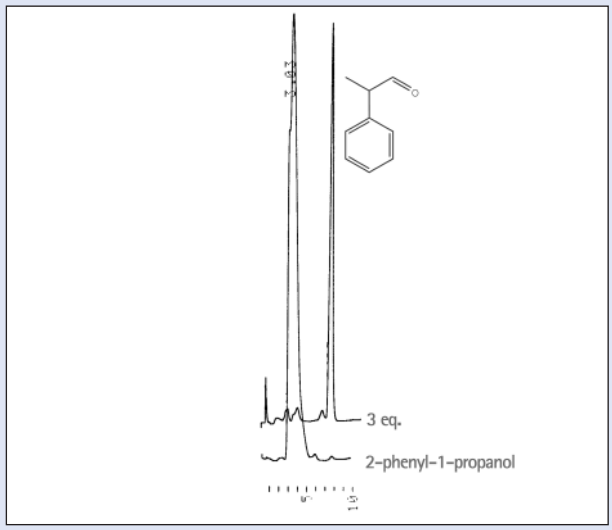

Figure 6: HPLC profiles showing the oxidation of 2-phenyl-1-propanol to 2-phenyl propanal with IBX-polystyrene.

References

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