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Polymer-Bound Oxidant : IBX Reagent

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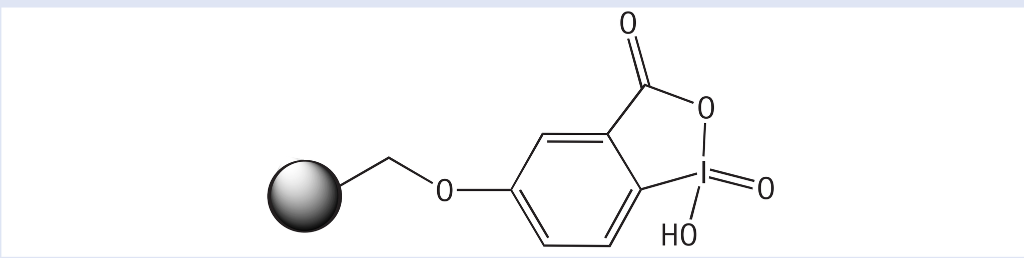
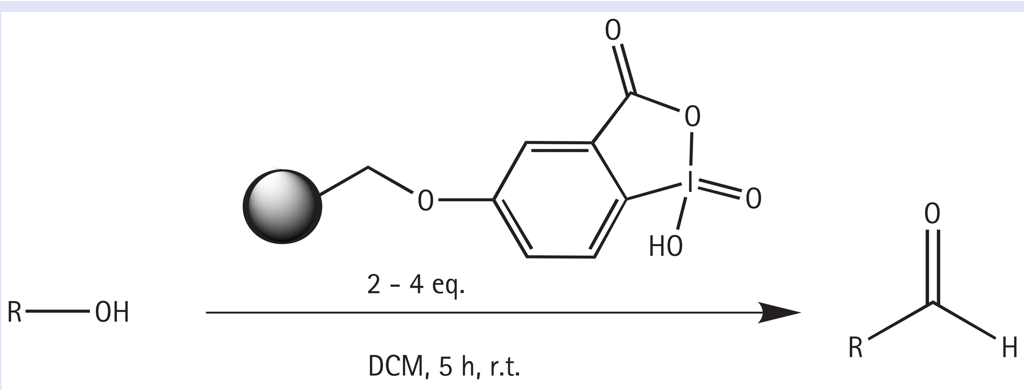
Introduction

Hypervalent iodine reagents have been used extensively in organic chemistry owing to their low toxicity, ready availability and ease of handling [1]. 1-Hydroxy-(*1H*)-benzo-1,2-iodoxol-3-one-1-oxide (IBX) oxidizes benzylic, allylic and aliphatic alcohols mildly and efficiently to carbonyl compounds in high yields. However, this reagent is poorly soluble in many organic solvents and sometimes can be difficult to be removed from the reaction mixture. The polymer-supported version of IBX *(01-64-0445)* overcomes these limitations and offers the additional benefits of being environmentally safe and recyclable [2-3].



Results and Discussion

The reaction kinetics of the supported IBX reagent were studied to develop optimized procedures as shown in Method 1. Cinnamyl alcohol, 1-phenylethanol, 3-phenyl-1-propanol and 2-phenyl-1-propanol were studied as additional examples in IBX oxidation. Results are presented in Table 1.



Optimization Conditions

4-Bromobenzylalcohol was oxidized to the corresponding aldehyde using Method 1 applying 1, 1.5, 2 and 3eq. of two different batches of IBX resin.

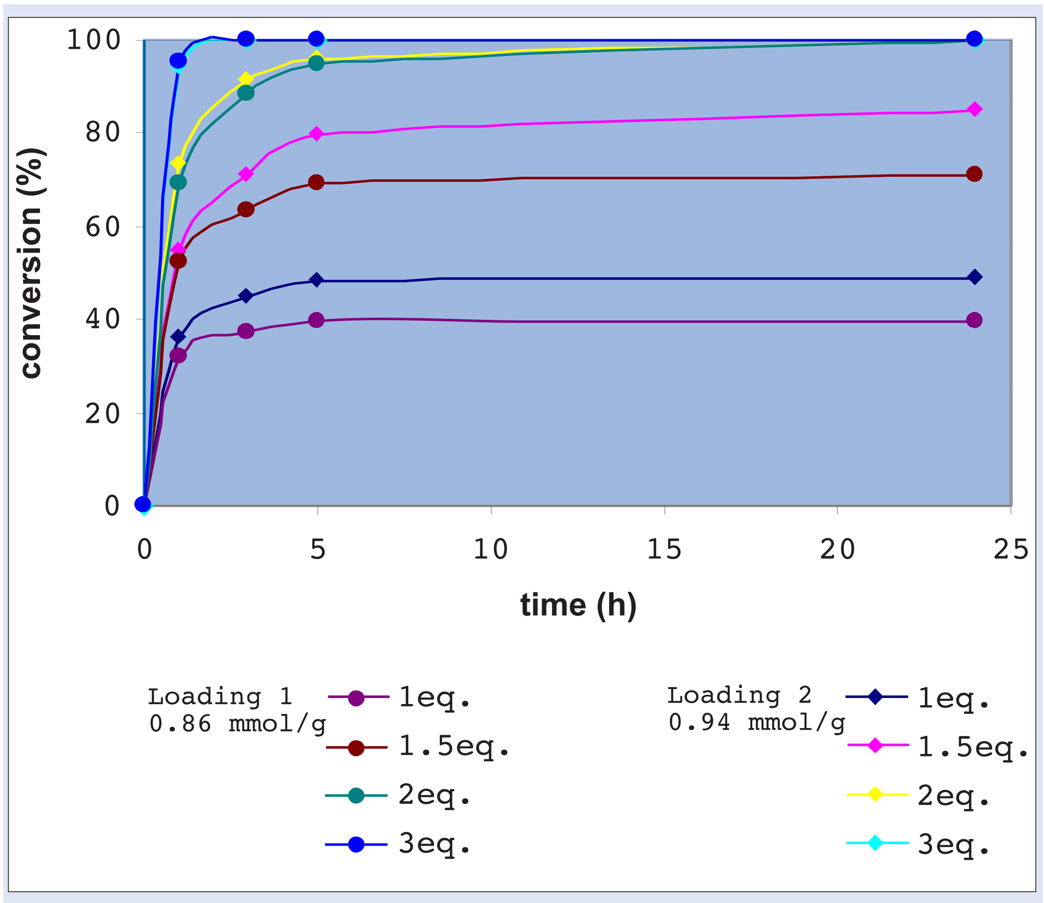


Fig. 1: Conversion of 4-bromobenzylalcohol to the corresponding aldehyde as determined by HPLC (HPLC conditions: Purospher STAR; Gradient: 35%-70%B in 10 min, 1 ml/min; A: 100% water; B: 100% acetonitrile).

Applications

Oxidation of	Cinnamyl alcohol	1-Phenylethanol	3-Phenyl-1-propanol	2-Phenyl-1-propanol
Purity of aldehyde %	98.6 (2eq. resin) 99.2 (3eq. resin)	98.8 (2eq. resin)	70 (3eq. resin)	90 (3eq. resin) 95 (4eq. resin)
Fig. 2	A	B	C	D

Table 1: Oxidation in parallel format using IBX supported reagent.

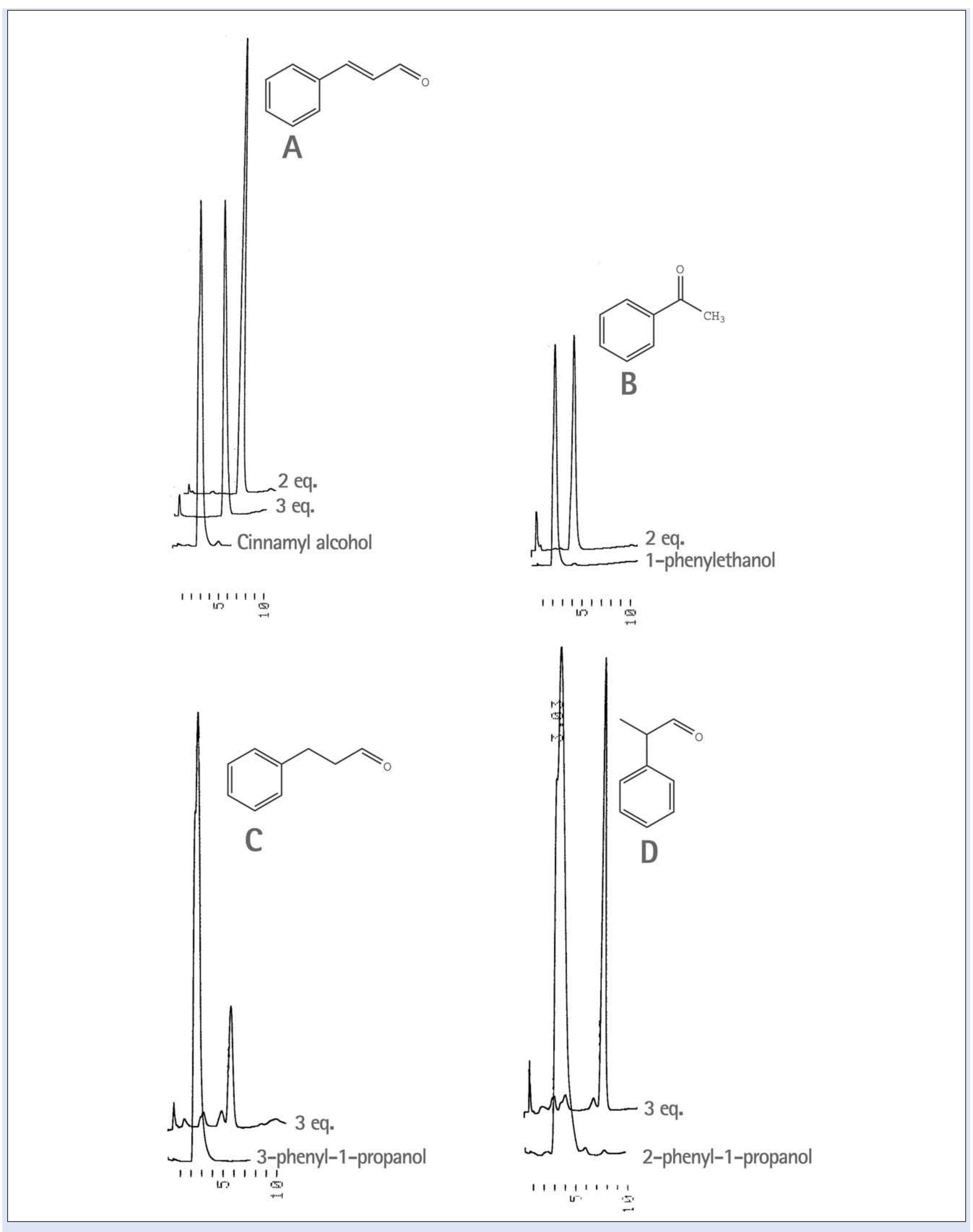
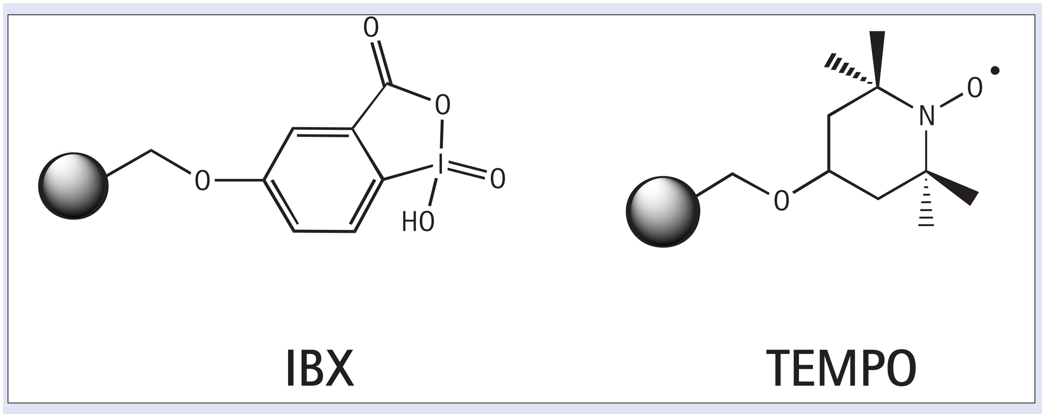


Fig. 2: HPLC traces of oxidation reactions using IBX resin as mentioned in Table 1 (HPLC conditions: Purospher STAR; Gradient: 35%-70%B in 10 min, 1 ml/min; A: 100% water; B: 100% acetonitrile).

Comparison of 2 oxidant reagents:

IBX and TEMPO resin

A comparison of 2 different polymer-bound oxidation reagents [4-6] is presented (Table 2) in order to have a complementary approach of reaction conditions in solution phase chemistry.
TEMPO resin pre-activated with N-chlorosuccinimide to oxoammonium salt can convert alcohols into corresponding aldehydes. TEMPO may also be used in catalytic quantity in combination with a co-oxidant (e.g. Oxone, BAIB).



	IBX	TEMPO		
		Stoechiometric	Catalytic + Oxone	Catalytic + BAIB
% Oxidation of alcohols	Method 1	Method 2	Method 3	Method 4
4-Br benzylalcohol	100 (2eq.)	99	97.5-98	Not determined
Cinnamyl alcohol	98.6 (2eq.) 99.2 (3eq.)	98.1	91.5	99.4
2-Phenyl-1-ethanol	77 (3eq.) 80 (4eq.)	34 P/18.6 R	54.3 P/45.7 R	98.8
1-Phenyl -1-ethanol	98.8 (2eq.)	99.5	97.1	53.4 P/46.6 R
2-Phenyl -1-propanol	90 (3eq.) 95 (4eq.)	0	0	39.6 P/5.4 R/ 55% impurities
3-Phenyl -1-propanol	70 (3eq.)	Not determined	Not determined	86.7
5-Phenyl -1-pentanol	68 (3eq.) 71 (4eq.)	68 P/31 R	42 P/23 R	67.5 P/32.5 R

Table 2: Oxidation of alcohols using IBX or TEMPO resin.

Abbreviations

P: Product
R: Reagent
IBX: 1-Hydroxy-(1H)-benzo-1,2-iodoxol-3-one-1-oxide
BAIB: [Bis(acetoxy)iodo]benzene
TEMPO: 2,2,6,6-Tetramethylpiperidinyl-1-oxy, free radical
Oxone®: Potassium peroxymonosulfate, the approximate empirical formula $2 KHSO_5.KHSO_4.K_2SO_4$

Method 1

1. Swell the resin (2-4eq.) in DCM for 15 min
2. Add the alcohol (1eq.)
3. Agitate 5 h and follow the reaction by HPLC
4. Remove the resin by filtration, wash with DCM and evaporate the combined filtrate to dryness

Method 2

A. Conversion of TEMPO resin to oxoammonium salt:

1. Dissolve N-chlorosuccinimide (5 eq.) in dry DCM
2. Add 4M HCl in dioxane (6 eq.) and stir for 5 min
3. Add to TEMPO resin (1 eq.), pre-swollen in DCM
4. Agitate gently for 15 min
5. Isolate resin by filtration and wash with dry DCM

B. Oxidation of alcohol with oxoammonium resin:

1. Dissolve alcohol (1 eq.) in dry DCM
2. Add freshly prepared resin (3-5 eq.) and agitate for 1 h (primary alcohol) or 2 h (secondary alcohol)
3. Remove resin by filtration and wash with DCM
4. Evaporate combined filtrates to dryness

Method 3

Oxidation of alcohol with catalytic amount of TEMPO and oxone:

1. Dissolve alcohol (1 eq.) in DCM
2. Add TBA-Br (0.04 eq.)
3. Add TEMPO resin (0.06 eq.)
4. Add oxone (2.2 eq.)
5. Agitate o/n at r.t.
6. Remove resin by filtration and wash with DCM
7. Evaporate combined filtrates to dryness

Method 4

Oxidation of alcohol with catalytic amount of TEMPO and BAIB:

1. Swell the resin (0.1 eq.) in DCM for 15 min
2. Add BAIB (1.1 eq.) to a solution of alcohol in DCM
3. Agitate 3-5 h and follow the reaction by HPLC
4. Remove the resin by filtration, wash with DCM
5. Wash with a saturated solution of $Na_2S_2O_3$, extract with DCM
6. Dry, evaporate the combined filtrates to dryness
7. Purify by chromatography

Conclusion

- The oxidation of primary, secondary, benzylic, allylic and aliphatic alcohols was achieved using IBX and TEMPO polymer-supported reagents
- IBX and TEMPO resins were compared
- 4 different methods can be used depending on the nature of the alcohols

TEMPO

Pre-activation of the resin when stoechiometric method used
Use in catalytic quantity in combination with co-oxidant (e.g. Oxone, BAIB)
Method 4 especially adapted for water soluble alcohols (sugar...)
Quantitative oxidation of 2-phenyl ethanol, a substrate difficult to oxidize, with method 4

IBX

Easier handling (no pre-activation)
Quantitative oxidation of 2-phenyl propanol
Higher conversion of 5-phenyl pentanol (71%)

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