

Preparation of resin bound [hydroxy(tosyloxy)iodo] benzene and its use in 5-benzoyldihydro-2(3H)-furanone synthesis

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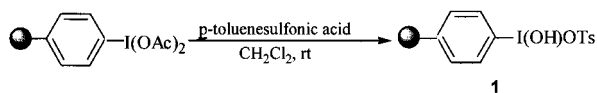
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A new type of polymer supported hypervalent iodine reagent, which is sufficiently reactive for the formation of 5-benzoyldihydro-2(3H)-furanone from 4-benzoylbutyric acid, has been prepared by a convenient method; the poly(4-iodostyrene), formed in the ractionization could be regenerated and recycled for reuse the same reaction.

Keywords: hypervalent iodine, 5-benzoyldihydro-2(3H)-furanone synthesis

Lactonisation methodology plays an important role in modern organic synthetic chemistry not only because lactones occur in nature in great abundance and variety,¹ but also because they constitute a particularly useful class of synthons.² The preparation of lactones was via intramolecular cyclisation of acyclic olefinic carboxylic acids.³ [Hydroxy(tosyloxy)iodo] benzene (HTIB) is an important hypervalent iodine reagent: it can offer a superior and general alternative to existing syntheses which involve the use of lachrymatory and toxic α -halogenoketones.⁴ Recently, Moriarty *et al.* have developed a simple and useful route to synthesise 5-benzoyldihydro-2(3H)-furanone by using HTIB.⁵ Despite the simple experimental operation and low toxicity, HTIB has a major shortcoming: the iodobenzene formed is difficult to separate from the product and is hard to reuse. Polymer supported hypervalent iodine could solve the problem. After the reaction, the poly(4-iodostyrene) formed could be easily removed from the solution just by filtration and reused. Some polymer supported trivalent iodine reagents have been synthesised, such as poly[styrene(iodosodiacetate)],⁶ phenyl polystyryliodonium bisulfate,⁷ and poly[styrene(iodosodifluoro)].⁸ In connection with our ongoing programme of the preparation and application of resin bound hypervalent iodine,⁹ we have immobilised [hydroxy(tosyloxy)iodo] benzene on polystyrene. In this paper, we report the multistep preparation of poly{[4-hydroxy(tosyloxy)iodo]styrene} and its application to the synthesis of 5-benzoyldihydro-2(3H)-furanone.

We first prepared the poly[styrene(iodosodiacetate)] from commercial polystyrene (MW = 250,000) according to the literature method.⁶ Then the poly[styrene(iodosodiacetate)] was added to a solution of *p*-toluenesulfonic acid in CH_2Cl_2 at room temperature. In a few minutes, the poly{[4-hydroxy(tosyloxy)iodo]styrene} was formed and it was collected by filtration (Scheme 1).



Scheme 1

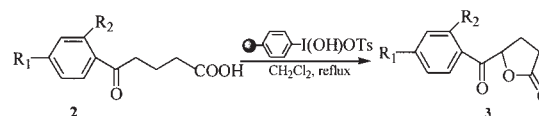
IR spectrum proved that the above conversion had occurred. The disappearance of 1645 cm^{-1} ($\text{C}=\text{O}$), 1290 cm^{-1} ($\text{O}-\text{C}$) and the emergence of 1186 , 1032 cm^{-1} ($\text{O}=\text{S}=\text{O}$) showed that the poly[styrene(iodosodiacetate)] had been converted into

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† This is a Short Paper, there is therefore no corresponding material in *J. Chem. Research (M)*.

poly{[4-hydroxy(tosyloxy)iodo]styrene} completely. The exact loading was determined by element analysis, which revealed the resin contained 1.91 mmol/g of the functional group.

4-Benzoylbutyric acid (**2**) was dissolved in dry CH_2Cl_2 , poly{[4-hydroxy(tosyloxy)iodo]styrene} was added and the solution was refluxed for 15–22 hours. The resulting solution was washed with saturated NaHCO_3 solution. After the organic layer was dried over MgSO_4 , CH_2Cl_2 was removed under vacuum and $\text{CH}_3\text{COOC}_2\text{H}_5$ was added to the resulting oil to precipitate poly(4-iodostyrene). The final products were purified by column chromatography (Scheme 2). The reaction conditions and yields are shown in Table 1.



Scheme 2

To show that poly{[4-hydroxy(tosyloxy)iodo]styrene} can be recycled a number of times, the oxidation of 4-benzoylbutyric acid (**2a**) to 5-benzoyldihydro-2(3H)-furanone (**3a**) was repeated four times using the same batch of supported [hydroxy(tosyloxy)iodo]benzene regenerated after each reaction. As seen in Table 2, the yields remain almost same as when the first prepared poly{[4-hydroxy(tosyloxy)iodo]styrene} was used.

In conclusion, the attachment of [hydroxy(tosyloxy)iodo] benzene to polystyrene lead to an air stable immobilised reagent that is as active as HTIB, and has the advantage that it can be regenerated numerous times. The poly(4-iodostyrene) formed is separated from product just by

Table 1 5-benzoyldihydro-2(3H)-furanone (**3**) obtained by oxidation of the corresponding keto acids with resin bound $\text{PhI}(\text{OH})\text{OTs}$

Entry	Product		Reaction time /h	m.p./°C		Yield /%
	R ¹	R ²		Found	Lit	
1	H	H	16	77–78	78–79 ¹⁰	63
2	Me	H	22	90–91		69
3	MeO	H	22	120–122	122–124 ¹⁰	55
4	Cl	H	21	93–94		73
5	Br	H	24	70–72		64
6	Me	Me	20	146		65
7	Et	H	15	66		62

Table 2 Reusability of resin bound Ph(OH)OTs (**1**)^a

Experiment	Yields using 1 (%)
1	63
2	62
3	60
4	58

^aOxidation of **2a** to **3a**.

filtration and the isolation of the pure product is achieved by passing the liquid through a short column of silica gel.

Experimental

Polystyrene (MW=250,000) was purchased from Acros. ¹H-NMR spectra were recorded on 60MHz on a Varian EM-300 spectrometer. Infrared spectra were recorded on a Perkin Elmer 683 spectrophotometer in KBr with absorption in cm⁻¹.

Synthesis of poly{[4-hydroxy(tosyloxy)iodo]styrene}: 2.0 g poly{styrene(iodoso diacetate)} was dissolved in 20 ml CH₂Cl₂, and 2.4 g *p*-toluenesulfonic acid was poured into the solution. After a few minutes, yellow solid appeared, and was isolated by vacuum filtration. The solid was washed with acetone(10 ml×2), ether(10 ml×2) to give 1.8g poly{[4-hydroxy(tosyloxy)iodo]styren}. S%: 6.10%. Functional group 1.91 mmol/g. IR ν_{max}/cm⁻¹ 3400, 1200, 1020, 817, 760, 700.

Synthesis of 4-benzoylbutyric acid (2).¹¹ **General procedure**: A solution of glutaric anhydride(1.14 g) in dry toluene was added with stirring to an ice cold suspension of powdered anhydrous AlCl₃ (3.35g) in dry toluene (5ml). The mixture was kept at room temperature for 12 hours and then warmed at 60–65°C for half an hour. The product was decomposed with ice and HCl and the excess of toluene removed by steam distillation. The solid product was extracted with hot NaHCO₃; the keto acid was precipitated with HCl, and crystallised from ethanol. The yield was 60%.

Synthesis of 5-benzoyldihydro-2(3H)-furanone (3). **General procedure**: 4-benzoylbutyric acid (1.0mmol, 0.19 g) was dissolved in 10 ml of dry CH₂Cl₂, poly{[4-hydroxy(tosyloxy)iodo]styrene} (1.7 mmol, 0.9 g) was added with stirring and the resulting slurry heated at reflux for 16 hours. Then the solution was cooled to room temperature and washed with saturated NaHCO₃ solution (2×10 ml) and water (5 ml). The organic layer was separated and dried over anhydrous MgSO₄, filtered and the solvent was removed under vacuum. Ethyl acetate was added to the resulting oil and filtered. The liquid layer was chromatographed upon silica gel (200–300 mesh) to give pure product. CHCl₃: CH₃COOC₂H₅ (9:1) was used as eluent.

3a: Yield 63%; white solid; m.p. 77–78°C (lit¹⁰ 78–79°C); ¹H-NMR (CDCl₃) δ: 7.98–8.00 (m, 2H, ArH) 7.27–7.65 (m, 3H, ArH), 5.80–5.83 (m, 1H,CH), 2.47–2.64 (m, 4H,2-CH₂); IR (KBr) ν (cm⁻¹): 1790, 1700, 1225, 1060; MS *m/z* (relative intensity) M⁺ 190 (1) 105 (100) 91 (100) 77 (31).

3b: Yield 69%; white solid; m.p. 90–91°C; ¹H-NMR (CDCl₃) δ: 8.00 (d, *J*=8Hz, 2H, ArH), 7.40 (d, *J*=8Hz, 2H, ArH), 5.62–5.75 (m, 1H, CH), 2.43–2.60 (m, 4H, 2×CH₂), 2.38 (s, 3H, CH₃); IR (KBr) ν (cm⁻¹): 1790, 1700, 1610, 1230, 1065; MS *m/z* (relative intensity) M⁺ 204 (1) 119 (100) 91 (28). Anal. Calcd for C₁₂H₁₂O₃: C, 70.57; H, 5.92. Found: C, 70.81; H, 5.87.

3c: Yield 55%; white solid; m.p. 120–122°C(lit¹⁰ 122–124°C); ¹H-NMR (CDCl₃) δ: 8.03 (d, *J*=8Hz, 2H, ArH), 7.10 (d, *J*=8Hz, 2H, ArH), 5.60–5.85 (m, 1H, CH), 3.87 (s, 3H, CH₃), 2.37–2.65 (m, 4H, 2×CH₂); IR (KBr) ν (cm⁻¹): 2835, 1783, 1680, 1610, 1270, 1230, 1070; MS *m/z* (relative intensity) M⁺ 220 (2) 135 (100) 77 (18).

3d: Yield 73%; white solid; m.p. 93–94°C; ¹H-NMR (CDCl₃) δ: 7.30–8.19 (m, 4H, ArH), 5.70–5.80 (m, 1H, CH), 2.40–2.60 (m, 4H, 2×CH₂); IR (KBr) ν (cm⁻¹): 1800, 1700, 1600, 1230, 1085; MS *m/z* (relative intensity) M+2 226 (0.4), M⁺ 224 (1), 139 (52), 91 (41), 43(100). Anal. Calcd for C₁₁H₉ClO₃: C, 58.81; H, 4.04. Found: C, 58.98; H, 4.01.

3e: Yield 64%; white solid; m.p. 70–72°C; ¹H-NMR (CDCl₃) δ: 7.70–8.00 (m, 4H, ArH), 5.70–5.80 (m, 1H, CH), 2.40–2.62 (m, 4H, 2×CH₂); IR (KBr) ν (cm⁻¹): 1790, 1695, 1600, 1225, 1060; MS *m/z* (relative intensity) 185 (17), 183 (17), 105 (100), 77 (35). Anal. Calcd for C₁₁H₉BrO₃: C, 49.10; H, 3.37. Found: C, 49.38; H, 3.29.

3f: Yield 65%; white solid; m.p. 146°C; ¹H-NMR (CDCl₃) δ: 6.95–7.70 (m, 3H, ArH), 5.40–5.60 (m, 1H, CH), 2.28–2.53 (m, 10H, 2×CH₂ and CH₃); IR (KBr) ν (cm⁻¹): 1800, 1700, 1610, 1220, 1060; MS *m/z* (relative intensity) M⁺ 218 (1), 133 (100). Anal. Calcd for C₁₃H₁₄O₃: C, 71.54; H, 6.47. Found: C, 71.68; H, 6.44.

3g: Yield 62%; white solid; m.p. 66–68°C; 7.85 (d, *J*=8Hz, 2H, ArH), 7.28 (d, *J*=8Hz, 2H, ArH), 5.63–5.77 (m, 1H, CH), 2.64–2.70 (m, 2H, CH₂), 2.32–2.54 (m, 4H, 2×CH₂), 1.38 (t, *J*=7.6Hz, 3H, CH₃); IR (KBr) ν (cm⁻¹): 1800, 1700, 1600, 1230, 1080; MS *m/z* (relative intensity) M⁺ 218 (0.5), 133 (100), 105(23). Anal. Calcd for C₁₃H₁₄O₃: C, 71.54; H, 6.47. Found: C, 71.80; H, 6.54.

Regeneration of poly{[4-hydroxy(tosyloxy)iodo]styrene}: The used poly (4-iodostyrene) was treated with peracetic acid to form and then converted into the poly{[4-hydroxy(tosyloxy)iodo]styrene} by the method previously described. S%: 6.06%. The loading of the resin: 1.89 mmol/g.

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