

The application of cross-linked poly[styrene(iodosodiacetate)] to the synthesis of 1,3,4-oxadiazoles[†]

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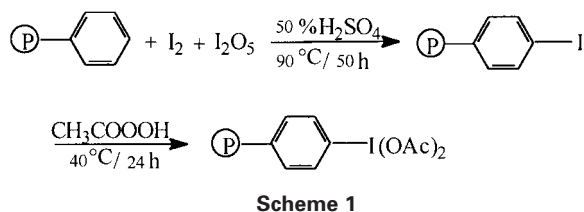
The 2% cross-linked poly[styrene(iodosodiacetate)] has been synthesised, and has been applied effectively to the synthesis of 1,3,4-oxadiazole derivatives, and regenerated and reused for the same reaction.

1,3,4-Oxadiazole derivatives are important substances in medicine and agrochemistry because of their special physiological properties.¹ It has been reported² that 1,3,4-oxadiazoles may be prepared by dehydration of 1,2-diacylhydrazines, and by chemical oxidation of aldehyde *N*-acylhydrazones by the very toxic oxidant lead tetraacetate.³

Phenyliodine diacetate (PID) is widely used in organic synthesis. It has some advantages such as the mild reaction conditions of its use, ease in handling, high selectivity and low toxicity.⁴ Dai *et al.* reported⁵ $\text{PhI}(\text{OAc})_2$ could be used to synthesis 1,3,4-oxadiazoles. But PID has many shortcomings: (1) the byproduct iodobenzene is difficult to remove from the product; (2) the iodobenzene is hard to be reused.

Recently we have developed 2% cross-linked poly[styrene(iodosodiacetate)] [CPSID] for organic synthesis. It is the ideal reagent to solve the problems because CPSID can be recovered just by filtration and reused. It is also environmentally safe.

The 2% cross-linked poly[styrene(iodosodiacetate)] was prepared as follows (Scheme 1): in presence of 50% sulfuric acid, commercially available 2% cross-linked polystyrene [CPS] (200–400 mesh) reacted with iodine and iodine pentoxide in nitrobenzene at 90 °C for 50 h to give iodinated polystyrene [CPIS].



Elemental analysis revealed that CPIS contains 33.5% iodine. This represents 2.64 mmol iodine/g indicating that 41.2% of the aromatic rings had been successfully iodinated. This intermediate was then nearly quantitatively converted into the poly[styrene(iodosodiacetate)] [CPSID] by treatment with freshly prepared peracetic acid at 40 °C overnight. The loading capacity of the polymer was obtained by iodometry and determined to be 1.99 mmol/g indicating that 98.5% of the iodinated benzene ring had been converted to phenyliodine diacetate. The resin product was best stored away from direct sunlight and in a refrigerator.

Then, we carried out the reaction by using 2% cross-linked poly[styrene(iodosodiacetate)] [CPSID] (Scheme 2) as oxidant. In presence of 2 equiv. $\text{NaOAc} \cdot 3\text{H}_2\text{O}$, the oxidative cyclization of aldehyde *N*-acylhydrazones took place smoothly at room temperature. After 30 minutes, 1,3,4-oxadiazoles were obtained in good yields.

Furthermore, the regeneration and reuse of cross-linked poly[styrene(iodosodiacetate)] from recovered poly(iodostyrene) were also studied. The result is also shown in Table 1.

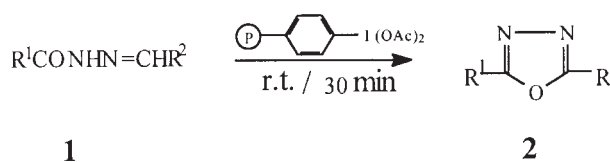


Table 1 Oxidative cyclization of aldehyde *N*-acylhydrazones by CPSID

Entry	Compound	R ¹	R ²	Product	Yield ^a (%)
1	1a	Ph	Me	2a	58
2	1b	Me	Ph	2a	50
3	1c	Ph	<i>n</i> -Pr	2b	65
4	1d	Ph	<i>n</i> -Bu	2c	68
5	1e	Ph	Ph	2d	30
6	1f	Bn	Me	2e	49
7	1g	Bn	<i>n</i> -Pr	2f	55
8	1h	Bn	<i>n</i> -Bu	2g	48
9	1i	Me	<i>n</i> -Pr	2h	24
10	1a^b	Ph	Me	2a	58

^aYield of isolated product based on 1.

^bReaction with regenerated CPSID.

In conclusion, 2% cross-linked poly[styrene(iodosodiacetate)] has good reactivity in oxidative cyclization of aldehyde *N*-acylhydrazones. After the reaction, poly(iodostyrene) can be recovered by simple filtration and the poly[styrene(iodosodiacetate)] can be regenerated and reused.

Experimental

2% Cross-linked polystyrene was purchased from Aldrich. ¹H-NMR spectra were recorded at 60MHz on a Varian EM-300 spectrometer of solutions in CDCl₃ or CCl₄. Infrared spectra were recorded on a Perkin Elmer 683 spectrophotometer in KBr.

The iodination of 2% cross-linked polystyrene: A 250 ml three necked round-bottomed flask was charged with 10 g polystyrene, 10 g iodine, 4g I₂O₅ in mixture of 4 ml CCl₄, 40 ml 50% H₂SO₄ and 120 ml of nitrobenzene. The reaction was carried out under reflux at 90 °C for 50 hours. The polymer was washed by 15 ml ether, acetone, then CH₂Cl₂ three times. 14.3 g of iodinated polystyrene were obtained. I%: 33.5%. About 41.2% benzene ring was iodinated. IR ν (cm⁻¹) 1000, 817, 760, 700.

Preparation of cross-linked poly[styrene(iodosodiacetate)]: Hydrogen peroxide (30%, 40 ml) was added dropwise to acetic anhydride (145 ml) at 40 °C and was stirred for another 4 hours. The temperature was not allowed to rise over 45 °C. To this solution, 2% cross-linked poly(iodostyrene) (6g) was added, and then the solution was kept at 40 °C overnight. The product was collected by filtration. IR ν (cm⁻¹) 1654, 1500, 1410, 1360, 1280, 1000, 817, 760, 700. The loading capacity of the polymer was obtained by idometry. The functional group is 1.99 mmol/g.

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

Typical procedure for preparation of 1,3,4-oxadiazoles: 1.2 mmol of CPSID was added to a stirred solution of 1 (1 mmol) and NaOAc·3H₂O (2 mmol) in methanol (8 ml) at room temperature. The mixture was stirred for 30 min and then the mixture was filtrated and the liquid was concentrated *in vacuo*. To the residue was added H₂O (8 ml) and the water layer extracted with ether (10 ml × 3). The organic layer was dried over MgSO₄ and concentrated. The residue was purified by column chromatography on silica gel using Et₂O-petroleum ether (1:2) as eluant;

2a: m.p. 67–69 °C (lit⁶ m.p. 67–69 °C); ¹H-NMR (CDCl₃) δ: 2.6 (s, 3H), 7.4–8.3 (m, 5H); IR (KBr) IR ν (cm⁻¹): 1580, 1490, 1445, 1250, 780, 710, 690

2b:⁶ clear oil; ¹H-NMR (CCl₄) δ: 1.1 (t, *J* = 7Hz, 3H), 1.5–2.4 (m, 2H), 7.3–8.5 (m, 5H); IR (neat) ν (cm⁻¹): 2950, 2850, 1580, 1560, 1455, 1185, 1140

2c:⁵ clear oil; ¹H-NMR (CCl₄) δ: 0.9 (t, *J* = 7Hz, 3H), 1.1–2.2 (m, 4H), 2.8 (t, *J* = 7Hz, 2H), 7.2–8.2 (m, 5H); IR (neat) ν (cm⁻¹): 2950, 2870, 1586, 1460, 1070, 1010, 780, 710, 690.

2d: m.p. 137–140 °C (lit² 141 °C); ¹H-NMR (CDCl₃) δ: 7.4–8.5 (m, 10H); IR (KBr) ν (cm⁻¹): 1550, 1485, 1450, 1070, 780, 705, 680.

2e:⁵ clear oil; ¹H-NMR (CCl₄) δ: 2.4 (s, 3H), 4.1 (s, 2H), 7.3 (s, 5H); IR (neat) ν (cm⁻¹): 1590, 1480, 1435, 1375, 1250, 1200, 1140, 1005, 930, 730, 700, 680, 640

2f:⁵ clear oil; ¹H-NMR (CCl₄) δ: 0.9 (t, *J* = 7 Hz, 3H), 1.5–2.0 (m, 2H), 2.7 (t, *J* = 7 Hz, 2H), 4.1 (s, 2H), 7.2 (s, 5H); IR (neat) ν (cm⁻¹): 1580, 1475, 1445, 1240, 1075, 1020, 965, 720, 695.

2g:⁵ clear oil; ¹H-NMR (CCl₄) δ: 0.9 (t, *J* = 7 Hz, 3H), 1.1–2.0 (m, 4H), 2.7 (t, *J* = 7Hz, 2H), 4.0 (s, 2H), 7.1 (s, 5H); IR (neat) ν (cm⁻¹): 1580, 1480, 1435, 1375, 1250, 1190, 1130, 1005, 930, 740, 690, 640.

2h:⁶ clear oil; ¹H-NMR (CCl₄) δ: 1.0 (t, *J* = 7 Hz, 3H), 1.8 (m, *J* = 7Hz, 2H), IR (neat) ν (cm⁻¹): 2950, 2860, 1585, 1555, 1450, 9225, 1180, 955.

Regeneration and reuse of CPSID from recovered poly (iodostyrene): After the reaction, the poly (iodostyrene) was recovered by simple filtration. Then, the recovered PIS was oxidised to CPSID with peracetic acid and was assayed again by iodometry. IR ν (cm⁻¹) 1654, 1500, 1410, 1360, 1280, 1000, 817, 760, 700. Functional group is 1.97 mmol/g. It was applied to the reaction and has the same activity as the first prepared CPSID.

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