The First Example of Polymer-supported Alkenyl Iodonium Salts: Efficient Synthesis of β-Functional Enamines

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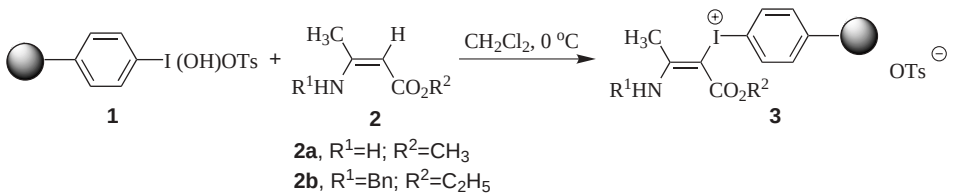
Abstract: Polymer-supported alkenyl(phenyl) iodonium salts were synthesized, which served as effective alkenyl transfer reagents for the preparation of β-functional enamines; the polymer support poly(4-iodostyrene) can be regenerated and recycled.

Key words: polymer-supported alkenylphenyl iodonium salts, poly(4-iodostyrene), β-functional enamines

Polymer-supported organic reagents have been extensively applied to the preparation of the organic molecules.[1] The most important point is that the regeneration and reuse of the recovered polymer-supported reagents are possible, thus providing an environmentally benign system. Hypervalent iodine reagents have attracted wide attention due to their unique chemical properties.[2] Among them, alkenyl(phenyl) iodonium salts are very important reagents as synthons of alkenyl cations in organic synthesis.[3] Most of the syntheses of alkenyl(phenyl) iodonium salts were realized by the reaction of an activated alkene with iodine(III) species[4] or addition of nucleophiles to alkynyl(phenyl) iodonium salts.[5] However, to the best of our knowledge, no examples of polymer-supported alkenyl(phenyl) iodonium salts have been reported. During continuing our efforts to develop new polymer-supported hypervalent iodine reagents,[6] we were interested in the synthesis of polymer-supported alkenyl iodonium salts. In this paper, we report the first preparation of polymer-supported alkenylphenyl iodonium salts, and their application as alkenyl transfer reagents to synthesize β-functional enamines.

We began our efforts to prepare the polymer-supported alkenyl(phenyl) iodonium salts by the treatment of poly{[4-hydroxy(tosyoxy)iodo]styrene}(resin **1**)[6b] with terminal alkenes, such as styrene and α-methylsyrene, or α,β-unsaturated ketones and esters, but no satisfactory results were got. Luckily, polymer-supported alkenyl(phenyl) iodonium salts were obtained when methyl-3-amino-crotonate (**2a**) and ethyl-3-benzylamino-crotonate (**2b**) were used following the conditions that Papoutsis[4c] et al. devised in the solution conditions (Scheme 1). The resin **1** and methyl-3-amino-crotonate (**2a**) or ethyl-3-benzylamino-crotonate (**2b**) were stirred at 0 °C for 6 hours. The resulting solution was evaporated in vacuo carefully and Et_2O was added to precipitate the white polymeric alkenyl(phenyl) iodonium salts[7] **3a** and **3b**. The elemental analysis of the nitrogen component is 3.09% (**3a**, N: 2.21mmol/g) and 2.44% (**3b**, N: 1.74 mmol/g) respectively, which implies the polymer-supported Koser's reagent (resin **1**) have been converted almost quantitatively to polymer-supported alkenyl(phenyl) iodonium salts **3**.

The conversion was also established by IR spectroscopy with the shifting of the characteristic peaks of -SO_2- from 1187 to 1170 cm^{-1} (**3a**) or 1171 cm^{-1} (**3b**), and the appearance of peaks at 3176 and 3076 cm^{-1} (NH_2, **3a)** or 3043cm^{-1} (BnNH, **3b**) and 1629 cm^{-1} (C=O, **3a**), or 1625 cm^{-1} (C=O, **3b**). The polymer-supported alkenyl(phenyl) iodonium salts are stable in air, and no decomposition was observed over a period of one week at room temperature, but it is better to store the resin products away from direct sunlight and in a refrigerator.



Scheme 1

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With these polymer supported alkenyl(phenyl) iodonium salts at hand, we investigated their reactions with various nucleophilic reagents to prepare β-functional enamines[8] (Scheme 2) at room temperature. The results are summarized in Table 1.

The recovered poly(4-iodostyrene) was dissolved in CH_2Cl_2 and precipitated by the addition of Et_2O to purify the resin. The regenerated resin was converted to polymer supported alkenyl(phenyl) iodonium salts according to the above methods. The β-functional enamine **4a** prepared with polymer-supported alkenyl(phenyl) iodonium salt **3a** was repeated and the yield remained constant (Table 1, Entry 12).

In conclusion, the polymer-supported alkenyl(phenyl) iodonium salts have firstly prepared as effective alkenyl transfer reagents for the preparation of β-functional enamines. The regenerated polymeric hypervalent iodonium salts showed the similar activity as newly prepared reagents. The β-functional enamines, which containing various functional groups, can obviously be applied for useful building block in organic synthesis. Further applications of the β-functional enamines and polymer-supported alkenyl(phenyl) iodonium salts are being studied.

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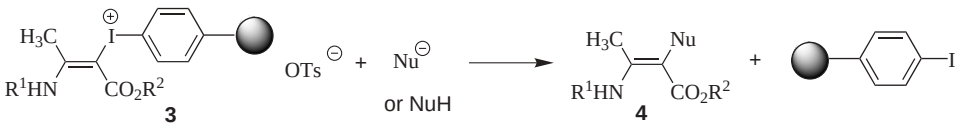

Scheme 2

Table 1 Preparation of β-Functional Enamines **4**

Entry	Nu or NuH	R^1	R^2	Product	Yield (%)[a]	Conditions
1	KSCN	H	CH_3	**4a**	83	$CHCl_3/H_2O$/12 h
2	$HN(Et)_2$	H	CH_3	**4b**	79	$CHCl_3$/12 h
3	Bu_4NBr	H	CH_3	**4c**	81	$CHCl_3$/12 h
4	NaCN	H	CH_3	**4d**	63	$CHCl_3/H_2O$/24 h
5	$NaSO_2Tol$	H	CH_3	**4e**	74	$CHCl_3/H_2O$/16 h
6	Morpholine	H	CH_3	**4f**	84	$CHCl_3$/12 h
7	$NaSC(S)N(CH_3)CH_2C_6H_5$	H	CH_3	**4g**	82	$CHCl_3/H_2O$/12 h
8	$KSP(O)(OEt)_2$	H	CH_3	**4h**	76	$CHCl_3/H_2O$/12 h
9	NaCN	Bn	C_2H_5	**4i**	68	$CHCl_3/H_2O$/24 h
10	KSCN	Bn	C_2H_5	**4j**	69	$CHCl_3/H_2O$/12 h
11	$HN(Et)_2$	Bn	C_2H_5	**4k**	66	$CHCl_3$/12 h
12[b]	KSCN	H	CH_3	**4a**	83	$CHCl_3/H_2O$/12 h

[a] Isolated yields.
[b] Using regenerated resin.

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(7) **Preparation of Polymer-supported Alkenyl Iodonium Tosylate 3**: To a solution of methyl-3-amino-crotonate (**2a**; 1.15 g, 10 mmol) or ethyl-3-benzylamino-crotonate (**2b**; 2.19 g, 10 mmol) in CH_2Cl_2 (30 mL), poly{[4-hydroxy(tosyloxy)iodo]styrene} (1.65 g, 3 mmol) was added. The suspension was stirred at 0 °C for 6 h or 2 h, respectively. After the reaction was complete, the CH_2Cl_2 was evaporated in vacuum to give oily residue. Et_2O (20 mL) was added to precipitate the product, which was filtered off and washed with acetone (10 mL × 2) and Et_2O (10 mL × 2) to afford the products. Compound **3a**: white powder, 1.61 g, N%, 3.09. IR (KBr): ν = 3176, 3076 1629, 1448, 1404, 1263, 1187, 1125, 1035, 1009, 814, 684 cm^{-1}. Compound **3b**: white powder, 1.78 g, N%, 2.44. IR (KBr): ν = 3043, 2920, 1625, 1487, 1449, 1170, 1124, 1034, 1009, 814, 683 cm^{-1}.

(8) **General Procedure for the Synthesis of β-Functional Enamines 4:** To a suspension of **3a** (1.0 g, N: 2.21 mmol/g) in $CHCl_3$ (10 mL) was added the solution of KSCN (0.1 g, 1 mmol) in water (3 mL). After the reaction was complete, the organic layer was separated and dried over anhyd $MgSO_4$. The solvent was removed under vacuum and Et_2O was added to the resulting oil to precipitate poly(4-iodostyrene). The solution was submitted to preparative TLC on silica gel with *n*-hexane–EtOAc (2:1, v/v) as the eluent to afford 143 mg (83%) of **4a**, white powder, mp 77–78 °C. IR (KBr): n = 3410, 3312, 2998, 2949, 1672, 1628, 1506, 1434, 1371, 1264, 1185, 1134, 1071, 778, 648 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): d = 9.26 (s, 1 H), 5.78 (s, 1 H), 3.77 (s, 3 H), 2.39 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): d = 168.8, 168.7, 113.5, 75.6, 52.0, 23.4. MS (EI): *m/z* (%) = 172 (38.9) [M^+], 113 (71.4), 87 (67.7), 59 (49.5), 42 (100). Anal. Calcd for $C_6H_8N_2O_2S$: C, 41.85; H, 4.68; N, 16.27. Found: C, 41.78; H, 4.59; N, 16.39.