SHORT PAPER

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Hypervalent iodine in synthesis 74: synthesis and reactivity of new functionalised alkenyliodonium salts[1†]

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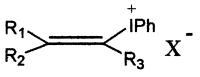
β-Amino substituted α,β-unsaturated ketones react with [hydroxy(tosyloxy)iodo]benzene to afford the corresponding alkenyl(phenyl)iodonium tosylates; these new α-acyl-β-aminoalkenyl(phenyl)iodonium tosylates offer an easy access to highly functionalised alkenes upon reaction with verious nucleophiles

During the last few years alkenyl(phenyl)iodonium salts **(1)** have risen from mere chemical curiosities to valuable synthetic intermediates.[2] Because of the excellent leaving group ability of a phenyliodonyl moiety, alkenyl(phenyl)iodonium salts undergo nucleophilic vinyl substitutions under mild conditions, thus providing a useful route for the synthesis of various kinds of olefins. Recently, some of functionalised alkenyl iodonium salts **(2)** have been prepared.[3] These compounds represent a potentially useful class of reagents that can be converted into functionalised alkenes. However, non-cyclic alkenyliodonium salts bearing an amino and acyl group on the vinylic carbon have not reported. Our research interest is in the synthetic application of alkenyl iodonium salts as alkenylating reagents of nucleophiles under mild conditions, which include the reactions of alkenyl iodonium salts with sodium dithiocarbamates, potassium carbonotrithioates, sodium tellurolates and selenolates, potassium phosphorothioates, phosphorodithioates and phosphoroselenoates.[4] In an extension of our investigations we have prepared α-acyl-β-aminoalkenyl(phenyl)iodonium salts and examined the reactions of these new alkenyliodonium salts with nucleophiles which provide an easy access to some highly functionalised alkenes.



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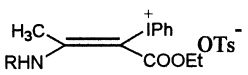

2

Herein we wish to report our results. At first, some of new α-acyl-β-aminoalkenyl(phenyl)iodonium salts were prepared. We found that the reaction of β-amino-α,β-unsaturated ketones **(3)** with [hydroxy(tosyloxy)iodo]benzene **(4)** occurred easily in methylene chloride. In fact, simple stirring of a mixture of the **(3)** and **(4)** in CH_2Cl_2 at ice-bath temperature for 45 minutes gave, after workup, the stable α-acyl-β-aminoalkenyl(phenyl)iodonium salts **(5)** (Scheme 1). The results are summarised in Table 1.

Then, using the **(5a)** as a representative compound we investigated the reactivity of these new functionalised alkenyliodonium salts **(5)** with nucleophilies. We found that the reaction of **(5a)** with several nucleophiles **(6)** occurred easily and was complete within 1 hour in DMF at room temperature in the presence of CuI (when the nucleophile was sodium nitrite, the reaction required cupric sulfate instead of CuI as catalyst) to form corresponding highly functionalised alkenes **(7)** with good yields (Scheme 2). The results are summarised in Table 1. The products were characterised by IR, NMR, MS and microanalyses.

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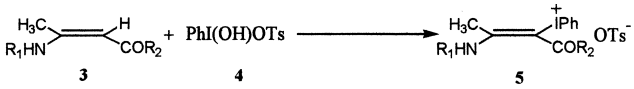
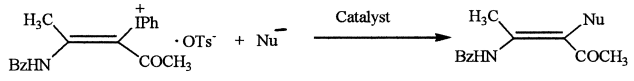
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*



3 **4** **5**

a: R_1=Bn, R_2=Me
b: R_1=Bn, R_2=Ph
c: R_1=Me, R_2=Me
d: R_1=Me, R_2=Ph

Scheme 1



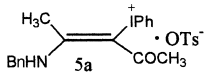
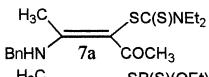
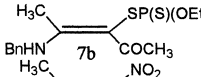
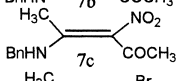
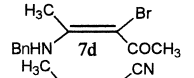
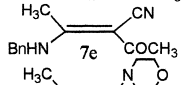
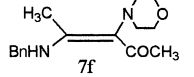
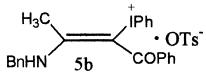
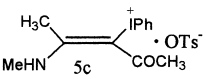
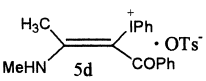
5a **6** **7**

a: $Et_2NC(S)S$–(Na^+salt)
b: $(Et_2O)_2P(S)S$–(K^+salt)
c: NO_2 (Na^+salt)
d: Br^-(n–Bu_4N^+salt)
e: CN^-(Na^+salt)
f:  from morpholine

a: Nu=$Et_2NC(S)S$–
b: Nu=$(Et_2O)_2P(S)S$–
c: Nu=–NO_2
d: Nu=–Br
e: Nu=–CN
f: Nu= 

Scheme 2

Table 1 Preparation and reactivity of iodonium salts

Entry	Iodonium salts **5**	Yield/%	Products **7**	Yield/%
1	 **5a**	51	 **7a**	92
2			 **7b**	83
3			 **7c**	41
4			 **7d**	57
5			 **7e**	63
6			 **7f**	78
7	 **5b**	68		
8	 **5c**	57		
9	 **5d**	62		

Bn = nenzyl

Although the configuration of the products **(7)** was not examined, we believed that the stereochemistry of the substitution may be analogous to our earlier reported reaction of alkenyl(phenyl)iodonium salts with benzotriazole which went with retention of configuration, which was confirmed by a single-crystal X-ray.[5]

In conclusion, in this paper we report, for the first time, the preparation of α-acyl-β-aminoalkenylphenyl)iodonium salts from β-amino substituted α,β-unsaturated ketones with [hydroxy(tosyloxy)iodo]benzene. These new alkenyliodonium salts upon reaction with nucleophiles offer a convenient route for the synthesis of a potentially useful class of intermediates which are difficult to obtain by other synthetic methods.

Experimental

Melting points were measured on a X_4-Data microscope melting point apparatus and are uncorrected. Microanalyses were obtained using a Carlo-Erba 1106. IR spectra were recorded with a Perkin Elmer 683 spectrometer. ^{1}H NMR spectra were obtained at 400MHz (AVANCE DMX400) for solutions in $CDCl_3$ with TMS as internal standard. Mass spectra were obtained by electron impact at 70eV (HP5989B).

Preparation of alkenyl(phenyl)iodonium salts **5a–d**: General method: PhI(OH)OTs (0.74g, 2 mmol) was added to a solution of methyl 3-benzylaminocrotonone (0.378 g, 2 mmol) in CH_2Cl_2(15 ml) and the suspension was stirred for 45min under 0°C. The resulting solution was concentrated under reduced pressure at room temperature to half of its volume and the iodonium salt, E-3-phenyliodonyl-4-benzylamino-3-penten-2-one tosylate **(5a)** was precipitated upon the addition of diethyl ether, 0.575 g, 51%. m.p. 182–184°C. IR (KBr)/ cm^{-1}: 3200–3100, 1665, 1280, 1180; ^{1}H NMR($CDCl_3$): δ 7.12–8.20 (m,14H), 4.04 (2H, d, *J*=6Hz), 3.36 (s, 3H), 2.51 (s, 3H), 2.30 (s, 3H); MS: 314(0.37), 204(3.38), 172(49.42), 155(4.26), 127(2.23), 106(100), 91(72.14), 77(27.18), 43(53.64); Anal. Calcd for $C_{25}H_{26}NO_4IS$: C, 53.29; H, 4.65; N, 2.49. Found: C, 53.56; H, 4.38; N, 2.75.

E-2-phenyliodonyl-3-benzylamino-1-phenylbut-2-en-1-one tosylate **5b**: m.p. 199–202°C. IR (KBr)/cm^{-1}: 3320–3210, 1610, 1320, 1140; ^{1}H NMR($CDCl_3$): δ 7.02–7.65 (m,19H), 4.60 (2H, d, *J*=6Hz), 2.29 (s, 3H), 2.03 (s, 3H); MS: 376(0.47), 204(1.03), 172(2.13), 155(1.62), 127(2.40), 105(38.60), 106(37.06), 91(100), 77(33.59); Anal. Calcd for $C_{30}H_{28}NO_4IS$: C, 57.60; H, 4.51; N, 2.24. Found: C, 57.98; H, 4.26; N, 2.60.

E-3-phenyliodonyl-4-methylamino-3-penten-2-one tosylate **5c**: m.p. 210–212°C. IR (KBr)/ cm^{-1}: 3320–3190, 1670, 1220, 1120; ^{1}H NMR($CDCl_3$): δ 7.13–7.90 (m, 9H), 3.47 (3H, d, *J*=6Hz), 3.20 (s, 3H), 2.45 (s, 3H), 2.23 (s, 3H); MS: 300(0.97), 204(3.66), 172(37.89), 155(5.88), 139(13.76), 127(1.52), 91(83.20), 77(18.25), 43(100); Anal. Calcd for $C_{19}H_{22}NO_4IS$: C, 46.83; H, 4.55; N, 2.87. Found: C, 47.09; H, 4.98; N, 3.16.

E-2-phenyliodonyl-3-methylamino-1-phenylbut-2- en-1-one tosylate **5d**: m.p. 225–230°C. IR (KBr)/cm^{-1}: 3320–3170, 1635, 1230, 1150; ^{1}H NMR($CDCl_3$): δ 6.98–7.70 (m,14H), 4.12 (3H, d, *J*=6Hz), 2.38 (s, 3H), 2.27 (s, 3H); MS: 316(6.98), 300(1.16), 204(1.44), 172(39.88), 155(6.52), 139(11.86), 127(1.08), 105(100), 91(79.56), 77(62.36); Anal. Calcd for $C_{24}H_{24}NO_4IS$: C, 52.47; H, 4.40; N, 2.55. Found: C, 52.81; H, 4.78; N, 2.86.

Preparation of substituted α,β-unsaturated ketones **7a–f**: *E-3-(diethylthiocarbamoylsulfanyl)-4-benzylamino-3-penten-2-one* **(7a)**: Iodonium salt **5a** (0.563g, 1 mmol) was added to a solution of Et_2NCS_2Na (0.225g, 1 mmol) and CuI (0.1 g) in DMF(20 ml) and the mixture was stirred for 1 h at room temperature. Saturated brine (30 ml) was added to the reaction mixture and the solution was extracted with CH_2Cl_2 (2×10ml). The organic extracts were dried, concentrated and chromatographed on silica column to afford, after iodobenzene, **7a** as oil, 0.309g, 92%; IR (neat)/cm^{-1}: 3240–3120, 1716, 1628, 1533, 1454, 1377, 1277, 1130, 1077, 695; ^{1}H NMR($CDCl_3$): δ 7.08–7.36 (m,5H), 5.48 (br, 1H), 4.89 (d, 2H, *J*=5Hz), 3.71 (q, 4H, *J*=7.2Hz), 2.35 (s,3H), 1.88 (s,3H), 1.09 (t, 6H, *J*=7.2Hz); MS: 336(M$^+$,1.95), 245(6.64), 116(5.36), 106(23.65), 91(100), 43(58.61); Anal. Calcd for $C_{17}H_{24}N_2OS_2$: C, 60.68; H, 7.19; N, 8.32; S, 19.06. Found; C, 61.05; H, 7.57; N, 7.66; S, 18.77.

E-3-(diethoxythiophosphorylsulfanyl)-4-benzylamino-3-penten-2-one **(7b)**: Oil; IR (neat)/cm^{-1}: 3340–3215, 1705, 1270, 1190; ^{1}H NMR($CDCl_3$): δ 6.90–7.40 (m,5H), 4.45 (d, 2H, *J*=6Hz), 5.80 (br, 1H), 4.05 (q, 4H, *J*=5Hz), 2.25 (s, 3H), 2.16 (s, 3H), 1.25 (t, 6H, *J*=5Hz); MS: 373(M$^+$, 3.13), 105(13.76), 91(100), 43(82.71); Anal. Calcd for $C_{16}H_{24}NO_3PS_2$: C, 51.46; H, 6.48; N, 3.75; S, 17.17. Found; C, 51.08; H, 5.89; N, 4.13; S, 16.79.

E-3-nitro-4-benzylamino-3-penten-2-one **(7c)**: m.p. 200°C(dec.); IR(KBr)/cm^{-1}: 3320–3200, 1685cm^{-1}, 1530, 1340, 1270, 1180; ^{1}H NMR($CDCl_3$): δ 11.40 (br, 1H), 7.30–8.10 (m, 5H), 4.53 (d, 2H, *J*=6Hz), 2.93 (s, 3H), 2.42 (s, 3H); MS: 234(M$^+$, 1.56), 142(1.62), 105(100), 91(2.09), 77(38.59), 43(22.48); Anal. Calcd for $C_{12}H_{14}N_2O_3$: C, 61.53; H,6.02; N,11.96. Found; C, 61.88; H, 5.73; N, 12.36.

E-3-bromo-4-benzylamino-3-penten-2-one **(7d)**: m.p. 130–132°C; IR(KBr)/cm^{-1}: 3400–3300, 1780, 1300, 1175; ^{1}H NMR($CDCl_3$): δ 7.21–7.68 (m,5H), 5.12 (br, 1H), 4.45 (d, 2H, *J*=6Hz), 2.50 (s, 3H), 2.12 (s,3H); MS: 269(M$^+$,13.21), 267(M$^+$,13.50), 254(0.71), 252(0.73), 91(100), 43(37.82); Anal. Calcd for $C_{12}H_{14}BrNO$: C, 53.75; H, 5.26; N, 5.22. Found; C, 54.31; H, 5.63; N, 5.57.

Z-3-cyano-4-benzylamino-3-penten-2-one **(7e)**: m.p. 195°C(dec.); IR(KBr)/cm^{-1}: 3340–3280, 2200, 1690; ^{1}H NMR($CDCl_3$): δ 8.28 (br, 1H), 7.10–7.72 (m, 5H), 4.56 (d, 2H, *J*=6Hz), 2.46 (s, 3H), 1.84 (s, 3H); MS: 214(M$^+$,20.80), 199(17.71), 105(100), 91(83.38), 43(62.16); Anal. Calcd for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.59; N, 13.07. Found; C, 72.49; H, 6.93; N, 12.85.

E-3-morpholino-4-benzylamino-3-penten-2-one **(7f)**: m.p. 156–160°C; IR(KBr)/cm^{-1}: 3300–3200, 1640, 1130; ^{1}H NMR($CDCl_3$): δ 7.10–7.63 (m,5H), 4.45 (d, 2H, *J*=6Hz), 3.01–3.60 (m, 8H), 2.42 (br, 1H), 2.20 (s,3H), 1.98 (s, 3H); MS: 274(M$^+$,18.93), 259(23.18), 105(43.68), 91(100), 43(37.26); Anal. Calcd for $C_{16}H_{22}N_2O_2$: C, 70.04; H, 8.08; N, 10.21. Found; C, 70.40; H, 7.83; N, 10.59.

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