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An exploration of the catalytic Sakurai reaction in the moisture stable ionic liquids [bmim]PF_6 and [bmim]BF_4

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Abstract

Several α,β-unsaturated ketones underwent the Sakurai reaction with allyltrimethylsilane in the presence of $InCl_3$ using [bmim]PF_6 or [bmim]BF_4 as the solvent. $InCl_3$ was a more effective catalyst in either of these two ionic liquids than in the normal solvent of choice, CH_2Cl_2. However, the choice of ionic liquid had little influence on yields of the δ,ε-unsaturated ketone product. We also investigated alternative classical solvents to CH_2Cl_2, i.e. THF and DMF and it was found that the Sakurai reaction did not occur in these under the general conditions used.

Keywords: Sakurai; Ionic liquid; Catalyst; Allyl coupling; $InCl_3$

The Sakurai reaction, i.e. the Lewis acid mediated addition of allyltrimethylsilane **1** with α,β-unsaturated ketones **2** to form δ,ε-unsaturated ketones **3**, Scheme 1, is considered to be one of the most efficient means of carbon–carbon bond formation both inter- and intramolecularly. It is of tremendous utility in the synthesis of natural products. For example, cyclisation of a trienone using ethylaluminium dichloride directly afforded nookatone, which is a flavour component of grapefruit. Treatment of the same trienone with fluoride ion gave a fused cyclooctane, an intermediate for neolemnanyl acetate, a natural product from the pacific soft coral lemnalia africana [1–18]. The range of Lewis acids that may be employed is extensive, however, recently the Sakurai reaction catalysed by the Lewis acid $InCl_3$ has been achieved with high reactivity and selectivity [19–23].

Over the last 5 years, there has been an interest in allylation reactions performed in ionic liquids. For example, the allylation of aldehydes to produce homoallylic alcohols has been carried out in both [bmim]PF_6 and [bmim]BF_4 using tetraallylstannane by Gordon and McClusky [24]. The palladium catalysed allylic allylation of 3-acetoxy-1,3-diphenylprop-1-ene using $Pd(OAc)_2/PPh_3$ in the presence of K_2CO_3 in the ionic liquid [bmim]BF_4 has also been achieved by Chen et al. [25].

We felt that by combining of the advantages of $InCl_3$, as applied to the extremely useful Sakurai chemical reaction, i.e. its easy handling, high reactivity, high selectivity and low toxicity, to the now well-established advantages of ionic liquids, i.e. their highly polar but non-co-ordinating property, their tuneable miscibility/immiscibility with a wide range of classical organic solvents and water, and their non-volatile nature [26,27], that we would produce a reaction system that would be very attractive to chemists. To this end, we sought to demonstrate through the use of some simple α,β-unsaturated ketones and allyltrimethylsilane that the Sakurai reaction could be performed in the presence of $InCl_3$ using [bmim]PF_6 or [bmim]BF_4 as the solvent.

A typical example of the experimental procedure is given for 6-hepten-2-one **5**: An oven-dried 50 ml round-bottom flask with a magnetic stirrer was charged with Indium chloride (0.22 g, 1.00 mmol) in 5 ml [bmim]PF_6. The flask was purged with argon for 10 min and then methyl vinyl ketone **4** (0.35 g, 5.00 mmol), chlorotrimethylsilane (2.17 g, 20.00 mmol) and allyltrimethylsilane (0.63 g, 5.00 mmol) were added. The mixture was stirred at room temperature for 3 h under argon. The reaction mixture was then extracted with diethyl ether (5 ml × 10 ml). The diethyl ether fractions were combined together, dried (anhydrous $MgSO_4$) and the solvent removed under vacuum to afford the crude

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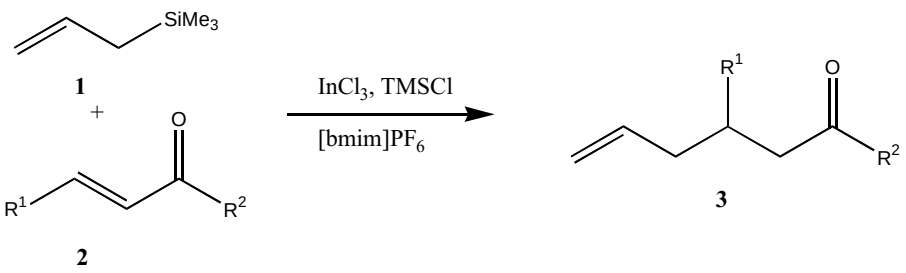
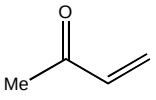
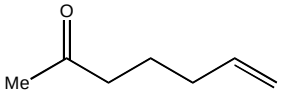
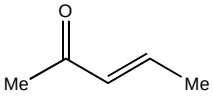
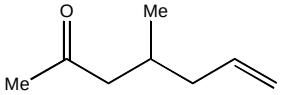
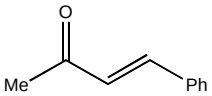
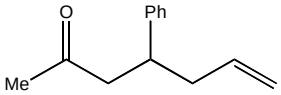
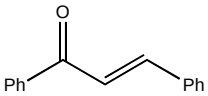
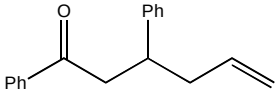
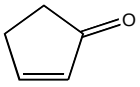
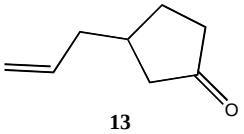
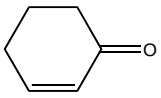
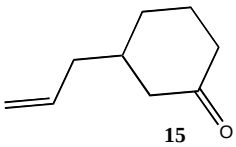
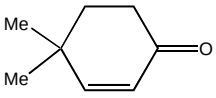
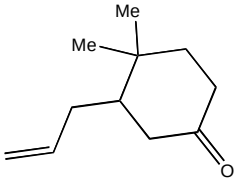
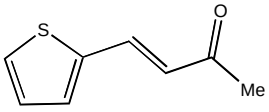
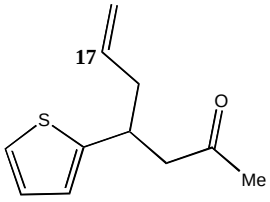
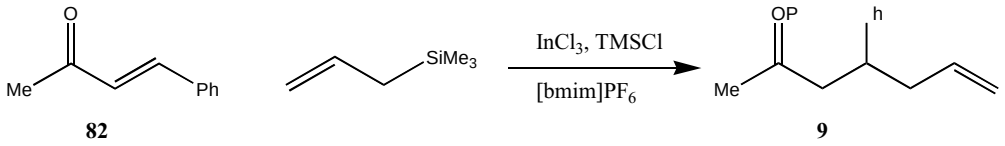


Scheme 1.

Table 1
Results of the Sakurai reaction in $[bmim]PF_6$ and $[bmim]BF_4$.

Entry	Substrate	Product	Yield (%)		
			[19]	$[bmim]PF_6$	$[bmim]BF_4$
1	 **4**	 **5**	62	54	56
2	 **6**	 **7**	77	71	68
3	 **8**	 **9**	81	85	82
4	 **10**	 **11**	89	82	83
5	 **12**	 **13**	64	68	74
6	 **14**	 **15**	73	75	76
7	 **16**		84	77	77
8	 **18**	 **17** **19**	89	91	88



82 **9**

Scheme 2.

product. This was subsequently purified by flash column chromatography on silica gel (hexane:ethyl acetate = 15:1) to give **5** (0.31 g, 54%). All compounds produced in the reactions had satisfactory analytical data.[1]

It was found that ionic liquid could enhance the yield in some cases (Table 1, entries 3, 5, 6 and 8). The reaction of methyl vinyl ketone with allyltrimethylsilane was more inefficient in an ionic liquid than in CH_2Cl_2, the yield decreased by 8% (Table 1, entry 1). For the reaction of 4-hexen-3-one with allyltrimethylsilane and the reaction of *trans*-chalcone with allyltrimethylsilane, the yields of both were lower than in CH_2Cl_2, it might be that the steric hindrance was increased in ionic liquid more than in CH_2Cl_2 (Table 1, entries 2 and 4). It was also found that the cyclic α,β-enone with substituents in the *ortho* position could decrease the yield by 7% (Table 1, entry 7).

It is worth noting that α,β-unsaturated esters such as methyl acrylate and methyl methacrylate did not undergo the Sakurai reaction in ionic liquid, which is equivalent to their reaction in CH_2Cl_2.

It was found that little difference occurred when the Sakurai reaction was carried out in different types of ionic liquids [bmim]PF_6 and [bmim]BF_4. This apparently shows that the different anions of ionic liquids used here have little influence on yields, and indeed on the mechanistic pathway of the reaction.

Other factors could influence yields were also investigated. The reaction of 4-phenyl-3-buten-2-one **8** with allyltrimethylsilane **1** to afford 4-phenyl-6-hepten-2-one **9**, Scheme 2, was carried out in the ionic liquid [bmim]PF_6 as a model for the investigation. It was found that Sakurai reaction could not happen in neither DMF nor in THF (Table 2, entries 1 and 2) and CH_2Cl_2 was the most suitable solvent amongst the classical organic solvents. But catalyst $InCl_3$ was more effective in ionic liquid than in CH_2Cl_2, product **9** was obtained in 85% yield (Table 2, entry 4) with 0.20 eq. of $InCl_3$ in ionic liquid other than in 81% yield (Table 2, entry 3) with 0.5 eq. of $InCl_3$ in CH_2Cl_2.

It was noticed that the reaction could happen without the presence of additive TMSCl, but the yield was lower even if more $InCl_3$ was added (Table 2, entries 5 and 6). Surprisingly, the additive TMSCl did not effect the yields for $TiCl_4$ and $AlCl_3$ (Table 2, entries 8 and 10).

Table 2
Results from variation of solvent, additive (TMSCl) and catalyst.

Entry	Solvent	Catalyst (eq.)	Additive (eq.)	Yield (%)
1	THF	$InCl_3$ (1.0)	TMSCl (4.0)	0
2	DMF	$InCl_3$ (0.5)	TMSCl (4.0)	0
3	CH_2Cl_2	$InCl_3$ (0.2)	TMSCl (4.0)	81
4	[bmim]PF_6	$InCl_3$ (0.5)	TMSCl (4.0)	85
5	[bmim]PF_6	$InCl_3$ (1.0)		71
6	[bmim]PF_6	$InCl_3$ (1.0)		59
7	CH_2Cl_2	$TiCl_4$ (1.0)		78
8	CH_2Cl_2	$TiCl_4$ (1.0)	TMSCl (4.0)	78
9	[bmim]PF_6	$AlCl_4$ (1.0)		0
10	[bmim]PF_6	$AlCl_4$ (1.0)	TMSCl (4.0)	0

[1] 6-Hepten-2-one **5**: ^{1}H NMR (400 MHz) ($CDCl_3$): δ 5.65–5.75 (ddt, J = 17.2 Hz, J = 10.0 Hz, J = 7.2 Hz, CH, 1H), 4.90–4.97(dd, J = 16.0 Hz,J = 9.2 Hz, CH_2, 2H), 2.40 (t, J = 7.50, CH_2, 2H), 2.10 (s, CH_3, 3H), 2.01(q, J = 7.5, CH_2, 2H), 1.64 (quint, J = 7.6 CH_2, 2H). ^{13}C NMR (100 MHz) ($CDCl_3$): δ 207.0, 136.0, 113.3, 40.9, 31.1, 28.4, 21.0 ppm. 5-Methyl-7-octen-3-one **7**: ^{1}H NMR (400 MHz) ($CDCl_3$): δ 5.73–5.84 (m, CH, 1H), 5.04–5.10 (dd, J = 16.4 Hz, J = 10.0 Hz, CH_2, 2H), 2.41–2.50 (m, CH_2CH, 3H), 2.10–2.27 (m, CH_2, 2H), 2.00–2.09 (m, CH_2, 2H), 1.10 (t, J = 6.4 Hz, CH_3, 3H), 0.95 (d, J = 6.4 Hz, CH_3, 3H). ^{13}C NMR (100 MHz) ($CDCl_3$): δ 211.9, 137.1, 116.8, 49.3, 41.6, 36.9, 29.3, 20.2, 8.2 ppm. 4-Phenyl-6-hepten-2-one **9**: ^{1}H NMR (400 MHz) ($CDCl_3$): δ 7.18–7.32 (m, C_6H_5–, 5H), 5.60–5.70 (ddt, J = 16.0 Hz, J = 10.0 Hz, J = 7.2 Hz, CH, 1H), 4.95–5.02 (dd, J = 17.8 Hz, J = 10.5 Hz, CH_2, 2H), 3.28 (quint, J = 7.2 Hz, CH, 1H), 2.75 (m, CH_2, 2H), 2.35 (m, CH_2, 2H), 2.00 (s, CH_3, 3H). ^{13}C NMR (100 MHz) ($CDCl_3$): δ 208.1, 144.5, 136.6, 129.2, 127.6, 126.9, 117.2, 49.9, 41.5, 41.2, 31.1 ppm. 1,3-Diphenyl-1-oxo-5-hexene **11**: ^{1}H NMR (400 MHz) ($CDCl_3$): δ 7.90(d, J = 7.2 Hz, 2H), 7.50 (t, J = 7.6 Hz, 1H), 7.40 (t, J = 7.6 Hz, 2H), 7.20–7.30(m, 4H), 7.10 (t, J = 7.6 Hz, 1H), 5.60–5.70 (ddt, J = 17.2 Hz, J = 10.0 Hz, J = 7.20 Hz, CH, 1H), 4.97–4.90 (m, CH_2, 2H), 3.40 (quint, J = 7.2 Hz, CH, 1H), 3.30 (d, J = 6.8 Hz, CH_2, 2H), 2.40 (m, CH_2, 2H). ^{13}C NMR (100 MHz) ($CDCl_3$): δ 199.3, 144.8, 137.6, 136.7, 133.4, 128.9, 128.8, 128.4, 128.0, 126.8, 117.2, 44.9, 41.1, 41.2 ppm. 3-Allyl cyclopentanone **13**: ^{1}H NMR (400 MHz) ($CDCl_3$): δ 5.78–5.88 (ddt, J = 17.2 Hz, J = 10.0 Hz, J = 7.2 Hz, CH, 1H), 5.05–5.12 (dd, J = 16.0 Hz, J = 9.2 Hz, CH_2, 2H), 2.15–2.45 (m, $CH_2CH_2CH_2CH$, 7H), 1.85–1.95 (dd, J = 9.2 Hz, 1H), 1.55–1.65 (m, 1H). ^{13}C NMR (100 MHz) ($CDCl_3$): δ 220.0, 136.7, 116.9, 45.2, 40.1, 38.9, 37.2, 29.5 ppm. 3-Allylcyclohexanone **15**: ^{1}H NMR (400 MHz) ($CDCl_3$): δ 5.78 (m, CH, 1H), 5.05–5.10 (m, CH_2, 2H), 2.38–2.50 (m, CH_2, 2H), 2.25–2.32 (m, CH, 1H), 2.00–2.19 (m, $2CH_2$, 4H), 1.82–2.00 (m, CH_2, 2H), 1.60–1.73 (m, CH, 1H), 1.30–1.45 (m, CH, 1H). ^{13}C NMR (100 MHz) ($CDCl_3$): δ 212.4, 136.2, 117.4, 48.3, 41.9, 41.4, 39.3, 31.4, 25.7 ppm. 3-Allyl-4,4-dimethylcyclohexenanone **17**: ^{1}H NMR (400 MHz) ($CDCl_3$): δ 5.70–5.60 (m, CH, 1H), 5.02–4.95 (m, CH_2, 2H), 2.40–2.22 (m, $2CH_2$, 4H), 2.02 (dd, J = 16.4 Hz, J = 10.1 Hz, CH, 1H), 1.75–1.52 (m, $2CH_2$, 4H), 1.05 (s, CH_3, 3H), 1.00 (s, CH_3, 3H). ^{13}C NMR (100 MHz) ($CDCl_3$): δ 212.4, 137.1, 117.0, 46.7, 43.0, 40.7, 38.7, 35.8, 33.1, 29.1, 19.9 ppm. 4-(2-Thienyl)-6-hepten-2-one **19**: ^{1}H NMR (400 MHz) ($CDCl_3$): δ 7.13 (dd, J = 6.0 Hz, J = 1.2 Hz, CH, 1H), 6.91 (dd, J = 6.0 Hz, J = 3.6 Hz, CH, 1H), 6.81 (d, J = 3.6 Hz, CH, 1H), 5.65–5.75 (ddt, J = 17.2 Hz, J = 10.0 Hz, J = 7.0 Hz, CH, 1H), 5.07–5.00 (m, CH_2, 2H), 3.51 (quint, J = 7.2 Hz, CH, 1H), 2.80–2.78 (dd, J = 1.2 Hz, J = 2.4 Hz, CH_2, 2H), 2.45–2.40 (m, CH_2, 2H), 2.10 (s, CH_3, 3H). ^{13}C NMR (100 MHz) ($CDCl_3$): δ 207.5, 148.3, 136.0, 127.0, 124.3, 123.5, 117.7, 50.6, 42.0, 36.3, 31.1 ppm.

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