SmI_3 mediated reginospecific Michael addition of ω-bromo-acetophenone to α,β-unsaturated alkynones

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SmI_3 mediated regiospecific Michael addition of ω-bromo-acetophenone to α,β-unsaturated alkynones was investigated. A new method for the synthesis of 1,5-dicarbonyl compounds was put forward. This reaction suffers from the influence of solvents seriously.

Keywords: SmI_3, Michael addition, acetophenone, alkynones

Michael addition is one of the classical organic reactions, which have played a great role in organic synthesis.[1] The wide utility of SmI_2 as reducing and coupling agent to effect carbon–carbon bond formation as well as functional group reduction has been explored.[2] However, compared with the application of samarium(II) species in organic synthesis, there are only limited reports on the application of samarium(III) species in organic synthesis.[3] Recently, the reports of using samarium(III) in organic chemistry are rapidly increased. For example, promoted by SmI_3 α-chloroketones can react with aldehyde to give α,β-unsaturated ketones;[4] Sasai reported that 1-chloro-2-heptanone is able to react with benzaldehyde to form α-chloro-β-hydroxy ketones at catalysis of Sm(HMDS);[5] at the aid of $Sm(OTf)_3$ and s-BuLi methyliodide has been added to carbonyl group of acetophenone,[6] Our group have also reported several methods on the application of samarium(III) species in organic synthesis.[7]

Here we wish to report the addition of ω-bromo-acetophenone to α,β-unsaturated alkynones mediated by SmI_3 to afford Michael addition products (Scheme 1).

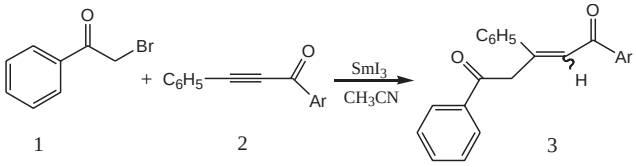
According to previous reports, in the case of Grignard reagents, both 1,2- and 1,4-additions were possible,[8, 9] the orientation depended on some effects such as the bulk of the substrates and reagents. Although many researches have been carried out on the subject by different authors no absolute conclusion can be reached.[9] It is interesting that the addition of ω-bromo-acetophenone to α,β-unsaturated alkynones mediated by SmI_3 only afforded Michael addition products in good yields under mild conditions. We did not obtain 1,2-nucleophilic addition production in our experiments.

In the course of our work, we found that the reaction is influenced by solvent. When tetrahydrofuran (THF) was used as the solvent, the product **3**' was obtained. (Scheme 2).

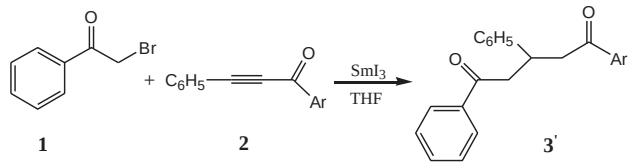
However, in *N*, *N*-dimethyl-formamide (DMF) no reaction occurs. The results are summarised in Table 1.

We suggest that, a samarium enolate is a reaction intermediate.[10] So we think that the possible mechanism of the reaction in CH_3CN should be following (Scheme 3). Because of chelation of Sm^{3+} with DMF in this solvent, a samarium enolate could not be formed. We do not know the mechanism of the reaction in THF.

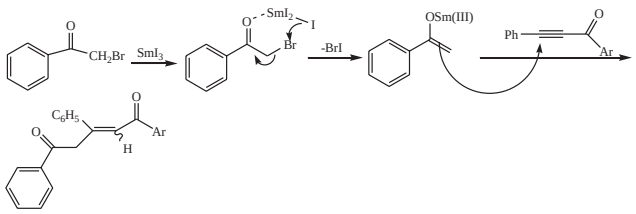
In conclusion, the addition of ω-bromo-acetophenone to α,β-unsaturated alkynones mediated by SmI_3 was explored. It is a regiospecific Michael addition and suffers from the influence of solvents seriously. The mild reaction conditions,



Scheme 1



Scheme 2



Scheme 3

Table 1 The results of the Michael addition reaction

Entry	Ar	Solvent	t/h[a]	Products	Yields/%[b]
1	C_6H_5	CH_3CN	4	**3a**	75
2	*p*-$CH_3OC_6H_4$	CH_3CN	6	**3b**	67
3	*p*-$CH_3C_6H_4$	CH_3CN	6	**3c**	75
4	*p*-ClC_6H_4	CH_3CN	6	**3d**	88[c], 86[d]
5	2,4-$Cl_2C_6H_4$	CH_3CN	6	**3e**	65
6	2, 6-$Cl_2C_6H_3$	CH_3CN	6	**3f**	61
7	2-furanyl	CH_3CN	6	**3g**	70
8	$CH_3CH_2CH_2$	THF	4	**3'h**	75[c], 70[d]
9	2-furanyl	THF	4	**3'i**	71
10	C_6H_5	THF	4	**3'j**	82
11	C_6H_5	DMF	24	**3k**	0[c,d]
12	*p*-ClC_6H_4	DMF	24	**3l**	0[c,d]

[a]Reaction time; [b]Isolated yields; [c]Reaction temperature 25 °C; [d]Reaction temperature 60 °C.

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readily available starting materials and simple operations make this method advantageous. A new method for the synthesis of 1,5-dicarbonyl compounds was presented.

Experimental

Melting points were uncorrected. IR spectra were recorded on a Bruker Vector-22 infrared spectrometer. ^{1}H NMR spectra were obtained with a Bruker AC-400 MHz spectrometer in $CDCl_3$ or DMSO-d_6 solution using TMS as the internal standard. Mass spectra were recorded on an HP 5989B MS spectrometer. Elemental analyses were performed on a Carlo Erba 1106 instrument. The reactions were performed in a Schlenk-type glass apparatus under a nitrogen atmosphere.

General procedure for the nucleophilic addition reaction of allylsamarium bromide to α,β-unsaturated alkynones: ω-Bromoacetophenone (1 mmol) and α,β-unsaturated alkynone (1 mmol) were added sequentially to the SmI_3 (1 mmol) in CH_3CN or THF. The mixture was stirred at room temperature until the reaction was complete, as shown by TLC. Then 2 ml 0.1 N HCl and 5 ml water were added. The reaction mixture was extracted with diethyl ether (3 × 10 ml), the diethyl ether solution was washed with saturated $Na_2S_2O_3$ (10 ml), then washed with water (10 ml) and dried over anhydrous Na_2SO_4. The solvent was removed by evaporation under reduced pressure. The crude product was purified by preparative TLC on silica gel (cyclohexane-ethyl acetate (10 : 1) as eluent).

Compound **3a**. m.p. 202–204 °C. δ_H(ppm) 8.13–8.11 (d, 2H, *J* = 8 Hz), 7.97–7.95 (d, 4H, *J* = 8 Hz), 7.60–7.43 (m, 9H), 4.80–4.77 (t, 1H), 3.77–3.76 (d, 2H, *J* = 4 Hz). ν_{max}(KBr)/cm^{-1}: 3422, 3065, 2918, 2985, 1676, 1596, 1447, 1220, 687. MS: *m/z*, 326 (M$^+$, 0.13), 249 (13.76), 105 (100), 77 (58.76), 51 (14.05), Anal. calcd. for $C_{23}H_{18}O_2$: C 84.64, H 5.55%, Found: C 84.58, H 5.42%.

Compound **3b**. m.p. 204–206 °C. δ_H(ppm) 8.22–8.20 (d, 2H, *J* = 8 Hz), 8.03–8.01 (d, 4H, *J* = 8 Hz), 7.68–7.40 (m, 8H), 4.26–4.23 (t, 1H), 3.78–3.77 (d, 2H, *J* = 4 Hz), 3.53 (s, 3H). ν_{max}(KBr)/cm^{-1}: 3424, 3067, 2915, 2982 1663, 1596, 1578, 1447, 1330, 1220, 1039, 715. MS: *m/z*, 356 (M$^+$, 0.10), 355 (20.00), 338 (24.00), 249 (10.25), 105 (100), 77 (62.73), 51 (15.56). Anal. calcd. for $C_{24}H_{20}O_3$: C 80.87, H 5.65%, Found: C 80.81, H 5.57%.

Compound **3c**. m.p. 194–196 °C. δ_H(ppm) 8.11–8.09 (d, 2H, *J* = 8 Hz), 8.02–8.00 (d, 4H, *J* = 8 Hz), 7.66–7.37 (m, 8H), 4.27–4.24 (t, 1H), 3.77–3.76 (d, 2H, *J* = 4 Hz), 2.35 (s, 3H). ν_{max}(KBr)/cm^{-1}: 3415, 2912, 2980, 1664, 1637, 1617, 1596, 1447, 1330, 1220, 715. MS: *m/z*, 340 (M$^+$, 0.20), 249 (9.16), 105 (100), 77 (63.91), 51 (16.33). Anal. calcd. for $C_{24}H_{20}O_2$: C 84.67, H 5.92%, Found: C 84.63, H 5.88%.

Compound **3d**. m.p. 140–141 °C. δ_H(ppm) 8.33–8.31 (d, 2H, *J* = 8 Hz), 8.12–8.10 (d, 4H, *J* = 8 Hz), 7.77–7.51 (m, 8H), 4.25–4.23 (t, 1H), 3.76–3.75 (d, 2H, *J* = 4 Hz). ν_{max}(KBr)/cm^{-1}: 3414, 3066, 2980, 2914, 1663, 1637, 1618, 1597, 1448, 1330, 1220, 1015, 715. MS: *m/z*, 360 (M$^+$, 0.12), 338 (38.00), 355 (24.60), 249 (12.60), 105 (100), 77 (61.87), 51 (14.56). Anal. calcd. for $C_{23}H_{17}ClO_2$: C 76.56, H 4.74, Cl 9.82%, Found: C 76.49, H 4.66, Cl 9.87%.

Compound **3e**. m.p. 206–208 °C. δ_H(ppm) 8.23–8.21 (d, 2H, *J* = 8 Hz), 8.11–8.09 (d, 4H, *J* = 8 Hz), 7.85–7.62 (m, 7H), 4.28–4.25 (t, 1H), 3.79–3.78 (d, 2H, *J* = 4 Hz). ν_{max}(KBr)/cm^{-1}: 3449, 3064, 1667, 1596, 1448, 1330, 1220, 1018, 712. MS: *m/z*, 395 (M$^+$, 0.65), 360 (1.66), 355 (24.00), 351 (28.38), 249 (10.47), 105 (100), 77 (70.72), 51 (14.56). Anal. calcd. for $C_{23}H_{16}Cl_2O_2$: C 69.88, H 4.08, Cl 17.94%, Found: C 69.81, H 4.02, Cl 17.77%.

Compound **3f**. m.p. 174–176 °C. δ_H(ppm) 8.22–8.20 (d, 2H, *J* = 8 Hz), 8.10–8.08 (d, 4H, *J* = 8 Hz), 7.86–7.60 (m, 7H), 4.28–4.25 (t, 1H), 3.78–3.77 (d, 2H, *J* = 4 Hz). ν_{max}(KBr)/cm^{-1}: 3447, 3066, 1667, 1595, 1446, 1331, 1221, 1018, 712. MS: *m/z*, 395 (M$^+$, 0.88), 360 (1.87), 355 (18.00), 351 (24.22), 249 (13.55), 105 (100), 77 (76.73), 51 (19.52). Anal. calcd. for $C_{23}H_{16}Cl_2O_2$: C 69.88, H 4.08, Cl 17.94%, Found: C 69.81, H 4.02, Cl 17.77%.

Compound **3g**. m.p. 168–170 °C. δ_H(ppm) 8.11–8.09 (d, 2H, *J* = 8 Hz), 7.95–7.93 (d, 4H, *J* = 8 Hz), 7.62–7.41 (m, 4H), 7.36–6.38 (m, 3H), 4.24–4.22 (t, 1H), 3.77–3.76 (d, 2H, *J* = 4 Hz). ν_{max}(KBr)/cm^{-1}: 3447, 3066, 2917, 1668, 1594, 1447, 1400, 1335, 1123, 1001, 755, 706. MS: *m/z*, 316 (M$^+$, 0.48), 249 (13.97), 105 (100), 77 (61.65), 57 (56.60), 43 (5.98). Anal. calcd. for $C_{21}H_{16}O_3$: C 79.33, H 5.09%, Found: C 79.26, H 5.11%.

Compound **3'h**. m.p. 132–134 °C. δ_H(ppm) 8.12–8.10 (d, 2H, *J* = 8 Hz), 7.96–7.94 (d, 4H, *J* = 8 Hz), 7.62–7.44 (m, 8H), 4.83–4.75 (m, 1H), 3.59–3.32 (dd, 4H). ν_{max}(KBr)/cm^{-1}: 2922, 1687, 1670, 758, 691. MS: *m/z*, 362 (M$^+$, 0.27), 339 (4.83), 234 (6.34), 251 (7.32), 105 (100), 77 (57.04), 51 (17.34). Anal. calcd. for $C_{23}H_{19}ClO_2$: C 76.13, H 5.27, Cl 9.77%, Found: C 76.22, H 5.22, Cl 9.70%.

Compound **3'i**. m.p. 110–112 °C. δ_H(ppm) 8.10–8.08 (d, 2H, *J* = 8 Hz), 7.95–7.93 (d, 4H, *J* = 8 Hz), 7.46–6.42 (m, 7H), 4.82–4.73 (m, 1H), 3.55–3.22 (dd, 4H). ν_{max}(KBr)/cm^{-1}: 2917, 1687, 1669, 755, 706, 691. MS: *m/z*, 318 (M$^+$, 0.20), 234 (6.45), 251 (8.19), 105 (100), 77 (57.04), 51 (17.88). Anal. calcd. for $C_{21}H_{18}O_3$: C 79.22, H 5.69%, Found: C 79.17, H 5.55%.

Compound **3'j**. m.p. 86–90 °C. δ_H(ppm) 8.13–8.11 (d, 2H, *J* = 8 Hz), 7.95–7.93 (d, 4H, *J* = 8 Hz), 7.64–7.44 (m, 9H), 4.82–4.75 (m, 1H), 3.59–3.32 (dd, 4H). ν_{max}(KBr)/cm^{-1}: 2917, 1675, 1670, 1595, 757, 709, 688. MS: *m/z*, 328 (M$^+$, 0.33), 251 (9.05), 234 (7.26), 105 (100), 77 (58.85), 51 (15.80). Anal. calcd. for $C_{23}H_{20}O_2$: C 84.12, H 6.13%, Found: C 84.20, H 6.11%.

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