

A Simple Access to Chalcones via Modified Mukaiyama Aldol Condensation Promoted by $\text{SmI}_3/\text{TMSCl}$

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Promoted by SmI_3 , acetophenones and benzaldehydes can undergo the Mukaiyama type aldol condensation in the presence of TMSCl to form chalcones in good yields.

Keywords samarium triiodide, condensation, chalcones

Chalcones and their derivatives are important intermediates in organic synthesis. They can undergo many kinds of reactions, through which a wide range of useful compounds have been prepared.¹ In addition, many chalcone derivatives display interesting pharmacological and biological activities.² Usually, the preparation of enones is achieved with NaOH , KOH or $\text{Ba}(\text{OH})_2$ in hydroalcoholic medium from benzaldehyde and ketones,³ but the use of a relatively strong base to effect dehydration and force the aldol condensation to completion is not always successful because the enones may undergo further condensation and lead to polymeric products. Furthermore, the dimerization of uncondensed aldehyde may also occur under strong alkaline conditions, particularly with the nitrobenzaldehydes. Recognized as a standard method for the preparation of cross aldol products, the Mukaiyama aldol condensation of trimethylsilylenol ether of ketones with aldehydes or ketones in the presence of TiCl_4 only gives β -hydroxy-ketones as the final products.⁴ In order to obtain α,β -unsaturated ketones, trifluoroacetic anhydride and triethylamine are needed to effect the dehydration of the reaction intermediates.⁵ Sev-

eral other methods have also been developed for the preparation of chalcones,⁶ but due to their importance, the development of novel synthetic methods remains an active research area.⁷

In the last decade the application of lanthanoid reagents in organic synthesis has been of great interest and the reports of using $\text{Sm}(\text{III})$ in organic chemistry are also rapidly increased recently. Fukuzawa reported that CeI_3 or CeCl_3/NaI could promote the aldol type reaction of α -haloketones and aldehydes to give enones.⁸ We found that the similar reaction could be efficiently promoted by SmI_3 .⁹ Unfortunately, when ketones (such as acetophenone) rather than α -haloketones were used under the same reaction conditions, no aldol condensation product could be obtained. More recently we found that promoted by SmI_3 the trimethylsilylenol ethers of cycloalkanone could undergo Mukaiyama-type aldol condensation with aldehydes to give α,α' -bis(substituted benzyldene)cycloalkanones in high yields.¹⁰ Herein we wish to report that SmI_3 mediated reaction of noncyclic ketones and benzaldehydes proceeded smoothly in the presence of TMSCl to form chalcones in good yields. The reaction was shown in Eq. (1) and the results were listed in Table 1.

The results show that this reaction provides an efficient access to chalcone derivatives. It is the first report

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Table 1 Preparation of chalcones promoted by SmI₃/TMSCl

Entry	Ar ¹	Ar ²	Yield (%) ^a
1	C ₆ H ₅	C ₆ H ₅	75
2	3-BrC ₆ H ₄	C ₆ H ₅	77
3	3-BrC ₆ H ₄	4-CH ₃ C ₆ H ₄	78
4	4-ClC ₆ H ₄	C ₆ H ₅	79
5	2-ClC ₆ H ₄	C ₆ H ₅	75
6	4-CH ₃ C ₆ H ₄	C ₆ H ₅	65
7	4-CH ₃ C ₆ H ₄	4-CH ₃ C ₆ H ₄	63
8	4-NO ₂ C ₆ H ₄	C ₆ H ₅	86
9	4-NO ₂ C ₆ H ₄	4-CH ₃ C ₆ H ₄	82
10	3-NO ₂ C ₆ H ₄	C ₆ H ₅	84
11	2-NO ₂ C ₆ H ₄	C ₆ H ₅	82

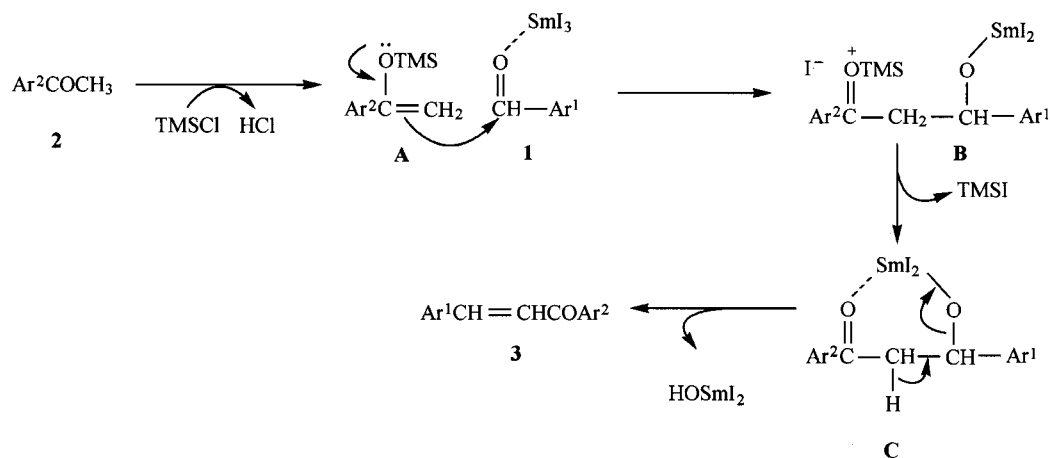
^a Isolated yields of chalcone derivatives; only the *trans* form products were obtained.

that SmI₃ can facilitate the aldol condensation of non-cyclic ketones with aldehydes to give enones. Generally, the yields of the products are to some extent affected by

the nature of the substituents on the phenyl ring of benzaldehydes (Table 1, Entries 6–9). As shown in Table 1, higher yields are obtained from the substrates with electron withdrawing groups, while the substrates with electron donating groups give chalcones in lower yields. In addition, it should be noted that in the absence of SmI₃ or TMSCl, the reaction did not occur (Table 1, Entry 1).

A plausible mechanism for the formation of chalcones is depicted in Scheme 1. This process may be initiated by the *in situ* generation of the trimethylsilylenol ether (A) of acetophenones (2). Promoted by SmI₃, A and benzaldehydes (1) undergo the Mukaiyama-type aldol condensation to give a presumed oxonium ion intermediate (B), which then extrudes TMSI (giving intermediate C) and a HOSmI₂ fragment sequentially to give chalcones (3) as the final products.

In summary, we have extended the scope of SmI₃ to a cross coupling reaction of noncyclic ketones with benzaldehydes, which provides a simple access to chalcones in satisfactory yields. Further studies on the application of SmI₃ in organic synthesis are currently underway in our laboratory.

Scheme 1

Experimental

Tetrahydrofuran was distilled from sodium-benzophenone ketyl immediately prior to use. Melting points were uncorrected. Infrared spectra were recorded on a Bruker Vector 22 spectrometer in KBr with absorption in cm⁻¹. ¹H NMR spectra were determined on a Bruker AC 80 spectrometer with CDCl₃ as solution. Chemical

shifts were expressed in ppm downfield from the internal standard tetramethylsilane. Mass spectra were recorded on an HP5989B mass spectrometer. Elemental analyses were carried out on a Carlo-Erba EA 1110 instrument.

General procedure for the preparation of chalcones

Under anhydrous conditions, a mixture of powdered

samarium (0.15 g, 1 mmol) and iodine (0.375 g, 3 mmol) in dry THF (20 mL) was stirred at room temperature until samarium disappeared. To the resulting pale yellow suspension of SmI₃ was added simultaneously acetophenone (1 mmol), aryl aldehyde (1 mmol) and TM-SCl (1 mmol). The mixture was stirred under reflux for 6 h. At completion, the reaction mixture was poured to 1 mol/L HCl (5 mL) and extracted with diethyl ether (3 × 15 mL). The combined extracts were washed subsequently with a saturated solution of Na₂S₂O₃ (15 mL) and a saturated solution of NaCl (15 mL) and dried over anhydrous Na₂SO₄. After evaporating the solvent under reduced pressure, the crude product was purified by preparative TLC on silica gel using ethyl acetate-cyclohexane (1:5) as eluent.

1,3-Diphenyl-2-propen-1-one (3a) Crystal, m.p. 53—55 °C (lit.¹¹ 55—56 °C); ¹H NMR (CDCl₃, 80 MHz) δ: 7.38—7.90 (m, ArH, = CH); IR (KBr) ν: 1660 (C=O) cm⁻¹.

3-(3-Bromophenyl)-1-phenyl-2-propen-1-one (3b) Crystal, m.p. 81—83 °C (lit.¹¹ 83—85 °C); ¹H NMR (CDCl₃, 80 MHz) δ: 7.18—7.95 (m, ArH, = CH); IR (KBr) ν: 1665 (C=O) cm⁻¹.

1-(4-Methylphenyl)-3-(3-bromophenyl)-2-propen-1-one (3c) Crystal, m.p. 107—110 °C; ¹H NMR (CDCl₃, 80 MHz) δ: 2.43 (s, 3H, CH₃), 7.26—7.94 (m, 10H, ArH, = CH); IR (KBr) ν: 1665 (C=O) cm⁻¹. MS (70 eV) *m/z* (%): 302 (M⁺ + 1, 48.8), 301 (M⁺, 36.5), 300 (M⁺ - 1, 48.8), 221 (73.9), 119 (100), 102 (56.9), 91 (87.28), 65 (49.57); Anal. calcd for C₁₆H₁₃BrO: C 50.30; H 3.69; found C 50.10, H 3.57.

3-(4-Chlorophenyl)-1-phenyl-2-propen-1-one (3d) Crystal, m.p. 110—111 °C (lit.¹¹ 112—113 °C); ¹H NMR (CDCl₃, 80 MHz) δ: 7.15—7.98 (m, ArH, = CH); IR (KBr) ν: 1665 (C=O) cm⁻¹.

3-(2-Chlorophenyl)-1-phenyl-2-propen-1-one (3e) Crystal, m.p. 48—49 °C (lit.¹¹ 49—51 °C); ¹H NMR (CDCl₃, 80 MHz) δ: 7.05—7.85 (m, ArH, = CH); IR (KBr) ν: 1665 (C=O) cm⁻¹.

3-(4-Methylphenyl)-1-phenyl-2-propen-1-one (3f) Crystal, m.p. 90—92 °C (lit.¹¹ 92—94 °C); ¹H NMR (CDCl₃, 80 MHz) δ: 2.28 (s, 3H, CH₃), 7.10—8.15 (m, 11H, ArH, = CH); IR (KBr) ν: 1658 (C=O) cm⁻¹.

1,3-Di(4-methylphenyl)-2-propen-1-one (3g)

Crystal, m.p. 93—94 °C (lit.¹¹ 94—95 °C); ¹H NMR (CDCl₃, 80 MHz) δ: 2.39 (s, 3H, CH₃), 2.44 (s, 3H, CH₃), 7.20—7.98 (m, 10H, ArH, = CH); IR (KBr) ν: 1658 (C=O) cm⁻¹.

3-(4-Nitrophenyl)-1-phenyl-2-propen-1-one (3h) Crystal, m.p. 159—160 °C (lit.¹¹ 160—161 °C); ¹H NMR (CDCl₃, 80 MHz) δ: 7.34—8.30 (m, ArH, = CH); IR (KBr) ν: 1668 (C=O) cm⁻¹.

1-(4-Methylphenyl)-3-(4-nitrophenyl)-2-propen-1-one (3i) Crystal, m.p. 168—170 °C; ¹H NMR (CDCl₃, 80 MHz) δ: 2.45 (s, 3H, CH₃), 7.32—8.29 (m, 10H, ArH, = CH); IR (KBr) ν: 1670 (C=O) cm⁻¹. MS (70 eV) *m/z* (%): 267 (M⁺, 72.07), 178 (28.08), 119 (94.10), 91 (100), 65 (61.49); Anal. calcd for C₁₆H₁₃NO₃: C 71.90, H 4.90, N 5.24; found C 71.68, H 4.71, N 5.31.

3-(3-Nitrophenyl)-1-phenyl-2-propen-1-one (3j) Crystal, m.p. 142—143 °C (lit.¹² 145—146 °C); ¹H NMR (CDCl₃, 80 MHz) δ: 7.25—8.05 (m, ArH, = CH); IR (KBr) ν: 1665 (C=O) cm⁻¹.

3-(2-Nitrophenyl)-1-phenyl-2-propen-1-one (3k) Crystal, m.p. 115—117 °C (lit.^{6b} 117—119 °C); ¹H NMR (CDCl₃, 80 MHz) δ: 7.30—8.15 (m, ArH, = CH); IR (KBr) ν: 1670 (C=O) cm⁻¹.

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