

Samarium (III) iodide promoted preparation of α,α' -bis (substituted benzylidene)cyclohexanones from benzaldehydes and cyclohexanone[†]

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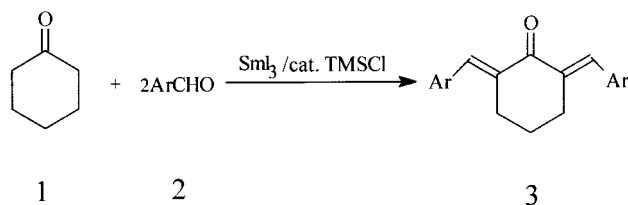
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Promoted by SmI_3 , cyclohexanone condenses with benzaldehydes in the presence of catalytic amount of SiMe_3Cl (TMSCl) to give 2,6-bis(substituted benzylidene)cyclohexanones under mild conditions in good yields.

α,α' -Bis(substituted benzylidene)cycloalkanones as useful precursors to potentially bioactive pyrimidine derivatives,¹ has attracted considerable attention in recent years. Hathaway *et al.* reported that this preparation is available by cross aldol-type reaction, but this traditional acid- or base- catalysed reaction suffers from the reverse reaction.² Metal chlorides (TiCl_4 , ZrCl_4 , or AlCl_3) are reported to prompt the self-condensation of ketones and aliphatic aldehydes rather than the cross-aldol condensation.³ Ogoshi *et al.*⁴ and Taichi Nakan *et al.*⁵ reported newer methods for the preparation of these cross-condensations. Whereas the former obtained α,α' -bis(benzylidene) cyclohexanones in 30% yields by the Rh(III)-porphyrin complex-catalysed reaction of cyclohexanone with benzaldehydes, and the latter investigated the cross-aldol condensation using $[\text{TiCp}_2\text{Ph}_2]$ as a catalyst and reported the reaction to give good yield. However, this reaction needs high temperature in a sealed ampoule. Recently, our group reported that SmI_3 is an efficient catalyst for the cross-aldol condensation of cyclopentenone with some aldehydes. But when cyclohexanone was used to react with benzaldehydes, the result disappointed us. Though they reacted under high temperature for one day, the yields were not more than 20%. More recently, our group has found that α,α' -bis(substituted benzylidene)cycloalkanones can be attained by the condensation reaction of trimethyl silyl enol ethers of cycloalkanone with aldehydes promoted by SmI_3 .⁶

In order to find a more available method for the preparation of 2,6-bis(substituted benzylidene)cyclohexanones, we studied the reaction of cyclohexanone with benzaldehydes in the presence of a catalytic amount of Me_3SiCl (TMSCl) promoted by SmI_3 . Now we would like to report our results as shown in Scheme 1. When **1** (1mmol) and **2** (2mmol) are added to an SmI_3 -THF solution in the presence of a catalytic amount of TMSCl, the condensation product **3** is formed in good yield (see Table 1).

We think that the above work may provide a useful method for the preparation of 2,6-bis(substituted benzylidene)cyclohexanones under milder conditions than those previously



Scheme 1

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

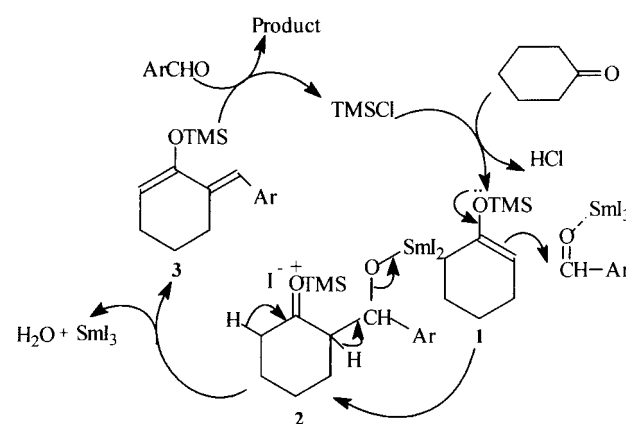
reported.³ In all cases the formation of α -mono(substituted benzylidene)cyclohexanones was not observed under the present reaction conditions.

The possible mechanism for the formation of 2,6-bisubstituted products is shown in Scheme 2. At first, prompted by SmI_3 the trimethyl silyl enol ether of cyclohexanone (**1**) is formed. Then via an ene-like path way,⁷ a α -proton maybe lost when a presumed oxonium ion intermediate (**2**) is formed. Another silyl enol ether molecule (**3**) is involved in the further reaction.

Table 1 Cross-condensation of cyclohexanone with benzaldehydes promoted by $\text{SmI}_3/\text{cat. TMSCl}$ in THF

Entry	Ar	Reaction conditions/ $^{\circ}\text{C}/\text{h}$	Yield*/%
a	C_6H_5	60, 8	85
b	$p\text{-CH}_3\text{C}_6\text{H}_4$	60, 8	80
c	$p\text{-CH}_3\text{OC}_6\text{H}_4$	60, 8	70
d	$p\text{-NO}_2\text{C}_6\text{H}_4$	60, 8	85
e	$m\text{-NO}_2\text{C}_6\text{H}_4$	60, 8	80
f	$p\text{-ClC}_6\text{H}_4$	60, 8	65
g	$2,4\text{-Cl}_2\text{C}_6\text{H}_3$	70, 10	75
h	2-furyl	70, 10	85
i	$\text{C}_6\text{H}_5\text{CH}=\text{CH}$	70, 10	75

*Isolated yields based on cyclohexanone



Scheme 2

In conclusion, $\text{SmI}_3/\text{cat. TMSCl}$ promotes a condensation reaction of cyclohexanone with some aldehydes, which has not been achieved satisfactorily by other reagents. Further studies to develop other new reactions using $\text{SmI}_3/\text{cat. TMSCl}$ are now in progress.

Experimental

Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use. Melting points were uncorrected. Infrared spectra

were recorded on a Perkin-Elmer 683 spectrometer in KBr with absorption in cm^{-1} . $^1\text{H-NMR}$ spectra were determined on a Bruker AC 80 spectrometer as CDCl_3 solutions. Chemical shifts were expressed in ppm downfield from internal standard tetramethylsilane. Mass spectra were recorded on an HP5989B Mass spectrometer. Elemental analyses were carried out on an EA 1110 instrument. SmI_2 was prepared from samarium power and iodine in dried THF.

General procedure for the synthesis of 2,6-bis(substitutedbenzylidene) cyclohexanones: Cyclohexanone (2.1 mmol), TMSCl (10 mol%) and aldehyde (4 mmol) were added to SmI_2 (1 mmol)-THF (15 ml) solution under a dinitrogen atmosphere, and stirred at a given temperature for a given time as shown in Table 1. At completion, the reaction mixture was poured on to 1N HCl (5 ml) and extracted with diethyl ether (3×15 ml). The combined extracts were washed with a saturated solution of $\text{Na}_2\text{S}_2\text{O}_3$ (15 ml) then a saturated solution of NaCl (15 ml) and dried over anhydrous Na_2SO_4 . After evaporating the solvent under reduced pressure, the crude solid products were separated. They were recrystallized from CHCl_3 and toluene.

Compound a: m.p. 115–116°C (lit.,⁶ 116–117°C). IR ν_{max} (cm^{-1}): 1670. $^1\text{H NMR}$ δ_{H} (ppm) 7.50–7.27 (m, 10 H), 7.78 (s, 2 H), 3.00–2.80 (t, 4 H), 1.91–1.34 (m, 2 H).

Compound b: m.p. 171–173°C (lit.,⁶ 172–173°C). IR ν_{max} (cm^{-1}): 1685. $^1\text{H NMR}$ δ_{H} (ppm) 7.63 (s, 2 H), 7.38–7.03 (m, 8 H), 3.00–2.78 (t, 4 H), 2.35 (s, 6 H), 2.06–1.87 (t, 2 H).

Compound c: m.p. 155–156°C (lit.,⁸ 156–157°C). IR ν_{max} (cm^{-1}): 1680. $^1\text{H NMR}$ δ_{H} (ppm) 7.60 (s, 2 H), 7.50–6.80 (m, 8 H), 3.50 (s, 6 H), 2.90–2.79 (t, 4 H), 1.87–1.35 (m, 2 H).

Compound d: m.p. 201–202°C (lit.,⁸ 200–203°C). IR ν_{max} (cm^{-1}): 1675. $^1\text{H NMR}$ δ_{H} (ppm) 8.10 (s, 2 H), 8.00–7.50 (m, 8 H), 2.90–2.79 (t, 4 H), 1.87–1.35 (m, 2 H).

Compound e: m.p. 189–192°C (lit.,⁸ 189–191°C). IR ν_{max} (cm^{-1}): 1680. $^1\text{H NMR}$ δ_{H} (ppm) 7.90 (s, 2 H), 7.80–7.50 (m, 8 H), 2.80–2.69 (t, 4 H), 1.85–1.30 (m, 2 H).

Compound f: mp 146–148°C (lit.,⁸ 145–149°C). IR ν_{max} (cm^{-1}): 1676. $^1\text{H NMR}$ δ_{H} (ppm) 7.75 (s, 2 H), 7.58–7.13 (m, 8 H), 3.00–2.78 (t, 4 H), 2.16–1.77 (t, 2 H).

Compound g: m.p. 162°C. IR ν_{max} (cm^{-1}): 1685. $^1\text{H NMR}$ δ_{H} (ppm) 7.80 (s, 2 H), 7.75–7.40 (m, 4 H), 2.90–2.69 (t, 4 H), 1.75–1.30 (m, 2 H).

Compound h: m.p. 138–139°C. IR ν_{max} (cm^{-1}): 300–2850, 1670, 1590, 1450, 1280–1120, 1010. $^1\text{H NMR}$ δ_{H} (ppm) 7.75–6.20 (m, 8 H), 3.34–2.43 (m, 6 H). m/z: 254.

Compound i: m.p. 178–180°C. (lit.,⁶ 179–180°C). IR ν_{max} (cm^{-1}): 3050, 2900, 1690, 1620–1600, 1440, 1250, 1180. $^1\text{H NMR}$ δ_{H} (ppm) 7.65 (m, 10 H), 7.35–7.02 (s, 2 H), 2.91–2.74 (t, 4 H), 1.75 (m, 2 H). m/z: 326.

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