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Samarium(III) Iodide Promoted Three-Component Coupling Reactions of Aldehydes, a-Haloketones, and Active Methylene or Methyl Compounds

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Samarium(III) Iodide Promoted Three-Component Coupling Reactions of Aldehydes, α-Haloketones, and Active Methylene or Methyl Compounds

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ABSTRACT

In the presence of samarium(III) iodide, the reaction of aldehydes, α -haloketones with malononitrile, ethylcyanoacetate or nitromethane proceeded very efficiently and furnished moderate to high yields of adducts.

Key Words: Samarium(III) iodide; Aldehydes; Alph-haloketones; Active methylene compounds; Three-component coupling reaction.

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ArCHO + PhCOCH₂Br + XCH₂Y
$$\xrightarrow{\text{SmI}_3}$$
 $\xrightarrow{\text{ArCHCH}_2\text{COPh}}$
| XCHY
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Table 1. Three-component coupling reactions promoted by SmI₃.

Entry	Ar	XCH ₂ Y	Yield (%) ^a
a	C ₆ H ₅	$CH_2(CN)_2$	75
b	p-CH ₃ C ₆ H ₄	$CH_2(CN)_2$	69
с	$p-\mathrm{ClC}_6\mathrm{H}_4$	$CH_2(CN)_2$	70
d	p-CH ₃ OC ₆ H ₄	$CH_2(CN)_2$	73
e	C_6H_5	NCCH ₂ CO ₂ Et	53
f	$p-CH_3C_6H_4$	NCCH ₂ CO ₂ Et	50
g	$p-\mathrm{ClC}_6\mathrm{H}_4$	NCCH ₂ CO ₂ Et	48
h	p-CH ₃ OC ₆ H ₄	NCCH ₂ CO ₂ Et	54
i	C_6H_5	CH_3NO_2	79
i	p-CH ₃ C ₆ H ₄	CH ₃ NO ₂	78
k	p-ClC ₆ H ₄	CH_3NO_2	79
1	p-CH ₃ OC ₆ H ₄	CH ₃ NO ₂	83

^aIsolated yield.

Herein, we wish to report our results on three-component coupling reactions of aldehydes, α -haloketone, and active methylene or methyl compounds promoted by SmI₃ in one pot to form the adducts (Sch. 1).

When aryl aldehydes (1) and α -haloketone (2) were treated with 2 equiv. SmI₃ for about 2 h at room temperature, almost all of them were consumed and the corresponding immediate products α,β -unsaturated ketones were formed, then a solution of active methylene or methyl compound (3) was added to the flask, the product 1,1-disubsituted-2-aryl-3-benzoyl-propane (4) can be obtained in moderate to fine yields. The results were summarized in Table 1.

From Table 1 we can find that the reactions of equimolar benzaldehydes, α -haloketones with malononitrile or nitromethane in the presence of two equivalent of SmI₃ gave the adducts in good yields; But when ethylcyanoacetate was used as nucleophilic reagent instead of malononitrile or nitromethane, the yields were comparatively low. However, the reactions of benzaldehydes, acetophone with active methylene

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compounds in the same conditions couldn't give the corresponding adducts. Besides, when the aliphatic aldehydes instead of the benzaldehydes, the corresponding products couldn't be obtained either.

In summary, we have found that samarium triiodide promotes the three-component coupling reactions of aldehydes, α -haloketones, and active methylene or methyl compounds (for example: malononitrile, ethylcyanoacetate, nitromethane) to form 1,1-disubstituted-2-aryl-3-benzoyl-propanes in moderate to high yields. Further studies to develop other new use of SmI₃ are now in progress.

EXPERIMENTAL

Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use. All reactions were conducted under a nitrogen atmosphere. Melting points were uncorrected. Infrared spectra were recorded on a Perkin-Elmer 683 spectrometer in KBr with absorptions in cm⁻¹. ¹H-NMR spectra were determined on a Bruker AC 80 spectrometer as CDCl₃ solutions. Chemical shifts were expressed in ppm downfield from internal standard tetramethylsilane. Mass spectra were recorded on HP5989B mass spectrometer. Elemental analyses were carried out on an EA 1110 instrument.

General Procedure for the Preparation of 1,1-Disubstituted-2-aryl-3-benzoyl-propane (4)

To a mixture of aldehyde (1 mmol) and α -haloketones (1 mmol) in anhydrous THF (3 mL) was added to a solution of SmI₃ (2 mmol, in 20 mL THF). The mixture was stirred to room temperature for 2 h, then a solution of active methylene compound (1 mmol) was added. The mixture was refluxed for 20–24 h, then water was added and the product was extracted with diethyl ether. The organic phase was collected, dried (Na₂SO₄), and evaporated to afford the crude product. The product was purified by preparative TLC on silica gel using cyclohexane and ethyl acetate (6:1) as eluent.

3-Benzoyl-1,1-dicyano-2-phenyl-propane (4a): M.p. 122–125°C, lit.,^[1] 125–126°C. ν_{max} (KBr)/cm⁻¹: 2260, 1680. δ_{H} (CDCl₃): 3.60–3.68 (2H, d, J = 7.2 Hz, CH₂), 3.85–4.18 (1H, m, CH), 4.60–4.66 (1H, d, J = 4.8 Hz, CH), 7.10–8.00 (10H, m, ArH).

3-Benzoyl-1,1-dicyano-2-(4-methylphenyl)-propane (4b): M.p. 126–128°C. ν_{max} (KBr)/cm⁻¹: 2255, 1675. δ_{H} (CDCl₃): 2.28 (3H, s, CH₃), 3.24–3.27

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(2H, d, J = 6.6 Hz, CH₂), 3.44–3.65 (1H, m, CH), 4.40–4.55 (1H, d, J = 4.2 Hz, CH), 6.92–8.03 (9H, m, ArH). m/z: 306 (M⁺, 1.3), 105 (100). Anal. calcd. for C₁₉H₁₆N₂O: C, 79.14; H, 5.59; N, 9.72. Found: C, 78.75; H, 5.78; N, 9.91.

3-Benzoyl-2-(4-chlorophenyl)-1,1-dicyano-propane (4c): M.p. 114–116°C, lit.,^[1] 115–116°C. ν_{max} (KBr)/cm⁻¹: 2255, 1680. δ_{H} (CDCl₃): 3.55–3.64 (2H, d, J=7.2 Hz, CH₂), 3.78–4.20 (1H, m, CH), 4.58–4.64 (1H, d, J=4.8 Hz, CH), 7.10–8.13 (9H, m, ArH).

3-Benzoyl-2-(4-methoxyphenyl)-1,1-dicyano-propane (4d): M.p. 117–119°C, lit.,^[1] 117°C. ν_{max} (KBr)/cm⁻¹: 2255, 1675. $\delta_{\rm H}$ (CDCl₃): 3.34–3.38 (2H, d, J = 7.2 Hz, CH₂), 3.48–3.94 (4H, m, CH, OCH₃), 4.47–4.54 (1H, d, J = 4.8 Hz, CH), 6.80–7.98 (9H, m, ArH).

3-Benzoyl-1-cyano-1-ethoxycarbonyl-2-phenyl-propane (4e): Oil. ν_{max} (KBr)/cm⁻¹: 2250, 1745, 1680. δ_{H} (CDCl₃): 0.93 (3H, t, J = 6.4 Hz, CH₃), 3.56–3.65 (2H, d, J = 7.2 Hz, CH₂), 3.86–4.15 (3H, m, CH, OCH₂), 4.52–4.56 (1H, d, J = 3.2 Hz, CH), 7.30–8.05 (10H, m, ArH). m/z: 321 (M⁺, 1.2), 105 (100).

3-Benzoyl-1-cyano-1-ethoxycarbonyl-2-(4-methylphenyl)-propane (4f): Oil. ν_{max} (KBr)/cm⁻¹: 2250, 1745, 1685. δ_{H} (CDCl₃): 1.09 (3H, t, J = 7.2 Hz, CH₃), 2.22 (3H, s, CH₃), 3.40–3.54 (2H, d, J = 7.5 Hz, CH₂), 3.72–4.24 (4H, m, 2CH, OCH₂), 7.00–7.97 (9H, m, ArH). m/z: 335 (M⁺, 1.3), 105 (100).

3-Benzoyl-1-cyano-1-ethoxycarbonyl-2-(4-chlorophenyl)-propane (4g): Oil. ν_{max} (KBr)/cm⁻¹: 2250, 1740, 1685. $\delta_{\rm H}$ (CDCl₃): 0.99 (3H, t, J = 7.2 Hz, CH₃), 3.59–3.67 (2H, d, J = 6.4 Hz, CH₂), 3.86–4.24 (3H, m, CH, OCH₂), 4.63–4.67 (1H, d, J = 3.2 Hz, CH), 7.21–7.90 (9H, m, ArH). m/z: 355 (M⁺, 1.4), 105 (100).

3-Benzoyl-1-cyano-1-ethoxycarbonyl-2-(4-methoxyphenyl)-propane (4h): Oil. ν_{max} (KBr)/cm⁻¹: 2250, 1745, 1685. δ_{H} (CDCl₃): 1.04 (3H, t, J = 7.2 Hz, CH₃), 3.37–3.55 (2H, d, J = 7.5 Hz, CH₂), 3.68–4.29 (7H, m, 2CH, OCH₃, OCH₂), 6.78–7.97 (9H, m, ArH). m/z: 351 (M⁺, 1.0), 105 (100).

4-Nitro-1,3-diphenyl-1-butanone (4i): M.p. 98–100°C, lit.,^[3,4] 100–101°C. ν_{max} (KBr)/cm⁻¹: 1685, 1545, 1375. δ_{H} (CDCl₃): 3.40–3.48 (2H, d, J = 6.4 Hz, CH₂), 4.00–4.34 (1H, m, CH), 4.66–4.77 (2H, d, J = 8.8 Hz, CH₂), 7.14–7.90 (10H, m, ArH).

4-Nitro-1-phenyl-3-(4-methylphenyl)-1-butanone (4j): M.p. 84–86°C. ν_{max} (KBr)/cm⁻¹: 1680, 1540, 1380. δ_{H} (CDCl₃): 2.30 (3H, s, CH₃), 3.38–3.46 (2H, d, J=6.6 Hz, CH₂), 4.01–4.71 (3H, m, CH, CH₂), 7.14–7.92 (9H, m, ArH). m/z: 237 (M-46, 1.2), 236 (3.5), 105 (100). Anal. calcd. for C₁₇H₁₇NO₃: C, 72.07; H, 6.05; N, 4.94. Found: C, 71.81; H, 5.95; N, 5.16.

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4-Nitro-1-phenyl-3-(4-chlorophenyl)-1-butanone (4k): M.p. 110–111°C. ν_{max} (KBr)/cm⁻¹: 1680, 1550, 1360. δ_{H} (CDCl₃): 3.44–3.52 (2H, d, J = 6.4 Hz, CH₂), 4.08–4.37 (1H, m, CH), 4.68–4.79 (2H, d, J = 8.8 Hz, CH₂), 7.14–8.01 (9H, m, ArH). m/z: 257 (M-46, 0.8), 256 (1.9), 105 (100). Anal. calcd. for C₂₀H₁₈ClNO₃: C, 63.27; H, 4.65; N, 4.61. Found: C, 63.10; H, 4.64; N, 4.63.

4-Nitro-1-phenyl-3-(4-methoxyphenyl)-1-butanone (4l): M.p. 64–66°C, lit.,^[2] 66°C. ν_{max} (KBr)/cm⁻¹: 1680, 1540, 1380. δ_{H} (CDCl₃): 3.38–3.46 (2H, d, J = 6.8 Hz, CH₂), 3.78 (3H, s, CH₃), 4.05–4.67 (3H, m, CH, CH₂), 6.79–7.90 (9H, m, ArH).

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