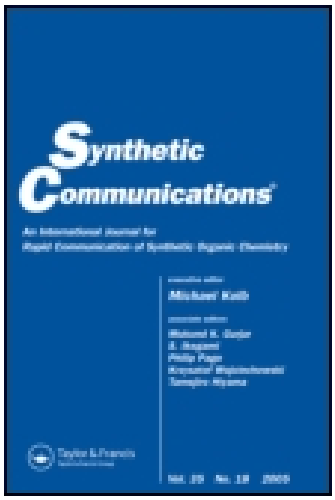


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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

Yongmin Ma [a] & Yongmin Zhang [a b]

[a] Department of Chemistry , Zhejiang University (Campus Xixi) , Hangzhou, P.R. China

[b] State Key Laboratory of Organometallic Chemistry , Shanghai Institute of Organic Chemistry , Chinese Academy of Sciences , Shanghai, P.R. China

Published online: 17 Aug 2006.

To cite this article: Yongmin Ma & Yongmin Zhang (2003) Samarium(III) Iodide Promoted Three-Component Coupling Reactions of Aldehydes, α-Haloketones, and Active Methylene or Methyl Compounds, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 33:5, 711-715, DOI: 10.1081/SCC-120016312

To link to this article: http://dx.doi.org/10.1081/SCC-120016312

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

SYNTHETIC COMMUNICATIONS®
Vol. 33, No. 5, pp. 711–715, 2003

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

Yongmin Ma[1] and Yongmin Zhang[1,2,*]

[1]Department of Chemistry, Zhejiang University (Campus Xixi), Hangzhou, P.R. China
[2]State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, P.R. China

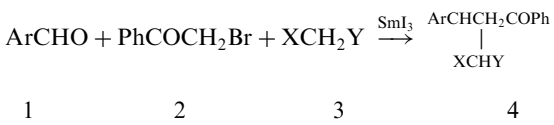
ABSTRACT

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.

*Correspondence: Yongmin Zhang, Department of Chemistry, Zhejiang University (Campus Xixi), Hangzhou, 310028, P.R. China; Fax: +86-571-88807077; E-mail: yminzhang@mail.hz.zj.cn.

DOI: 10.1081/SCC-120016312 0039-7911 (Print); 1532-2432 (Online)



1 2 3 4

Scheme 1.

Table 1. Three-component coupling reactions promoted by SmI_3.

Entry	Ar	XCH_2Y	Yield (%)[a]
a	C_6H_5	$CH_2(CN)_2$	75
b	*p*-$CH_3C_6H_4$	$CH_2(CN)_2$	69
c	*p*-ClC_6H_4	$CH_2(CN)_2$	70
d	*p*-$CH_3OC_6H_4$	$CH_2(CN)_2$	73
e	C_6H_5	$NCCH_2CO_2Et$	53
f	*p*-$CH_3C_6H_4$	$NCCH_2CO_2Et$	50
g	*p*-ClC_6H_4	$NCCH_2CO_2Et$	48
h	*p*-$CH_3OC_6H_4$	$NCCH_2CO_2Et$	54
i	C_6H_5	CH_3NO_2	79
j	*p*-$CH_3C_6H_4$	CH_3NO_2	78
k	*p*-ClC_6H_4	CH_3NO_2	79
l	*p*-$CH_3OC_6H_4$	CH_3NO_2	83

[a]Isolated 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 SmI_3 in one pot to form the adducts (Sch. 1).

When aryl aldehydes (**1**) and α-haloketone (**2**) were treated with 2 equiv. SmI_3 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 SmI_3 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

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 SmI_3 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}. ^{1}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 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 SmI_3 (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 (Na_2SO_4), 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 ($CDCl_3$): 3.60–3.68 (2H, d, $J = 7.2$ Hz, CH_2), 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 ($CDCl_3$): 2.28 (3H, s, CH_3), 3.24–3.27

(2H, d, $J = 6.6$ Hz, CH_2), 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 $C_{19}H_{16}N_2O$: 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 ($CDCl_3$): 3.55–3.64 (2H, d, $J = 7.2$ Hz, CH_2), 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. δ_H ($CDCl_3$): 3.34–3.38 (2H, d, $J = 7.2$ Hz, CH_2), 3.48–3.94 (4H, m, CH, OCH_3), 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 ($CDCl_3$): 0.93 (3H, t, $J = 6.4$ Hz, CH_3), 3.56–3.65 (2H, d, $J = 7.2$ Hz, CH_2), 3.86–4.15 (3H, m, CH, OCH_2), 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 ($CDCl_3$): 1.09 (3H, t, $J = 7.2$ Hz, CH_3), 2.22 (3H, s, CH_3), 3.40–3.54 (2H, d, $J = 7.5$ Hz, CH_2), 3.72–4.24 (4H, m, 2CH, OCH_2), 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. δ_H ($CDCl_3$): 0.99 (3H, t, $J = 7.2$ Hz, CH_3), 3.59–3.67 (2H, d, $J = 6.4$ Hz, CH_2), 3.86–4.24 (3H, m, CH, OCH_2), 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 ($CDCl_3$): 1.04 (3H, t, $J = 7.2$ Hz, CH_3), 3.37–3.55 (2H, d, $J = 7.5$ Hz, CH_2), 3.68–4.29 (7H, m, 2CH, OCH_3, OCH_2), 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 ($CDCl_3$): 3.40–3.48 (2H, d, $J = 6.4$ Hz, CH_2), 4.00–4.34 (1H, m, CH), 4.66–4.77 (2H, d, $J = 8.8$ Hz, CH_2), 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 ($CDCl_3$): 2.30 (3H, s, CH_3), 3.38–3.46 (2H, d, $J = 6.6$ Hz, CH_2), 4.01–4.71 (3H, m, CH, CH_2), 7.14–7.92 (9H, m, ArH). *m/z*: 237 (M-46, 1.2), 236 (3.5), 105 (100). Anal. calcd. for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 71.81; H, 5.95; N, 5.16.

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 ($CDCl_3$): 3.44–3.52 (2H, d, $J = 6.4$ Hz, CH_2), 4.08–4.37 (1H, m, CH), 4.68–4.79 (2H, d, $J = 8.8$ Hz, CH_2), 7.14–8.01 (9H, m, ArH). *m/z*: 257 (M-46, 0.8), 256 (1.9), 105 (100). Anal. calcd. for $C_{20}H_{18}ClNO_3$: 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 ($CDCl_3$): 3.38–3.46 (2H, d, $J = 6.8$ Hz, CH_2), 3.78 (3H, s, CH_3), 4.05–4.67 (3H, m, CH, CH_2), 6.79–7.90 (9H, m, ArH).

ACKNOWLEDGMENTS

We are grateful to the National Natural Science Foundation of China (Project No. 29872010) and the NSF of Zhejiang Province, China for financial support.

REFERENCES

1. Krauze, A.; Bomika, Z.; Shestopalov, A.M.; Radinovskaya, L.A.; Pelcers, J.; Duburs, G.; Sharanin, Yu.A.; Promonenkov, V.K. Khim Geterotisikl. Soedin **1998**, *3*, 377.
2. Davey, W.; Tievey, D.J. J. Chem. Soc. **1958**, 2276.
3. Gracia-Raso, A.; Garcia-Raso, J.; Campaner, B.; Mestres, R.; Sinisterra, J.V. Synthesis **1982**, 1037.
4. Pedro, V.; Jose, I.B.; Anton, V.F. Tetrahedron Lett. **1991**, *32* (39), 5375.

Received in the Netherlands February 15, 2002

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016