

Note

An Efficient Mg/SmI₂ Catalytic System for the Intermolecular Deoxygenative Coupling of Amides and Ketones[†]

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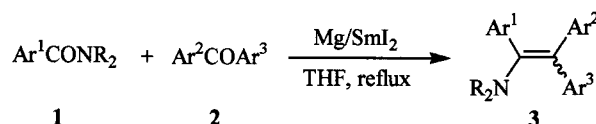
The intermolecular deoxygenative coupling of ketones with amides induced by Mg/SmI₂ catalyst was studied and a series of enamines was synthesized in moderate yields under mild and neutral conditions.

Keywords magnesium, samarium diiodide, ketone, amide, enamine

The intermolecular or intramolecular reductive deoxygenation of carbonyl compounds to olefins under the influence of low-valent titanium reagents, commonly referred to as “McMurry reaction”, has been tremendously exploited by chemists since its debut in the early 1970s.¹ A lot of other functional groups (such as ketones, aldehydes, esters) can be coupled. Füstner² reported the intramolecular reductive cyclization of oxoamides to give indoles promoted by low-valent titanium. Ogawa *et al.*³ reported the first deoxygenative coupling of amides promoted by Sm/SmI₂ or Yb/YbI₂. In contrast, the intermolecular reductive deoxygenation coupling reaction of amides and ketones has remained largely unexplored possibly due to the low reactivity of amides.⁴ We postulated that the requisite reagents for the desired coupling reaction of amides and ketones should possess both powerful reducing ability and good oxophilicity. The low-valent titanium reagent (TiCl₄/Sm, TiCl₄/Zn)⁵ would appear to be suitable candidates but, actually, these reagents did not work well. Our group has reported the intermolecular reductive de-

oxygenative coupling of amides and ketones promoted by Sm/SmI₂.⁶ Since magnesium has a strong reducing power similar to that of samarium and also is more stable in air, these properties of magnesium promoted us to use the more convenient and cheaper metallic magnesium directly instead of samarium. Here we wish to report that a magnesium⁷/samarium diiodide⁸ mixed reagent successfully promotes the intermolecular deoxygenative coupling of ketones and amides, which provides a powerful tool for preparing enamines in moderate yields (Scheme 1).

Scheme 1



The results are summarized in Table 1. When amides **1** and ketones **2** were treated with Mg/SmI₂ catalyst in anhydrous THF at 67 °C under a nitrogen atmosphere, the deep blue color of the mixture changed into brownish red immediately and the products **3** were obtained after the reaction was carried out for a given time (Table 1). However, the desired products were not obtained in the absence of either magnesium or samarium diiodide. Meanwhile, chloro and alkoxy groups could not be reduced under the reaction conditions and have no effect on the yield of intermolecular reductive coupling

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Table 1 Deoxygenative coupling of amides and ketones induced by Mg/SmI₂

Entry	Ar ¹	NR ²	Ar ²	Ar ³	t (h)	Product	Yield (%) ^a
1	C ₆ H ₅	NEt ₂	C ₆ H ₅	C ₆ H ₅	6	3a	65, 0 ^b , 49 ^c
2	C ₆ H ₅	NEt ₂	C ₆ H ₅	4-CH ₃ C ₆ H ₄	6	3b	60
3	C ₆ H ₅	NEt ₂	C ₆ H ₅	4-ClC ₆ H ₄	6	3c	57
4	C ₆ H ₅	NEt ₂	C ₆ H ₅	4-C ₆ H ₅ C ₆ H ₄	6	3d	63
5	C ₆ H ₅	Piperidine	C ₆ H ₅	4-CH ₃ C ₆ H ₄	5	3e	68
6	4-CH ₃ OC ₆ H ₄	NEt ₂	C ₆ H ₅	C ₆ H ₅	6	3f	65
7	4-ClC ₆ H ₄	NEt ₂	C ₆ H ₅	C ₆ H ₅	7	3g	63
8	4-ClC ₆ H ₄	Piperidine	C ₆ H ₅	C ₆ H ₅	6	3h	67
9	CH ₃ (CH ₂) ₄	NEt ₂	C ₆ H ₅	C ₆ H ₅	10	3i	0 ^d
10	C ₆ H ₅	NEt ₂	C ₆ H ₅	CH ₃	10	3j	0 ^d

^a Isolated yields; ketone (1 mmol), amide (1 mmol), Mg (6 mmol) and SmI₂ (0.6 mmol) were used. ^b In the absence of Mg or SmI₂.

^c Ketone (1 mmol), amide (1 mmol), Mg (6 mmol) and SmI₂ (0.2 mmol) were used.

product. All reactions are completed in 5–7 h under reflux to give the products in satisfactory yields. Unfortunately, when the substrates are *N,N*-diethylhexanoamide and benzophenone, or *N,N*-diethylbenzamide and acetophenone, the reaction results in a complex mixture under the same conditions.

In conclusion, we have demonstrated that Mg/SmI₂ catalyst system can be used for the intermolecular deoxygenative coupling of ketones and amides to yield enamines. Thus it provides a very convenient and practical method in terms of mild reaction condition, simple operation and moderate yields.

Experimental

General

Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use. Melting points were uncorrected. Infrared spectra were recorded on a Bruker Vector 22 spectrometer in KBr with absorptions reported in cm⁻¹. ¹H NMR spectra were determined on a Bruker AC-400 or a Bruker AC-80 spectrometer using CDCl₃ as the solvent and chemical shifts were given relative to tetramethylsilane. Mass spectra were recorded on an HP5989B Mass spectrometer.

General procedure for the synthesis of compounds 3

A solution of amides (1 mmol) and ketones (1 mmol) in dry THF (2 mL) was added to the solution of SmI₂ (0.6 mmol) and Mg (6 mmol) in THF (15 mL) at

67 °C under a nitrogen atmosphere. After being stirred for a given time (Table 1, the reaction was monitored by TLC), the solvent was removed under reduced pressure. Then the residue was purified by chromatography on silica gel (200–300 mesh) using petroleum ether (60–90 °C) as eluant to give the pure products.

3a Light green crystals, yield 65%, m. p. 96–98 °C (lit.⁶ m. p. 96–98 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 7.20–7.28 (m, 6H), 7.08–7.11 (m, 4H), 6.82–6.92 (m, 5H), 2.71 (q, *J* = 7.04 Hz, 4H), 0.98 (t, *J* = 7.04 Hz, 6H); IR (KBr) ν: 3085, 2970, 1594, 1580, 1557 cm⁻¹.

3b Light green crystals (*Z* + *E*), yield 60%, m. p. 115–118 °C (lit.⁶ m. p. 117–118 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 7.27–7.09 (m, 9H), 6.90–6.72 (m, 5H), 2.73–2.66 (m, 4H), 2.33 (s, 1.52H), 2.15 (s, 1.48H), 0.95–1.00 (m, 6H); IR (KBr) ν: 2967, 2925, 1590, 1581, 1507 cm⁻¹.

3c Light green crystals (*Z* + *E*), yield 57%, m. p. 106–108 °C (lit.⁶ m. p. 104–105 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 7.46–7.10 (m, 9H), 7.11–6.76 (m, 5H), 2.75–2.67 (m, 4H), 0.95–1.01 (m, 6H); IR (KBr) ν: 2968, 2930, 1596, 1578, 1489 cm⁻¹.

3d Light green crystals (*Z* + *E*), yield 63%, m. p. 117–119 °C (lit.⁶ m. p. 120–122 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 7.62 (d, *J* = 8.42 Hz, 1H), 7.53–7.09 (m, 14H), 6.89–6.87 (m, 4H), 2.68–2.78 (m, 4H), 0.96–1.02 (m, 6H); IR (KBr) ν: 3023, 2965, 1594, 1579, 1485 cm⁻¹.

3e Light green crystals (*Z* + *E*), yield 68%,

m.p. 142—145 °C (lit.⁶ m.p. 138—139 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 7.27—7.34 (m, 3H), 7.08—7.12 (m, 5H), 6.75—6.99 (m, 6H), 2.54 (brs, 4H), 2.34 (s, 1.53H), 2.16 (s, 1.47H), 1.44 (brs, 6H); IR (KBr) ν: 3019, 2970, 2928, 1595, 1558, 1507 cm⁻¹.

3f Light green crystals, yield 65%, m.p. 123—125 °C (lit.⁶ m.p. 123—124 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 7.19—7.02 (m, 8H), 6.77—6.67 (m, 6H), 3.71 (s, 3H), 2.72 (q, *J* = 7.2 Hz, 4H), 0.96 (t, *J* = 7.2 Hz, 6H); IR (KBr) ν: 2966, 1605, 1579, 1507 cm⁻¹.

3g Light green crystals, yield 63%, m.p. 114—116 °C (lit.⁶ m.p. 113—114 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 7.23—7.05 (m, 8H), 6.97—6.79 (m, 6H), 2.65 (q, *J* = 7.0 Hz, 4H), 0.94 (t, *J* = 7.0 Hz, 6H); IR (KBr) ν: 3085, 2970, 1594, 1580, 1557 cm⁻¹.

3h Light green crystals, yield 67%, m.p. 145—147 °C (lit.⁶ m.p. 145—147 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 7.26—7.29 (m, 4H), 7.17—7.19 (m, 1H), 7.06—7.10 (m, 4H), 6.94—6.97 (m, 3H), 6.83—6.85 (m, 2H), 2.52 (s, 4H), 1.45 (s, 6H); IR (KBr) ν: 3094, 2931, 2849, 2785, 1596, 1549, 1487 cm⁻¹.

References

- For reviews of low-valent titanium, see:
 - McMurry, J. E. *Acc. Chem. Res.* **1974**, *7*, 281.
 - McMurry, J. E. *Acc. Chem. Res.* **1983**, *16*, 405.
 - McMurry, J. E. *Chem. Rev.* **1989**, *89*, 1513.
 - Lenoir, D. *Synthesis* **1989**, 883.
 - Füstner, A.; Bogdanovi, B. *Angew. Chem., Int. Ed.* **1996**, *35*, 2443.
- Füstner, A.; Hupperts, A. *J. Am. Chem. Soc.* **1995**, *117*, 4468.
- Ogawa, A.; Takami, N.; Sekiguchi, M.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1992**, *114*, 8729.
 - Ogawa, A.; Nanke, T.; Takami, N.; Sekiguchi, M.; Ryu, I.; Kambe, N.; Sonoda, N. *Appl. Organomet. Chem.* **1995**, *9*, 461.
- Fleming, I.; Ghosh, U.; Mack, S. R.; Clark, B. P. *Chem. Commun.* **1998**, 711.
 - Bravo-Zhivotovskii, D. A.; Pigarev, S. D.; Kalikman, I. D.; Vyazankina, O. A.; Vyazankin, N. S. *J. Organomet. Chem.* **1983**, *248*, 51.
 - Bravo-Zhivotovskii, D. A.; Pigarev, S. D.; Kalikman, I. D.; Vyazankina, O. A.; Vyazankin, N. S. *Zh. Obshch. Khim.* **1983**, *53*, 1838.
- The reaction of *N,N*-diethylbenzamide and benzophenone with TiCl₄/Sm or TiCl₄/Zn resulted in the formation of a complex mixture (67 °C, 10 h).
- Xu, X.-L.; Zhang, Y.-M. *Tetrahedron* **2002**, *58*, 503.
- For the reaction of Mg/SmI₂, see:
 - Nomura, R.; Matsuno, T.; Endo, T. *J. Am. Chem. Soc.* **1996**, *118*, 11666.
 - Annunziatu, R.; Benaglia, M.; Cinquini, M.; Cozzi, F.; Raimondi, L. *Tetrahedron Lett.* **1998**, *39*, 3333.
- For reviews, see:
 - Krief, A.; Laval, A. M. *Chem. Rev.* **1999**, *99*, 745.
 - Molander, G. A. *Acc. Chem. Res.* **1998**, *31*, 603.
 - Molander, G. A.; Harris, C. R. *Tetrahedron* **1998**, *54*, 3321.
 - Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307.
 - Imamota, T. *Lanthanides in Organic Synthesis*, Academic Press, London, **1994**, Chapter 4.
 - Molander, G. A. *Chem. Rev.* **1992**, *92*, 29.
 - Curran, D. P.; Fevig, T. L.; Jasperse, C. P.; Totleben, M. J. *Synlett* **1992**, 943.

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