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Intermolecular deoxygenative coupling of diarylketones and arylamides induced by Sm/SmI_2 system

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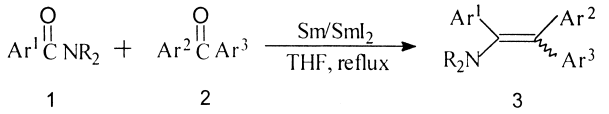
Abstract—In the presence of Sm/SmI_2, the intermolecular deoxygenative coupling reaction of diarylketones and arylamides proceeded very efficiently to give enamines in good to excellent yields under mild conditions. © 2002 Elsevier Science Ltd. All rights reserved.

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 synthetic chemists since its debut in the early 1970s.[1] Fürstner reported the intramolecular reductive cyclization of oxoamides to give indoles promoted by low-valent titanium.[2] In marked contrast, the intermolecular reductive deoxygenation coupling reaction of amides and ketones has remained largely unexplored, possibly due to the amides' low reactivity.[3] To the best of our knowledge, no literature has been reported on the intermolecular reductive deoxygenation coupling of amides and ketones up to date. We postulated that the requisite reagents for the desired coupling reaction of amides and ketones should possess both powerful reducing ability and good oxophilicity. A low-valent titanium reagent ($TiCl_4$/Sm, $TiCl_4$/Zn)[4] or samarium diiodide[5] would appear to be suitable candidates but, in fact, these reagents did not work well. Here we wish to report that a samarium/samarium diiodide mixed reagent successfully promotes the intermolecular deoxygenative coupling of diarylketones and arylamides, which provides a powerful tool for preparing enamines in good to excellent yields (Scheme 1).



Scheme 1.

As can be seen in the experiments varying the molar ratio of Sm/SmI_2 (Table 1), the yield of coupling product was dependent on the amount of samarium metal. The coupling reaction with Sm proceeded in the presence of a catalytic amount of SmI_2.

Table 2 lists examples of the intermolecular deoxygenative coupling of ketones and amides. At the same time, chloro, alkoxyl groups could not be reduced under the reaction conditions and have no influence on the rate of intermolecular reductive coupling. All the reactions were complete within 3–4 h under reflux conditions to give satisfactory yields without any additives such as HMPA or NiI_2. Unfortunately, when the substrate is *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 Sm/SmI_2 system can be used for the intermolecular deoxygenative coupling of diarylketones and arylamides to yield enamines. This appears to be a very convenient and practical method in terms of mild reaction condition, simple operation and high yields.

Table 1. Deoxygenative coupling of *N*,*N*-diethylbenzamide (1 mmol) and benzophenone (1 mmol)

Entry	Sm (mmol)	SmI_2 (mmol)	Time (h)	Yield (%)[a]
1	0	3.3	6	0[b]
2	0.4	3	3	55
3	1.1	2.2	3	72
4	2.2	1.1	3	80
5	2.2	1.1	6	57
6	3	0.3	4	60

[a] Isolated yield.
[b] A complex mixture.

Keywords: samarium; samarium (II) iodide; diarylketones; arylamides; enamines; intermolecular deoxygenative coupling.

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Table 2. Sm/SmI_2 induced reductive coupling of amides and ketones[5]

Entry	Ar^1	NR_2	Ar^2	Ar^3	Time (h)	Yield[a] (%)
3a	C_6H_5	NEt_2	C_6H_5	C_6H_5	3	80
3b	C_6H_5	NEt_2	C_6H_5	$4\text{-}CH_3C_6H_4$	3	78
3c	C_6H_5	NEt_2	$4\text{-}CH_3C_6H_4$	$4\text{-}CH_3C_6H_4$	3	76
3d	C_6H_5	NEt_2	C_6H_5	$4\text{-}ClC_6H_4$	4	68
3e	C_6H_5	NEt_2	C_6H_5	$4\text{-}C_6H_5C_6H_4$	3	81
3f	C_6H_5	Piperidine	C_6H_5	$4\text{-}CH_3C_6H_4$	3	83
3g	$4\text{-}CH_3OC_6H_4$	NEt_2	C_6H_5	C_6H_5	3	75
3h	$4\text{-}CH_3OC_6H_4$	NEt_2	C_6H_5	$4\text{-}CH_3C_6H_4$	3	73
3i	$4\text{-}CH_3OC_6H_4$	NEt_2	$4\text{-}CH_3C_6H_4$	$4\text{-}CH_3C_6H_4$	3	67
3j	$4\text{-}CH_3OC_6H_4$	NEt_2	C_6H_5	$4\text{-}C_6H_5C_6H_4$	3	75
3k	$4\text{-}ClC_6H_4$	NEt_2	C_6H_5	C_6H_5	4	67
3l	$4\text{-}ClC_6H_4$	NEt_2	C_6H_5	$4\text{-}CH_3C_6H_4$	4	65
3m	$4\text{-}ClC_6H_4$	Piperidine	C_6H_5	C_6H_5	4	63
3n	$CH_3(CH_2)_4$	NEt_2	C_6H_5	C_6H_5	6	0[b]
3o	C_6H_5	NEt_2	C_6H_5	CH_3	6	0[b]

Ketone (1 mmol), amide (1 mmol), Sm (1.1 mmol) and SmI_2 (2.2 mmol) were used.
[a] Isolated yields.
[b] A complex mixture; ketone (1 mmol), amide (1 mmol), Sm (1.1 mmol), SmI_2 (2.2 mmol) and HMPA (1 mL) were used.

1. Experimental

Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use. All reactions were conducted under a nitrogen atomsphere. Melting points are uncorrected. ^1H NMR spectra were recorded on a Bruker AC-80 or AC-400 instrument as $CDCl_3$ solutions using TMS as internal standard. Chemical shifts (δ) are reported in ppm and coupling constants J are given in Hz. IR spectra were recorded using KBr disks with a Bruker Vector-22 infrared spectrometer. Elemental analyses were performed on a EA-1110 instrument. Metallic samarium and all solvents were purchased from commercial sources, without further purification before use.

1.1. General procedure for the synthesis of compounds 3

A solution of amides(1 mmol) and ketones(1 mmol) in dry THF (3 mL) was added to the solution of SmI_2 (2.2 mmol) and Sm (1 mmol) in THF (22 mL) at 67°C under a nitrogen atmosphere. After being stirred for a given time (Table 2, the reaction was monitored by TLC), the solvent was removed under reduced pressure. Then the residue was purified by column gel silca (200–300 mesh) using petroleum (60–90°C) as eluant to give pure product.

1.1.1. 1,2,2-Triphenyl-1-*N*,*N*-diethylaminoethylene 3a. Light green crystals, yield: 80%, mp: 96–98°C. δ_H: 7.20–7.28 (6H, m), 7.08–7.11 (4H, m), 6.82–6.92 (5H, m), 2.68–2.73 (4H, q, J=7.0 Hz), 0.96–0.99 (6H, t, J=7.0 Hz). ν_{max}(KBr)/cm^{-1}: 3085, 2970, 1594, 1580, 1557. *m/z*(%): 327 (M^+, 100), 298 (56). Anal. $C_{24}H_{25}N$. Calcd C, 88.03; H, 7.69; N, 4.28. Found C, 88.21; H, 7.78; N, 4.03%.

1.1.2. 1,2-Diphenyl-2-(4-methylphenyl)-1-*N*,*N*-diethylaminoethylene 3b (*Z* and *E*). Light green crystals, yield: 78%, mp: 117–118°C. δ_H: 7.09–7.27 (9H, m), 6.72–6.90 (5H, m), 2.66–2.73 (4H, m), 2.33 (1.57H, s), 2.15 (1.43H, s), 0.95v1.00 (6H, m). ν_{max}(KBr)/cm^{-1}: 2967, 2925, 1590, 1581, 1507. *m/z* (%): 341 (M^+, 100), 326 (1.54), 312 (22.75). Anal. $C_{25}H_{27}N$. Calcd C, 87.93; H, 7.97; N, 4.10. Found C, 87.81; H, 7.78; N, 4.03%.

1.1.3. 1-Phenyl-2,2-di(4-methylphenyl)-1-*N*,*N*-diethylaminoethylene 3c. Light green crystals, yield: 76%, mp: 136–137°C. δ_H: 7.26–7.28 (2H, d), 7.05–7.12 (7H, m), 6.72–6.74 (4H, m), 2.65–2.71 (4H, q, J=7.0 Hz), 2.31 (1.5H, s), 2.14 (1.5H, s), 0.95–0.98 (6H, t, J=7.0 Hz). ν_{max}(KBr)/cm^{-1}: 3075, 2967, 1580, 1550. *m/z* (%): 355 (M^+, 100), 340 (1.79), 326 (19.89), 119 (22.32). Anal. $C_{26}H_{29}N$. Calcd C, 87.84; H, 8.22; N, 3.94. Found C, 88.01; H, 8.09; N, 3.85%.

1.1.4. 1,2-Diphenyl-2-(4-chlorophenyl)-1-*N*,*N*-diethylaminoethylene 3d (*Z* and *E*). Light green crystals, yield: 68%, mp: 104–105°C. δ_H: 7.10–7.46 (9H, m), 7.09–6.76 (5H, m), 2.67–2.75 (4H, m), 0.95–1.01 (6H, m). ν_{max}(KBr)/cm^{-1}: 2968, 2930, 1596, 1578, 1489 *m/z* (%): 361 (M^+, 12.25), 363 (M^++2, 2.85), 332 (8.73), 328 (5.33), 105 (100). Anal. $C_{24}H_{24}ClN$. Calcd C, 79.65; H, 6.68; N, 3.87. Found C, 79.52; H, 6.81; N, 3.99%.

1.1.5. 1,2-Diphenyl-2-(4-phenylphenyl)-1-*N*,*N*-diethylaminoethylene 3e (*Z* and *E*). Light green crystals, yield: 81%, mp: 120–122°C. δ_H: 7.60–7.62 (2H, d), 7.09–7.53 (13H, m), 6.87–6.89 (4H, m), 2.68–2.78 (4H, m), 0.96–1.02 (6H, m). ν_{max}(KBr)/cm^{-1}: 3023, 2965, 1594, 1579, 1485. *m/z* (%): 403 (M^+, 100), 374 (17.33). Anal. $C_{30}H_{29}N$. Calcd C, 89.29; H, 7.24; N, 3.47. Found C, 89.11; H, 7.43; N, 3.29%.

1.1.6. 1,2-Diphenyl-2-(4-methylphenyl)-1-piperidylethylene 3f (*Z* and *E*). Light green crystals, yield: 83%, mp: 138–139°C. δ_H: 7.27–7.34 (3H, m), 7.08–7.12 (5H, m), 6.75–6.99 (6H, m), 2.54 (4H, brs), 2.34 (1.56H, s), 2.16 (1.44H, s), 1.44 (6H, brs). ν_{max}(KBr)/cm^{-1}: 3019, 2970, 2928, 1595, 1558, 1507. *m/z* (%): 353 (M^+, 100), 338 (1.27), 262 (22.53), 247 (24.4). Anal. $C_{26}H_{27}N$. Calcd C, 88.34; H, 7.69; N, 3.96. Found C, 88.47; H, 7.65; N, 3.87%.

1.1.7. 1-(4-Methoxyphenyl)-2,2-diphenyl-1-*N*,*N*-diethylaminoethylene 3g. Light green crystals, yield: 75%, mp: 123–124°C. δ_H: 7.02–7.19 (8H, m), 6.67–6.83 (6H, m), 3.71 (3H, s), 2.74–2.69 (4H, q, J=7.2 Hz), 0.98–0.95 (6H, t, J=7.2 Hz). ν_{max}(KBr)/cm^{-1}: 2966, 1605, 1579, 1507. *m/z* (%): 357 (M^+, 100), 328 (66.45). Anal.

$C_{25}H_{27}NO$. Calcd C, 83.99; H, 7.61; N, 3.92. Found C, 84.10; H, 7.52; N, 3.79%

1.1.8. 1-(4-Methoxyphenyl)-2-phenyl-2-(4-methylphenyl)-1-*N*,*N*-diethylaminoethylene 3h (*Z* and *E*). Light green crystals, yield: 73%, mp: 116–117°C. δ_H: 7.07–7.26 (7H, m), 7.08–7.12 (6H, m), 3.71 (1.24H, s), 3.69 (1.76H, s), 2.67–2.71 (4H, m), 2.33 (1.76H, s), 2.16 (1.24H, s), 0.95–0.99 (6H, m). ν_{max}(KBr)/cm^{-1}: 3025, 2970, 1605, 1585, 1507. *m*/*z* (%): 371 (M^+, 100), 356 (1.41), 342 (46.93). Anal. $C_{26}H_{29}NO$. Calcd C, 84.05; H, 7.86; N, 3.77. Found C, 84.21; H, 7.69; N, 3.85%.

1.1.9. 1-(4-Methoxyphenyl)-2,2-di(4-methylphenyl)-1-*N*,*N*-diethylaminoethylene 3i (*Z* and *E*). Light green crystals, yield: 67%, mp: 133–134°C. δ_H: 7.08–7.19 (6H, m), 6.64–6.82 (6H, m), 3.70 (3H, s), 2.64–2.70 (4H, q, *J*=7.0 Hz), 2.36 (3H, s), 2.16 (3H, s), 0.95–0.98 (6H, t, *J*=7.0 Hz). ν_{max}(KBr)/cm^{-1}: 3075, 2966, 1605, 1570, 1508. *m*/*z* (%): 385 (M^+, 100), 356 (38.75), 266 (20.23). Anal. $C_{27}H_{31}NO$. Calcd C, 84.11; H, 8.10; N, 3.63. Found C, 83.97; H, 7.92; N, 3.84%.

1.1.10. 1-(4-Methoxyphenyl)-2-phenyl-2-(4-phenylphenyl)-1-*N*,*N*-diethylaminoethylene 3j (*Z* and *E*). Light green crystals, yield: 75%, mp: 139–140°C. δ_H: 7.24–7.53 (11H, m), 6.88–6.92 (4H, m), 6.66–6.68 (2H, d), 3.72 (3H, s), 2.66–2.72 (4H, m), 0.97–1.00 (6H, m). ν_{max}(KBr)/cm^{-1}: 2965, 1604, 1579, 1485, 1441. *m*/*z* (%): 433 (M^+, 100), 404 (65.86), 252 (24.37), 181 (53.29). Anal. $C_{31}H_{31}NO$. Calcd C, 85.87; H, 7.21; N, 3.23. Found C, 85.74; H, 7.06; N, 3.41%.

1.1.11. 1-(4-Chlorophenyl)-2,2-diphenyl-1-*N*,*N*-diethylaminoethylene 3k. Light green crystals, yield: 67%, mp: 113–114°C. δ_H: 7.23–7.05 (8H, m), 6.97–6.79 (6H, m), 2.67–2.62 (4H, q, *J*=7.0 Hz), 0.96–0.92 (6H, t, *J*=7.0 Hz). ν_{max}(KBr)/cm^{-1}: 3085, 2970, 1594, 1580, 1557. *m*/*z* (%): 361 (M^+, 100), 363 (M^++2, 34.94), 332 (52.77), 334 (14.69). Anal. $C_{24}H_{24}ClN$. Calcd C, 79.65; H, 6.68; N, 3.87. Found C, 79.57; H, 6.49; N, 3.69%.

1.1.12. 1-(4-Chlorophenyl)-2-phenyl-2-(4-methylphenyl)-1-*N*,*N*-diethylaminoethylene 3l (*Z* and *E*). Light green crystals, yield: 65%, mp: 118–119°C. δ_H: 7.17–7.25 (5H, m), 7.03–7.08 (4H, m), 6.72–6.94 (4H, m), 2.63–2.70 (4H, m), 2.28 (1.55H, s), 2.17 (1.45H, s), 0.94–0.99 (6H, m). ν_{max}(KBr)/cm^{-1}: 3070, 2926, 1577, 1550, 1507, 1488. *m*/*z* (%): 375 (M^+, 100), 377 (M^++2, 36.63), 360 (3.66), 346 (36.85), 256 (13.98), 119 (75.90). Anal. $C_{25}H_{26}ClN$. Calcd C, 79.87; H, 6.97; N, 3.72. Found C, 79.69; H, 6.85; N, 3.63%.

1.1.13. 1-(4-Chlorophenyl)-2,2-diphenyl-1-piperidylethylene 3m. Light green crystals, yield: 63%, mp: 145–147°C. δ_H: 7.26–7.29 (4H, m), 7.17–7.19 (1H, m), 7.06–7.10 (4H, m), 6.94–6.97 (3H, m), 6.83–6.85 (2H, m), 2.52 (4H, s), 1.45 (6H, s). ν_{max}(KBr)/cm^{-1}: 3094, 2931, 2849, 2785, 1596, 1549, 1487. *m*/*z* (%): 373 (M^+, 100), 375 (34), 281 (53), 283 (23). Anal. $C_{25}H_{24}ClN$. Calcd C, 80.30; H, 6.47; N, 3.75. Found C, 80.45; H, 6.65; N, 3.59%.

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