Samarium diiodide promoted one-pot syntheses of amides from azides and esters

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A one-pot synthesis of amides from azides and esters was realized in a SmI_2-THF system under mild conditions and various amides were prepared in this way with good to excellent yields.

Keywords: samarium diiodide, one-pot syntheses, amides

Generally, the transformation of amides from azides involves two steps: (1) the reduction of nitro compounds to amines; (2) the acylation of the corresponding amines with an acylating agent.[1] Though a large number of excellent methods are available for the conversion of azides to amines, relatively fewer literature methods concern the direct transformation of azides to amides. With zinc and ammonium chloride as reducing agent, acyl azides were reduced to the corresponding amides while alkyl azides were reduced to amines in the same conditions.[2a] The combination of carboxylic acid, sodium iodide and metal exchanged montmorillonite was an effective system for the reductive acylation of azides to prepare amides.[2b] In addition, thioacetic acid was found to achieve the reduction of azides which occurred with concomitant acetylation affording the corresponding acetamide.[3a,3b] Barua *et al*. reported a combination of Ac_2O and TMSCl could effect the conversion of azides to acetamides in one pot.[3c] Recently, AlI_3/Ac_2O in CH_3CN was reported to transform azides into the corresponding acetamides directly.[4] Most of the above methods focus on the generation of acetamides. Besides, Kotsuki *et al*. described that Et_3SiH and di-*tert*-butyl dicarbonate in the presence of a catalytic amount of 20% Degassa $Pd(OH)_2/C$ could realize the conversion of azides to *N*-(*tert*-butoxycarbonyl)amines in one step.[5] To our best knowledge, a general one-pot transformation of azides to various amides with esters as acylating reagents has not been investigated. Here we wish to disclose a successful one-pot preparation of various amides from azides and esters mediated by SmI_2.

Azides could be reduced by SmI_2 to afford the corresponding amines in good yield,[6] but further investigation concerning their *in situ* transformation into amides has not been conducted. It has been reported that reduction of azides in aprotic solvent such as THF could lead to a living nitrogen anion,[7] which is more active than the corresponding amine and might be acylated by esters (relatively weaker acylating agents). These considerations prompted us to investigate the possibility of one-pot reductive acylation of azides to prepare amides upon treatment with samarium diiodide and esters in THF.

As shown in Scheme 1, when a mixture of azide and ester was added simultaneously to the SmI_2-THF solution, the corresponding amides were obtained with excellent yield under mild conditions. The results are listed in Table 1. The one-pot reductive acylation of phenyl azide with ordinary esters was completed within 10 minutes at room temperature under neutral conditions (no extra catalysts such as bases are needed for the acylation process, Table 1, entries 1-3). As for alkyl azides such as benzyl azide and *n*-butyl azide, a little longer time (30 minutes) was required for the completion of the reductive acylation (Table 1, entries 4-6).

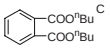
Other esters, such as ethyl acetate and methyl benzoate, could complete the acylation process efficiently. α,β-Unsaturated esters such as ethyl acrylate and methyl cinamate as the acylating agents were also explored (Scheme 2). To our delight, the corresponding α,β-unsaturated amides were obtained almost exclusively (Table 1, entries 7 and 8). It should be noted that a 1,4-Michael addition product was not obtained under the reaction conditions.

Besides, 1,4-γ-butyrolactone could act as an efficient acylating agent as well (Scheme 3). It was found that the ring opening of the lactone took place smoothly to afford the γ-hydroxy amides in good yields (Table 1, entry 7).

Finally, the reductive bis-acylation of phenyl azide with butyl *o*-phthalates as the bis-acylation agent under the SmI_2-THF conditions was investigated (Scheme 4). It was found that again the expected *N*-phenylphthalimide was formed albeit with relatively lower yields and prolonged time (Table 1, entry 10).

In conclusion, mediated by samarium diiodide, the one-pot syntheses of several types of amides including α, β-unsaturated amides, γ-hydroxy amides and an imide from azides in the presence of esters were successfully realised. The reaction undergoes smoothly at room temperature and

Table 1 One-pot syntheses of amides from azides in the presence of esters mediated by SmI_2

Entry	Azides	Esters[a]	Amides	Time/min	Yields[b]/%
1	$C_6H_5N_3$	$CH_3COOC_2H_5$	$CH_3CONHC_6H_5$ **3a**	10	91
2	$C_6H_5N_3$	$C_6H_5COOCH_3$	$C_6H_5CONH\ C_6H_5$ **3b**	10	95
3	$C_6H_5N_3$	$2\text{-}ClC_6H_5COOC_2H_5$	$2\text{-}ClC_6H_4CONH\ C_6H_5$ **3c**	10	92
4	$C_6H_5CH_2N_3$	$CH_3COOC_2H_5$	$CH_3CONHCH_2C_6H_5$ **3d**	30	82
5	$C_6H_5CH_2N_3$	$C_6H_5COOC_2H_5$	$C_6H_5CONHCH_2C_6H_5$ **3e**	30	90
6	$n\text{-}C_4H_9N_3$	$C_6H_5COOC_2H_5$	$n\text{-}C_4H_9NHCOC_6H_5$ **3f**	30	76
7	$C_6H_5N_3$	$CH_2=CHCOOC_2H_5$	$CH_2=CHCONH\ C_6H_5$ **3g**	60	90
8	$C_6H_5N_3$	$C_6H_5CH=CHCOOC_2H_5$	$C_6H_5CH=CHCONHC_6H_5$ **3h**	60	82
9	$C_6H_5N_3$		$HOCH_2CH_2CH_2CONHPh$ **3i**	10	87
10	$C_6H_5N_3$		 **3j**	60	58

[a]1.1 Equiv. of esters were used for the acylation process unless otherwise specified. [b]Isolated yields based on azides. [c]0.55 equiv. of the ester was used.

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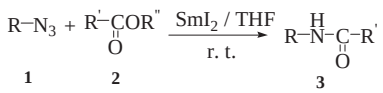
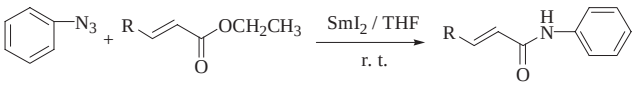


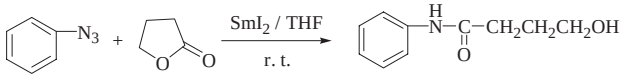
R = Ph, $PhCH_2$, *n*-Butyl

Scheme 1

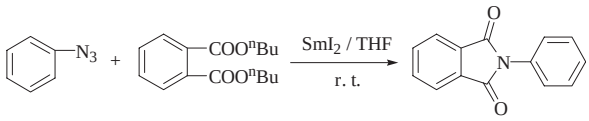


R = Ph, H

Scheme 2



Scheme 3



Scheme 4

under neutral conditions. In combination with the high yields, the simplified procedure and the ready access to the starting materials, the present method may be attractive for the preparation of amides.

Experimental

General: Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use. All reactions were conducted under a nitrogen atmosphere. ^{1}H NMR spectra were recorded on a Bruker AC-400 instrument as $CDCl_3$ solutions using TMS as an internal standard. Chemical shifts (δ) were 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. Metallic samarium and all solvents were purchased from commercial sources and were used without further purification. Phenyl azide,[8] benzyl azide[9] and *n*-butyl azide[10] was synthesised according to literature procedures.

General procedure for the reductive acylation of azides with samarium diiodide and esters: A mixture of the azides (1 mmol) and esters (1.1 mmol) in anhydrous THF (2 ml) was added by syringe to the solution of 2.2 mmol SmI_2 in dry THF (15 ml) at room temperature under nitrogen atmosphere. After completion of the reaction (the reaction time was indicated in the Table 1), 0.1 N of hydrochloride acid (3 ml) was added. The resulting mixture was extracted with ether (3 × 20 ml). The combined organic extracts were washed with saturated brine (15 ml) and dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure gave a residue, which was either recrystallised in EtOH or purified by preparative TLC on silica gel using ethyl acetate-cyclohexane (1:4) as eluent to give the pure amides.

Compound **3a:** White solid. m.p. 116–118 °C (lit. 115–116 °C).[11] ν_{max}(KBr)/cm^{-1}: 3294, 3021, 1663, 1598, 1369. δ_H ($CDCl_3$): 7.5 (2H, d, *J* = 8.0 Hz), 7.30–7.35 (2H, m), 7.10–7.16 (2H, m), 2.18 (3H, s).

Compound **3b:** White solid. m.p. 163–164 °C (lit. 163 °C).[11] ν_{max}(KBr)/cm^{-1}: 3446, 3348, 3054, 1655, 1600. δ_H ($CDCl_3$): 7.83–7.89 (3H,m), 7.5 (2H, d, *J* = 8.0 Hz), 7.47–7.58 (3H, m), 7.35–7.40 (2H, m), 7.16 (1H, t, *J* = 8.0 Hz).

Compound **3c:** White solid. m.p. 100–101 °C (lit. 99 °C).[11] ν_{max}(KBr)/cm^{-1}: 3240, 3189, 3081, 1642, 1600, 760. δ_H ($CDCl_3$): 7.90 (1H, s), 7.77–7.80 (1H, d, *J* = 8.0 Hz), 7.64–7.66 (2H, d, *J*= 8.0 Hz), 7.37–7.46 (5H, m), 7.18 (1H, m).

Compound **3d:** White solid. m.p. 56–59 °C (lit. 56–58 °C).[2] ν_{max}(KBr)/cm^{-1} : 3356, 2974, 1653, 1553, 1456, 1371. δ_H ($CDCl_3$): 7.23–7.32 (5H, m), 6.30 (1H, s), 4.36 (2H, d, *J* = 6.0 Hz), 1.96 (3H,s).

Compound **3e:** White solid. m.p. 105–107 °C (lit. 105–106 °C).[11] ν_{max}(KBr)/cm^{-1}: 3327, 3059, 3030, 1641, 1602, 1577, 1452. δ_H ($CDCl_3$): 7.79 (1H, d, *J* = 8.0 Hz), 7.26–7.51 (9H, m), 6.37 (1H,s), 4.66 (2H, d, *J* = 4 Hz).

Compound **3f:** oil.[12] ν_{max}(KBr)/cm^{-1}: 3315, 3064, 3030, 1637, 1541, 1490, 1466, 1377. δ_H ($CDCl_3$): 7.75 (2H, d, *J* = 8.0 Hz), 7.33–7.46 (3H, m), 6.58 (1H, s), 3.37–3.43 (2H, m), 1.52–1.59 (2H, m), 1.33–1.39 (2H, m), 0.91 (3H, t, *J* = 8.0 Hz).

Compound **3g:** White solid. m.p. 100–102 °C (lit. 104 °C).[13] ν_{max}(KBr)/cm^{-1}: 3415, 3267, 3207, 3141, 3095, 1667, 1637, 1607,1497, 1441. δ_H ($CDCl_3$): 7.12–7.59 (6H, m), 6.25 (1H, dd, *J* = 8Hz, 16Hz), 5.78 (1H, dd, *J* = 4Hz, 8Hz), 6.45 (1H, dd, *J* = 16 Hz, 4 Hz).

Compound **3h:** White solid. m.p. 153–155 °C (lit. 154–156 °C).[14] ν_{max}(KBr)/cm^{-1}: 3417, 1661, 1624,1596,1577,1507. δ_H($CDCl_3$): 7.75–7.79 (1H, d, *J* = 16 Hz), 733–7.66 (11H, m), 6.53–6.57 (1H, d, *J*= 16 Hz).

Compound **3i:** White solid. m.p. 59–62 °C (lit.[15] 60–63°C). ν_{max}(KBr)/cm^{-1}: 3430, 3155, 2927, 2852, 1667, 1599. δ_H($CDCl_3$): 8.41 (1H, s), 7.03–7.49 (5H, m), 3.58–3.71 (2H, m,), 2.75 (1H, br, s), 2.43 (2H, t, *J* 6.8 Hz), 1.87–1.90 (2H, m).

Compound **3j:** Light yellow solid. m.p. 207–219 °C (lit. 210°C).[11] ν_{max}(KBr)/cm^{-1}: 3470, 3074, 1779, 1735, 1708, 1660, 1594. δ_H($CDCl_3$): 7.96–7.98 (2H, m), 7.79–7.81 (2H, m), 7.50–7.54 (2H, m), 7.40–7.46 (3H, m).

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References

1 (a) D.A. Evans and J.A. Ellman, *J. Am. Chem. Soc.* 1989, **111**, 1063; (b) D.A. Evans, T.C. Britton, J.A. Ellman and R.L. Dorow, *J. Am. Chem. Soc*. 1990, **112**, 4011; (c) K.C. Nicolaou, T. Caulfield, H. Kataoka and T. Kumazawa, *J. Am. Chem. Soc.* 1988, **110**, 7910; (d) T.J. Collins, R.D. Powell, C. Slebodnick and E.S. Uffelman, *J. Am. Chem. Soc*. 1991, **113**, 8419; (e) D.A. Evans, J.A. Ellman and K.M. DeVries, *J. Am. Chem. Soc.* 1989, **111**, 8912; (f) S. Takano, T. Sugihara, S. Satoh and K. Ogasawara, *J. Am. Chem. Soc.* 1988, **110**, 6467; (g) D.L. Boger, M.A. Patane and J. Zhou, *J. Am. Chem. Soc.* 1994, **116**, 8544.

2 (a) W. Lin, X. Zhang, Z. He, Y. Jin, L. Gong and A. Mi, *Synth. Commun.* 2002, **32**, 3279; (b) B.M. Choudary, V.S.R. Kalluri and L.K. Mannepalli, 2004, *US Pat* 6,673,967. 5 pp.

3 (a) T. Rosen, I.M. Lico and D.T.W. Chu, *J. Org. Chem.* 1988, **53**, 1580; (b) F. Fazio and C.-H. Wong, *Tetrahedron. Lett.* 2003, **44**, 9083; (c) A. Barua, G. Bez and N.C. Barua, *Synlett* 1999, 553.

4 G. Bez, *Synth. Commun*. 2002, **32**, 3625.

5 H. Kotsuki, T. Ohishi and T. Araki, *Tetrahedron Lett.* 1997, **38**, 2129.

6 C. Goulaouic-Dubois and M. Hesse, *Tetrahedron Lett.* 1995, **36**, 7427.

7 W. Zhong, Y. Zhang and X. Chen, *Tetrahedron Lett.* 2001, **42**, 73.

8 R.O. Lindsay and C.F.H. Alien, *Org. Syntheses*, Collect. Vol III, Wiley, New York, 1955, 710.

9 N. Wang and J. Li, *Huaxue Shij*i, 1995, **17**, 46.

10 A. Koziara, K. Osowska-Pacewicka, S. Zawadzki and A. Zwierzak, *Synthesis* 1985, 202.

11 J. Buckingham, *Dictionary of Organic Compounds*, 5th edn; Chapman and Hall, New York, 1982.

12 E.F. Pratt and J. Lasky, *J. Am. Chem. Soc.* 1956, **78**, 4310.

13 Y. Ogata, K. Tkagi and I. Ishino, *J. Org. Chem.* 1971, **36,** 3975.

14 G. Alberghina, A. Arcoria and S. Fisichella, *J. Org. Chem.* 1978, **43**, 1122.

15 M.C. Venuti and O. Ort, *Synthesis* 1988, 985.