SHORT PAPER

A novel synthesis of *N*-substituted 2-(benzotriazol-1-yl) acetamides promoted by samarium diiodide[†] Weike Su^{*}, Bibo Yang and Yongshu Li

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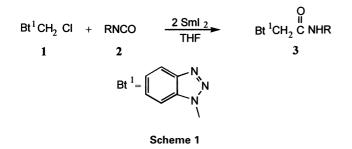
1-(Chloromethyl)benzotriazole undergo reaction with isocyanates promoted by samarium diiodide to afford *N*-substituted 2-(benzotriazol-1-yl)acetamides in good yields under mild and neutral conditions.

Keywords: samarium diiodide, benzotriazoles, isocyanates, reductive coupling

Samarium diiodide (SmI_2) , a reliable, mild, neutral, selective and versatile single-electron transfer agent, has been extensively applied in organic synthesis in the last decade¹. The pioneering work of Kagan with SmI₂ has served to demonstrate the scope of this reagent in synthetic organic chemistry.² For example, Barbier and Reformatsky reactions, pinacol couplings and ketone–olefin reductive couplings have all been reported using SmI₂ as the reagent.

As a result of the prominent work of Katritzky's group, benzotriazole has become a versatile synthetic auxiliary.³ Among numerous N-derivatives of benzotriazole, the 1-chloromethyl compound (Bt1CH2Cl) has played an important role in the introduction of other heteroatom groups. Work with this compound has mainly been focused on halogen displacement in Bt¹CH₂Cl by a wide range of oxygen, sulfur, nitrogen, phosphorus and carbon nucleophiles.⁴ Zhang and coworkers have reported that the reaction of 1-(chloromethyl)benzotrizole with diorganyl disulfides, diselenides and ditellurides in the presence of SmI₂ results in the formation of unsymmetrical α -(benzotriazol-1-yl-substituted) sulfides, selenides and tellurides, respectively, which can be subjected to further transformations.⁵ They have also reported the Barbier reaction of 1-(chloromethyl)benzotriazole with aldehydes and ketones mediated by SmI₂.6

We report here a facile synthesis of *N*-substituted 2-(benzotriazol-1-yl)acetamides by the reaction of 1-(chloromethyl) benzotriazole with isocyanates promoted by SmI_2 in THF (Scheme 1).



In the absence of SmI_2 no reaction took place between 1-(chloromethyl)benzotriazole and isocyanates, at 0°C, room temperature, or even on prolonged reflux, despite the reactivity of the isocyanates. However, the reaction proceeded smoothly and quickly to completion after the SmI_2 was introduced, and *N*-substituted 2-(benzotriazol-1-yl)acetamides were obtained in good yields under mild and neutral conditions. We also

investigated the reaction of Bt^1CH_2Cl with methylenedi-(*p*-phenylisocyanate) (4) promoted by SmI_2 and obtained the desired product 5 (Scheme 2). The results are listed in Table 1.

In summary, the SmI_2 -mediated reaction of 1-(chloromethyl)benzotriazole and isocyanates affords a novel route to *N*-substituted 2-(benzotriazol-1-yl)acetamides under mild and neutral conditions. Further studies to develop other new reactions using SmI_2 are now in progress.

Experimental

Tetrahydrofuran (THF) was distilled from sodium/benzophenone immediately prior to use. All reactions were carried on under a dry nitrogen atmosphere. Infrared spectra were recorded on a Perkin-Elmer 683 spectrometer in KBr. ¹H NMR spectra were determined on a Bruker AC-80 instrument with DMSO-d₆ as solvent; chemical shifts are expressed in ppm downfield from internal tetramethylsilane. Mass spectra were recorded on a HP 5989B MS spectrometer. Microanalysis was carried out on a Carlo-Erba 1106 instrument.

General procedure: A solution of 1-(chloromethyl)benzotriazole (1 1 mmol) and isocyanate (2; 1 mmol, or 4; 0.5 mmol) in anhydrous THF (5 ml) was added to a blue-black solution of SmI₂ (2 mmol) in THF (20 ml) under a dry nitrogen atmosphere. Then the mixture was stirred for a given time (see Table 1; monitored by TLC). After the reaction was complete the reaction mixture was treated with 0.1 N HCl and then extracted with ethyl acetate (3 × 30 ml). The combined organic extracts were washed with saturated aqueous Na₂S₂O₃, brine and dried over anhydrous MgSO₄. After the solvent was evaporated under reduced pressure, the crude products were purified by preparative TLC on silica gel using ethyl acetate–cyclohexane (1:2) as eluent. **3a** (R = i-Pr): m.p. 146–147°C; ¹H NMR: δ 0.80 (6H, d, *J* = 6.6 Hz,

3a (R = i-Pr): m.p. 146–147°C; ¹H NMR: δ 0.80 (6H, d, *J* = 6.6 Hz, 2 × CH₃), 2.52 (1H, m, *J* = 6.6 Hz, CH), 4.22 (2H, s, CH₂), 5.10 (1H, br s, NH), 7.19–7.46 (3H, m, ArH), 7.92–8.03 (1H, m, ArH); IR: v_{max} 3400, 3050, 2977, 2860, 1665, 1530, 1090, 750 cm⁻¹; MS *m*/*z* (%) 219 (M⁺+1, 3), 218 (M⁺, 2), 134 (35), 133 (4), 105 (4), 77 (100). Anal. calcd for C₁₁H₁₄N₄O: C 60.55, H 6.42, N 25.69; found C 60.56, H 6.36, N 25.66%.

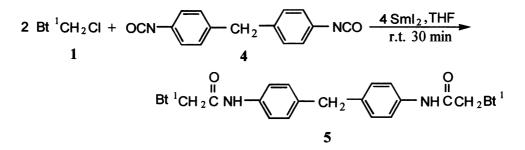
3b (R = *n*-Bu): m.p. 160–161°C; ¹H NMR: δ 0.84 (3H, t, *J* = 6.9 Hz, CH₃), 1.16–1.49 (4H, m, CH₂CH₂), 3.19 (2H, t, *J* = 5.9 Hz, CH₂), 4.33 (2H, s, CH₂), 5.31 (1H, br s, NH), 7.22–7.59 (3H, m, ArH), 7.98–8.07 (1H, m, ArH); IR: v_{max} 3302, 3090, 3064, 2930, 2861, 1661, 1558, 1100, 751 cm⁻¹; MS *m*/*z* (%) 233 (M⁺+1, 4), 232 (M⁺, 3), 133 (9), 132 (36), 106 (13), 105 (45), 104 (70), 77 (100). Anal. calcd for C₁₂H₁₆N₄O: C 62.07, H 6.90, N 24.14; found C 62.06, H 6.96, N 24.19%.

3c (R = Ph): m.p. 170–171 C; ¹H NMR: δ 4.28 (2H, s, CH₂), 5.46 (1H, br s, NH), 7.16–7.60 (8H, m, ArH), 8.00–8.13 (1H, m, ArH); IR: v_{max} 3440, 2988, 2911, 1666, 1501, 1100, 756 cm⁻¹; MS *m*/*z* (%) 253 (M⁺+1, 3), 252 (M⁺, 14), 133 (6), 132 (31), 106 (11), 105 (26), 104 (43), 77 (100). Anal. calcd for C₁₄H₁₂N₄O: C 66.67, H 4.76, N 22.22; found C 66.62, H 4.78, N 22.19%.

3d (R = 2-ClC₆H₄): m.p. 174–175°C; ¹H NMR: δ 4.32 (2H, s, CH₂), 5.40 (1H, br s, NH), 7.10–7.65 (7H, m, ArH), 8.02–8.10 (1H, m, ArH); IR: v_{max} 3455, 2997, 2908, 1666, 1522, 1072, 706 cm⁻¹; MS *m*/*z* (%) 288 (M⁺+2, 4), 287 (M⁺+1, 3), 286 (M⁺, 11), 154 (9), 153 (33), 133 (10), 132 (48), 105 (36), 104 (59), 77 (100). Anal. calcd for C₁₄H₁₁ClN₄O: C 58.64, H 3.84, N 19.55; found C 58.60, H 3.78, N 19.55%.

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[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.



Scheme 2

 Table 1
 Reaction of Bt¹CH₂Cl with isocyanates RNCO promoted by Sml₂

Product	R	T/°C	Time/min	Yield*/%
3a	i-Pr	0	5	65
3b	n-Bu	0	5	68
3c	C ₆ H ₅	0	8	81
3d	2-CIC ₆ H ₄	5	10	83
3e	3-CIC ₆ H ₄	10	15	79
3f	4-CIC ₆ H ₄	10	8	86
3g	2-EtC ₆ H ₄	5	10	80
3ĥ	2,6-i-Pr ₂ C ₆ H ₃	15	20	86
5	$CH_2(C_6H_4)_2$	15	30	78

* Isolated yields based on 1-(chloromethyl)benzotriazole.

3e (R = 3-ClC₆H₄): m.p. 179–180 C; ¹H NMR: δ 4.32 (2H, s, CH₂), 5.53 (1H, br s, NH), 6.96–7.62 (7H, m, ArH), 8.00–8.11 (1H, m, ArH); IR: v_{max} 3441, 2997, 2913, 1665, 1544, 1052, 700 cm⁻¹; MS *m*/*z* (%) 288 (M⁺+2, 4), 287 (M⁺+1, 3), 286 (M⁺, 12), 154 (7), 153 (23), 133 (11), 132 (61), 105 (40), 104 (58), 77 (100). Anal. found C 58.65, H 3.89, N 19.57%.

3f (R = 4-ClC₆H₄): m.p. 188–190°C; ¹H NMR: δ 4.30 (2H, s, CH₂), 5.40 (1H, br s, NH), 7.28–7.54 (7H, m, ArH), 8.03–8.11 (1H, m, ArH); IR: v_{max} 3449, 3000, 2910, 1667, 1532, 1060, 694 cm⁻¹; MS *m*/*z* (%) 288 (M⁺+2, 4), 287 (M⁺+1, 3), 286 (M⁺, 12), 153 (34), 133 (12), 132 (60), 105 (52), 104 (69), 77 (100). Anal. found C 58.67, H 3.80, N 19.54%.

 $\begin{array}{l} \textbf{3g} \ (\text{R}=2\text{-}\text{EtC}_6\text{H}_4)\text{: m.p. }181\text{-}182^\circ\text{C}\text{; }^{1}\text{H}\ \text{NMR: }\delta\ 1.18\ (3\text{H, t}, J=6\ \text{Hz, CH}_3), 2.70\ (2\text{H, m}, J=6\ \text{Hz, CH}_2), 4.28\ (2\text{H, s, CH}_2), 5.22\ (1\text{H, br s, NH}), 7.27\text{-}7.68\ (7\text{H, m, ArH}), 8.07\text{-}8.17\ (1\text{H, m, ArH})\text{; IR: }\nu_{\text{max}}\ 3452,\ 2982,\ 2877,\ 1664,\ 1530,\ 1455,\ 740\ \text{cm}^{-1}\text{; MS}\ m/z\ (\%)\ 281\ (\text{M}^++1,\ 3),\ 280\ (\text{M}^+,\ 11),\ 133\ (5),\ 132\ (56),\ 106\ (3),\ 105\ (34),\ 104\ (39),\ 77\ (100).\ \text{Anal. calcd for }C_{16}\text{H}_{16}\text{N}_4\text{O: C}\ 68.57,\ \text{H}\ 5.71,\ \text{N}\ 20.00\text{;}\ found\ C\ 68.51,\ \text{H}\ 5.75,\ \text{N}\ 19.95\%. \end{array}$

3h (R = 2,6-i-Pr₂C₆H₃): m.p. 202 C; ¹H NMR: δ 0.90 (12H, d, *J* = 6.8 Hz, 4 × CH₃), 2.56 (2H, m, *J* = 6.8 Hz, CH), 4.24 (2H, s, CH₂), 5.49 (1H, br s, NH), 6.95–7.61 (6H, m, ArH), 8.01–8.12 (1H, m, ArH); IR: v_{max} 3408, 3035, 2961, 2867, 1665, 1533, 1457, 746 cm⁻¹; MS *m*/*z* (%) 337 (M⁺+1, 1), 336 (M⁺, 1), 204 (25), 133 (53), 132 (13), 106 (36), 105 (22), 104 (48), 77 (100). Anal. calcd for C₂₀H₂₄N₄O: C 71.43, H 7.14, N 16.67; found C 71.40, H 7.10, N 16.65%.

5: m.p. 266°C; ¹H NMR: δ 3.88 (2H, s, CH₂), 4.94 (4H, s, 2 × CH₂), 5.50 (2H, br s, NH), 7.19–7.76 (14H, m, ArH), 7.96–8.12 (2H, m, ArH); IR: ν_{max} 3455, 2992, 2896, 1664, 1550, 1116, 751 cm⁻¹; MS *m*/*z* (%) 516 (M⁺, 3), 253 (2), 252 (13), 251 (3), 133 (7), 132 (40), 106 (12), 105 (33), 104 (58), 77 (100). Anal. calcd for C₂₉H₂₄N₈O₂: C 67.44, H 4.65, N 21.71; found C 67.47, H 4.69, N 21.69%

We are grateful to the Natural Science Foundation of Zhejiang province (Project No.201062) and the Center of Engineering Research of Zhejiang University of Technology for financial help.

Received 29 January 2002; accepted 9 June 2002 Paper 02/1223

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