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Lewis-acid mediated acetamidation of *N*-protected bromomethylindoles

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A facile $ZnBr_2$-mediated acetamidation of various types of *N*-protected 2/3-bromomethylindoles is reported. Upon interaction of bromomethylindoles with acetonitrile in the presence of anhydrous $ZnBr_2$ at reflux followed by aqueous work up led to the isolation of respective acetamidomethylindoles in good yields.

Keywords: Bromomethylindole, Lewis acid, acetamidation, aminomethylindoles

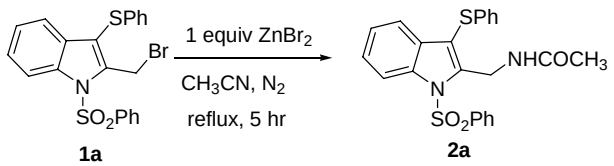
During the past fifty years, a plethora of substituted indole derivatives have been synthesized due to their undisputable importance in nature where this particular heterocycle is embedded in countless number of natural products and medicinally important compounds[1]. The fact that *N*-protected 2/3-methylindole can be easily allylic brominated using NBS led to the syntheses of a wide variety of hitherto inaccessible indole derivatives[2]. In particular, synthetic utility of bromomethylindoles has been well exploited to the syntheses of different types of indole based natural products[3].

Results and Discussion

In continuation of our work on studies related to the synthetic elaboration of bromomethylindoles[4] we required different types of 2-acetamidomethylindoles towards the synthesis of medicinally important β-carboline alkaloids *via* non-tryptamine pathways[5]. In this regard, a survey of literature indicated that Kacan and McKillop reported a simple preparation of *N*-benzylacetamide *via* interaction of benzyl chlorides with acetonitrile using $FeCl_3.6H_2O$ as catalyst[6]. Subsequently, Karabulut and Kacan extended the methodology to the synthesis of different types of *N*-benzylamides *via* interaction of benzyl methyl ether with alkyl/aryl nitrile[7]. Recently, acetamidation at benzylic positions were performed using I_2 (Ref. 8), H_2SO_4 (Ref. 9), $Bi(OTf)_3$ (Ref. 10), $ZrOCl_2$ (Ref. 11) as well as $Ce(SO_4)_2$ (Ref. 12). Nevertheless, these recent developments are yet to be applied for indolylmethylbromides. It should be noted that once different types of 2/3-acetamidomethylindoles are easily accessible its further transformation into the required β/γ-carbolines could be achieved *via* alkylation followed by cyclization. Very recently, Lewis acid-mediated arylation and annulation reactions of *N*-protected bromomethylindoles have been reported from our lab[13].

As a representative case, reaction of bromo compound **1a** with acetonitrile in the presence of 1 eq. of anhydrous $ZnBr_2$ at reflux followed by work-up and crystallization furnished required acetamidomethyl indole **2a** in 81% of yield (**Scheme I**).

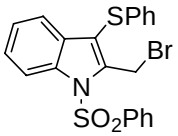
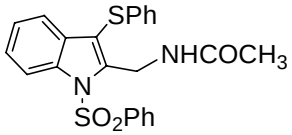
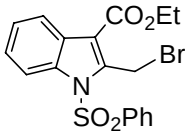
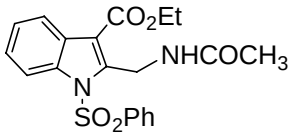
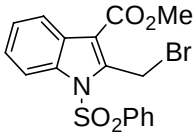
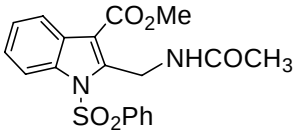
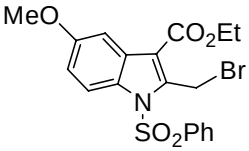
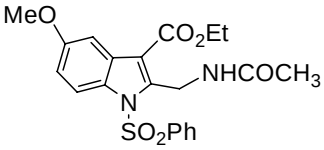
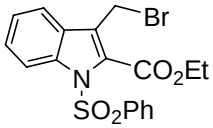
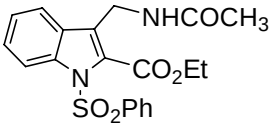
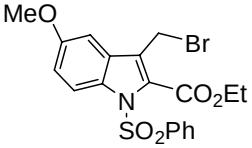
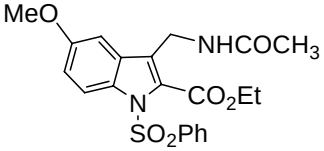
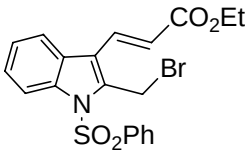
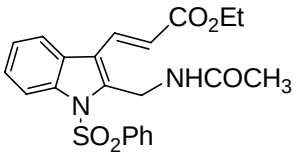
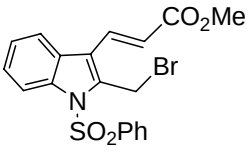
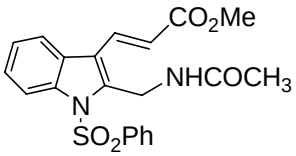
The one-pot acetamidation reaction was tested with different types of bromomethyl compounds **1a-o** and the results obtained are presented in **Table I**. The acetamidation reactions could be successfully performed with bromomethylindoles **1b-f** containing ester unit at 2/3-position (entries 2-6). As expected, 3-bromomethylindoles **1e-f** containing electron withdrawing ester group afforded better yield of acetamidomethylindoles **2e-f** than the respective 2-bromomethylindoles **1b-d**. The presence of electron releasing 5-methoxy group has slightly enhanced yields of acetamidation products in 2-bromomethylindole **1d** as well as 3-bromomethylindole **1f**. The acetamidation of 3-vinyl ester tethered



1a **2a**

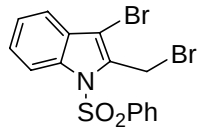
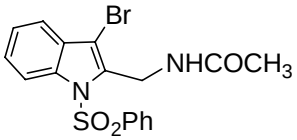
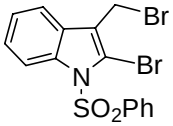
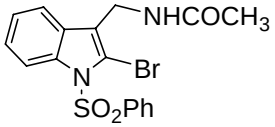
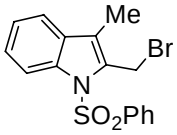
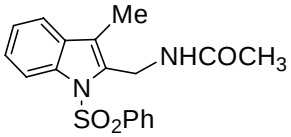
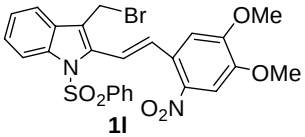
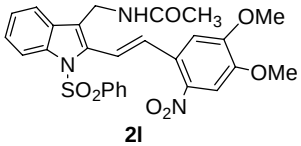
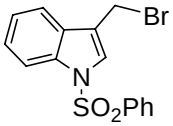
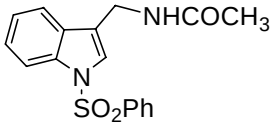
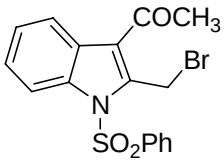
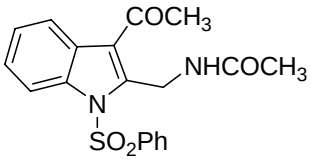
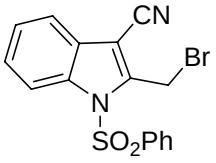
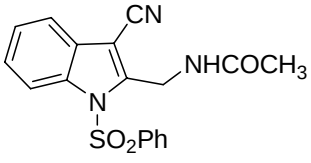
Scheme I

Table I — $ZnBr_2$ catalyzed acetamidation of bromomethylindoles **1a-o** with acetonitrile

Bromomethylindoles	Amide products	Time (h)	Yield (%)
 **1a**	 **2a**	5	81
 **1b**	 **2b**	12	57
 **1c**	 **2c**	11	60
 **1d**	 **2d**	7	71
 **1e**	 **2e**	8	68
 **1f**	 **2f**	6	73
 **1g**	 **2g**	8	77
 **1h**	 **2h**	7	79

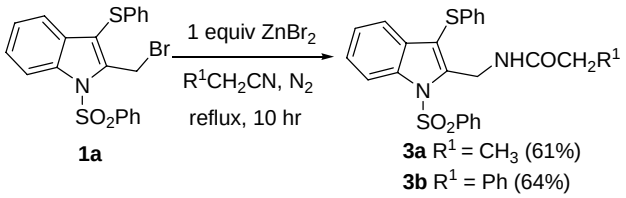
—Contd

Table I — $ZnBr_2$ catalyzed acetamidation of bromomethylindoles **1a-o** with acetonitrile**—***Contd*

Bromomethylindoles	Amide products	Time (h)	Yield (%)
 **1i**	 **2i**	10	72
 **1j**	 **2j**	9	74
 **1k**	 **2k**	7	74
 **1l**	 **2l**	6	65
 **1m**	 **2m**	8	72
 **1n**	 **2n**	20	0
 **1o**	 **2o**	18	0

2-bromomethylindoles **1g** and **1h** were achieved in 77% and 79% yields, respectively. Reaction of 2-bromomethylindoles containing functionalities such as Br, Me and arylvinyl units also led to the isolation of respective acetamidomethylindoles (entries 9-13). Surprisingly, the acetamidation reaction of 2-bromomethylindoles **1n** or **1o** containing electron withdrawing ketone or cyanide function failed to produce the expected aceatmidomethylindoles even after prolonged reaction period, only the respective starting bromo compounds were recovered unchanged (entries 14-15).

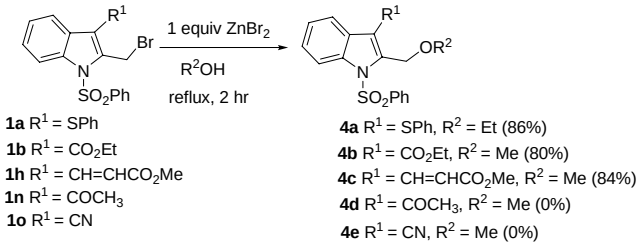
The $ZnBr_2$-mediated acetamidation reaction was found to be successful with propionitrile as well as



Scheme II

Table II — Lewis acid catalyzed acetamidation of **1a** with acetonitrile

Entry	Lewis acid	Time (h)	Yield of **2a** (%)
1	20 mol% $InBr_3$	4	86
2	1eq. $ZnBr_2$	5	81
3	1eq. $CuCl_2$	12	0
4	1eq. $FeCl_3$	14	70
5	1eq. $NiBr_2$	18	0
6	1eq. $Sc(OTf)_3$	16	0



Scheme III

benzylnitrile to afford the respective products **3a**/**3b** in slightly diminished yields (**Scheme II**).

The acetamidation reaction was then tested different types of Lewis acid using bromo compound **1a** and the results obtained are presented in **Table II**. The expected product **2a** was obtained in excellent yield using 20 mole% of expensive indium bromide. The acetamidation reaction required longer reaction time with anhydrous $FeCl_3$. Use of other Lewis acids such as $CuCl_2$, $NiBr_2$ and $Sc(OTf)_3$ for acetamidation of bromomethylindole **1a** was found to be unsuccessful.

Finally, a smooth $ZnBr_2$-mediated etherification of bromomethylindoles **1a-b** and **1h** could be achieved in methanol at reflux to furnish the respective products **4a-c** (**Scheme III**). It should be noted that the reaction of bromomethylindoles with methanol using K_2CO_3 as a base always led to the formation of the respective ether along with cleavage of the 1-phenylsulfonyl unit. Similar to the aceamidation reaction, etherification was also failed with 2-bromomethylindoles containing ketone or cyanide function at the indole-3-position.

Experimental Section

All melting points were uncorrected. Reagents were purchased from commercial sources and used as received without purification. Solvents were dried by standard procedures. Column chromatography was carried on silica gel (grade 60, mesh size 230-400, Merck). IR spectra were recorded on a Shimadzu FT-IR 8300 instrument. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as an internal standard on a JEOL GSX 400 and Bruker-300 spectrometers. Chemical shift values were quoted in ppm and coupling constants were quoted in Hz. Chemical shift multiplicities were reported as s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Mass spectra were recorded on a JEOL DX 303 HF spectrometer. Elemental analyses were carried out on a Perkin-Elmer series II 2400 (IIT Madras) equipment.

General procedure for acetamidation of bromomethylindole 1a-ousing $ZnBr_2$

To a solution of substrate **1a** (1.09 mmole) in dry acetonitrile (20 mL), $ZnBr_2$ (1.11 mmole), was added. The reaction-mixture was then refluxed for 5 hr under N_2 atmosphere. It was then poured over ice-water (30 mL) containing 1 mL of Conc..HCl, extracted with $CHCl_3$ (3 × 10 mL) and dried (Na_2SO_4). Removal of solvent followed by crystallization from methanol afforded amide **2a-o**.

Synthesis of indolyldimethylether

To a solution of substrate **1b** (1.18 mmole) in dry methanol (20 mL), $ZnBr_2$ (1.19 mmole), was added. The reaction-mixture was then refluxed for 2 hr under N_2 atmosphere. It was then poured over ice-water (30 mL) containing 1 mL of Conc.HCl, extracted with $CHCl_3$ (3 × 10 mL) and dried (Na_2SO_4). Removal of solvent followed by column chromatographic purification (silica gel, EtOAc-hexane 90:10) afforded product **4a-c**.

1-Phenylsulfonyl-*N*-((3-(phenylthio)-1*H*-indol-2-yl)methyl)acetamide, 2a. Yield: (0.38 g, 81%); colourless solid; m.p. 150°C; IR (KBr): 3417, 1674, 1361, 1174 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.20 (d, *J* = 8.4 Hz, 1 H), 7.76 (d, *J* = 7.5 Hz, 2 H), 7.60 (t, *J* = 7.5 Hz, 1 H), 7.48-7.35 (m, 4 H), 7.23 (t, *J* = 7.5 Hz, 1 H), 7.12-7.07 (m, 3 H), 6.99-6.96 (m, 2 H), 6.41 (t, *J* = 5.4 Hz, 1 H), 5.01 (d, *J* = 6.0 Hz, 2 H), 1.89 (s,

3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 169.4, 140.6, 138.1, 136.7, 136.0, 134.4, 130.4, 129.6, 128.9, 127.2, 126.2, 126.1, 125.7, 124.5, 120.8, 115.3, 115.0, 35.4, 23.1; MS (EI): *m/z* (%) 436 (M^+, 69%); Anal. Calcd for $C_{23}H_{20}N_2O_3S_2$: C, 63.28; H, 4.62; N, 6.42; S, 14.69. Found: C, 63.53; H, 4.77; N, 6.18; S, 14.97%.

Ethyl-1-phenylsulfonyl-2-(acetamidomethyl)-1*H*-indole-3-carboxylate, 2b. Yield: (0.27 g, 57%); colourless solid; m.p. 202°C; IR (KBr): 3257, 1705, 1647, 1370, 1180 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16 (d, *J* = 8.1 Hz, 1 H), 8.06 (d, *J* = 7.8 Hz, 1 H), 7.88 (d, *J* = 8.1 Hz, 2 H), 7.70-7.62 (m, 2 H), 7.52 (t, *J* = 7.8 Hz, 1 H), 7.39-7.31 (m, 2 H), 5.15 (d, *J* = 4.5 Hz, 2 H), 4.39 (q, *J* = 7.2 Hz, 2 H), 3.27 (s, 1 H), 1.86 (s, 3 H), 1.41 (t, *J* = 6.9 Hz, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 169.4, 163.2, 141.9, 137.5, 135.1, 134.6, 129.5, 126.4, 126.2, 125.5, 124.3, 121.7, 114.2, 114.1, 60.4, 34.4, 22.1, 13.9; MS (EI): *m/z* (%) 400 (M^+, 43%); Anal. Calcd for $C_{20}H_{20}N_2O_5S$: C, 59.99; H, 5.03; N, 7.00; S, 8.01. Found: C, 59.79; H, 5.33; N, 7.25; S, 8.21%.

Methyl-1-phenylsulfonyl-2-(acetamidomethyl)-1*H*-indole-3-carboxylate, 2c. Yield: (0.28 g, 60%); colourless solid; m.p. 180°C; R_f (40% EtOAc-hexane) 0.44; IR (KBr): 3264, 1711, 1650, 1375, 1176 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8.1 Hz, 1 H), 7.97 (d, *J* = 8.4 Hz, 1 H), 7.75 (d, *J* = 7.8 Hz, 2 H), 7.50 (t, *J* = 7.8 Hz, 1 H), 7.38 (t, *J* = 7.8 Hz, 2 H), 7.33-7.22 (m, 2 H), 6.56 (s, 1 H), 5.15 (d, *J* = 5.7 Hz, 2 H), 3.89 (s, 3 H), 1.88 (s, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 170.1, 164.6, 141.8, 138.3, 135.9, 134.6, 129.7, 126.8, 126.4, 126.0, 124.8, 122.4, 114.8, 114.4, 52.0, 34.9, 23.0; MS (EI): *m/z* (%) 386 (M^+, 65%); Anal. Calcd for $C_{19}H_{18}N_2O_5S$: C, 59.06; H, 4.70; N, 7.25; S, 8.30. Found: C, 59.23; H, 4.90; N, 7.04; S, 8.56%.

Ethyl-1-phenylsulfonyl-2-(acetamidomethyl)-5-methoxy-1*H*-indole-3-carboxylate, 2d Yield: (0.34 g, 71%); colourless solid; m.p. 142-44°C; IR (KBr): 3264, 1712, 1645, 1362, 1186 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.08 (d, *J* = 9.3 Hz, 1 H), 7.80 (d, *J* = 7.8 Hz, 2 H), 7.56 (t, *J* = 7.8 Hz, 2 H), 7.46 (t, *J* = 7.8 Hz, 2 H), 6.99 (dd, *J* = 2.4 Hz, *J* = 9.3 Hz, 1 H), 6.43 (s, 1 H), 5.20 (d, *J* = 5.7 Hz, 2 H), 4.45 (q, *J* = 6.9 Hz, 2 H), 3.85 (s, 3 H), 1.94 (s, 3 H), 1.45 (t, *J* = 6.9 Hz, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 169.5, 164.2, 157.2, 142.4, 138.3, 134.5, 130.5, 129.6, 128.2, 126.4, 115.4, 115.2, 114.7, 104.3, 61.1, 55.6, 34.8, 23.2, 14.3; MS (EI): *m/z* (%) 430 (M^+, 54%); Anal. Calcd for $C_{21}H_{22}N_2O_6S$: C, 58.59; H, 5.15; N, 6.51; S, 7.45. Found: C, 58.79; H, 5.25; N, 6.28; S, 7.68%.

Ethyl-1-phenylsulfonyl-3-(acetamidomethyl)-1*H*-indole-2-carboxylate, 2e. Yield: (0.32 g, 68%); colourless solid; m.p.122 °C; IR (KBr): 3260, 1730, 1643, 1367, 1184 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (d, *J* = 8.4 Hz, 1 H), 7.85 (d, *J* = 7.5 Hz, 2 H), 7.63 (d, *J* = 7.8 Hz, 1 H), 7.47 (t, *J* = 6.9 Hz, 1 H), 7.39-7.31 (m, 3 H), 7.23-7.18 (m, 1 H), 6.03 (s, 1 H), 4.49 (d, *J* = 5.7 Hz, 2 H), 4.37 (q, *J* = 6.9 Hz, 2 H), 1.86 (s, 3 H), 1.30 (t, *J* = 6.9 Hz, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 169.8, 162.1, 138.0, 136.9, 133.9, 129.7, 129.0, 128.4, 127.3, 127.1, 125.5, 124.5, 121.3, 115.1, 62.6, 32.8, 23.1, 14.1; MS (EI): *m/z* (%) 400 (M^+, 49%); Anal. Calcd for $C_{20}H_{20}N_2O_5S$: C, 59.99; H, 5.03; N, 7.00; S, 8.01. Found: 59.77; H, 5.30; N, 7.29; S, 8.23%.

Ethyl-1-phenylsulfonyl-3-(acetamidomethyl)-5-methoxy-1*H*-indole-2-carboxylate, 2f. Yield: (0.35 g, 73%); colourless solid; m.p. 98-100°C; IR (KBr): 3273, 1721, 1657, 1370, 1179 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.81-7.76 (m, 3 H), 7.45-7.07 (m, 4 H), 6.92 (d, *J* = 8.7 Hz, 1 H), 6.04 (s, 1 H), 4.45 (d, *J* = 5.7 Hz, 2 H), 4.37 (q, *J* = 6.9 Hz, 2 H), 3.72 (s, 3 H), 1.86 (s, 3 H), 1.30 (t, *J* = 6.9 Hz, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 169.9, 162.2, 157.2, 137.6, 133.9, 131.5, 130.3, 129.6, 128.9, 127.0, 126.3, 117.2, 116.3, 102.8, 62.6, 55.8, 32.9, 23.2, 14.1; MS (EI): *m/z* (%) 430 (M^+, 64%); Anal. Calcd for $C_{21}H_{22}N_2O_6S$: C, 58.59; H, 5.15; N, 6.51; S, 7.45. Found: C, 58.39; H, 5.23; N, 6.26; S, 7.67%.

(E)-Ethyl-1-phenylsulfonyl-3-(2-(acetamidomethyl)-1*H*-indol-3-yl)acrylate, 2g. Yield: (0.36 g, 77%); colourless solid; m.p. 174°C; IR (KBr): 3334, 1678, 1627, 1373, 1183 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.24 (d, *J* = 16.2 Hz, 1 H), 8.17 (d, *J* = 8.4 Hz, 1 H), 7.80 (d, *J* = 7.5 Hz, 1 H), 7.74 (d, *J* = 7.8 Hz, 2 H), 7.57 (t, *J* = 7.5 Hz, 1 H), 7.47-7.29 (m, 4 H), 6.60 (s, 1 H), 6.57 (d, *J* = 16.2 Hz, 1 H), 4.85 (d, *J* = 6.0 Hz, 2 H), 4.27 (q, *J* = 7.2 Hz, 2 H), 1.97 (s, 3 H), 1.33 (t, *J* = 6.9 Hz, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 170.0, 166.9, 138.3, 137.5, 136.6, 135.1, 134.4, 129.7, 127.3, 126.1, 125.9, 124.7, 121.3, 120.9, 118.7, 114.8, 60.6, 34.4, 23.1, 14.3; MS (EI): *m/z* (%) 426 (M^+, 39%); Anal. Calcd for $C_{22}H_{22}N_2O_5S$: C, 61.96; H, 5.20; N, 6.57; S, 7.52. Found: C, 61.70; H, 5.41; N, 6.69; S, 7.30%.

(E)-Methyl-1-phenylsulfonyl-3-(2-(acetamidomethyl)-1*H*-indol-3-yl)acrylate, 2h. Yield: (0.37 g, 79%); colourless solid; m.p. 156°C; IR (KBr): 3264, 1711, 1650, 1375, 1176 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.26 (d, *J* = 16.2 Hz, 1 H), 8.18 (d, *J* = 7.8 Hz, 1 H), 7.81 (d, *J* = 7.8 Hz, 1 H), 7.75 (d, *J* = 8.1

Hz, 2 H), 7.59 (t, *J* = 7.2 Hz, 1 H), 7.48-7.27 (m, 4 H), 6.59 (s, 1 H), 6.59 (d, *J* = 16.2 Hz, 1 H), 4.85 (d, *J* = 6.0 Hz, 2 H), 3.83 (s, 3 H), 1.99 (s, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 169.9, 167.2, 138.3, 137.5, 136.6, 135.3, 134.4, 129.7, 127.2, 126.1, 126.0, 124.8, 120.9, 118.7, 114.8, 51.8, 34.4, 23.1; MS (EI): *m*/*z* (%) 412 (M^+, 51%); Anal. Calcd for $C_{21}H_{20}N_2O_5S$: C, 61.15; H, 4.89; N, 6.79; S, 7.77. Found: C, 61.35; H, 4.65; N, 6.98; S, 7.59%.

1-Phenylsulfonyl-*N*-((3-bromo-1*H*-indol-2-yl)methyl)acetamide, **2i**. Yield: (0.34 g, 72%); colourless solid; m.p. 149-51°C; IR (KBr): 3262, 1644, 1371, 1178 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06 (d, *J* = 8.1 Hz, 1 H), 7.64 (d, *J* = 7.8 Hz, 2 H), 7.47-7.18 (m, 6 H), 6.35 (s, 1 H), 4.77 (d, *J* = 5.7 Hz, 2 H), 1.88 (s, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.2, 138.1, 137.3, 134.4, 129.4, 127.2, 127.1, 125.6, 124.5, 121.2, 119.3, 115.2, 110.8, 34.9, 22.8; MS (EI): *m*/*z* (%) 408 (M^++2, 44%), 406 (M^+, 44%); Anal. Calcd for $C_{17}H_{15}BrN_2O_3S$: C, 50.13; H, 3.71; N, 6.88; S, 7.87. Found: C, 50.34; H, 3.91; N, 6.68; S, 7.59%.

1-Phenylsulfonyl-*N*-((2-bromo-1*H*-indol-3-yl)methyl)acetamide, **2j**. Yield: (0.35 g, 74%); colourless solid; m.p. 137-39°C; IR (KBr): 3275, 1638, 1377, 1182, cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.28 (d, *J* = 8.1 Hz, 1 H), 7.91 (d, *J* = 7.8 Hz, 2 H), 7.59 (t, *J* = 7.5 Hz, 2 H), 7.49-7.28 (m, 4 H), 5.79 (s, 1 H), 4.53 (d, *J* = 4.8 Hz, 2 H), 1.98 (s, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.3, 138.1, 137.2, 134.4, 129.4, 127.1, 127.0, 125.6, 124.4, 121.1, 119.3, 115.1, 110.8, 34.8, 22.9; MS (EI): *m*/*z* (%) 408 (M^++2, 56%), 406 (M^+, 56%); Anal. Calcd for $C_{17}H_{15}BrN_2O_3S$: C, 50.13; H, 3.71; N, 6.88; S, 7.87. Found: C, 50.36; H, 3.90; N, 6.63; S, 7.99%.

1-Phenylsulfonyl-*N*-((3-methyl-1*H*-indol-2-yl)methyl)acetamide, **2k**. Yield: (0.35 g, 74%); colourless solid; m.p. 106-08°C; IR (KBr): 3265, 1666, 1362, 1178 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.1 Hz, 1 H), 7.70 (d, *J* = 7.5 Hz, 2 H), 7.54-7.36 (m, 2 H), 7.35-7.23 (m, 4 H), 6.60 (s, 1 H), 4.72 (d, *J* = 6.3 Hz, 2 H), 2.36 (s, 3 H), 1.97 (s, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 169.6, 138.6, 136.5, 133.7, 131.6, 130.2, 129.1, 126.8, 126.0, 123.7, 121.9, 119.5, 114.9, 34.3, 23.2, 8.9; MS (EI): *m*/*z* (%) 342 (M^+, 70%); Anal. Calcd for $C_{18}H_{18}N_2O_3S$: C, 63.14; H, 5.30; N, 8.18; S, 9.36. Found: C, 63.38; H, 5.10; N, 8.46; S, 9.46%.

1-Phenylsulfonyl-*N*-((2-(4,5-dimethoxy-2-nitrostyry)-1*H*-indol-3-yl)methyl)acetamide, **2l**. Yield: (0.31 g, 65%); yellow solid; m.p. 148°C; IR (KBr): 3268, 1666, 1517, 1363, 1329, 1178 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.08 (d, *J* = 8.4 Hz, 1 H), 7.67 (d, *J* = 7.5 Hz, 2 H), 7.61 (s, 1 H), 7.56 (d, *J* = 7.8 Hz, 1 H), 7.42-7.38 (m, 2 H), 7.33-7.19 (m, 6 H), 5.83 (s, 1 H), 4.54 (d, *J* = 5.1 Hz, 2 H), 4.0 (s, 3 H), 3.92 (s, 3 H), 1.87 (s, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 170.0, 153.8, 149.0, 140.1, 137.8, 136.2, 136.1, 134.0, 131.8, 130.0, 129.2, 127.8, 126.8, 125.8, 124.4, 122.2, 120.2, 120.1, 114.9, 110.2, 107.9, 56.6, 56.5, 34.1, 23.2; MS (EI): *m*/*z* (%) 535 (M^+, 35%); Anal. Calcd for $C_{27}H_{25}N_3O_7S$: C, 60.55; H, 4.71; N, 7.85; S, 5.99. Found: C, 60.40; H, 4.90; N, 7.99; S, 5.79%.

1-Phenylsulfonyl-*N*-((1*H*-indol-3-yl)methyl)acetamide, **2m**. Yield: (0.34 g, 72%); colourless solid; m.p. 80-82°C; IR (KBr): 3310, 1662, 1365, 1177 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.22 (s, 1 H), 7.96 (d, *J* = 8.1 Hz, 1 H), 7.86 (d, *J* = 7.8 Hz, 1 H), 7.54-7.49 (m, 3 H), 7.41 (t, *J* = 7.8 Hz, 2 H), 7.32 (t, *J* = 7.2 Hz, 1 H), 7.24 (d, *J* = 8.4 Hz, 1 H), 5.96 (s, 1 H), 4.50 (d, *J* = 5.4 Hz, 2 H), 1.96 (s, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 170.1, 138.1, 135.3, 133.9, 129.7, 129.4, 127.2, 126.8, 125.2, 124.1, 123.5, 119.8, 113.6, 34.5, 23.2; MS (EI): *m*/*z* (%) 328 (M^+, 67%); Anal. Calcd for$C_{17}H_{16}N_2O_3S$: C, 62.18; H, 4.91; N, 8.53; S, 9.76. Found: C, 62.01; H, 4.70; N, 8.78; S, 9.98%.

1-Phenylsulfonyl-*N*-((3-(phenylthio)-1*H*-indol-2-yl)methyl)propionamide, **3a**. Yield: (0.30 g, 61%); colorless solid; m.p. 136°C; IR (KBr): 3315, 1655, 1375, 1186 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.18 (d, *J* = 8.4 Hz, 1 H), 7.74 (d, *J* = 7.8 Hz, 2 H), 7.58 (t, *J* = 7.2 Hz, 1 H), 7.44 (t, *J* = 8.1 Hz, 3 H), 7.36 (t, *J* = 7.2 Hz, 1 H), 7.26-7.19 (m, 1 H), 7.10-7.05 (m, 3 H), 6.97-6.94 (m, 2 H), 6.34 (t, *J* = 5.4 Hz, 1 H), 5.00 (d, *J* = 6.0 Hz, 2 H), 2.12 (q, *J* = 7.8 Hz, 2 H), 1.07 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 173.1, 140.7, 138.1, 136.7, 136.1, 134.4, 130.4, 129.6, 128.8, 127.2, 126.2, 126.1, 125.7, 124.6, 120.8, 115.3, 115.0, 35.3, 29.5, 9.6; MS (EI): *m*/*z* (%) 450 (M^+, 50%); Anal. Calcd for $C_{24}H_{22}N_2O_3S_2$: C, 63.98; H, 4.92; N, 6.22; S, 14.23. Found: C, 63.78; H, 4.81; N, 6.45; S, 14.05%.

1-Phenylsulfonyl-2-phenyl-*N*-((3-(phenylthio)-1*H*-indol-2-yl)methyl)acetamide, **3b**. Yield: (0.36 g, 64%); Thick liquid; IR (KBr): 3271, 1637, 1373, 1178 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 (d, *J* = 8.4 Hz, 1 H), 7.68 (d, *J* = 7.5 Hz, 2 H), 7.55 (t, *J* = 7.2 Hz, 1 H), 7.42-7.36 (m, 4 H), 7.33-7.25 (m, 3 H), 7.21-7.16 (m, 3 H), 7.09-7.05 (m, 3 H), 6.95-6.92 (m, 2 H), 6.43 (t, *J* = 6.0 Hz, 1 H), 4.96 (d, *J* = 6.0 Hz, 2 H), 3.48 (s, 2 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 170.4, 140.4, 138.0, 136.7, 136.0, 134.6, 134.3, 130.4, 129.5,

129.4, 128.9, 128.8, 127.3, 127.2, 126.2, 126.1, 125.7, 124.6, 120.8, 115.3, 115.0, 43.7, 35.6; MS (EI): *m*/*z* (%) 512 (M^+, 59%); Anal. Calcd for $C_{29}H_{24}N_2O_3S_2$: C, 67.94 H, 4.72; N, 5.46; S, 12.51. Found: C, 67.75; H, 4.52; N, 5.65; S, 12.77%.

1-Phenylsulfonyl-2-(ethoxymethyl)-3-(phenylthio)-1*H*-indole, **4a**. Yield: (0.39 g, 85%); Thick liquid; IR (KBr): 1373, 1178 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.18 (d, *J* = 8.4 Hz, 1 H), 8.10 (d, *J* = 7.5 Hz, 2 H), 7.52-7.31 (m, 5 H), 7.21-7.02 (m, 6 H), 5.11 (s, 2 H), 3.52 (q, *J* = 6.9 Hz, 2 H), 1.11 (t, *J* = 6.9 Hz, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 141.2, 138.9, 136.6, 136.2, 133.9, 129.8, 129.0, 127.4, 126.9, 126.1, 125.7, 124.1, 120.6, 114.8, 114.2, 65.9, 62.0, 15.1; MS (EI): *m*/*z* (%) 423 (M^+, 52%); Anal. Calcd for $C_{23}H_{21}NO_3S_2$: C, 65.22; H, 5.00; N, 3.31; S, 15.14. Found: C, 65.01; H, 5.27; N, 3.54; S, 15.42%.

Ethyl-1-phenylsulfonyl-2-(methoxymethyl)-1*H*-indole-3-carboxylate, 4b. Yield: (0.35 g, 80%); colourless solid; m.p. 106°C; IR (KBr): 1706, 1379, 1184 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.19-8.00 (m, 4 H), 7.56-7.29 (m, 5 H), 5.33 (s, 2 H), 4.43 (q, *J* = 6.9 Hz, 2 H), 3.38 (s, 3 H), 1.45 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 164.2, 142.4, 138.9, 135.9, 134.0, 129.4, 129.0, 127.2, 126.7, 125.8, 124.4, 122.5, 114.5, 62.8, 60.9, 57.9, 14.4; MS (EI): *m*/*z* (%) 373 (M^+, 76%); Anal. Calcd for $C_{19}H_{19}NO_5S$: C, 61.11; H, 5.13; N, 3.75; S, 8.59. Found: C, 61.39; H, 5.41; N, 3.98; S, 8.37%.

(E)-Methyl-1-phenylsulfonyl-3-(2-(methoxymethyl)-1*H*-indol-3-yl)acrylate, 4c. Yield: (0.37 g, 84%); colourless solid; m.p. 130-32°C; IR (KBr): 1719, 1372, 1175 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.21 (d, *J* = 8.1 Hz, 1 H), 8.02 (d, *J* = 7.8 Hz, 2 H), 7.93 (d, *J* = 16.2 Hz, 1 H), 7.80 (d, *J* = 7.5 Hz, 1 H), 7.52 (d, *J* = 7.2 Hz, 1 H), 7.45-7.27 (m, 4 H), 6.58 (d, *J* = 16.2 Hz, 1 H), 4.96 (s, 2 H), 3.83 (s, 3 H), 3.43 (s, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 167.4, 138.6, 137.5, 136.6, 134.9, 133.9, 129.1, 127.1, 126.9, 126.0, 124.3, 120.5, 119.4, 115.0, 63.2, 58.1, 51.8; MS (EI): *m*/*z* (%) 385 (M^+, 62%); Anal. Calcd for $C_{20}H_{19}NO_5S$: C, 62.32; H, 4.97; N, 3.63; S, 8.32. Found: C, 62.07; H, 4.79; N, 3.90; S, 8.58%.

Conclusion

In conclusion, we have synthesized wide variety of *N*-phenylsulfonyl-2/3-acetamidomethylindoles *via* interaction of bromomethylindoles with acetonitrile using $ZnBr_2$ as catalyst. Using similar conditions, etherification of representative bromomethylindoles were also achieved. The $ZnBr_2$-mediated one-pot acetamidation procedure developed herein is simple, clean and economically viable for the synthesis of various types of 2/3-aminomethylindoles. Further work on transformation of these functionalized 2/3-acetamidomethylindoles into the respective β/γ-carbolines is in progress.

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