Supplementary material:

AN EFFICIENT SYNTHESIS OF N-SULPHONYL *β*-ARYLMETHYLALANINATES FROM SERINE *VIA* RING OPENING OF N-SULPHONYL AZIRIDINE-2 CARBOXYLATE

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EXPERIMENTAL

General Information

All reactions were conducted using oven-dried glassware under an atmosphere of nitrogen (N_2) or argon (Ar). All reagents used were of commercial grade and used without further purification. Solvents were dried and distilled following the usual protocols. Column chromatography was carried out using silica gel (100–200 mesh). TLC was performed on aluminium-backed plates coated with Silica Gel 60 with F-254 indicator. The ^{1}H NMR spectra were recorded with a 400 MHz and ^{13}C NMR spectra were recorded with a 100 MHz using $CDCl_3$. DMSO-d_6, ^{1}H NMR chemical shifts are expressed in parts per million (δ) relative to $CDCl_3$ (δ = 7.26) and DMSO-d_6 (δ = 2.49); ^{13}C NMR chemical shifts are expressed in parts per million (δ) relative to the $CDCl_3$ (δ =77.0). High resolution mass spectra (HRMS) were obtained under positive electron spray ionization (m/z values are given).Liquid chromatography Mass spectrometer (LC-MS) spectra were obtained under positive electron spray ionization (m/z values are given). Melting point of synthesized compound/s was uncorrected and determined by capillary method.

1. methyl 2-amino-3-hydroxypropanoate (2)

In inert atmosphere DL-Serine (9.59 mmol) was dissolved in methanol (2 mL / mmol) and cooled to < 0° C (salt/ice). Thionyl chloride (56.69 mmol, 5.9eq.) was added slowly by syringe, reaction mixture was refluxed for 3 h, TLC was monitored in BuOH: Acetic acid: Water (3:1:1) system and then concentrated, coevaporated with ether. Product obtained **(2)** was *white*

crystalline solid (90 % yield). mp 162-164º C. Product was confirmed by LC-MS (ESI) m/z: 120.1 (MH^+). Anal. calcd. for $C_4H_9NO_3$: C, 40.33; H, 7.62; N, 11.76; found: C, 40.29; H, 7.59; N, 11.73. HRMS (ESI) m/z: (MH^+) calcd. for $C_4H_9NO_3$: 120.0678; found: 120.0680.

2. methyl 3-hydroxy-2-(tritylamino)propanoate (3a)

Method A: methyl 2-amino-3-hydroxypropanoate **(2)** (1.29 mmol) was suspended in CH_2Cl_2 (2 mL/mmol) under N_2. At RT, TMSCl (4. 51 mmol, 3.5eq) was added via syringe, and the mixture was heated at reflux for 1h. The solution was allowed to cool to RT, and triethylamine (4.51 mmol, 3.5eq) in CH_2Cl_2 (0.8 mL) was added slowly, whereupon the mixture became difficult to stir. The mixture was then heated at reflux for 45 min. Upon cooling to 0º C, MeOH (.07 mL) in CH_2Cl_2 (0.33 mL) was added, followed by the addition of triethylamine (1.29 mmol, 1eq) and triphenylmethyl chloride (1.29 mmol,1eq) in 2 portions over 15 min. The reaction was allowed to stir overnight. MeOH (0.25mL) and triethylamine (0.18mL) were then added, and the mixture was stirred for an additional 15 min. All solvents were removed under vacuum, and the crude acid was dissolved in EtOAc (15 mL) and washed with a 5% citric acid solution (3 × 4 mL) and then with H_2O (3 × 4 mL). The organic layer was dried (Na_2SO_4), filtered, and concentrated. Purification was done as per method B.

Method B: methyl 2-amino-3-hydroxypropanoate **(2)** (1.29 mmol) was dissolved in chloroform (1.5mL/mmol), to this stirring triethylamine (16.13 mmol, 2.5eq.) was added in inert atmosphere. Reaction mixture was cooled 0º C & to this trityl chloride (1.29 mmol, 1eq.) was added. Reaction mixture was stirred 0°C to RT for 2 h. Reaction mixture was diluted with CH_2Cl_2 and washed with $NaHCO_3$ (2 times) and then with brine. Organic part was dried over sodium sulphate and evaporated under reduced pressure.TLC was monitored in 30% EA/Hex solution. Compound was visible in UV light and also ninhydrin active. Purification was done by column chromatography (silica G 100-200); product was eluted using 10 to 50 % EA/ Hex as mobile phase. Product isolated **(3a)** was *white crystalline solid* (86 % yield). Mp 74-78º C (lit [1] Mp 77-78ºC); ^{1}H NMR, 400 MHz in $CDCl_3$: 1H (t, *J*=7.4, δ=2.26), 1H (s, δ=2.97), 3H (s, δ=3.29), 2H (d, *J*=8.58, δ=3.54), 1H (m, δ=3.69), 3H (t, *J*=7.12, δ=7.18), 2H (dd, *J*=7.9, 4.4, δ=7.24), 4H (m, δ=7.27-7.19), 6H (m, δ=7.47-7.42). ^{13}C NMR, 100 MHz in $CDCl_3$ δ: 51.8(-*C*H_3), 61.6(-*C*-OH), 74.9(-*C*-NH_2), 75.5(-*C*-Ph_3), 126.2, 127.0, 129.2, 145.0(–*C*H $_{Aromatic}$), 171.2(-CO_2-). LC-MS (ESI) m/z: 362.2 (MH^+). Anal. calcd. for $C_{23}H_{23}NO_3$: C, 76.43; H, 6.41; N, 3.88; found: C, 76.40; H, 6.39; N, 3.85. HRMS (ESI) m/z: (MH^+) calcd. for $C_{23}H_{23}NO_3$: 362.1743; found: 362.1741.

3. methyl 2-((tert-butoxycarbonyl) amino)-3-hydroxypropanoate (3b)

methyl 2-amino-3-hydroxypropanoate **(2)** (3.22mmol) was reconstituted in CH_2Cl_2 and triethylamine (8.06 mmol, 2.5 eq) was added dropwise at 0ºC in presence of nitrogen, to this stirring solution di-tertbutyl dicarbonate (3.86mmol, 1.2eq.) was added in one portion. The reaction mixture was stirred until the starting material was consumed, as determined by TLC (1:1 EA/ Hex) & observed in Ninhydrin stain .The reaction mixture was concentrated and dissolved in EtOAc (15 mL) and then washed with saturated $NaHCO_3$ (aq) (3 mL) followed by brine. Organic part was dried over sodium sulphate and evaporated under reduced pressure. Purification was done by column chromatography (silica G 100-200); product was eluted using 10 to 30% EA/ Hex as mobile phase. Product isolated was *brown oil* (76 % yield). ^{1}H NMR, 400

MHz in $CDCl_3$: 9H(s, δ=1.44), 1H(s, δ=2.1) 3H(s, δ=3.78), 2H (d, *J*=6.664, δ=3.92), 1H (s, δ=4.38), 1H (s, δ=5.40). ^{13}C NMR, 100 MHz in $CDCl_3$ δ: 28.4 (-*C*H_{3Boc}), 51.8 (-*C*H_3), 59.6(-*C*-NH_2), 62.4 (-*C*-OH), 79.6 (-*C*-CH_{3Boc}), 156.0(-*C*O_{2Boc}), 171.4 (-*C*O_2-). LC-MS (ESI) m/z: 220.2 (MH^+). Anal. calcd. for $C_9H_{17}NO_5$: C, 49.31; H, 7.82; N, 6.39; found: C, 49.27; H, 7.77; N, 6.35. HRMS (ESI) m/z: (MH^+) calcd. for $C_9H_{17}NO_5$: 220.1146; found: 220.1143.

4. methyl 2-(((benzyloxy)carbonyl)amino)-3-hydroxypropanoate (3c)

Method A: methyl 2-amino-3-hydroxypropanoate **(2)** (19.04mmol) was dissolve in H_2O (34 mL). To this $NaHCO_3$ (59.02mmol, 3.1eq) was added. This mixture was cooled in ice bath to 0º C. To this at stirring, solution of benzylchloroformate (9.0mL, 50% sol in toluene) and ether (16 mL) was added and allowed to stir at 0^0 C for 3 h. Then allowed it to warm to RT and stirred for overnight. Reaction mixture was filtered and filtrate was washed with diethyl ether (2mL). Aqueous layer was acidified to pH ~3 with citric acid and extracted with EtOAc. Organic layer was dried over sodium sulphate. TLC was monitored in 30% EA/Hex and in BuOH: AA: H_2O (3:1:1).Product obtained as *white crystalline solid* (62 % yield).

Method B: methyl 2-amino-3-hydroxypropanoate **(2)** (19.04mmol) was dissolved in H_2O (34mL). To this MgO (59.02mmol, 3.1eq) and ether (16 mL) was added. This mixture was cooled in ice bath to 0º C. To this at stirring, solution of benzylchloroformate (9.0 mL, 50% sol in toluene) was added and allowed to stir at 0º C for 2 h. Then allowed it to warm to RT for an additional 30min. Reaction mixture was filtered and filtrate was washed with diethyl ether (2mL). Aqueous layer was acidified to pH ~3 with citric acid and extracted with EtOAc. Organic layer was dried over sodium sulphate. TLC was monitored in 30% EA/Hex and in BuOH: AA: H_2O (3:1:1).Product obtained as *white crystalline solid* (74 % yield). Mp 116-120º C (lit [2] Mp 118-120º C); ^1H NMR, 400 MHz in DMSO-d_6 : 1H (m, δ=3.31-3.25), 3H (s, δ=3.78), 2H (dd, *J*=10.6, 3.8, δ=4.22), 2H (d, *J*=4.35, δ=5.12), 3H (m, δ=7.28-7.23), 2H (m, δ=7.40-7.34). ^{13}C NMR, 100 MHz in DMSO-d_6; δ: 51.8 (-*C*H_3), 59.5(-*C*-NH_2), 62.3 (-*C*-OH), 66.7(-*C*H_2-O_{CBz}), 127.1, 127.6, 128.9, 136.1 (-*C*H $_{Aromatic\ CBz}$), 155.9 (-*C*$O_{2\ CBz}$), 171.4 (-*C*O_2-). LC-MS (ESI) m/z: 254.2 (MH^+). Anal. calcd. for $C_{12}H_{15}NO_5$: C, 56.91; H, 5.97; N, 5.53; found: C, 56.85; H, 5.93; N, 5.48.HRMS (ESI) m/z: (MH^+) calcd. for $C_{12}H_{15}NO_5$: 254.2378; found: 254.2375.

General procedure for cyclization of N-protected aziridines.

(3a) or (3b) or (3c) (8.3mmol) was stripped twice with dry dioxane. It was dissolved in dry toluene (18 mL/ mmol) then triethyl amine (24.9mmol, 3 eq.) was added in inert atmosphere. Temperature was cooled down to -50°C and sulfuryl chloride (9.96 mmol, 1.2 eq.) was added slowly drop wise. Reaction mixture was allowed to warm at RT slowly. pH of the reaction should be basic. Progress of reaction was monitored with TLC in 5% to 10% EA/ Hex. Reaction mixture was diluted with ethyl acetate and washed with brine twice. Organic part was dried over sodium sulphate and evaporated under reduced pressure. Compound was visible in UV light and also ninhydrin active. Purification was done by column chromatography (silica G 100-200) product was eluted using 1 to 10 % EA/ Hex as mobile phase.

5. methyl 1-tritylaziridine-2-carboxylate (4a)

Product isolated was *off white solid*, mp 130-132º C (lit [3]130-131º C), (88% yield). ^{1}H NMR 400 MHz in $CDCl_3$, 1H (d, *J*=6.24, δ=1.40), 1H (d, *J*=3.6, δ=1.87), 3H (s, δ=3.7), 4H (m, δ=7.09-7.03), 5H (m, δ=7.22-7.17), 6H (d, *J*=7.44, δ=7.48). ^{13}C NMR, 100 MHz in $CDCl_3$ δ: 22.2 (-*C*H_2 *Aziridine*), 37.3 (-*C*H *Aziridine*), 51.8 (-*C*H_3), 85.0 (-*C*-Ph_3), 126.2, 127.0, 129.2, 145.0 (-*C*H *Aromatic*), 171.2(-*C*O_2-). LC-MS (ESI) m/z: 344.1 (MH^+). Anal. calcd. for $C_{23}H_{21}NO_2$: C, 80.44; H, 6.16; N, 4.08; found: C, 80.37; H, 6.09; N, 4.17.HRMS (ESI) m/z: (MH^+) calcd. for $C_{23}H_{21}NO_2$: 344.1645; found: 344.1641.

6. 1-tert-butyl 2-methyl aziridine-1, 2-dicarboxylate (4b)

Product isolated was *brown oil* (78% yield). ^{1}H NMR, 400 MHz in $CDCl_3$: 9H (s, δ=1.42), 2H (d, *J*=8.794, δ=2.10), 1H (m, δ=3.32-3.27), 3H (s, δ=3.78). ^{13}C NMR, 100 MHz in DMSO δ: 28.3 (-*C*H_{3Boc}), 31.3 (-*C*H Aziridine), 37.2 (-*C*H_2 Aziridine), 51.8 (-*C*H_3), 79.8 (-*C*-CH_{3Boc}), 154.2 (-*C*O_2 *Boc*), 171.4 (-*C*O_2-). LC-MS (ESI) m/z: 202.2 (MH^+). Anal. calcd. for $C_9H_{15}NO_4$: C, 53.72; H, 7.51; N, 6.96; found: C, 53.79; H, 7.45; N, 6.88.HRMS (ESI) m/z: (MH^+) calcd. for $C_9H_{15}NO_4$: 202.1078; found: 202.1073.

7. 1-benzyl 2-methyl aziridine-1, 2-dicarboxylate (4c)

Product isolated was *yellow oil* (65 % yield). ^{1}H NMR 400 MHz in $CDCl_3$, 1H (m, δ=1.92-1.86), 1H (m, δ=2.14-2.09), 1H (t, *J*=4.318, δ=2.43), 3H (s, δ=3.72), 2H (m, δ=7.73-7.67), 1H (m, δ=7.81-7.86), 2H (d, *J*=4.673, δ=8.23). ^{13}C NMR, 100 MHz in $CDCl_3$ δ: 31.3 (-*C*H Aziridine), 37.2 (-*C*H_2 Aziridine), 51.8 (-*C*H_3), 67.3 (-*C*H_2-O_{CBz}), 127.1, 127.6, 128.9, 136.1 (-*C*H Aromatic CBz), 154.3 (-*C*O_2 CBz), 171.4 (-*C*O_2-). LC-MS (ESI) m/z: 236.2 (MH^+). Anal. calcd. for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.95; found: C, 61.29; H, 5.49; N, 5.90. HRMS (ESI) m/z: (MH^+) calcd. for $C_{12}H_{13}NO_4$: 236.2437; found: 236.2435.

8. methyl aziridine-2-carboxylate (5)

Method A

Compound (**4a-c**) (0.7288 mmol to 3.4mmol) was dissolved in solution of CH_2Cl_2 : MeOH (1:1). Solution was cooled to the -10ºC and TFA (28.53mmol, 14 eq.) was added slowly in an inert atmosphere. Reaction mixture was maintained at -10º C for 3 h and the reaction was monitored by TLC, but it was found that compound was forming salt with TFA. Work up of reaction was done by diluting it with ethyl acetate and water, mixture was extracted between ethyl acetate twice .Ethyl acetate part was discarded and aqueous part was concentrated on under reduced pressure with striping with toluene.

Method B

To solution of compounds (**4a-c**) (0.7288 mmol-3.4mmol) in MeOH: CH_2Cl_2 (1:1, 6 mL), TFA (28.53mmol, 14 eq.) was added under nitrogen atmosphere at 0º C over 20 min. Reaction mixture was stirred for 3 h at 0º C. Upon completion of reaction it was concentrated. To the crude material, ether (6mL) was added and concentrated under reduced pressure; this was repeated 3-4 times to remove excess TFA. The residue was partitioned between EtOAc (2.2 mL)

and water (2 × 3 mL). Ethyl acetate part was discarded and aqueous part was concentrated under reduced pressure with striping with toluene. Product obtained was *oily* (82% yield). ^{1}H NMR 400 MHz in $CDCl_3$, 1H (m, δ=1.93-1.68), 1H (m, δ=2.14-2.18), 1H (t, δ=2.43), 3H (s, δ=3.76). ^{13}C NMR, 100 MHz in $CDCl_3$ δ: 27.0 (-*C*H$_2$ *Aziridine*), 30.4 (-*C*H *Aziridine*), 51.8 (-*C*H$_3$), 171.4 (-*C*O$_2$-). LC-MS (ESI) m/z: 102.1 (MH^+). Anal. calcd. for $C_4H_7NO_2$: C, 47.52; H, 6.98; N, 13.85; found: C, 47.39; H, 7.08; N, 13.76. HRMS (ESI) m/z: (MH^+) calcd. for $C_4H_7NO_2$: 102.0578; found: 102.0575.

9. methyl 1-tosylaziridine-2-carboxylate (6a)

Immediately to above [methyl aziridine-2-carboxylate (**5**), method B], activated potassium carbonate (5.05 mmol, 5eq.) was added at RT followed by *p*-tosyl chloride (2.02 mmol, 2eq.) in CH_2Cl_2 (2.5mL) was added. This was allowed to stir overnight. Solvent was removed under reduced pressure, diluted with H_2O (7mL) and washed with CH_2Cl_2 (2mL). Aqueous layer was acidified with citric acid solution and extracted with ethyl acetate. Ethyl acetate part was dried over sodium sulphate and evaporated under reduced pressure. TLC was monitored in EA/Hex sol. Purification was done by column chromatography (silica G 100-200), product was eluted using 12 to 18 % EA/ Hex as mobile phase. Product isolated was *brown oil* (80% yield). ^{1}H NMR 400 MHz in $CDCl_3$. δ: 2H (dd, *J*=8.3, 3.5 Hz, δ=2.14), 3H (m, δ=2.34-2.28), 1H (d, *J*=4.12, δ=2.54), 3H (s, δ=3.73), 2H (d, *J*=7.92, δ=7.34), 2H (d, *J*=8.0, δ=7.83). ^{13}C NMR, 100 MHz in $CDCl_3$ δ: 21.5 (-*C*H$_3$ *p-tosyl*), 31.9 (-*C*H *Aziridine*), 37.2 (-*C*H$_2$ *Aziridine*), 51.8 (-*C*H$_3$ *ester*), 128.3, 129.3, 137.6, 140.2 (-*C*H *Aromatic*), 167.8 (-*C*O$_2$-). LC-MS (ESI) m/z: 256.1 (MH^+). Anal. calcd. for $C_{11}H_{13}NO_4S$: C, 51.75; H, 5.13; N, 5.49; found: C, 51.63; H, 5.17; N, 5.40. HRMS (ESI) m/z: (MH^+) calcd. for $C_{11}H_{13}NO_4S$: 256.2912; found: 256.2909.

10. methyl 1-((4-nitrophenyl)sulfonyl)aziridine-2-carboxylate (6b)

Immediately to above [methyl aziridine-2-carboxylate (**5**), method B], activated potassium carbonate (5.05 mmol, 5eq.) was added at RT followed by p-nitrobenzenesulphonyl chloride (3.89 mmol, 1.05 eq.) in CH_2Cl_2 (2.5mL). This was allowed to stir overnight. Solvent was removed under reduced pressure, diluted with H_2O (7 mL) and washed with CH_2Cl_2 (2 mL). Aqueous layer was acidified with citric acid solution and extracted with ethyl acetate. Ethyl acetate part was dried over sodium sulphate and evaporated under reduced pressure. TLC was monitored in EA/Hex sol. Purification was done by column chromatography (silica G 100-200), product was eluted using 14 to 18 % EA/ Hex as mobile phase. Product isolated was *yellow solid*. mp 54-58º C (lit[4] mp 55-58º C); (84 % yield). ^{1}H NMR, 400 MHz in DMSO-d_6. δ: 2H (dd, *J*=7.4, 3.5, δ=2.10), 3H (m, δ=2.31-2.27), 1H (d, *J*=4.62, δ=2.46), 2H (d, *J*=8.67, δ=7.31), 2H (d, *J*=8.13, δ=7.88). ^{13}C NMR, 100 MHz in DMSO-d_6 δ: 31.9 (-*C*H *Aziridine*), 37.2 (-*C*H$_2$ *Aziridine*), 51.8 (-*C*H$_3$ *ester*), 124.6, 128.3, 146.1, 151.4 (-*C Aromatic*), 167.8 (-*C*O$_2$-). LC-MS (ESI) m/z: 287.2 (MH^+). Anal. calcd. for $C_{10}H_{10}N_2O_6S$: C, 41.96; H, 3.52; N, 9.79; found: C, 42.11; H, 3.42; N, 9.67. HRMS (ESI) m/z: (MH^+) calcd. for $C_{10}H_{10}N_2O_6S$: 287.2673; found: 287.2670.

Typical procedure for synthesis of N-*p*-tosyl *β*-arylmethylalaninates (7a-e) and *N*-*p*-nosyl *β*-arylmethylalaninates (8a-e).

A mixture of compound (**6a**) (50mg, 0.196mmoles) or (**6b**) (50 mg, 0.174 mmoles) and various aryl moieties (1.5 eq) (as nucleophiles) in 1 mL CH_2Cl_2 or $CHCl_3$ added in tightly capped test

tube (seal tube) followed by addition of various catalyst (0.2-0.4 eq.)at suitable temperature were mixed with 2-5 mL of CH_2Cl_2 and reacted in a same tightly capped test tube for overnight (12 h).Reactions were monitored by TLC. After confirmation of new spot, crude mixtures were analyzed for LC-MS and products were confirmed by m/z obtained. The reaction mixture was diluted with 5mL water and extracted with EtOAc and washed with brine. The extract was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel 2:8 EA/Hex as mobile phase.

11. methyl 3-(1-methyl-1H-indol-3-yl)-2-(4-methylphenylsulfonamido) propanoate (7a)

Product isolated as *brown oil*. ^{1}H NMR, 400 MHz in DMSO-d_6 δ: 3H (s, δ=2.38), 1H (dd, J= 8.4, 5.4 Hz, δ=3.48), 1H (d, J = 12.0 Hz, δ=3.26), 6H (m, δ=3.70-3.63), 1H (dd, J = 8.0, 6.0, Hz, δ=4.12), 2H (m, δ=7.19-7.12), 1H (s, δ=7.24), 1H (d, J = 5.9 Hz, δ=7.30), 2H (m, δ=7.40-7.34), 1H (d, J = 7.9 Hz, δ=7.55), 2H (m, δ=7.74-7.68), 1H (s, δ=8.05). ^{13}C NMR, 100 MHz in DMSO-d_6 δ: 21.7 (-*C*H_3 *p-tosyl*), 29.6 (-*C*H_2-*N*-methylIndole), 34.6 (-*C*H_3 *N-methylindole*), 51.8 (-*C*H_3*ester*), 59.7 (-*C*H-NH- *p-tosyl*), 109.6, 113.7, 117.8, 119.7, 121.4, 127.5, 128.3, 129.3, 133.2, 137.6, 140.2, 141.8 (-*C Aromatic*), 172.6 (-*C*O_2-). LC-MS (ESI) m/z: 387.3 (MH^+). Anal. calcd. for $C_{20}H_{22}N_2O_4S$: C, 62.16; H, 5.74; N, 7.25; found: C, 62.25; H, 5.68; N, 7.18. HRMS (ESI) m/z: (MH^+) calcd. for $C_{20}H_{22}N_2O_4S$: 387.4613; found: 387.4611.

12. methyl 2-(4-methylphenylsulfonamido)-3-(1H-pyrrol-2-yl) propanoate (7b)

Product isolated as *pale yellow oil*. ^{1}H NMR 400 MHz in $CDCl_3$. δ: 3H (s, δ=2.36), 1H (dd, J=7.4, 3.4 Hz, δ=3.09), 1H (d, J = 10.3 Hz, δ=3.39), 3H (s, δ=3.62), 1H (m, δ=3.78-3.73), 2H (m, δ=5.81-5.75), 1H (s, δ=6.72), 2H (d, J = 4.3 Hz, δ=7.36), 3H (m, δ=7.79-7.74), ^{13}C NMR, 100 MHz in $CDCl_3$ δ: 21.4 (-*C*H_3 *p-tosyl*), 28.4 (-*C*H_2-*pyrrole*), 51.8 (-*C*H_3*ester*), 59.5 (-*C*H-NH- *p-tosyl*), 107.6, 108.8, 118.2, 128.7, 130.3, 141.2, 143.2, (-*C Aromatic*), 171.6 (-*C*O_2-). LC-MS (ESI) m/z: 323.3 (MH^+). Anal. calcd. for $C_{15}H_{18}N_2O_4S$: C, 55.88; H, 5.63; N, 8.69; found: C, 56.06; H, 5.55; N, 8.78. HRMS (ESI) m/z: (MH^+) calcd. for $C_{15}H_{18}N_2O_4S$: 323.3854; found: 323.3851.

13. methyl 3-(furan-2-yl)-2-(4-methylphenylsulfonamido) propanoate (7c)

Product isolated as *colourless oil*. ^{1}H NMR 400 MHz in $CDCl_3$. δ: 3H (s, δ=2.36), 1H (dd, J = 7.7, 1.6 Hz, δ=2.89), 1H (d, J = 9.6 Hz, δ=3.18), 3H (m, δ=3.66), 1H (m, δ=3.78-3.73), 1H (d, δ=5.81-5.75), 1H (m, δ=6.44-6.38), 2H (d, J = 5.4 Hz, δ=7.42), 3H (m, δ=7.79-7.74), ^{13}C NMR, 100 MHz in $CDCl_3$ δ: 21.4 (-*C*H_3 *p-tosyl*), 31.8 (-*C*H_2- *furan*), 51.5 (-*C*H_3*ester*), 56.5 (-*C*H-NH- *p-tosyl*), 105.6, 110.6, 128.7, 130.3, 137.9, 141.2, 141.8, 156.2, (-*C Aromatic*), 171.6 (-*C*O_2-). LC-MS (ESI) m/z: 324.3 (MH^+). Anal. calcd. for $C_{15}H_{17}NO_5S$: C, 55.71; H, 5.30; N, 4.33. found: C, 55.63; H, 5.38; N, 4.21; HRMS (ESI) m/z: (MH^+) calcd. for $C_{15}H_{17}NO_5S$: 324.3628; found: 324.3685.

14. methyl 2-(4-methylphenylsulfonamido)-3-(thiophen-2-yl) propanoate (7d)

Product isolated as *brown oil*. ^{1}H NMR 400 MHz in $CDCl_3$. δ: 3H (s, δ=2.36), 1H (dd, J= 7.9, 4.4 Hz, δ=3.12), 1H (dd, J = 9.6, 3.2 Hz, δ=3.32), 3H (m, δ=3.66), 1H (m, δ=3.84-3.78), 2H (m, δ=6.92-6.87), 3H (m, δ=7.46-7.41), 3H (m, δ=7.79-7.74), ^{13}C NMR, 100 MHz in $CDCl_3$ δ: 21.4 (-*C*H_3 *p-tosyl*), 31.2 (-*C*H_2- *thiofuran*), 51.8 (-*C*H_3*ester*), 58.7 (-*C*H-NH- *p-tosyl*), 126.2,127.4,128.2, 128.7, 129.6, 130.3, 132.8, 137.7, 141.5 (-*C Aromatic*), 171.6 (-*C*O_2-). LC-MS (ESI) m/z: 340.2

(MH^+). Anal. calcd. for $C_{15}H_{17}NO_4S_2$: C, 53.08; H, 5.05; N, 4.13; found: C, 53.27; H, 5.12; N, 4.03. HRMS (ESI) m/z: (MH^+) calcd. for $C_{15}H_{17}NO_4S_2$: 340.4367; found: 340.4365.

15. methyl 3-(3,4-dimethoxyphenyl)-2-(4-methylphenylsulfonamido) propanoate (7e)

Product isolated as *colourless oil*. ^{1}H NMR 400 MHz in DMSO-d_6 δ: 3H (s, δ=2.38), 1H (dd, J=9.2, 4.4 Hz, δ=2.96), 1H (d, J = 8.4 Hz, δ=3.24), 3H (s, δ=3.71), 6H (s, δ=3.82), 1H (dd, J = 8.2, 5.4 Hz, δ=4.12), 1H (s, δ=6.52), 2H (m, δ=6.78-6.73), 1H (m, δ=6.89-6.84), 2H (m, δ=7.40-7.34), 3H (m, δ=7.79-7.74), ^{13}C NMR, 100 MHz in DMSO-d_6 δ: 21.7 (-*C*$H_{3\ p\text{-}tosyl}$), 37.3 (-*C*H_2-*dimethylcatechol*), 51.8 (-*C*H_{3ester}), 55.8 (-*C*$H_{3dimethylcatechol}$), 59.7 (-*C*H-NH- *p-tosyl*), 112.4, 113.2, 128.1, 128.8, 129.3, 129.9, 141.3, 141.8, 147.1, 149.5 (-*C* $_{Aromatic}$), 171.7 (-*C*O_2-). LC-MS (ESI) m/z: 394.2 (MH^+). Anal. calcd. for $C_{19}H_{23}NO_6S$: C, 58.00; H, 5.89; N, 3.56; found: C, 57.92; H, 5.81; N, 3.68. HRMS (ESI) m/z: (MH^+) calcd. for $C_{19}H_{23}NO_6S$: 394.4576; found: 394.4573.

16. methyl 3-(1-methyl-1H-indol-3-yl)-2-(4-nitrophenylsulfonamido) propanoate (8a)

Product isolated as *dark brown oil*. ^{1}H NMR 400 MHz in $CDCl_3$. 1H (d, J= 3.9 Hz, δ=3.24), 1H (dd, J = 12.0, 5.7 Hz, δ=3.46), 6H (m, δ=3.71-3.66), 1H (dd, J = 8.4, 6.2, Hz, δ=3.90), 1H (m, δ=7.00-6.94), 1H (d, J = 7.3 Hz, δ=7.42), 2H (m, δ=7.56-7.50), 1H (s, δ=7.76), 2H (m, δ=8.16-8.10), 2H (m, δ=8.40-8.34), ^{13}C NMR, 100 MHz in $CDCl_3$ δ: 29.8 (-*C*H_2-*N*-methylIndole), 34.2 (-*C*$H_{3\ N\text{-}methylindole}$), 52.2 (-*C*$H_{3ester}$), 59.3 (-*C*H-NH- *p-nosyl*), 108.8, 118.4, 119.6, 124.1, 124.4, 127.5, 128.3, 129.3, 137.6, 149.8,150.7, 151.5 (-*C* $_{Aromatic}$), 171.2 (-*C*O_2-). LC-MS (ESI) m/z: 418.1 (MH^+). Anal. calcd. for $C_{19}H_{19}N_3O_6S$: C, 54.67; H, 4.59; N, 10.07; found: C, 54.78; H, 4.47; N, 10.21. HRMS (ESI) m/z: (MH^+) calcd. for $C_{19}H_{19}N_3O_6S$: 418.4355; found: 418.4352.

17. methyl 2-(4-nitrophenylsulfonamido)-3-(1H-pyrrol-2-yl) propanoate (8b)

Product isolated as *dark brown oil*. ^{1}H NMR 400 MHz in $CDCl_3$. δ: 1H (dd, J=8.4, 2.4 Hz, δ=3.14), 1H (d, J = 6.3 Hz, δ=3.36), 3H (s, δ=3.62), 1H (m, δ=4.12-4.07), 1H (d, J = 5.4 Hz, δ=5.76), 1H (m, δ=6.08-6.03), 1H (m, δ=6.73-6.67), 1H (s, δ=7.78), 2H (m, δ=8.18-8.13), 2H (m, δ=8.42-8.36).^{13}C NMR, 100 MHz in $CDCl_3$ δ: 28.4 (-*C*H_2-*pyrrole*), 51.8 (-*C*H_{3ester}), 59.3 (-*C*H-NH- *p-nosyl*), 107.6, 108.8, 118.2, 124.4, 128.7, 141.2, 150.4, 151.2 (-*C* $_{Aromatic}$), 171.6 (-*C*O_2-). LC-MS (ESI) m/z: 354.3 (MH^+). Anal. calcd. for $C_{14}H_{15}N_3O_6S$: C, 47.59; H, 4.28; N, 11.89; found: C, 47.52; H, 4.38; N, 11.94. HRMS (ESI) m/z: (MH^+) calcd. for $C_{14}H_{15}N_3O_6S$: 354.3507; found: 354.3504.

18. methyl 3-(furan-2-yl)-2-(4-nitrophenylsulfonamido)propanoate (8c)

Product isolated as *brown oil*. ^{1}H NMR 400 MHz in $CDCl_3$. δ: 1H (dd, J = 9.2, 4.6 Hz, δ=2.89), 1H (d, J = 7.4 Hz, δ=3.14), 3H (m, δ=3.66), 1H (m, δ=3.82-3.77), 1H (m, δ=5.91-5.85), 1H (m, δ=6.44-6.38), 1H (m, δ=7.61-7.56), 1H (m, δ=7.76-7.71), 2H (m, δ=8.18-8.13), 2H (m, δ=8.42-8.36). ^{13}C NMR, 100 MHz in $CDCl_3$ δ: 31.8 (-*C*H_2- *furan*), 51.6 (-*C*H_{3ester}), 56.5 (-*C*H-NH- *p-nosyl*), 106.1, 110.2, 124.4, 128.6, 141.6, 150.8, 151.4, 155.2 (-*C* $_{Aromatic}$), 171.6 (-*C*O_2-). LC-MS (ESI) m/z: 355.1 (MH^+). Anal. calcd. for $C_{14}H_{14}N_2O_7S$: C, 47.46; H, 3.98; N, 7.91; found: C, 47.38; H, 4.08; N, 7.84. HRMS (ESI) m/z: (MH^+) calcd. for $C_{14}H_{14}N_2O_7S$: 355.0517; found: 355.0513.

19. methyl 2-(4-nitrophenylsulfonamido)-3-(thiophen-2-yl)propanoate (8d)

Product isolated as *yellow semisolid*. ^{1}H NMR 400 MHz in $CDCl_3$. δ: 1H (dd, J= 10.6, 5.4 Hz, δ=2.94), 1H (dd, J = 8.4, 4.2 Hz, δ=3.32), 3H (m, δ=3.66), 1H (m, δ=3.84-3.78), 2H (m, δ=6.92-6.87), 1H (m, δ=7.46-7.41), 2H (m, δ=8.18-8.13), 2H (m, δ=8.42-8.36). ^{13}C NMR, 100 MHz in $CDCl_3$ δ: 31.2 (-*C*H_2- *thiofuran*), 51.8 (-*C*H_3 *ester*), 59.4 (-*C*H-NH- *p-nosyl*), 125.4, 127.4, 128.2, 129.1, 137.7, 150.8, 151.2 (-*C* *Aromatic*), 171.6 (-*C*O_2-). LC-MS (ESI) m/z: 371.3 (MH^+). Anal. calcd. for $C_{14}H_{14}N_2O_6S_2$: C, 45.40; H, 3.81; N, 7.56; found: C, 45.48; H, 3.78; N, 7.71. HRMS (ESI) m/z: (MH^+) calcd. for $C_{14}H_{14}N_2O_6S_2$: 371.4056; found: 371.4054.

20. methyl 3-(3,4-dimethoxyphenyl)-2-(4-nitrophenylsulfonamido)propanoate (8e)

Product isolated as *brown semisolid*. ^{1}H NMR 400 MHz in DMSO-d_6 δ: 1H (d, J=6.2 Hz, δ=2.94), 1H (dd, J = 8.4, 3.4 Hz, δ=3.18), 3H (s, δ=3.66), 6H (s, δ=3.82), 1H (dd, J = 8.2, 5.4 Hz, δ=3.88), 2H (m, δ=6.78-6.72), 1H (m, δ=6.88-6.83), 2H (m, δ=8.18-8.13), 2H (m, δ=8.42-8.36). ^{13}C NMR, 100 MHz in DMSO-d_6 δ: 36.4 (-*C*H_2-*dimethylcatechol*), 51.8 (-*C*H_3 *ester*), 55.9 (-*C*H_3 *dimethylcatechol*), 59.2 (-*C*H-NH- *p-tosyl*), 112.1, 113.2, 124.5, 128.6, 128.8, 129.7, 147.1, 149.5, 150.8, 151.3 (-*C* *Aromatic*), 171.7 (-*C*O_2-). LC-MS (ESI) m/z: 425.2 (MH^+). Anal. calcd. for $C_{18}H_{20}N_2O_8S$: C, 50.94; H, 4.75; N, 6.60; found: C, 51.08; H, 4.66; N, 6.71. HRMS (ESI) m/z: (MH^+) calcd. for $C_{18}H_{20}N_2O_8S$: 425.2384; found: 425.2383.

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