Synthesis of Cyclic Sulfonamide via Pd-Catalyzed Cross Coupling Reaction: An expedient approach to polycyclic sultams.

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Experimental section:

General: Melting points were determined in open capillaries and are uncorrected. IR spectra were run for KBr discs on a PerkinElmer 120-000A apparatus ($\nu_{\text{max}}$ in cm$^{-1}$) and $^1$H-NMR spectra were determined for solutions in CDCl$_3$ with TMS as internal standard on a Bruker DPX-400. $^{13}$C-NMR spectra were determined for solutions in CDCl$_3$ on a Bruker DPX-75. HRMS was recorded on a Qtof Micro YA263 instrument. Silica gel (60-120 mesh) was used for chromatographic separation. Silica gel-G [E-Mark (India)] was used for TLC. Petroleum-ether refers to the fraction between 60 and 80 $^0$C.

General procedure for the preparation of compound 3a-f:
A mixture of sulfonamides 1a-c (4.13 mmol), 2-bromobenzyl bromides 2a,b (10.33 mmol) and anhydrous K$_2$CO$_3$ (3 g) in anhydrous EMK (20 mL) in the presence of catalytic amount of NaI was refluxed for 12 h. After cooling, the mixture was filtered and the solvent was removed. The residual mass was extracted with dichloromethane (3 X 30 mL). The dichloromethane extract was washed with water (3 X 30 mL) followed by brine (1 X 10 mL) and dried (Na$_2$SO$_4$). Removal of dichloromethane gave a crude product, which was purified by chromatography (silica gel, EtOAc-pet ether, 1:9) to afford the bromo derivatives 3a-f.

Compound 3a: White solid, mp 133-134 $^0$C, yield 95%. IR (KBr, cm$^{-1}$) $\nu_{\text{max}}$: 1342, 1160; $^1$H-NMR (CDCl$_3$, 400 MHz) $\delta$: 2.45 (s, 3H), 4.50 (s, 4H), 6.99 (t, 2H, $J$ = 7.8 Hz), 7.13 (t, 2H, $J$ = 8.4 Hz), 7.33 (t, 6H, $J$ = 8.4 Hz), 7.73 (d, 2H, $J$ = 8.2 Hz); $^{13}$C-NMR
(CDCl₃, 75 MHz) δ: 21.4, 52.2, 123.2, 127.2, 128.8, 129.7, 130.0, 132.4, 134.7, 136.4, 143.5; HRMS: Calculated for C₂₁H₁₉Br₂NO₂S: 529.9335 [M+Na], 531.9381 [M+2+Na], 533.9339 [M+4+Na]. Found: 529.9401 [M+Na], 531.9401 [M+2+Na], 533.9401 [M+4+Na].

**Compound 3b:** White solid, mp 110-111 °C, yield 92%. IR (KBr, cm⁻¹) νmax: 1341, 1163; ¹H-NMR (CDCl₃, 400 MHz) δ: 2.45 (s, 3H), 3.67 (s, 6H), 4.45 (s, 4H), 6.55 (dd, 2H, J = 8.8, 3.0 Hz), 6.86 (d, 2H, J = 3 Hz), 7.21 (d, 2H, J = 8.7 Hz), 7.34 (d, 2H, J = 8.2 Hz), 7.77 (d, 2H, J = 8.2 Hz); MS (m/z): 567 [M⁺], 569 [M+2], 571 [M+4]. Anal. Calcd. for C₂₁H₂₁Br₂NO₂S: C, 48.52; H, 4.07; N, 2.46 %. Found: C, 48.61; H, 4.12; N, 2.55 %.

**Compound 3c:** White solid, mp 80-82 °C, yield 94%. IR (KBr, cm⁻¹) νmax: 1327, 1157; ¹H-NMR (CDCl₃, 400 MHz) δ: 4.54 (s, 4H), 6.99 (t, 2H, J = 7.6 Hz), 7.13 (t, 2H, J = 7.4 Hz), 7.30 (d, 2H, J = 7.6 Hz), 7.35 (d, 2H, J = 7.8 Hz), 7.51 (t, 2H, J = 7.5 Hz), 7.59 (t, 1H, J = 7.1 Hz), 7.84 (d, 2H, J = 7.5 Hz); MS (m/z); 493 [M⁺], 495 [M+2], 497 [M+4]. Anal. Calcd. for C₂₀H₁₇Br₂NO₂S: C, 48.51; H, 3.46; N, 2.83 %. Found: C, 48.65; H, 3.58; N, 2.73 %.

**Compound 3d:** White solid, mp 81-82 °C, yield 89%. IR (KBr, cm⁻¹) νmax: 1343, 1168; ¹H-NMR (CDCl₃, 400 MHz) δ: 3.67 (s, 6H), 4.48 (s, 4H), 6.56 (dd, 2H, J = 8.7, 2.5 Hz), 6.87 (d, 2H, J = 1.9 Hz), 7.23 (t, 2H, J = 5.8 Hz), 7.54 (t, 2H, J = 7.2 Hz), 7.64 (d, 2H, J = 8.5 Hz); MS (m/z): 553 [M⁺], 555 [M+2], 557 [M+4]. Anal. Calcd. for C₂₂H₂₁Br₂NO₂S: C, 47.59; H, 3.81; N, 2.52 %. Found: C, 47.51; H, 3.89; N, 2.55 %.

**Compound 3e:** White solid, mp 161-162 °C, yield 87%. IR (KBr, cm⁻¹) νmax: 3450, 3361, 1307, 1142; ¹H-NMR (CDCl₃, 400 MHz) δ: 4.13 (bs, 2H), 4.47 (s, 4H), 6.69 (d, 2H, J = 8.4 Hz), 6.98 (t, 2H, J = 7.6 Hz), 7.13 (t, 2H, J = 7.4 Hz), 7.33 (d, 4H, J = 7.6 Hz), 7.64 (d, 2H, J = 8.5 Hz); MS (m/z): 508 [M⁺], 510 [M+2], 512 [M+4]. Anal. Calcd. for C₂₀H₁₈Br₂N₂O₂S: C, 47.08; H, 3.56; N, 5.49 %. Found: C, 46.99; H, 3.60; N, 5.41 %.

**Compound 3f:** White solid, mp 105-106 °C, yield 90%. IR (KBr, cm⁻¹) νmax: 3479, 3374, 1594, 1324, 1154; ¹H-NMR (CDCl₃, 400 MHz) δ: 3.68 (s, 6H), 4.15 (bs, 2H), 4.42 (s, 4H), 6.55 (dd, 2H, J = 8.7, 2.8 Hz), 6.70 (d, 2H, J = 8.4 Hz), 6.90 (d, 2H, J = 2.7 Hz), 7.21 (d, 2H, J = 8.7 Hz), 7.67 (d, 2H, J = 8.6 Hz); MS (m/z): 568 [M⁺], 570 [M+2], 572
[M+4]. Anal. Calcd. for C$_{22}$H$_{22}$Br$_2$N$_2$O$_4$: C, 46.33; H, 3.89; N, 4.91 %. Found: C, 46.45 ; H, 4.07; N, 4.99 %.

**Compound 3g**: White gummy, yield 95%. IR (KBr, cm$^{-1}$) $\nu_{\text{max}}$: 1341, 1163; $^1$H-NMR (CDCl$_3$, 400 MHz) $\delta$: 2.45 (s, 3H), 3.83 (s, 3H), 4.45 (s, 2H), 4.49 (s, 2H), 6.55 (dd, 1H, $J = 8.7, 2.7$ Hz), 6.81 (d, 1H, $J = 2.5$ Hz ), 7.00 (t, 1H, $J = 7.5$ Hz), 7.15 (t, 1H, $J = 7.4$ Hz), 7.20 (d, 1H, $J = 8.8$ Hz), 7.31-7.37 (m, 4H), 7.75 (d, 2H, $J = 8.0$ Hz); MS (m/z): 537 [M$^+$], 539 [M+2], 541 [M+4]. Anal. Calcd. for C$_{22}$H$_{21}$Br$_2$N$_2$O$_4$: C, 49.00; H, 3.92; N, 2.60 %. Found: C, 49.12 ; H, 4.00; N, 2.52 %.

**Compound 3h**: Yellow viscous, yield 65%. IR (KBr, cm$^{-1}$) $\nu_{\text{max}}$: 3450, 1307, 1142; $^1$H-NMR (CDCl$_3$, 300 MHz) $\delta$: 4.2 (s, 2H), 7.49-7.54 (m, 1H), 7.60-7.66 (m, 1H), 7.77-7.83 (m, 2H ), 8.22 (d, 2H, $J = 7.5$ Hz), 8.64 (d, 1H, $J = 2.1$ Hz), 8.75 (d, 1H, $J = 1.5$ Hz); MS (m/z): 370 [M$^+$], 372 [M+2]. Anal. Calcd. for C$_{13}$H$_{11}$BrN$_2$O$_4$: C, 42.06; H, 2.99; N, 7.55 %. Found: C, 42.18 ; H, 3.21; N, 7.50 %.

**General procedure for the synthesis of the compounds 7(a-f) by the Heck reaction:**
A mixture of 3a (200 mg, 0.39 mmol), tetrabutylammonium bromide (153 mg, 0.47 mmol) and dry potassium acetate (106 mg, 1.08 mmol) was taken in dry N,N-dimethylformamide (5 mL) under a nitrogen atmosphere. Pd(OAc)$_2$ (9 mg, 0.039 mmol) was added and the reaction mixture was stirred at 120$^\circ$C for 10 h. The reaction mixture was cooled and water (25 mL) was added. The aqueous layer was extracted with ethyl acetate (3 X 30 mL) and the organic layer was washed with water (2 X 40 mL), followed by brine (30 mL). The organic layer was dried (Na$_2$SO$_4$), and the solvent was removed in vacuo. The crude product was purified by silica gel column chromatography using ethyl acetate: pet ether (1:9) to afford the product 7a. The other substrate 3 (b-f) were similarly treated to give products 7 (b-f).

**Compound 7a**: White solid, mp 241-242 $^\circ$C, yield 85%. IR (KBr, cm$^{-1}$) $\nu_{\text{max}}$: 1462, 1317, 1149; $^1$H-NMR (CDCl$_3$, 400 MHz) $\delta$: 2.52 (s, 3H), 3.86 (d, 1H, $J = 15.1$ Hz), 4.11 – 4.19 (q, 2H, $J = 11.8$ Hz), 4.45 (d, 1H, $J = 15.1$ Hz), 7.34 – 7.37 (m, 1H), 7.39 – 7.44 (m, 2H), 7.49 – 7.54 (m, 3H), 7.57 – 7.62 (m, 3H), 8.25 (d, 1H, $J = 8.2$ Hz); $^{13}$C-NMR (CDCl$_3$, 75 MHz) $\delta$: 21.5, 48.6, 49.2, 127.3, 127.4, 127.6, 128.5, 128.8, 129.0, 129.2, 129.7, 130.9, 133.7, 134.6, 136.2, 137.5, 139.5, 141.2, 144.9; HRMS: Calculated for C$_{21}$H$_{17}$NO$_2$S: 370.0878 [M+Na]. Found: 370.0878 [M+Na].
**Compound 7b:** White solid, mp 223-224 °C, yield 80%. IR (KBr, cm\(^{-1}\)) \(\nu_{\text{max}}\): 1303, 1148; \(^1\)H-NMR (CDCl\(_3\), 400 MHz) \(\delta\): 3.75 (d, 1H, \(J = 15\) Hz), 3.86 (s, 3H), 3.89 (s, 3H), 4.05 (d, 1H, \(J = 11.4\) Hz), 4.14 (d, 1H, \(J = 11.5\) Hz), 4.42 (d, 1H, \(J = 15\) Hz), 6.99 (d, 2H, \(J = 6.6\) Hz), 7.07 (d, 1H, \(J = 8.6\) Hz), 7.29 (d, 1H, \(J = 8.0\) Hz), 7.45 (s, 1H), 7.51 (d, 1H, \(J = 8.5\) Hz), 7.70 (d, 1H, \(J = 9.2\) Hz), 8.21 (d, 1H, \(J = 8.1\) Hz); HRMS: Calculated for C\(_{23}\)H\(_{21}\)NO\(_4\)S: 430.1086 [M+Na]. Found: 430.1089 [M+Na].

**Compound 7c:** White solid, mp 173-174 °C, yield 92%. IR (KBr, cm\(^{-1}\)) \(\nu_{\text{max}}\): 1315, 1152; \(^1\)H-NMR (CDCl\(_3\), 400 MHz) \(\delta\): 3.87 (d, 1H, \(J = 14.5\) Hz), 4.07 (d, 1H, \(J = 11.4\) Hz), 4.17 (d, 1H, \(J = 11.4\) Hz), 4.48 (d, 1H, \(J = 15.0\) Hz), 7.42 (d, 2H, \(J = 6.8\) Hz), 7.54-7.58 (m, 6H), 7.73 (d, 2H, \(J = 9.0\) Hz), 8.38 (d, 1H, \(J = 8.2\) Hz); HRMS: Calculated for C\(_{20}\)H\(_{15}\)NO\(_2\)S: 356.0722 [M+Na]. Found: 356.0721 [M+Na].

**Compound 7d:** White solid, mp 199-200 °C, yield 87%. IR (KBr, cm\(^{-1}\)) \(\nu_{\text{max}}\): 1312, 1156; \(^1\)H-NMR (CDCl\(_3\), 400 MHz) \(\delta\): 3.76 (d, 1H, \(J = 15.2\) Hz), 3.86 (s, 3H), 3.89 (s, 3H), 4.06 (d, 1H, \(J = 11.5\) Hz), 4.14 (d, 1H, \(J = 11.4\) Hz), 4.42 (d, 1H, \(J = 15.2\) Hz), 6.99 (d, 2H, \(J = 6.6\) Hz), 7.09 (d, 1H, \(J = 8.5\) Hz), 7.47-7.53 (m, 2H), 7.65-7.72 (m, 3H), 8.34 (d, 1H, \(J = 8.0\) Hz); MS (m/z): 393 \([\text{M}^+\]). Anal. Calcd. for C\(_{22}\)H\(_{19}\)NO\(_4\)S: C, 67.16; H, 4.87; N, 3.56 %. Found: C, 67.27; H, 4.83; N, 3.67 %.

**Compound 7e:** White solid, mp 290-291 °C, yield 84%. IR (KBr, cm\(^{-1}\)) \(\nu_{\text{max}}\): 3478, 3382, 1288, 1139; \(^1\)H-NMR (CDCl\(_3\), 400 MHz) \(\delta\): 3.83 (d, 1H, \(J = 15.1\) Hz), 4.09 (d, 1H, \(J = 11.9\) Hz), 4.20 (d, 1H, \(J = 11.8\) Hz), 4.27 (bs, 2H), 4.48 (d, 1H, \(J = 14.9\) Hz), 6.69 (d, 1H, \(J = 8.7\) Hz), 6.89 (d, 1H, \(J = 1.7\) Hz), 7.34-7.40 (m, 4H), 7.49 (t, 2H, \(J = 8.4\) Hz), 7.59 (d, 1H, \(J = 7.6\) Hz), 8.11 (d, 1H, \(J = 8.6\) Hz); MS (m/z): 348 \([\text{M}^+\]). Anal. Calcd. for C\(_{20}\)H\(_{16}\)N\(_2\)O\(_2\)S: C, 68.94; H, 4.63; N, 8.04 %. Found: C, 68.80; H, 4.74; N, 8.23 %.

**Compound 7f:** White solid, mp 206-207 °C, yield 81%. IR (KBr, cm\(^{-1}\)) \(\nu_{\text{max}}\): 3482, 3369, 1308, 1142; \(^1\)H-NMR (CDCl\(_3\), 400 MHz) \(\delta\): 3.72 (d, 1H, \(J = 15.0\) Hz), 3.85 (s, 3H), 3.87 (s, 3H), 4.02 (d, 1H, \(J = 11.4\) Hz), 4.16 (d, 1H, \(J = 11.5\) Hz), 4.23 (bs, 2H), 4.43 (d, 1H, \(J = 15.2\) Hz), 6.63 (d, 1H, \(J = 8.8\) Hz), 6.82 (d, 1H, \(J = 1.7\) Hz), 6.98 (d, 2H, \(J = 6.8\) Hz), 7.04 (d, 1H, \(J = 8.4\) Hz), 7.45 (d, 1H, \(J = 8.6\) Hz), 7.77 (d, 1H, \(J = 8.4\) Hz), 8.07 (d, 1H, \(J = 8.7\) Hz); MS (m/z): 408 \([\text{M}^+\]). Anal. Calcd. for C\(_{22}\)H\(_{20}\)N\(_2\)O\(_4\)S: C, 64.69; H, 4.94; N, 6.86 %. Found: C, 64.86; H, 4.90; N, 6.76 %. 


**Compound 7g:** White solid, mp 198-200 °C, yield 81%. IR (KBr, cm\(^{-1}\)) \(\nu_{\text{max}}\): 1303, 1148; \(^1\)H-NMR (CDCl\(_3\), 400 MHz) \(\delta\): 2.50 (s, 3H), 3.75 (d, 1H, \(J = 15\) Hz), 3.86 (s, 3H), 4.06 (d, 2H, \(J = 6.8\) Hz), 4.4 (d, 1H, \(J = 15\) Hz), 7.08 (d, 1H, \(J = 8.6\) Hz), 7.35 (t, 1H, \(J = 7.5\) Hz), 7.43-7.48 (m, 2H), 7.54 (d, 2H, \(J = 8.8\) Hz), 7.93 (d, 1H, \(J = 7.5\) Hz), 8.21 (d, 1H, \(J = 8.1\) Hz); MS (m/z): 377 [M\(^+\)]. Anal. Calcd. for C\(_{22}\)H\(_{19}\)NO\(_3\)S: C, 70.00; H, 5.07; N, 3.71 %. Found: C, 70.14 ; H, 5.17; N, 3.59 %.

**Compound 7h:** Yellow solid, mp 152-154 °C, yield 60%. IR (KBr, cm\(^{-1}\)) \(\nu_{\text{max}}\): 3482, 1308, 1142; \(^1\)H-NMR (CDCl\(_3\), 300 MHz) \(\delta\): 4.2 (d, 2H, \(J = 1.8\) Hz), 7.51-7.54 (m, 2H), 7.69-7.73 (m, 1H ), 7.87 (d, 1H, \(J = 9.0\) Hz), 8.07 (d, 1H, \(J = 2.8\) Hz), 8.11 (d, 1H, \(J = 2.1\) Hz), 8.90 (d, 1H, \(J = 3.0\) Hz); MS (m/z): 290 [M\(^+\)]. Anal. Calcd. for C\(_{13}\)H\(_{10}\)N\(_2\)O\(_4\)S: C, 53.79; H, 3.47; N, 9.65 %. Found: C, 53.68 ; H, 3.61; N, 9.53 %.