Supporting Information

Regio- and Diastereoselective Cycloaddition of Azomethine Ylide with Benzylidenemalononitrile: Assembly of a New Set of Multisubstituted 4,4-Dicyanopyrrolidine-2-Carboxylate and Nornicotine Scaffolds

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X-ray Structure of compound 8c
X-ray Structure of compound 8d
X-ray Structure of compound 9b
X-ray Structure of compound 9c
**General:** Melting points of compounds are uncorrected. FT-IR spectra of compounds were recorded as KBr pellets or thin films. $^1$H NMR and $^{13}$C NMR spectra of compounds were recorded on 400 MHz and 100 MHz spectrometers, respectively. Column chromatography purification of crude reaction mixture was performed on silica (100-200 mesh). Reactions were carried out under an inert atmosphere wherever required. Solutions were dried with anhydrous magnesium sulfate. Reagents were added to the reaction flask through syringe. Thin layer chromatography (TLC analysis) was performed on silica gel plates or neutral alumina plates and the components were visualized by observation under iodine chamber. Isolated yields of all the products were reported (yields were not optimized). Ratios of diastereomers were determined from NMR spectrum of crude reaction mixture or after isolation/column purification.

**General procedure for catalytic 1, 3-dipolar cycloadditon of azomethine ylides with benzylidenemalononitrile:** Under a nitrogen atmosphere AgOAc (10 mol%) in anhydrous DCM (1 mL) was stirred for 30 min; to this mixture were sequentially added a solution of N-benzylideneiminoglycinates (0.5 mmol) and benzylidenemalononitrile (0.5 mmol) in 4 mL DCM and Et$_3$N (40 mol%) and stirred for 12 h in the absence of light at r.t. The reaction mixture was filtered through a celite pad. The filtrate was directly evaporated and the residue was purified by column chromatography.

**Analytical data of the products:**

Following the general procedure described above 7a was obtained after purification by silica column chromatography (EtOAc:Hexane = 30:70); colorless solid, mp: 156-158 °C; FT-IR (KBr): 3341, 2954, 1737 and 1221 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.64 (d, 2H, $J = 8.1$ Hz), 7.46 (d, 4H, $J = 8.1$ Hz), 7.30 (d, 2H, $J = 8.1$ Hz), 4.94 (s, 1H), 4.51 (d, 1H, $J = 8.1$ Hz), 4.14 (d, 1H, $J = 8.1$ Hz), 3.75 (s, 3H), 2.99 (br s, 1H), 2.41 (s, 3H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 173.3, 139.8, 136.0, 132.3, 130.0, 129.4, 129.2, 128.7, 128.2, 113.5, 111.4, 69.7, 60.9, 58.0, 53.2, 50.8, 21.3; HRMS (ESI) calcd for C$_{21}$H$_{19}$ClN$_3$O$_2$ [M+H]$^+$ 380.1166 found [M+H]$^+$ 380.1171.
Following the general procedure described above \(7b\) was obtained after purification by silica column chromatography (EtOAc:Hexane = 30:70); colorless solid, mp:170-172 °C; FT-IR (KBr): 3343, 2902, 1737 and 1247 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.57 (d, 2H, \(J = 8.1\) Hz), 7.46 (d, 2H, \(J = 8.1\) Hz), 7.31-7.27 (m, 4H), 4.92 (s, 1H), 4.51 (d, 1H, \(J = 8.1\) Hz), 4.15 (d, 1H, \(J = 8.1\) Hz), 3.76 (s, 3H), 2.97 (brs, 1H), 2.41 (s, 6H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 173.4, 140.1, 139.6, 130.6, 130.0, 129.7, 129.6, 128.3, 127.2, 113.8, 111.7, 70.4, 61.0, 58.1, 53.1, 50.9, 21.3, 21.2; HRMS (ESI) calcd for C\(_{22}\)H\(_{22}\)N\(_3\)O\(_2\) [M+H]\(^+\) 360.1712 found [M+H]\(^+\) 360.1716.

Following the general procedure described above \(7c\) was obtained after purification by silica column chromatography (EtOAc:Hexane = 30:70); colorless solid, mp: 99-101 °C; FT-IR (KBr): 3345, 2983, 1731 and 1218 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.58 (d, 2H, \(J = 8.1\) Hz), 7.46 (d, 2H, \(J = 8.1\) Hz), 7.30-7.27 (m, 4H), 4.93 (s, 1H), 4.47 (d, 1H, \(J = 8.1\) Hz), 4.26-4.16 (m, 2H), 4.13 (d, 1H, \(J = 8.1\) Hz), 2.96 (br s, 1H), 2.41 (s, 6H), 1.21 (t, 3H, \(J = 7.1\) Hz); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 172.8, 140.0, 139.5, 130.7, 129.9, 129.8, 129.6, 128.3, 127.2, 113.9, 111.7, 70.4, 62.2, 61.2, 58.2, 50.9, 21.3, 21.3, 14.1; HRMS (ESI) calcd for C\(_{23}\)H\(_{24}\)N\(_3\)O\(_2\) [M+H]\(^+\) 374.1869 found [M+H]\(^+\) 374.1873.

Following the general procedure described above \(7d\) was obtained after purification by silica column chromatography (EtOAc:Hexane = 30:70); colorless solid, mp: 146-148 °C; FT-IR (KBr): 3339, 2954, 1736 and 1221 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.99-7.97 (m, 1H), 7.48 (d, 2H, \(J = 8.1\) Hz), 7.35-7.27 (m, 5H), 6.33 (s, 1H), 4.51 (d, 1H, \(J = 7.9\) Hz), 4.20 (d, 1H, \(J = 7.9\) Hz), 3.77 (s, 3H), 2.86 (br s, 1H), 2.58 (s, 3H), 2.42 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\),
100 MHz): δ 173.4, 139.7, 136.9, 131.7, 131.1, 130.0, 129.7, 129.6, 128.4, 127.5, 126.5, 114.2, 111.8, 65.5, 60.8, 58.7, 53.1, 49.5, 21.3, 19.8; HRMS (ESI) calcd for C$_{22}$H$_{22}$N$_3$O$_2$ [M+H]$^+$ 360.1712 found [M+H]$^+$ 360.1711.

Following the general procedure described above 7e was obtained after purification by silica column chromatography (EtOAc:Hexane = 30:70); colorless solid; mp:153-155 °C; FT-IR (KBr): 3346, 2954, 1737 and 1220 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): δ 8.05 (dd, 1H, $J_1$ = 7.9, $J_2$ = 2.0 Hz), 7.49-7.46 (m, 3H), 7.44-7.36 (m, 2H), 7.30 (d, 2H, $J$ = 7.9 Hz), 5.61 (s, 1H), 4.51 (d, 1H, $J$ = 8.1 Hz), 4.20 (d, 1H, $J$ = 8.1 Hz), 3.77 (s, 3H); 13C NMR (CDCl$_3$, 100 MHz): δ 173.1, 139.7, 134.2, 131.6, 130.9, 130.0, 129.5, 128.4, 127.3, 113.4, 111.6, 64.9, 60.7, 58.7, 53.2, 49.2, 21.3; HRMS (ESI) calcd for C$_{21}$H$_{19}$ClN$_3$O$_2$ [M+H]$^+$ 380.1166 found [M+H]$^+$ 380.1167.

Following the general procedure described above 7f was obtained after purification by silica column chromatography (EtOAc:Hexane = 35:65); colorless solid; mp:140-142 °C; FT-IR (KBr): 3345, 2955, 1737 and 1249 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): δ 7.61 (d, 2H, $J$ = 8.7 Hz), 7.46 (d, 2H, $J$ = 8.0 Hz), 7.28 (d, 2H, $J$ = 8.0 Hz), 6.99 (d, 2H, $J$ = 8.7 Hz), 4.90 (d, 1H, $J$ = 3.8 Hz), 4.50 (d, 1H, $J$ = 8.0 Hz), 4.14 (d, 1H, $J$ = 8.0 Hz), 3.85 (s, 3H), 3.75 (s, 3H), 2.95 (br s, 1H), 2.41 (s, 3H); 13C NMR (CDCl$_3$, 100 MHz): δ 173.4, 160.9, 139.6, 130.0, 130.0, 128.6, 128.3, 125.4, 114.3, 113.8, 111.7, 70.2, 60.9, 57.9, 55.4, 53.1, 51.0, 21.3; HRMS (ESI) calcd for C$_{22}$H$_{22}$N$_3$O$_3$ [M+H]$^+$ 376.1661 found [M+H]$^+$ 376.1668.

Following the general procedure described above 7g (mixture of isomers) was obtained after purification by silica column chromatography (EtOAc:Hexane = 30:70); colorless semi solid;
FT-IR (DCM): 3343, 2955, 1738 and 1244 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): δ 7.49-6.99 (m, 8H), 4.95 (s, 1H), 4.53 (d, 1H, \(J = 8.1\) Hz), 4.18 (d, 1H, \(J = 8.1\) Hz), 3.86 (s, 3H), 3.74 (s, 3H), 2.41 (s, 3H). (The \(^1\)H NMR given here for major isomer); \(^13\)C NMR (CDCl\(_3\), 100 MHz): δ 173.3, 171.4, 160.0, 159.9, 139.7, 139.6, 135.3, 130.9, 130.1, 130.0, 129.7, 129.6, 128.6, 128.3, 119.6, 119.4, 115.9, 115.7, 113.8, 112.8, 112.5, 111.7, 70.5, 70.2, 60.9, 60.5, 58.1, 57.7, 55.4, 55.3, 53.1, 53.0, 50.8, 48.9, 21.3, 21.1 (The \(^13\)C NMR given here for mixture of isomers); HRMS (ESI) calcd for C\(_{22}\)H\(_{22}\)N\(_3\)O\(_3\) [M+H]\(^+\) 376.1661 found [M+H]\(^+\) 376.3090.

Following the general procedure described above 7h (mixture of isomers) was obtained after purification by silica column chromatography (EtOAc:Hexane = 30:70); colorless solid, mp:138-140 °C; FT-IR (KBr): 3340, 2955, 1737 and 1247 cm\(^{-1}\); \(^1\)H NMR(CDCl\(_3\), 400 MHz): δ 7.85 (dd, 1H, \(J_1 = 7.7, J_2 = 1.4\) Hz), 7.47-6.95 (m, 7H), 5.46 (s, 1H), 4.46 (d, 1H, \(J = 8.0\) Hz), 4.18 (d, 1H, \(J = 8.0\) Hz), 3.90 (s, 3H), 3.75 (s, 3H), 2.40 (s, 3H). (The \(^1\)H NMR given here for major isomer); \(^13\)C NMR (CDCl\(_3\), 100 MHz): δ 173.1, 171.0, 157.3, 157.0, 139.5, 139.4, 130.8, 130.6, 130.0, 129.9, 128.8, 128.6, 128.4, 128.0, 127.8, 123.9, 122.6, 121.0, 120.8, 114.5, 114.2, 114.0, 112.2, 110.8, 110.5, 67.1, 63.7, 63.1, 61.3, 59.1, 58.4, 55.1, 55.1, 53.0, 52.9, 49.4, 48.8, 21.3 (The \(^13\)C NMR given here for mixture of isomers); HRMS (ESI) calcd for C\(_{22}\)H\(_{22}\)N\(_3\)O\(_3\) [M+H]\(^+\) 376.1661 found [M+H]\(^+\) 376.1667.

Following the general procedure described above 7i (mixture of isomers) was obtained after purification by silica column chromatography (EtOAc:Hexane = 35:65); colorless solid, mp: compound decomposes after 128 °C; FT-IR (KBr): 3340, 2956, 1738 and 1223 cm\(^{-1}\); \(^1\)H NMR(CDCl\(_3\), 400 MHz): δ 8.63-8.62 (m, 1H), 8.33 (d, 1H, \(J = 7.9\) Hz), 8.03 (d, 1H, \(J = 7.9\) Hz), 7.47 (d, 2H, \(J = 8.1\) Hz), 7.47-7.28 (m, 2H), 5.09 (s, 1H), 4.57 (d, 1H, \(J = 8.2\) Hz), 4.16 (d, 1H, \(J = 8.2\) Hz), 3.76 (s, 3H), 3.13 (br s, 1H), 2.41 (s, 3H); \(^13\)C NMR (CDCl\(_3\), 100 MHz): δ 173.1, 148.6, 140.0, 136.4, 133.5, 130.5, 130.4, 129.1, 128.5, 128.2, 125.0, 122.5, 113.2, 111.1, 69.2, 60.9, 57.9, 53.3, 50.6, 21.3 (The \(^1\)H and \(^13\)C NMR given here for major isomer); HRMS (ESI) calcd for C\(_{21}\)H\(_{19}\)N\(_4\)O\(_4\) [M+H]\(^+\) 391.1406 found [M+H]\(^+\) 391.1416.
Following the general procedure described above **7j** (mixture of isomers) was obtained after purification by silica column chromatography (EtOAc:Hexane = 50:50); colorless semi solid; FT-IR (DCM): 3345, 2960, 1736 and 1266 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.45 (d, 2H, \(J = 8.2\) Hz), 7.30-7.27 (m, 3H), 7.20 (dd, 1H, \(J_1 = 8.4, J_2 = 2.1\) Hz), 6.93 (d, 1H, \(J = 8.4\) Hz), 4.90 (s, 1H), 4.50 (d, 1H, \(J = 8.4\) Hz), 4.13 (d, 1H, \(J = 8.4\) Hz), 3.94 (s, 3H), 3.91 (s, 3H), 3.74 (s, 3H), 2.40 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 173.4, 150.3, 149.2, 139.6, 129.8, 129.1, 128.3, 125.9, 120.0, 113.9, 111.9, 111.1, 109.9, 70.4, 60.8, 57.9, 56.0, 53.1, 50.9, 21.2 (The \(^1\)H and \(^{13}\)C NMR given here for major isomer); HRMS (ESI) calcld for C\(_{23}\)H\(_{24}\)N\(_3\)O\(_4\) [M+H]\(^{+}\) 406.1767 found [M+H]\(^{+}\) 406.1772.

Following the general procedure described above **7k** was obtained after purification by silica column chromatography (EtOAc:Hexane = 35:65); colorless solid, mp:144-146 °C; FT-IR (KBr): 3346, 2958, 1738 and 1213 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.84 (d, 2H, \(J = 8.2\) Hz), 7.75 (d, 2H, \(J = 8.2\) Hz), 7.46 (d, 2H, \(J = 8.1\) Hz), 7.32-7.28 (m, 2H), 5.02 (s, 1H), 4.54 (d, 1H, \(J = 8.2\) Hz), 4.15 (d, 1H, \(J = 8.2\) Hz), 3.77 (s, 3H), 3.02 (br s, 1H), 2.42 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 173.2, 139.9, 137.8, 132.2 (d, \(J_{C-F} = 33\) Hz), 130.1, 129.2, 128.2, 127.9, 126.0 (q, 2H, \(J = 14.6\) Hz), 113.4, 111.2, 69.6, 60.9, 58.1, 53.2, 50.6, 21.3; HRMS (ESI) calcld for C\(_{22}\)H\(_{19}\)F\(_3\)N\(_3\)O\(_2\) [M+H]\(^{+}\) 414.1429 found [M+H]\(^{+}\) 414.1432.

Following the general procedure described above **7l** (mixture of isomers) was obtained after purification by silica column chromatography (EtOAc:Hexane = 55:45); colorless semi solid;
FT-IR (DCM): 3336, 2956, 1738 and 1255 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.49 (d, 2H, \(J = 8.7\) Hz), 7.27 (d, 1H, \(J = 2.0\) Hz), 7.20 (dd, 1H, \(J_1 = 8.7, J_2 = 2.0\) Hz), 7.00 (d, 2H, \(J = 8.3\) Hz), 6.93 (d, 1H, \(J = 8.3\) Hz ), 4.89 (s, 1H), 4.47 (d, 1H, \(J = 8.2\) Hz), 4.12 (d, 1H, \(J = 8.2\) Hz), 3.95 (s, 3H), 3.92 (s, 3H), 3.85 (s, 3H), 3.75 (s, 3H), 2.95 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 173.4, 160.5, 150.3, 149.2, 129.9, 129.6, 125.9, 124.5, 119.9, 114.6, 113.9, 111.9, 111.1, 110.0, 70.3, 61.0, 57.7, 56.0, 55.9, 55.3, 53.1, 51.1 (The \(^1\)H and \(^{13}\)C NMR given here for major isomer); HRMS (ESI) calcd for C\(_{23}\)H\(_{24}\)N\(_3\)O\(_5\) [M+H]\(^+\) 422.1716 found [M+H]\(^+\) 422.1721.

Following the general procedure described above 7m was obtained after purification by silica column chromatography (EtOAc:Hexane = 30:70); colorless solid, mp: 148-150 °C; FT-IR (KBr): 3345, 2955, 1738 and 1221 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.57-7.46 (m, 6H), 7.29-7.27 (m, 2H), 4.92 (s, 1H), 4.46 (d, 1H, \(J = 8.0\) Hz), 4.16 (d, 1H, \(J = 8.0\) Hz), 3.71 (s, 3H), 2.98 (br s, 1H), 2.41 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 172.9,140.2, 135.8, 131.3, 130.3, 129.8, 129.7, 129.6, 127.1, 113.5, 111.5, 70.4, 61.0, 57.6, 53.2, 50.7, 21.3; HRMS (ESI) calcd for C\(_{21}\)H\(_{19}\)ClN\(_3\)O\(_2\) [M+H]\(^+\) 380.1166 found [M+H]\(^+\) 380.1167.

Following the general procedure described above 8a (mixture of isomers) was obtained after purification by silica column chromatography (EtOAc:Hexane = 30:70); colorless semi solid; FT-IR (DCM): 3338, 2955, 1737 and 1219 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.53 (dd, 1H, \(J_1 = 1.8, J_2 = 0.7\) Hz), 7.44 (d, 2H, \(J = 8.2\) Hz), 7.29 (d, 2H, \(J = 8.2\) Hz), 6.70 (d, 1H, \(J = 3.4\) Hz), 6.48-6.47 (m, 1H), 5.04 (s, 1H), 4.51 (d, 1H, \(J = 8.7\) Hz ), 4.18 (d, 1H, \(J = 8.7\) Hz), 3.74 (s, 3H), 2.41 (s, 3H) (The \(^1\)H NMR given here for major isomer); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 172.6, 171.4, 148.1, 147.0, 144.1, 144.0, 139.8, 139.7, 130.0, 129.6, 129.2, 128.8, 128.5, 128.3, 113.3, 113.1, 113.0, 111.6, 111.0, 110.9, 110.5, 110.0, 65.5, 65.1, 63.3, 61.0, 58.2, 57.6, 53.2, 53.1, 49.4, 48.0, 21.3 (The \(^{13}\)C NMR values given here for mixture of isomers); HRMS (ESI) calcd for C\(_{19}\)H\(_{18}\)N\(_3\)O\(_3\) [M+H]\(^+\) 336.1348 found [M+H]\(^+\) 336.1359.
Following the general procedure described above 8b (mixture of isomers) was obtained after purification by silica column chromatography (EtOAc:Hexane = 90:10); colorless semi solid; FT-IR (DCM): 3321, 2954, 1738 and 1219 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 8.70 (d, 1H, J = 4.8 Hz), 7.84-7.80 (m, 1H), 7.60 (d, 1H, J = 8.0 Hz), 7.45 (d, 2H, J = 8.0 Hz), 7.41-7.36 (m, 1H), 7.30-7.27 (m, 2H), 5.11 (s, 1H), 4.65 (d, 1H, J = 9.4 Hz), 4.40 (d, 1H, J = 9.4 Hz), 3.74 (s, 3H), 2.39 (s, 3H) (The ¹H NMR given here for major isomer); ¹³C NMR (CDCl₃, 100 MHz): δ 172.5, 171.1, 153.1, 151.9, 149.9, 149.6, 139.7, 139.5, 137.4, 130.0, 129.2, 128.7, 128.5, 128.4, 124.7, 124.7, 122.9, 122.5, 113.8, 113.7, 113.3, 111.3, 71.7, 71.3, 64.6, 61.8, 59.6, 59.2, 53.1, 53.0, 50.4, 48.6, 21.2 (The ¹³C NMR values given here for mixture of isomers); HRMS (ESI) calcd for C₂₀H₁₉N₄O₂ [M+H]⁺ 347.1508 found [M+H]⁺ 347.1518.

Following the general procedure described above 8c was obtained after purification by silica column chromatography (EtOAc:Hexane = 35:65); colorless solid, mp:154-156 °C; FT-IR (KBr): 3338, 2955, 1738 and 1124 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 7.53-7.39 (m, 6H), 7.13 (dd, 1H, J₁ = 4.9, J₂ = 3.7 Hz), 5.26 (d, 1H, J = 4.9 Hz), 4.47 (dd, 1H, J₁ = 8.4, J₂ = 1.4Hz), 4.12 (d, 1H, J = 8.4 Hz), 3.75 (s, 3H), 3.26 (br s, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ 172.6, 136.5, 135.9, 130.8, 130.0, 129.6, 127.5, 126.9, 126.8, 113.2, 111.3, 66.9, 60.8, 57.4, 53.3, 51.0; HRMS (ESI) calcd for C₁₈H₁₅N₃O₂ S [M+H]⁺ 372.0573 found [M+H]⁺ 372.0578.

Following the general procedure described above 8d was obtained after purification by silica column chromatography (EtOAc:Hexane = 30:70); colorless solid, mp: 153-155 °C; FT-IR (KBr): 3346, 2984, 1731 and 1218 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 7.45 (d, 2H, J = 8.1 Hz), 7.42 (dd, 1H, J₁ = 5.1, J₂ = 1.2 Hz), 7.40 (dd, 1H, J₁ = 3.7, J₂ = 0.7 Hz), 7.29 (d, 2H, J =
Following the general procedure described above 8e (mixture of isomers) was obtained after purification by silica column chromatography (EtOAc:Hexane = 35:65); colorless semi solid; FT-IR (DCM): 3351, 2971, 1736 and 1219 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.83 (d, 1H, $J =$ 8.6 Hz), 7.41-7.36 (m, 4H), 7.11 (dd, 1H, $J_1 = 5.0$, $J_2 = 3.6$ Hz), 6.92 (d, 2H, $J =$ 8.6 Hz), 5.24 (s, 1H), 4.45 (d, 1H, $J =$ 8.5 Hz), 4.10 (d, 1H, $J =$ 8.5 Hz), 3.72 (s, 3H) (The $^1$H NMR values given here for major isomer); $^{13}$C NMR (CDCl$_3$ + DMSO, 100 MHz): $\delta$ 173.1, 171.2, 159.4, 158.4, 137.0, 135.3, 133.9, 132.3, 129.9, 129.6, 128.4, 127.4, 126.6, 126.8, 126.4, 116.1, 113.6, 111.7, 66.7, 66.2, 63.6, 60.9, 57.7, 55.7, 53.1, 51.4; 49.5 (The $^{13}$CNMR values given here for mixture of isomers); HRMS (ESI) caled for C$_{18}$H$_{16}$N$_3$O$_3$S [M+H]$^+$ 354.0912 found [M+H]$^+$ 354.0916.

Following the general procedure described above 8f was obtained after purification by silica column chromatography (EtOAc:Hexane = 30:70); colorless solid, mp:120-122 $^\circ$C; FT-IR (KBr): 3345, 2960, 1738 and 1219 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 8.00 (dd, 1H, $J_1 = 9.5$, $J_2 = 2.2$ Hz), 7.56 (dd, 1H, $J_1 = 1.8$, $J_2 = 0.6$ Hz), 7.49-7.36 (m, 3H), 6.63 (d, 1H, $J =$ 3.4 Hz), 6.49 (dd, 1H, $J_1 = 3.4$, $J_2 = 1.8$ Hz), 5.56 (dd, 1H, $J =$ 5.0 Hz), 4.56 (dd, 1H, $J_1 = 8.1$, $J_2 = 2.2$ Hz), 4.40 (d, 1H, $J =$ 8.1 Hz), 3.83 (s, 3H), 2.91 (br s, 1H); $^{13}$C NMR (CDCl$_3$, 100MHz): $\delta$ 172.6, 146.4, 144.2, 134.2, 131.1, 131.0, 130.0, 129.4, 127.4, 113.0, 111.2, 111.0, 110.3, 64.5, 59.3, 53.4, 52.5, 47.3; HRMS (ESI) caled for C$_{18}$H$_{15}$ClN$_3$O$_3$ [M+H]$^+$ 356.0802 found [M+H]$^+$ 356.0802.
Following the general procedure described above 8g (mixture of isomers) was obtained after purification by silica column chromatography (EtOAc:Hexane = 30:70); colorless semi-solid; FT-IR (DCM): 3344, 2953, 1741 and 1243 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 7.55 (d, 2H, J = 8.1 Hz), 7.42 (dd, 1H, J₁ = 5.2, J₂ = 1.1 Hz), 7.36 (dd, 1H, J = 3.6 Hz), 7.28 (d, 2H, J = 7.8 Hz), 7.15-7.13 (m, 1H), 4.92 (s, 1H), 4.51 (s, 2H), 3.79 (s, 3H), 2.41 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 172.7, 140.2, 134.8, 130.3, 129.7, 127.8, 127.1, 127.6, 126.6, 113.5, 114.4, 70.1, 62.5, 53.7, 53.3, 51.3, 21.3 (The ¹H and ¹³CNMR values given here for major isomers); HRMS (ESI) calcd for C₁₉H₁₈N₃O₂S [M+H]⁺ 352.1120 found [M+H]⁺ 352.1130.

Following the general procedure described above 8h was obtained after purification by silica column chromatography (EtOAc:Hexane = 35:65); colorless solid, mp: 144-146 °C; FT-IR (KBr): 3345, 2954, 1737 and 1238 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 7.53 (d, 2H, J = 8.1 Hz), 7.28 (d, 2H, J = 8.1 Hz), 6.71 (dd, 1H, J₁ = 2.5, J₂ = 1.8 Hz), 6.55 (dd, 1H, J₁ = 3.8, J₂ = 1.8 Hz), 6.21 (dd, 1H, J₁ = 3.8, J₂ = 2.5 Hz), 4.90 (d, 1H, J = 5.0 Hz), 4.49 (d, 1H, J = 8.0 Hz), 4.39 (d, 1H, J = 8.0 Hz), 3.79 (s, 6H), 2.93 (br s, 1H), 2.40 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 172.9, 140.2, 134.8, 130.3, 129.7, 127.0, 124.7, 124.3, 114.3, 115.6, 109.9, 108.0, 70.7, 63.1, 53.2, 50.4, 49.7, 34.2, 21.3; HRMS (ESI) calcd for C₂₀H₂₁N₄O₂ [M+H]⁺ 349.1665 found [M+H]⁺ 349.1674.

Following the general procedure described above 8i was obtained after purification by silica column chromatography (EtOAc:Hexane = 100:0); colorless solid, mp: 138-140 °C; FT-IR (KBr): 3338, 2954, 1738 and 1182 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 8.79 (d, 1H, J = 1.9 Hz), 8.73 (dd, 1H, J₁ = 4.8, J₂ = 1.3 Hz), 7.99-7.28 (m, 6H), 4.94 (s, 1H), 4.48 (d, 1H, J = 7.9 Hz), 4.21 (d, 1H, J = 7.9 Hz), 3.77 (s, 3H), 3.03 (br s, 1H), 2.41 (s, 3H); ¹³C NMR (CDCl₃+DMSO, 100 MHz): δ 172.6, 150.8, 149.9, 140.1, 135.7, 130.2, 129.6, 129.1, 127.1, 124.0, 113.3, 111.5, 70.4, 60.9, 55.5, 53.2, 50.5, 21.3; HRMS (ESI) calcd for C₂₀H₁₉N₄O₂ [M+H]⁺ 347.1508 found [M+H]⁺ 347.1508.
Following the general procedure described above 9a was obtained after purification by silica column chromatography (EtOAc:Hexane = 100:0); colorless solid, mp:132-134 °C; FT-IR (KBr): 3338, 2955, 1738 and 1253 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 8.89 (d, 1H, \(J = 2.1\) Hz), 8.73 (dd, 1H, \(J_1 = 4.8, J_2 = 1.4\) Hz), 8.11-8.08 (m, 1H), 7.50 (d, 2H, \(J = 8.8\) Hz), 7.44 (dd, 1H, \(J_1 = 7.9, J_2 = 4.8\) Hz), 7.01 (d, 2H, \(J = 8.8\) Hz), 4.99 (s, 1H), 4.50 (d, 1H, \(J = 8.2\) Hz), 4.14 (d, 1H, \(J = 8.2\) Hz), 3.86 (s, 3H), 3.76 (s, 3H), 3.03 (br s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 173.2, 160.6, 151.4, 148.9, 135.2, 130.0, 129.6, 124.0, 123.9, 114.7, 113.2, 111.3, 68.1, 61.0, 57.8, 55.4, 53.3, 50.8; HRMS (ESI) calcd for C\(_{20}\)H\(_{19}\)N\(_4\)O\(_3\) [M+H]\(^+\) 363.1457 found [M+H]\(^+\) 363.1460.

Following the general procedure described above 9b was obtained after purification by silica column chromatography (EtOAc:Hexane = 90:10); colorless solid, mp: 157-159 °C; FT-IR (KBr): 3348, 2955, 2210, 1734 and 1220 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 8.89 (d, 1H, \(J = 1.9\) Hz), 8.73 (dd, 1H, \(J_1 = 4.8, J_2 = 1.3\) Hz), 8.09 (d, 1H, \(J = 8.0\) Hz), 7.47-7.42 (m, 3H), 7.29 (d, 2H, \(J = 8.0\) Hz), 5.00 (s, 1H), 4.54 (d, 1H, \(J = 8.2\) Hz), 4.15 (d, 1H, \(J = 8.2\) Hz), 3.76 (s, 3H), 3.06 (br s,1H), 2.41 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 173.2, 151.3, 148.8, 139.9, 135.3, 130.1, 129.9, 129.2, 128.2, 123.9, 113.2, 111.2, 68.2, 60.9, 58.0, 53.3, 50.7, 21.3; HRMS (ESI) calcd for C\(_{20}\)H\(_{19}\)N\(_4\)O\(_2\) [M+H]\(^+\) 347.1508 found [M+H]\(^+\) 347.1501.

Following the general procedure described above 9c was obtained after purification by silica column chromatography (EtOAc:Hexane = 100:0); colorless solid, mp:152-154 °C; FT-IR
(KBr): 3337, 2957, 1738 and 1218 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 8.89 (d, 1H, \(J = 2.2\) Hz), 8.74 (dd, 1H, \(J_1 = 4.9, J_2 = 1.7\) Hz), 8.09-8.07 (m, 1H), 7.45-7.36 (m, 3H), 7.15 (dd, 1H, \(J_1 = 5.1, J_2 = 3.7\) Hz), 5.00 (d, 1H, \(J = 3.9\) Hz), 4.54-4.49 (m, 2H), 3.81 (s, 3H), 3.03 (br s, 1H); \(^1\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 172.5, 151.6, 149.0, 135.1, 134.3, 129.5, 127.9, 127.8, 126.9, 123.9, 112.9, 110.9, 67.9, 62.3, 53.7, 53.4, 51.0; HRMS (ESI) calcd for C\(_{17}\)H\(_{15}\)N\(_4\)O\(_2\)S [M+H]\(^+\) 339.0916 found [M+H]\(^+\) 339.0911.

**General procedure for the preparation of 10a and 10b:** Cycloadducts 7a or 7b (1 mmol) in DCM (5 mL) was stirred for 5 min, and then triethyl amine (2 mmol) was added followed by acryloyl chloride (2 mmol) drop wise with cooling. Further, the reaction mixture was stirred for overnight under nitrogen atmosphere. After this period, the reaction mixture was quenched with water and extracted using DCM, combined the organic layers evaporated and the resulting crude mixture was subjected to column chromatography which gave the compounds 10a and 10b.

**General procedure for the azomethine ylide cycloaddition and preparation of 11a,b or 12a,b:** A mixture of pyrrolidine derivative 10a or 10b (0.14 mmol), glycine (0.28 mmol) or N-benzyl glycine hydrochloride (0.21 mmol) and paraformaldehyde (0.70 mmol) in toluene (1 mL) was heated at 110 °C for 12 h under nitrogen atmosphere. After this period, the reaction mixture was evaporated and the resulting crude reaction mixture was purified through chromatography which afforded the corresponding products 11a,b or 12a,b.

Following the general procedure described above 10a was obtained after purification by silica column chromatography (EtOAc:Hexane = 25:75); colorless solid; mp:222-224 °C; FT-IR (KBr): 2958, 1738, 1675, 1416 and 1218 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.51-7.44 (m, 6H), 7.30 (d, 2H, \(J = 8.0\) Hz), 6.30 (d, 1H, \(J = 16.4\) Hz), 5.78-5.70 (m, 2H), 5.48 (d, 1H, \(J = 10.5\) Hz), 5.28 (d, 1H, \(J = 10.5\) Hz), 4.15-4.10 (m, 1H), 3.72 (s, 3H), 2.41 (s, 3H); \(^1\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 169.7, 165.3, 140.7, 137.0, 132.0, 130.0, 128.5, 127.4, 125.3, 112.0, 110.4, 69.2, 62.9, 54.3, 53.3, 52.0, 21.3; HRMS (ESI) calcd for C\(_{24}\)H\(_{21}\)ClN\(_3\)O\(_3\) [M+H]\(^+\) 434.1271 found [M+H]\(^+\) 434.1247.
Following the general procedure described above, \textbf{10b} was obtained after purification by silica column chromatography (EtOAc:Hexane = 25:75); colorless solid; mp: 198-200 °C; FT-IR (KBr): 2954, 1738, 1655, 1416 and 1218 cm\(^{-1}\); \( ^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 7.46 (d, 2H, \( J = 8.1 \) Hz), 7.39 (d, 2H, \( J = 8.1 \) Hz), 7.31-7.28 (m, 4H), 6.28 (dd, 1H, \( J_1 = 16.6, J_2 = 1.3 \) Hz), 5.78 (dd, 1H, \( J_1 = 16.6, J_2 = 10.4 \) Hz), 5.68 (s, 1H), 5.43 (dd, 1H, \( J_1 = 10.4, J_2 = 1.3 \) Hz), 5.30 (d, 1H, \( J = 11.2 \) Hz), 4.10 (d, 1H, \( J = 11.2 \) Hz), 3.71 (s, 3H), 2.41 (s, 3H), 2.40 (s, 3H); \( ^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 169.9, 165.5, 141.0, 140.5, 130.4, 130.3, 130.2, 129.4, 128.3, 127.6, 127.0, 125.6, 112.2, 110.6, 69.8, 62.9, 54.3, 53.2, 52.3, 21.4, 21.3; HRMS (ESI) calcd for C\(_{25}\)H\(_{23}\)N\(_3\)NaO\(_3\) [M+Na]\(^+\) 436.1637 found [M+Na]\(^+\) 436.1624.

Following the general procedure described above, \textbf{11a} was obtained after purification by alumina column chromatography (EtOAc:Hexane = 45:55); colorless solid; mp: 218-220 °C; FT-IR (KBr): 2952, 1750, 1662, 1411 and 1218 cm\(^{-1}\); \( ^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 7.53-7.28 (m, 8H), 5.61 (s, 1H), 5.24 (d, 1H, \( J = 11.2 \) Hz), 4.06 (d, 1H, \( J = 11.2 \) Hz), 3.68 (s, 3H), 2.89 (t, 1H, \( J = 8.1 \) Hz), 2.64-2.58 (m, 2H), 2.40 (s, 3H), 2.36-2.32 (m, 3H), 2.30 (s, 3H), 1.93-1.89 (m, 1H); \( ^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 175.8, 169.6, 140.6, 137.0, 132.1, 130.2, 130.1, 128.2, 125.3, 112.0, 110.4, 69.4, 63.1, 60.1, 55.9, 54.3, 53.2, 52.0, 42.7, 41.5, 28.5, 21.3; HRMS (ESI) calcd for C\(_{27}\)H\(_{26}\)ClN\(_4\)O\(_3\) [M+H]\(^+\) 491.1850 found [M+H]\(^+\) 491.1852.
Following the general procedure described above 11b was obtained after purification by alumina column chromatography (EtOAc:Hexane = 45:55); colorless solid; mp: 190-192 °C; FT-IR (KBr): 2954, 1753, 1449 and 1218 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 7.44-7.27 (m, 8H), 5.59 (s, 1H), 5.24 (d, 1H, J = 11.2 Hz), 4.04 (d, 1H, J = 11.2 Hz), 3.68 (s, 3H), 2.87 (t, 1H, J = 8.8 Hz), 2.73-2.55 (m, 3H), 2.40 (s, 3H), 2.39 (s, 3H), 2.37-2.32 (m, 2H), 2.29 (s, 3H), 1.93-1.88 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ 176.0, 169.8, 141.0, 140.4, 130.5, 130.4, 130.1, 128.3, 126.9, 125.6, 112.3, 110.6, 69.9, 63.0, 60.1, 56.0, 54.2, 53.1, 52.2, 42.6, 41.5, 28.5, 21.3, 21.3; HRMS (ESI) calcd for C₂₈H₃₁N₄O₃ [M+H]⁺ 471.2396 found [M+H]⁺ 471.2411.

Following the general procedure described above 12a was obtained after purification by silica column chromatography (EtOAc:Hexane = 65:35); colorless semi solid; FT-IR (DCM): 2953, 1749, 1661, 1409 and 1218 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 7.53-7.28 (m, 13H), 5.59 (s, 1H), 5.22 (d, 1H, J = 11.2 Hz), 4.03(d, 1H, J = 11.2 Hz), 3.69 (s, 3H), 3.60 (s, 2H), 3.02 (t, 1H, J = 8.0 Hz), 2.77-2.62 (m, 2H), 2.40 (s, 3H), 2.39-2.34 (m, 3H), 1.94-1.91 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ 175.7, 169.5, 140.6, 138.2, 130.2, 130.1, 128.9, 128.4, 128.2, 127.3, 125.3, 112.0, 110.4, 69.3, 63.1, 59.8, 57.9, 54.2, 53.8, 53.2, 52.0, 42.2, 27.8, 21.3; HRMS (ESI) calcd for C₃₃H₃₂ClN₄O₃ [M+H]⁺ 567.2163 found [M+H]⁺ 567.2175.
Following the general procedure described above 12b was obtained after purification by silica column chromatography (EtOAc:Hexane = 65:35); colorless semi solid; FT-IR (DCM): 2952, 1749, 1660, 1411 and 1218 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.44-7.26 (m, 13H), 5.56 (s, 1H), 5.23 (d, 1H, $J = 11.2$ Hz), 4.03 (d, 1H, $J = 11.2$ Hz), 3.69 (s, 3H), 3.58 (s, 2H), 2.99 (t, 1H, $J = 8.5$ Hz), 2.72-2.67 (m, 2H), 2.40 (s, 3H), 2.40 (s, 3H), 2.37-2.31 (m, 3H), 1.95-1.90 (m, 1H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 176.0, 169.7, 141.0, 140.4, 138.6, 130.5, 130.4, 130.1, 128.9, 128.3, 128.3, 127.1, 127.0, 125.6, 112.3, 110.6, 69.8, 63.1, 60.0, 58.0, 54.2, 53.9, 53.1, 52.3, 42.1, 27.9, 21.3, 21.3; HRMS (ESI) calcd for C$_{34}$H$_{35}$N$_4$O$_3$ [M+H]$^+$ 547.2709 found [M+H]$^+$ 547.2719.
SpinWorks 3: RK 968

[Chemical structure image]

PPM

8.05  7.95  7.85  7.75  7.65  7.55  7.45  7.35  7.25  7.15

1.05  2.08  5.65
SpinWorks 3: RK 1002

7h
Isolated as mixture of isomers
SpinWorks 3: RK 1009 R

Isolated as mixture of isomers
Isolated as mixture of isomers
SpinWorks 3: RK 1023

Isolated as mixture of isomers

![Chemical Structure Image]
Isolated as mixture of isomers

SpinWorks 3: RK 994
isolated as a mixture of isomers
SpinWorks 3: RK 1007 R
PROTON CDCl3 /qpt/topspin nmr su 43

Isolated as a mixture of isomers
Isolated as a mixture of isomers
Isolated as a mixture of isomers
Isolated as a mixture of isomers
Isolated as a mixture of isomers
Isolated as a mixture of isomers
SpinWorks 3: RK 1046
PROTON CDCl3/opti/topspin nmr au 17

Isolated as a mixture of isomers
SpinWorks 3: RK 1046

Isolated as a mixture of isomers
SpinWorks 3: RK 1117
PROTON CDCl3 /opt/topspin nmrsu 3

![NMR Spectrum Image]

10a

[Chemical Structure Image]