One-pot, three-component route to spiropyrrolidine derivatives via a 1,3-dipolar cycloaddition reaction

Guo-Liang Feng[a]*, Hong-Li Zhang[a] and Li-Jun Geng[a,b]

[a]*School of Science, Hebei University of Science and Technology, Yuhua East Road, Shijiazhuang 050018, P. R. China*

[b]*Department of Chemistry, School of Science, Tianjin University, Weijin Road, Tianjin 300072, P. R. China*

A series of novel spiropyrrolidine derivatives were synthesised via three-component 1,3-dipolar cycloaddition reactions of 1-(1-methylpyrrole-2-yl)-3-aryl-2-cyano-1-propenones, isatin and sarcosine in refluxing methanol. The method affords a fast one-pot synthesis of spiroheterocycles in high yields. Their structures were established by ^{1}H NMR, IR and elementary analysis.

Keywords: spiropyrrolidine derivatives, 1-(1-methylpyrrole-2-yl)-3-aryl-2-cyano-1-propenones, isatin, sarcosine, 1,3-dipolar cycloaddition reaction

Multicomponent 1,3-dipolar cycloaddition are considered to be one of the most useful processes for the construction of a variety of five-membered heterocyclic compounds, such as pyrrolidines, pyrrolines and pyrroles.[1,2] These strategies offer significant advantages over more traditional approaches, allowing the construction of complex structures from easily available starting materials in a single operation without the need for the isolation of intermediates. Azomethine ylides, which are zwitterionic and are composed of one positively charged nitrogen atom and two terminal sp^2-hybridised carbon atoms, have gained significance in recent years for the construction of nitrogen containing five-membered heterocycles.[3–6] Spiroheterocycles including spiropyrrolidines represent an important class of substances characterised by their high biological activities.[7–10] Oxindole derivatives at C3 as spiro-carbo- have served as potential synthetic intermediates for the total synthesis of alkaloids, drug intermediates and clinical pharmaceuticals.[11,12]

Recently, we described a new and efficient synthesis of pyridine derivatives by multicomponent reactions.[13,14] In the light of our interest in multicomponent syntheses, we now describe an efficient method for the preparation of spiropyrrolidine derivatives by the 1,3-dipolar cycloaddition of azomethine ylides from isatin and sarcosine with 1-(1-methylpyrrole-2-yl)-3-aryl-2-cyano-1-propenones in methanol (Scheme 1).

1-(1-Methylpyrrole-2-yl)-3-aryl-2-cyano-1-propenones **1** were prepared through a reaction of 3-(1-methylpyrrole-2-yl)-3-oxopropanenitrile **5** and aromatic aldehydes **6 in** refluxing glycol monomethyl ether (Scheme 2).

In our initial study, the different refluxing solvents were tested in the synthesis of **4a**. The results were summarised in Table 1. The reactions in 1,4-dioxane and glycol monomethyl ether provided none of the desired product. When the reactions were carried out in ethanol, ethanol/water or methanol/water, compound **4a** was obtained in moderate yields (Table 1, entries 1–5). However, the reaction proceeded well in methanol to give a good yield of 83% in a short time (Table 1, entry 6).

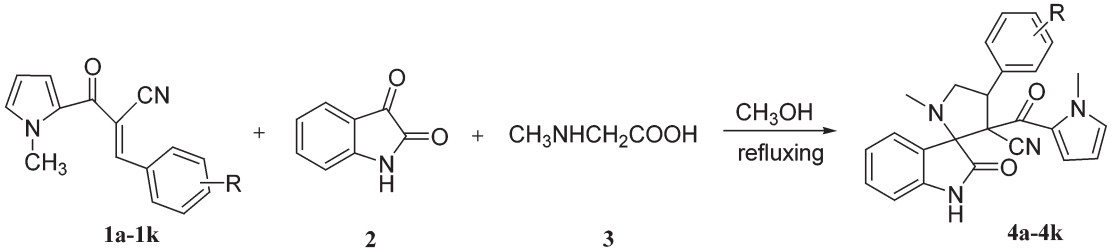
To extend the scope of this new procedure for the synthesis of spiropyrrolidines, a series of reactions were carried out with substituted derivatives **1** under these optimised conditions. We found that the reaction proceeded smoothly and the desired products were obtained in excellent yields. Interestingly, the electronic effect of the substituent on the aromatic ring had no significant influence on the reaction yields (Table 2).

The structures of the compounds **4a**–**k** were fully supported by IR, ^{1}H NMR and elementary analysis as demonstrated

Table 1 Optimisation of reaction conditions for the three-component reactions

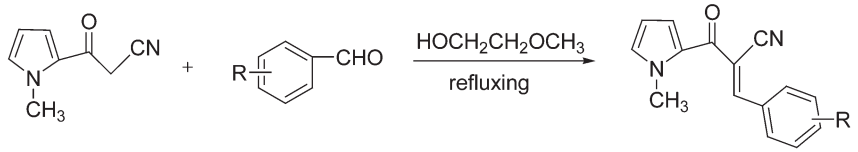
Entry	Solvent	Time/h	Yield/%[a]
1	1,4-dioxane	8	0
2	glycol monomethyl ether	8	0
3	ethanol	5	63
4	Ethanol : water(1:1)	5.5	32
5	Methanol : water(1:1)	4	44
6	methanol	2	83

[a]Isolated yield.



1a-1k 2 3 4a-4k

Scheme 1



5 6 1a-1k

Scheme 2

* Correspondent. E-mail: fgl197012@163.com

Table 2 Three-component synthesis of spiropyrrolidines in methanol

Entry	R	Product[a]	Time/h	Yield/%[b]	M. p. (°C)
1	H	**4a**	2	83	208–209 °C
2	4-CH_3	**4b**	2	84	233–234 °C
3	4-N(CH_3)$_2$	**4c**	1.5	76	209 °C
4	2-OCH_3	**4d**	1.5	88	193–195 °C
5	4-CH(CH_3)$_2$	**4e**	1.5	86	217–218 °C
6	3,4-(CH_3)$_2$	**4f**	1.5	89	231 °C
7	2,4-(CH_3)$_2$	**4g**	1.5	88	229–230 °C
8	3-NO_2	**4h**	2	82	202–203 °C
9	4-NO_2	**4i**	2	83	217–218 °C
10	2,4-Cl_2	**4j**	2	85	205–206 °C
11	3,4-(CH=CH-CH=CH)	**4k**	2	87	222–223 °C

[a] The products were characterised by ^{1}H NMR, IR and elementary analysis.
[b] Isolated yield.

for compound **4a**. The IR spectrum of **4a** showed two peaks at 1724 cm^{-1} and 1618 cm^{-1} which correspond to the isatin and 1-(1-methylpyrrole-2-yl)-3-aryl-2-cyano-1-propenones ring carbonyls, respectively. The peak at 2236 cm^{-1} correspond to the CN. In the ^{1}H NMR spectrum of **4a**, the –NH proton exhibited a singlet at δ 8.01. The –NCH_3 protons of the pyrrolidine exhibited a singlet at δ 2.23. The stereochemistry of the products has not been established.

Based on the above results, a possible mechanism for the reaction was proposed (Scheme 3). The isatin **2** reacts with sarcosine **3** to give intermediate **7** which underwent thermal decarboxylation leading to the azomethine ylides **8**. 1,3-Dipolar cycloaddition of 1-(1-methylpyrrole-2-yl)-3-aryl-2-cyano-1-propenones **1** with azomethine ylides **8** produced spiropyrrolidines **4**.

In summary, we have synthesised a number of interesting novel spiro compounds starting from 1-(1-methylpyrrole-2-yl)-3-aryl-2-cyano-1-propenones by 1,3-dipolar cycloaddition reaction. The experimental simplicity, compatibility with various functional groups, short reaction times and efficient yields made this procedure attractive to synthesise a variety of these derivatives.

Experimental

Melting points were recorded on an electrothermal digital melting point apparatus and are uncorrected. ^{1}H NMR spectra were determined on a Varian VXP-500 spectrometer using $CDCl_3$ as solvent and tetramethylsilane (TMS) as internal reference. IR spectra was obtained on a Nicolet FT-IR 6700 spectrophotometer using KBr pellets. Elementary analyses were performed by a Carlo-Erba EA1110 CNNO-S analyser.

Synthesis of **4a**–**k**: A mixture of 1-(1-methylpyrrole-2-yl)-3-aryl-2-cyano-1-propenone **1** (1mmol), isatin **2** (1mmol), sarcosine **3** (1mmol) and methanol (20 mL) was refluxed for the specified period of time. After complete conversion as indicated by TLC, the mixture was allowed to cool to room temperature and the solvent was removed in vacuo. The crude product was extracted with dichloromethane and washed with H_2O (3×15 mL) and the organic layer dried over $MgSO_4$. The solvent was removed *in vacuo* and the crude product was subjected to flash chromatography to afford the pure product (**4a–k**).

4a: ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.60 (s, 2H), 7.36–7.26 (m, 4H), 7.20–7.17 (m, 2H), 6.67 (t, 2H, *J* = 8.5 Hz), 6.13 (dd, 1H, *J* = 4.5 Hz and *J* = 2.0 Hz), 5.64 (dd, 1H, *J* = 4.5 Hz and *J* = 2.0 Hz), 5.38 (dd, 1H, *J* = 10.0 Hz and *J* = 7.0 Hz), 3.80–3.70 (m, 5H), 2.23 (s, 3H). IR(KBr): 3339, 3064, 3031, 2943, 2864, 2236, 1724, 1618, 1522, 1467 cm^{-1}. Anal. Calcd for $C_{25}H_{22}N_4O_2$: C, 73.15; H, 5.40; N, 13.65; Found: C, 73.04; H, 5.43; N, 13.53%.

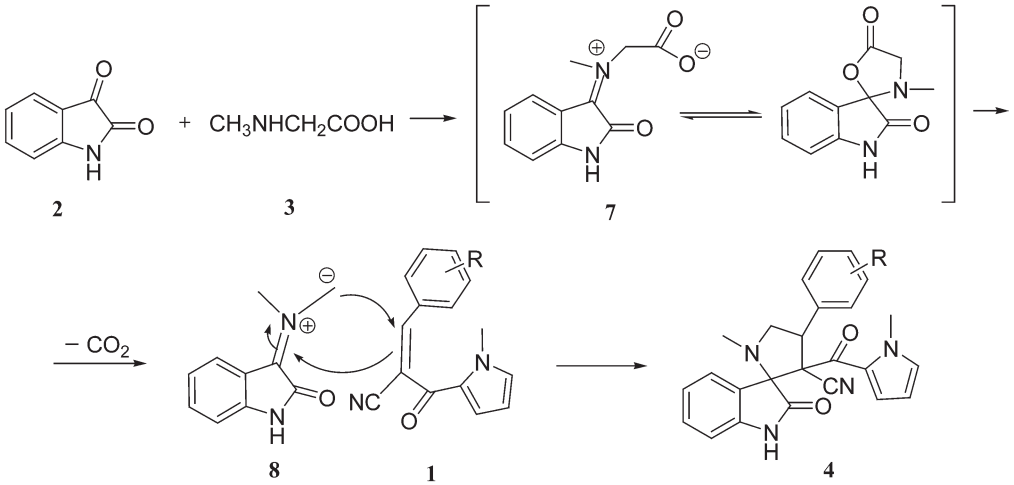
4b: ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.00 (s, 1H), 7.50 (d, 2H, *J* = 8.5 Hz), 7.37 (s, 1H), 7.32–7.28 (m, 1H), 7.20–7.16 (m, 3H), 6.71–6.67 (m, 2H), 6.16 (dd, 1H, *J* = 4.5 Hz and *J* = 2.0 Hz), 5.65 (dd, 1H, *J* = 4.5 Hz and *J* = 2.0 Hz), 5.36 (dd, 1H, *J* = 10.0 Hz and *J* = 7.0 Hz), 3.78–3.71 (m, 5H), 2.35 (s, 3H), 2.23 (s, 3H). IR(KBr): 3318, 3107, 2960, 2865, 2238, 1726, 1615, 1517, 1471 cm^{-1}. Anal. Calcd for $C_{26}H_{24}N_4O_2$: C, 73.56; H, 5.70; N, 13.20; Found: C, 73.62; H, 5.83; N, 13.31%.

4c: ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.44 (d, 2H, *J* = 7.0 Hz), 7.28 (s, 1H), 7.18–7.15 (m, 2H), 6.70–6.65 (m, 4H), 6.15 (dd, 1H, *J* = 4.5 Hz and *J* = 2.0 Hz), 5.66 (dd, 1H, *J* = 4.5 Hz and *J* = 2.0 Hz), 5.26 (dd, 1H, *J* = 10.0 Hz and *J* = 7.0 Hz), 3.75 (s, 3H), 3.72–3.69 (m, 2H), 2.93 (s, 6H), 2.23 (s, 3H). IR(KBr): 3314, 3103, 2961, 2856, 2790, 2239, 1724, 1715, 1618, 1512, 1470 cm^{-1}. Anal. Calcd for $C_{27}H_{27}N_5O_2$: C, 71.50; H, 6.00; N, 15.44; Found: C, 71.60; H, 6.11; N, 15.35%.

4d: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.88 (s, 1H), 7.29–7.26 (m, 3H), 7.12 (t, 1H, *J* = 7.5 Hz), 7.06 (t, 1H, *J* = 7.5 Hz), 6.79 (d, 1H, *J* = 8.0 Hz), 6.66–6.63 (m, 2H), 6.11 (dd, 1H, *J* = 4.5 Hz and *J* = 2.0 Hz), 5.67 (dd, 1H, *J* = 4.5 Hz and *J* = 2.0 Hz), 5.63 (dd, 1H, *J* = 9.5 Hz and *J* = 7.0 Hz), 3.78 (s, 3H), 3.71–3.68 (m, 2H), 3.34 (s, 3H), 2.18 (s, 3H). IR(KBr):3450, 3301, 2980, 2858, 2236, 1736, 1617, 1470 cm^{-1}. Anal. Calcd for $C_{26}H_{24}N_4O_3$: C, 70.89; H, 5.49; N, 12.72; Found: C, 70.78; H, 5.42; N, 12.84%.

4e: ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.00 (s, 1H), 7.51 (d, 2H, *J* = 8.0 Hz), 7.42–7.25 (m, 2H), 7.20–7.15 (m, 3H), 6.68 (d, 1H, *J* = 7.5 Hz), 6.65 (t, 1H, *J* = 2.0 Hz), 6.10 (dd, 1H, *J* = 4.5 Hz and *J* = 2.5 Hz), 5.63 (dd, 1H, *J* = 4.5 Hz and *J* = 2.5 Hz), 5.34 (d, 1H, *J* = 8.5 Hz), 3.75–3.71 (m, 5H), 2.92–2.86 (m, 1H), 2.23 (s, 3H), 1.24 (d, 6H, *J* = 7.0 Hz). IR(KBr): 3310, 3104, 2961, 2859, 2793, 2362, 1726, 1713, 1616, 1521, 1472 cm^{-1}. Anal. Calcd for $C_{28}H_{28}N_4O_2$: C, 74.31; H, 6.24; N, 12.38; Found: C, 74.36; H, 6.23; N, 12.31%.

4f: ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.34–7.27 (m, 4H), 7.17 (t, 1H, *J* = 7.5 Hz), 7.10 (d, 1H, *J* = 7.5 Hz), 6.68–6.64 (m, 2H), 6.13 (dd, 1H, *J* = 4.0 Hz and *J* = 2.5 Hz), 5.64 (dd, 1H, *J* = 4.5 Hz and



Scheme 3

J = 2.5 Hz), 5.26 (dd, 1H, *J* = 10.0 Hz and *J* = 7.0 Hz), 3.76 (s, 3H), 3.74–3.70 (m, 2H), 2.25 (s, 3H), 2.24 (s, 3H) 2.22 (s, 3H). IR(KBr): 3314, 3106, 2862, 2380, 1742, 1612, 1470 cm^{-1}. Anal. Calcd for $C_{27}H_{26}N_4O_2$: C, 73.95; H, 5.98; N, 12.78; Found: C, 73.97; H, 6.12; N, 12.85%.

4g: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95–7.90 (m, 2H), 7.31 (t, 1H, *J* = 7.5 Hz), 7.23 (s, 1H), 7.20 (d, 1H, *J* = 8.0 Hz), 7.12 (t, 1H, *J* = 8.0 Hz), 6.86 (s, 1H), 6.76 (d, 1H, *J* = 8.0 Hz), 6.69 (s, 1H), 6.11 (t, 1H, *J* = 2.5 Hz), 5.67 (dd, 1H, *J* = 4.5 Hz and *J* = 2.5 Hz), 5.39 (dd, 1H, *J* = 9.5 Hz and *J* = 5.5 Hz), 3.75–3.69 (m, 4H), 3.55–3.50 (m, 1H), 2.32 (s, 3H), 2.18 (s, 3H), 2.05 (s, 3H). IR(KBr): 3310, 3108, 2857, 2360, 1749, 1614, 1465 cm^{-1}. Anal. Calcd for $C_{27}H_{26}N_4O_2$: C, 73.95; H, 5.98; N, 12.78; Found: C, 73.87; H, 5.91; N, 12.75%.

4h: ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.50 (s, 1H), 8.16 (d, 1H, *J* = 7.5 Hz), 7.99–7.96 (m, 2H), 7.54 (t, 1H, *J* = 8.0 Hz), 7.34–7.31 (m, 1H), 7.25–7.23 (m, 1H), 7.18 (s, 1H), 6.70 (s, 1H), 6.66 (d, 1H, *J* = 7.5 Hz), 6.17(dd, 1H, *J* = 4.5 Hz and *J* = 2.5 Hz), 5.66 (dd, 1H, *J* = 4.5 Hz and *J* = 2.5 Hz), 5.56 (dd, 1H, *J* = 10.0 Hz and *J* = 5.5 Hz), 3.83 (t, 1H, *J* = 9.5 Hz), 3.80 (s, 3H), 3.70 (dd, 1H, *J* = 9.5 Hz and *J* = 6.0 Hz), 2.25 (s, 3H). IR(KBr): 3319, 3107, 2957, 2863, 2240, 1730, 1615, 1520, 1468 cm^{-1}. Anal. Calcd for $C_{25}H_{21}N_5O_4$: C, 65.93; H, 4.65; N, 15.38; Found: C, 65.88; H, 4.75; N, 15.40%.

4i: ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.23 (s, 2H), 7.99 (s, 1H), 7.78 (s, 2H), 7.32–7.29 (m, 1H), 7.26–7.14 (m, 2H), 6.70 (t, 1H, *J* = 2.0 Hz), 6.66 (d, 1H, *J* = 7.5 Hz), 6.18 (dd, 1H, *J* = 5.0 Hz and *J* = 2.0 Hz), 5.66 (dd, 1H, *J* = 4.0 Hz and *J* = 2.0 Hz), 5.56 (dd, 1H, *J* = 10.0 Hz and *J* = 6.0 Hz), 3.81 (t, 1H, *J* = 9.5 Hz), 3.79 (s, 3H), 3.68 (dd, 1H, *J* = 10.0 Hz and *J* = 6.0 Hz), 2.24 (s, 3H). IR(KBr): 3325, 3092, 2972, 2867, 2235, 1724, 1618, 1523, 1470 cm^{-1}. Anal. Calcd for $C_{25}H_{21}N_5O_4$: C, 65.93; H, 4.65; N, 15.38; Found: C, 65.95; H, 4.71; N, 15.47%.

4j: ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.00 (s, 1H), 7.85 (s, 1H), 7.44 (dd, 1H, *J* = 8.5 Hz and *J* = 2.0 Hz), 7.34–7.31 (m, 1H), 7.26 (s, 1H), 7.12 (t, 1H, *J* = 7.5 Hz), 6.76 (d, 1H, *J* = 8.0 Hz), 6.74 (s, 1H), 6.24 (dd, 1H, *J* = 4.5 Hz and *J* = 2.5 Hz), 5.73 (dd, 1H, *J* = 4.5 Hz and *J* = 2.5 Hz), 5.66 (dd, 1H, *J* = 9.5 Hz and *J* = 5.0 Hz), 5.30 (s, 1H), 3.81 (t, 1H, *J* = 9.5 Hz), 3.77(s, 3H), 3.47 (dd, 1H, *J* = 9.5 Hz and *J* = 5.0 Hz), 2.18 (s, 3H). IR(KBr): 3318, 3106, 2970, 2862, 2359, 1738, 1617, 1470 cm^{-1}. Anal. Calcd for $C_{25}H_{20}N_4O_2Cl_2$: C, 62.64; H, 4.21; N, 11.69; Found: C, 62.69; H, 4.16; N, 11.77%.

4k: ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14–8.04 (m, 2H), 7.85–7.81 (m, 3H), 7.76 (dd, 1H, *J* = 8.5 Hz and *J* = 2.0 Hz), 7.45 (dd, 2H, *J* = 6.5 Hz and *J* = 3.0 Hz), 7.33–7.29 (m, 1H), 7.26–7.19 (m, 2H), 6.68 (d, 1H, *J* = 7.5 Hz), 6.64 (t, 1H, *J* = 1.5 Hz), 6.13 (dd, 1H, *J* = 4.5 Hz and *J* = 1.5 Hz), 5.58–5.53 (m, 2H), 3.86 (d, 2H, *J* = 8.5 Hz), 3.78 (s, 3H), 2.28 (s, 3H). IR(KBr): 3288, 3107, 2861, 2360, 1742, 1613, 1469, 1404, 1362 cm^{-1}. Anal. Calcd for $C_{29}H_{24}N_4O_2$: C, 75.63; H, 5.25; N, 12.17; Found: C, 75.66; H, 5.39; N, 12.13%.

Synthesis of **1a**–k: A mixture of **5** (0.45 g, 3 mmol), **6** (3 mmol) and glycol monomethyl ether (10 mL) were refluxed for 2 h (the progress was monitored by TLC). After completion of the reaction, the mixture was allowed to cool to room temperature and the crude products were precipitated. The crude product was chromatographed on silica gel (200–300 mesh) using a mixture of petroleum ether and dichloromethane as eluent to afford the pure product **1a–k**.

1a: ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 8.09 (s, 1H), 8.00–7.98 (m, 2H), 7.54–7.49 (m, 3H), 7.37 (dd, 1H, *J* = 1.5 Hz and *J* = 4.0 Hz), 6.97 (d, 1H, *J* = 1.5 Hz), 6.23 (dd, 1H, *J* = 2.5 Hz and *J* = 4.0 Hz), 3.98 (s, 3H). Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.32; H, 5.09; N, 11.91%.

1b: ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 8.07 (s, 1H), 7.90 (d, 2H, *J* = 8.5 Hz), 7.36 (dd, 1H, *J* = 1.5 Hz and *J* = 4.5 Hz), 7.31 (d, 2H, *J* = 8.5 Hz), 6.95 (t, 1H, *J* = 2.0 Hz), 6.20 (dd, 1H, *J* = 2.0 Hz and *J* = 4.5 Hz), 3.98 (s, 3H), 2.44 (s, 3H). Anal. Calcd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.72; H, 5.69; N, 11.10%.

1c: ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 8.07 (s, 1H), 7.99 (dd, 2H, *J* = 1.5 Hz and *J* = 7.5 Hz), 7.37 (dd, 1H, *J* = 1.5 Hz and *J* = 4.0 Hz), 6.89 (t, 1H, *J* = 1.5 Hz), 6.71 (d, 2H, *J* = 7.5 Hz), 6.19 (dd, 1H, *J* = 2.5 Hz and *J* = 4.0 Hz), 3.96 (s, 3H), 3.11 (s, 6H). Anal. Calcd for $C_{17}H_{17}N_3O$: C, 73.10; H, 6.13; N, 15.04. Found: C, 73.19; H, 6.17; N, 15.08%.

1d: ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 8.56 (s, 1H), 8.30 (dd, 1H, *J* = 1.5 Hz and *J* = 8.0 Hz), 7.52–7.48 (m, 1H), 7.31 (dd, 1H, *J* = 1.5 Hz and *J* = 4.0 Hz), 7.08 (t, 1H, *J* = 7.5 Hz), 6.97–6.95 (m, 2H), 6.21 (dd, 1H, *J* = 2.5 Hz and *J* = 4.0 Hz), 3.98 (s, 3H), 3.89 (s, 3H). Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.19; H, 5.37; N, 10.48%.

1e: ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 8.05 (s, 1H), 7.86 (d, 2H, *J* = 8.5 Hz), 7.36 (dd, 1H, *J* = 1.5 Hz and *J* = 4.0 Hz), 7.30 (d, 2H, *J* = 8.5 Hz), 6.95 (t, 1H, *J* = 2.0 Hz), 6.20 (dd, 1H, *J* = 2.0 Hz and *J* = 4.5 Hz), 3.98 (s, 3H), 2.90–2.85 (m, 1H), 1.23 (d, 6H, *J* = 7.0 Hz). Anal. Calcd for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.06. Found: C, 77.69; H, 6.43; N, 10.08%.

1f: ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 8.04 (s, 1H), 7.79 (d, 1H, *J* = 8.0 Hz), 7.76 (s, 1H), 7.35 (dd, 1H, *J* = 1.5 Hz and *J* = 4.0 Hz), 7.26 (d, 1H, *J* = 7.5 Hz), 6.95 (t, 1H, *J* = 1.5 Hz), 6.21 (dd, 1H, *J* = 2.5 Hz and *J* = 4.5 Hz), 3.97 (s, 3H), 2.34 (s, 3H), 2.33 (s, 3H). Anal. Calcd for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.19; H, 6.19; N, 10.48%.

1g: ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 8.36 (s, 1H), 8.20 (d, 1H, *J* = 8.0 Hz), 7.36 (dd, 1H, *J* = 1.5 Hz and *J* = 4.0 Hz), 7.15 (d, 1H, *J* = 8.0 Hz), 7.15 (s, 1H), 6.96 (t, 1H, *J* = 1.5 Hz), 6.22 (dd, 1H, *J* = 2.5 Hz and *J* = 4.5 Hz), 3.99 (s, 3H), 2.40 (s, 3H), 2.38 (s, 3H). Anal. Calcd for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.32; H, 6.09; N, 10.53%.

1h: ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 8.70 (s, 1H), 8.41 (d, 1H, *J* = 8.0 Hz), 8.39–8.37 (m, 1H), 8.11 (s, 1H), 7.73 (t, 1H, *J* = 8.0 Hz), 7.40 (dd, 1H, *J* = 1.5 Hz and *J* = 4.0 Hz), 7.01 (t, 1H, *J* = 1.5 Hz), 6.26 (dd, 1H, *J* = 2.5 Hz and *J* = 4.0 Hz), 4.00 (s, 3H). Anal. Calcd for $C_{15}H_{11}N_3O_3$: C, 64.05; H, 3.94; N, 14.94. Found: C, 64.09; H, 3.87; N, 14.93%.

1i: ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 8.36–8.34 (m, 2H), 8.14–8.10 (m, 3H), 7.40 (dd, 1H, *J* = 1.5 Hz and *J* = 4.5 Hz), 7.02 (t, 1H, *J* = 1.5 Hz), 6.26 (dd, 1H, *J* = 2.5 Hz and *J* = 4.0 Hz), 4.00 (s, 3H). Anal. Calcd for $C_{15}H_{11}N_3O_3$: C, 64.05; H, 3.94; N, 14.94. Found: C, 64.11; H, 3.95; N, 14.87%.

1j: ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 8.36 (s, 1H), 8.20 (d, 1H, *J* = 8.5 Hz), 7.53 (d, 1H, *J* = 2.0 Hz), 7.41 (d, 1H, *J* = 8.5 Hz), 7.34 (dd, 1H, *J* = 1.5 Hz and *J* = 4.5 Hz), 7.00 (t, 1H, *J* = 2.0 Hz), 6.24 (dd, 1H, *J* = 2.5 Hz and *J* = 4.0 Hz), 3.99 (s, 3H). Anal. Calcd for $C_{15}H_{10}Cl_2N_2O$: C, 59.04; H, 3.30; N, 9.18. Found: C, 59.09; H, 3.21; N, 9.23%.

1k: ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 8.40 (s, 1H), 8.25 (s, 1H), 8.20 (dd, 1H, *J* = 1.5 Hz and *J* = 8.5 Hz), 7.96–7.93 (m, 2H), 7.89 (d, 1H, *J* = 8.0 Hz), 7.62 (t, 1H, *J* = 8.0 Hz), 7.56 (t, 1H, *J* = 8.0 Hz), 7.41 (dd, 1H, *J* = 1.5 Hz and *J* = 4.0 Hz), 6.98 (t, 1H, *J* = 1.5 Hz), 6.24 (dd, 1H, *J* = 2.5 Hz and *J* = 4.5 Hz), 4.00 (s, 3H). Anal. Calcd for $C_{19}H_{14}N_2O$: C, 79.70; H, 4.93; N, 9.78. Found: C, 79.79; H, 4.87; N, 9.69%.

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