A Novel and Simple Synthesis of 9*H*-Pyrimido[4,5-*b*]indoles under Microwave Irradiation and Solvent-Free Conditions

Mehdi Adib,*[a] Bagher Mohammadi,[a] Hamid Reza Bijanzadeh[b]

[a] School of Chemistry, University College of Science, University of Tehran, P.O. Box 14155-6455, Tehran, Iran
Fax +98(21)66495291; E-mail: madib@khayam.ut.ac.ir

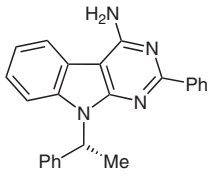
[b] Department of Chemistry, Tarbiat Modarres University, P.O. Box 14115-175, Tehran, Iran

Received 14 May 2007

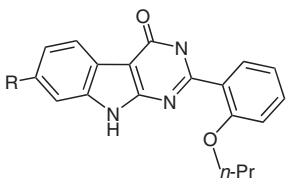
Abstract: A novel synthesis of 9*H*-pyrimido[4,5-*b*]indoles is described from a simple microwave-assisted reaction between oxindoles and aryl nitriles under solvent-free conditions in good to excellent yields.

Key words: 9*H*-pyrimido[4,5-*b*]indoles, oxindoles, aryl nitriles, solvent-free synthesis, cyclizations, heterocycles

Pyrimido[4,5-*b*]indoles, fused tricyclic 6:5:6 compounds with three nitrogen atoms (2:1:0; positions 1, 3, and 9, and bicyclic 5:6 analogues, pyrrolo[2,3-*d*]pyrimidines), are of interest because of their extensive use as active ingredients of pharmaceutical preparations.[1,2] Recently some of these compounds have been reported as useful new drugs in treatment of myocardial injury, pulmonary hypertension, renal failure, Huntington's chorea, as well as neurodegenerative disorders such as Parkinson's disease, Alzheimer's disease and focal ischemia.[2] Furthermore, some examples have been used as A1 and A3 adenosine receptor antagonists (Figure 1, **1**),[3] bronchodilators (Figure 1, **2**),[4] blood platelet aggregation inhibitors,[5] antihypertensive agents,[5] epidermal growth factor receptor tyrosine kinase (EGFRTK) inhibitors,[2] mitogen-activated protein kinase (MAPK) inhibitors,[2] and antagonists at CRF1 receptors.[6]



1, a potent A1 adenosine receptor antagonist



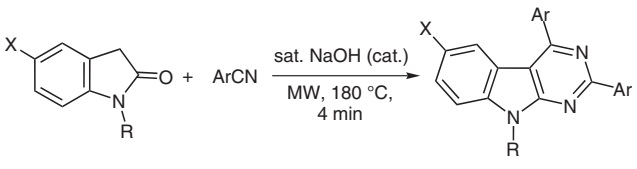
2, R = MeS, NH_2, MeNH active bronchodilators

Figure 1 Examples of biologically active pyrimido[4,5-*b*]indoles.

So far, several synthetic methods have been reported for the preparation of pyrimido[4,5-*b*]indole ring systems. The most common synthetic routes involve ring closure of 2,3-functionalized indoles, e.g. 2-aminoindole-3-carboxylates or 2-aminoindole-3-carbonitriles with CN atom fragments such as formamide or cyanamide.[2,7] Other synthetic approaches involve: reaction of 2-ethoxy-3-benzylidenindolenine tetrafluoroborate with amidines, guanidine and thiourea,[8] extension of the Nenitzescu reaction,[9] heteroannulation of 2-[bis(methylthio)methylene]-1-methyl-3-oxoindole with β-substituted β-lithioaminoacrylonitriles, malononitrile and guanidine,[10] palladium-catalyzed arylation of pyrimidine substrates,[11] addition of glycine ethyl ester to 2,4,6-trichloropyrimidine,[12] aza-wittig-type reaction of bisiminophosphoranes with aromatic isocyanates,[13] cyclization of 4-azidouracils[14] and 6-(phenylhydrazino)uracils,[15] and also oxidation of the corresponding 5,6,7,8-tetrahydropyrimido[4,5-*b*]indoles.[16] Most of the reported synthetic methods suffer from disadvantages such as the use of volatile organic solvents, unsatisfactory product yields and relatively long reaction times. In addition, in some of these methods the reactants such as 2,3-functionalized indoles, β-substituted β-lithioaminoacrylonitriles, bisiminophosphoranes, or uracil derivatives have to be synthesized first, hence these methods are relatively expensive and time-consuming.

The application of microwave irradiation in organic synthesis for conducting reactions at highly accelerated rates is an emerging technique.[17] In fact, in recent years, the use of microwaves have become popular among synthetic organic chemists both to improve classical organic reactions (shortening reaction times and/or improving yields) as well as to promote new reactions.

As part of our ongoing program to develop new facile methods for the preparation of biologically active heterocyclic compounds from readily available building blocks, we report herein a new facile method for the synthesis of pyrimido[4,5-*b*]indoles. Thus, oxindoles **3** react with a range of aryl nitriles **4** under microwave irradiation[18] and solvent-free conditions to produce 9*H*-pyrimido[4,5-*b*]indoles **5a–s** in 69–85% yields (Scheme 1, Table 1).



3 **4** **5**

Scheme 1

SYNLETT 2008, No. 2, pp 0177–0180
Advanced online publication: 21.12.2007
DOI: 10.1055/s-2007-1000872; Art ID: D14607ST

The reactions were carried out by first mixing the oxindole and the nitrile. Then, a catalytic amount of saturated aqueous NaOH solution was added and the reaction mixture was irradiated in a microwave oven at 180 °C for four minutes (progress of the reaction was followed by TLC monitoring minute by minute). TLC and ^{1}H NMR analysis of the reaction mixtures clearly indicated the formation of pyrimido[4,5-*b*]indole derivatives **5** in good to excellent yields.[19]

Table 1 Synthesis of 9*H*-Pyrimido[4,5-*b*]indoles **5a–s**

5	R	X	Ar	Yield (%)[a]
a	H	H	Ph	80
b	H	H	2-MeC_6H_4	74
c	H	H	4-MeC_6H_4	78
d	H	H	4-MeOC_6H_4	75
e	H	H	3-O_2NC_6H_4	84
f	H	H	4-O_2NC_6H_4	85
g	H	H	4-FC_6H_4	84
h	H	H	2-ClC_6H_4	80
i	H	H	3-ClC_6H_4	85
j	H	H	4-ClC_6H_4	85
k	H	H	2-BrC_6H_4	79
l	H	H	3-BrC_6H_4	84
m	H	H	4-BrC_6H_4	85
n	Me	H	Ph	77
o	Me	H	4-BrC_6H_4	82
p	Me	H	4-MeC_6H_4	75
q	H	Br	4-MeC_6H_4	70
r	H	Br	3-BrC_6H_4	73
s	H	Br	3-ClC_6H_4	69

[a] Isolated yields.

The structures of the isolated products **5a–s** were corroborated by IR, ^{1}H NMR and ^{13}C NMR spectroscopy, mass spectrometry, and elemental analysis.[19,20]

In conclusion, we have developed a novel microwave-assisted synthesis of pyrimido[4,5-*b*]indoles of potential synthetic and pharmacological interest. The use of commercial materials, fewer reagents and atomic economy, good to excellent yields, short reaction times, and solvent-free conditions are the main advantages of this method. This method presents a straightforward procedure for the synthesis of pyrimido[4,5-*b*]indoles.

Acknowledgment

This research was supported by the Research Council of University of Tehran as a research project (6102036/1/02).

References and Notes

(1) Delia, T. J.; Hurst, D. T. In *Comprehensive Heterocyclic Chemistry II*, Vol. 7; Katritzky, A. R.; Rees, C. W.; Scriven, E. V. F., Eds.; Pergamon Press: London, **1996**, Chap. 7, 229–281; and references therein.
(2) Lowinger, T.; Shimazaki, M.; Sato, H.; Tanaka, K.; Tsuno, N.; Marx, K.; Yamamoto, M.; Urbahns, K.; Gantner, F.; Okigami, H.; Nakashima, K.; Takeshita, K.; Bacon, K. B.; Komura, H.; Yoshida, N. PCT Int. Appl., WO03037898, **2003**.
(3) Hess, S.; Muller, C. E.; Frobenius, W.; Reith, U.; Klotz, K. N.; Eger, K. *J. Med. Chem.* **2000**, *43*, 4636.
(4) Coates, W. J. US Patent 5162316, **1992**.
(5) Monge, A.; Palop, J. A.; Goni, T.; Parrado, P.; Martinez, F.; Fernandezalvarez, E. *An. Quim., Ser. C* **1988**, *84*, 38.
(6) Yuan, J.; Hutchison, A. US Patent 6495688, **2002**.
(7) Glushkov, R. G.; Volskova, V. A.; Magidson, O. Y. *Khim.-Farm. Zh.* **1967**, *1*, 25.
(8) Borovik, V. P.; Shkurko, O. P. *Russ. Chem. Bull.* **2002**, *51*, 2129.
(9) (a) Dotzauer, B.; Troschütz, R. *Synlett* **2004**, 1039. (b) Bernier, J.-L.; Hénichart, J.-P. *J. Org. Chem.* **1981**, *46*, 4197.
(10) Kumar, U. K. S.; Yadav, A. K.; Venkatesh, C.; Ila, H.; Junjappa, H. *ARKIVOC* **2004**, *(viii)*, 20.
(11) Zhang, Y. M.; Razler, T.; Jackson, P. F. *Tetrahedron Lett.* **2002**, *43*, 8235.
(12) Bundy, G. L.; Banitt, L. S.; Dobrowolski, P. J.; Palmer, J. R.; Schwartz, T. M.; Zimmermann, D. C.; Lipton, M. F.; Mauragis, M. A.; Veley, M. F.; Appell, R. B.; Clouse, R. C.; Daugs, E. D. *Org. Process Res. Dev.* **2001**, *5*, 144.
(13) (a) Molina, P.; Arques, A.; Alias, A.; Vinader, M. V. *Tetrahedron Lett.* **1991**, *34*, 4401. (b) Molina, P.; Fresneda, P. M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1819.
(14) Lapachev, V. V.; Stadlbauer, W.; Kappe, T. *Monatsh. Chem.* **1988**, *119*, 97.
(15) Wright, G. E. *J. Heterocycl. Chem.* **1976**, *13*, 539.
(16) Eger, K.; Lanzner, W.; Rothenhaüsler, K. *Liebigs Ann. Chem.* **1993**, *5*, 465.
(17) *Microwaves in Organic Synthesis*, 2nd reprint; Loupy, A., Ed.; Wiley-VCH: Weinheim, **2004**.
(18) The experiments were performed using a microwave oven (ETHOS 1600, Milestone) with a power of 600 W specially designed for organic synthesis.
(19) Full spectroscopic assignment of compound **5a** has been made in: Borovik, V. P.; Shakirov, M. M.; Shkurko, O. P.; Vorozhtsov, N. N. *Khim. Geterotsikl. Soedin.* **2003**, 1531.
(20) **Preparation of 2,4-Diphenyl-9*H*-pyrimido[4,5-*b*]indole (5a); General Procedure**: A mixture of oxindole (0.13 g, 1 mmol), benzonitrile (0.31 g, 3 mmol), and a catalytic amount of sat. aq NaOH solution was irradiated in a microwave oven at 180 °C for 4 min (progress of the reaction was followed by TLC monitoring minute by minute). Then the reaction mixture was cooled to r.t. and the residue was purified by column chromatography [using *n*-hexane–EtOAc (4:1) as eluent, Merck silica gel 60 mesh]. The solvent was removed and the product was recrystallized from 95% EtOH.
Selected Data:
Compound **5a**: colorless crystals; mp 300–302 °C. IR (KBr): 3225 (NH), 1580, 1547, 1482, 1443, 1398, 1365, 1255, 1209, 760, 744, 693 cm^{-1}. ^{1}H NMR (500.1 MHz, DMSO-d_6):

δ = 7.21 (t, *J* = 7.7 Hz, 1 H, CH), 7.52 (t, *J* = 7.5 Hz, 1 H, CH), 7.53–7.59 (m, 3 H, 3 × CH), 7.60 (d, *J* = 8.1 Hz, 1 H, CH), 7.65–7.72 (m, 3 H, 3 × CH), 7.83 (d, *J* = 8.0 Hz, 1 H, CH), 8.04 (dd, *J* = 1.5, 8.0 Hz, 2 H, 2 × CH), 8.58 (dd, *J* = 1.5, 8.2 Hz, 2 H, 2 × CH), 12.53 (br, 1 H, NH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 108.91 (C), 111.99 (CH), 118.82 (C), 120.56, 121.78, 127.36, 127.79, 128.47, 128.63, 128.78, 129.93, 130.13 (9 × CH), 138.10, 138.58, 139.38, 157.35, 159.02, 159.29 (6 × C). MS: *m*/*z* (%) = 321 (27) [M$^+$], 320 (67) [M$^+$ – 1], 242 (14), 190 (26), 164 (14), 105 (58), 84 (44), 77 (76), 57 (86), 43 (100). Anal. Calcd for $C_{22}H_{15}N_3$ (321.38): C, 82.22; H, 4.70; N, 13.07. Found: C, 82.1; H, 4.8; N, 12.8.

Compound **5c**: colorless crystals; mp 295–296 °C. IR (KBr): 3285 (NH), 1587, 1549, 1433, 1397, 1368, 1252, 1214, 1179, 796, 739, 718 cm^{-1}. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ = 2.40, 2.49 (2 × s, 6 H, 2 × Me), 7.20 (t, *J* = 7.2 Hz, 1 H, CH), 7.36 (d, *J* = 7.5 Hz, 2 H, 2 × CH), 7.47–7.51 (m, 3 H, 3 × CH), 7.58 (d, *J* = 7.8 Hz, 1 H, CH), 7.86 (d, *J* = 7.7 Hz, 1 H, CH), 7.93 (d, *J* = 7.4 Hz, 2 H, 2 × CH), 8.46 (d, *J* = 7.6 Hz, 2 H, 2 × CH), 12.45 (br s, 1 H, NH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 20.93, 21.01 (2 × Me), 108.51 (C), 111.78 (CH), 118.89 (C), 120.56, 121.76, 127.20, 127.75, 128.73, 129.08, 129.16 (7 × CH), 135.43, 135.76, 138.95, 139.65, 139.81, 157.21, 159.10, 159.42 (8 × C). MS: *m*/*z* (%) = 349 (30) [M$^+$], 348 (100) [M$^+$ – 1], 334 (27), 273 (18), 107 (45), 102 (14), 91 (64), 77 (40), 57 (33). Anal. Calcd for $C_{24}H_{19}N_3$ (349.44): C, 82.49; H, 5.48; N, 12.03. Found: C, 82.3; H, 5.7; N, 11.7.

Compound **5f**: colorless crystals; mp 320 °C (dec.). IR (KBr): 3260 (NH), 1585, 1543, 1525, 1479, 1440, 1396, 1345, 1255, 1210, 798 cm^{-1}. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ = 7.25 (t, *J* = 7.5 Hz, 1 H, CH), 7.55 (dd, *J* = 7.5, 7.7 Hz, 1 H, CH), 7.60 (d, *J* = 7.7 Hz, 1 H, CH), 7.88 (d, *J* = 7.9 Hz, 1 H, CH), 7.92 (d, *J* = 8.5 Hz, 2 H, 2 × CH), 7.95 (d, *J* = 8.6 Hz, 2 H, 2 × CH), 8.65 (d, *J* = 8.5 Hz, 2 H, 2 × CH), 8.89 (d, *J* = 8.6 Hz, 2 H, 2 × CH), 12.05 (br, 1 H, NH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 110.25 (C), 112.11 (CH), 119.71 (C), 120.09, 122.18, 127.64, 127.75, 128.95, 129.14, 131.66 (7 × CH), 136.44, 138.71, 139.98, 147.51, 148.60, 157.69, 158.50, 159.33 (8 × C). MS: *m*/*z* (%) = 411 (19) [M$^+$], 410 (100) [M$^+$ – 1], 381 (23), 365 (9), 353 (44), 335 (15), 289 (31), 148 (60), 115 (23), 76 (36). Anal. Calcd for $C_{22}H_{13}N_5O_4$ (411.38): C, 64.23; H, 3.19; N, 17.02. Found: C, 64.1; H, 3.3; N, 16.9.

Compound **5g**: colorless crystals; mp 276–277 °C. IR (KBr): 3200 (NH), 1575, 1485, 1439, 1402, 1360, 1257, 1220, 1091, 902, 785, 741, 700 cm^{-1}. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ = 7.23 (t, *J* = 7.9 Hz, 1 H, CH), 7.28 (dd, $^3J_{FH}$ = 8.8 Hz, $^3J_{HH}$ = 8.8 Hz, 2 H, 2 × CH), 7.46 (dd, $^3J_{FH}$ = 8.8 Hz, $^3J_{HH}$ = 8.7 Hz, 2 H, 2 × CH), 7.55 (dd, *J* = 7.4, 7.8 Hz, 1 H, CH), 7.67 (d, *J* = 8.1 Hz, 1 H, CH), 7.94 (d, *J* = 8.0 Hz, 1 H, CH), 8.17 (dd, $^4J_{FH}$ = 5.5 Hz, $^3J_{HH}$ = 8.7 Hz, 2 H, 2 × CH), 8.70 (dd, $^4J_{FH}$ = 5.7 Hz, $^3J_{HH}$ = 8.8 Hz, 2 H, 2 × CH), 11.40 (br s, 1 H, NH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 110.16 (C), 112.77 (CH), 115.97 (d, $^2J_{FC}$ = 22.0 Hz, CH), 116.44 (d, $^2J_{FC}$ = 22.0 Hz, CH), 120.43 (C), 121.88, 123.15, 128.45 (3 × CH), 131.27 (d, $^3J_{FC}$ = 8.6 Hz, CH), 132.27 (d, $^3J_{FC}$ = 8.6 Hz, CH), 135.94 (d, $^4J_{FC}$ = 3.2 Hz, C), 136.43 (d, $^4J_{FC}$ = 3.3 Hz, C), 140.25, 158.76, 159.58, 160.18 (4 × C), 164.81 (d, $^1J_{FC}$ = 245.4 Hz, CF), 165.30 (d, $^1J_{FC}$ = 245.4 Hz, CF). MS: *m*/*z* (%) = 357 (77) [M$^+$], 356 (100) [M$^+$ – 1], 260 (6), 233 (8), 208 (13), 178 (9), 149 (5), 114 (4), 95 (8), 69 (13), 57 (10). Anal. Calcd for $C_{22}H_{13}F_2N_3$ (357.36): C, 73.94; H, 3.67; N, 11.76. Found: C, 73.8; H, 3.9; N, 11.6.

Compound **5i**: colorless crystals; mp 233–235 °C. IR (KBr): 3140 (NH), 1587, 1539, 1364, 1249, 1210, 1071, 763, 739, 692 cm^{-1}. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ = 7.21 (t, *J* = 7.5 Hz, 1 H, CH), 7.52 (t, *J* = 7.7 Hz, 1 H, CH), 7.53–7.57 (m, 2 H, 2 × CH), 7.59 (d, *J* = 8.0 Hz, 1 H, CH), 7.69–7.73 (m, 2 H, 2 × CH), 7.76 (d, *J* = 8.0 Hz, 1 H, CH), 7.97 (d, *J* = 6.7 Hz, 1 H, CH), 8.02 (s, 1 H, CH), 8.46 (d, *J* = 7.5 Hz, 1 H, CH), 8.48 (s, 1 H, CH), 12.59 (s, 1 H, NH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 109.40 (C), 112.06 (CH), 118.40 (C), 120.87, 121.77, 126.29, 127.30, 127.47, 127.80, 128.50, 129.85, 129.89, 130.39, 130.58 (11 × CH), 133.41, 133.50, 139.31, 139.98, 140.34, 156.99, 157.29, 157.78 (8 × C). MS: *m*/*z* (%) = 392 (17) [M^{+37}Cl$_2$], 390 (56) [M^{+37}Cl^{35}Cl], 388 (100) [M^{+35}Cl$_2$], 354 (10), 250 (9), 215 (13), 188 (15), 137 (27), 111 (32), 75 (15). Anal. Calcd for $C_{22}H_{13}Cl_2N_3$ (390.27): C, 67.71; H, 3.36; N, 10.77. Found: C, 67.7; H, 3.4; N, 10.5.

Compound **5j**: colorless crystals; mp 300–302 °C. IR (KBr): 3290 (NH), 1577, 1545, 1480, 1429, 1395, 1365, 1249, 1215, 1085, 1008, 844, 799, 740 cm^{-1}. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ = 7.23 (t, *J* = 7.5 Hz, 1 H, CH), 7.53 (dd, *J* = 7.4, 7.8 Hz, 1 H, CH), 7.59 (d, *J* = 7.8 Hz, 1 H, CH), 7.61 (d, *J* = 8.5 Hz, 2 H, 2 × CH), 7.76 (d, *J* = 8.3 Hz, 2 H, 2 × CH), 7.82 (d, *J* = 8.0 Hz, 1 H, CH), 8.06 (d, *J* = 8.3 Hz, 2 H, 2 × CH), 8.55 (d, *J* = 8.5 Hz, 2 H, 2 × CH), 12.59 (s, 1 H, NH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 109.04 (C), 111.97 (CH), 118.51 (C), 120.90, 121.91, 127.70, 128.59, 128.81, 129.48, 130.67 (7 × CH), 134.83, 135.08, 136.76, 137.14, 139.19, 157.10, 157.74, 158.26 (8 × C). MS: *m*/*z* (%) = 392 (3) [M^{+37}Cl$_2$], 390 (9) [M^{+37}Cl^{35}Cl], 388 (4) [M^{+35}Cl$_2$], 263 (32), 226 (44), 200 (48), 165 (7), 164 (35), 105 (16), 77 (100), 57 (29), 51 (47). Anal. Calcd for $C_{22}H_{13}Cl_2N_3$ (390.27): C, 67.71; H, 3.36; N, 10.77. Found: C, 67.6; H, 3.5; N, 10.7.

Compound **5l**: colorless crystals; mp 208–211 °C. IR (KBr): 3100 (NH), 1586, 1536, 1362, 1249, 1210, 1062, 772, 741, 716, 698 cm^{-1}. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ = 7.21 (t, *J* = 7.4 Hz, 1 H, CH), 7.48 (dd, *J* = 7.7, 8.2 Hz, 1 H, CH), 7.52 (dd, *J* = 7.4, 8.3 Hz, 1 H, CH), 7.59 (d, *J* = 8.0 Hz, 1 H, CH), 7.64 (dd, *J* = 7.8, 8.7 Hz, 1 H, CH), 7.67 (d, *J* = 8.0 Hz, 1 H, CH), 7.75 (d, *J* = 7.9 Hz, 1 H, CH), 7.86 (d, *J* = 7.8 Hz, 1 H, CH), 8.01 (d, *J* = 7.4 Hz, 1 H, CH), 8.15 (s, 1 H, CH), 8.50 (d, *J* = 7.6 Hz, 1 H, CH), 8.63 (s, 1 H, CH), 12.58 (1 H, s, NH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 109.37 (C), 112.04 (CH), 118.38 (C), 120.83, 121.74, 121.92, 121.93, 126.65, 127.77, 127.82, 130.22, 130.63, 130.80, 131.34 (11 × CH), 132.72, 132.74, 139.30, 140.15, 140.53, 156.94, 157.17, 157.64 (8 × C). MS: *m*/*z* (%) = 481 (6) [M^{+81}Br$_2$], 479 (85) [M^{+81}Br^{79}Br], 477 (6) [M^{+79}Br$_2$], 400(16), 319 (17), 216 (20), 181 (32), 155 (28), 114 (30), 102 (100), 75 (88), 52 (38). Anal. Calcd for $C_{22}H_{13}Br_2N_3$ (479.17): C, 55.15; H, 2.73; N, 8.77. Found: C, 54.9; H, 2.9; N, 8.6.

Compound **5n**: colorless crystals; mp 160–162 °C. IR (KBr): 1579, 1550, 1486, 1439, 1400, 1395, 1250, 1210, 758, 740 cm^{-1}. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ = 3.05 (s, 3 H, Me), 7.20 (t, *J* = 7.7 Hz, 1 H, CH), 7.49–7.57 (m, 4 H, 4 × CH), 7.62 (d, *J* = 7.8 Hz, 1 H, CH), 7.64–7.71 (m, 3 H, 3 × CH), 7.92 (d, *J* = 7.9 Hz, 1 H, CH), 8.00 (d, *J* = 7.8 Hz, 2 H, 2 × CH), 8.50 (d, *J* = 7.9 Hz, 2 H, 2 × CH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 40.25 (Me), 107.05 (C), 110.23 (CH), 117.78 (C), 119.18, 120.03, 127.15, 127.55, 127.95, 128.09, 128.45, 129.33, 130.64 (9 × CH), 138.39, 139.14, 139.97, 156.79, 158.64, 159.20 (6 × C). MS: *m*/*z* (%) = 335 (100) [M$^+$], 258 (14), 230 (23), 129 (18), 105 (43), 103 (39), 77 (55), 57 (40). Anal. Calcd for $C_{23}H_{17}N_3$ (335.41): C, 82.36; H, 5.11; N, 12.53. Found: C, 82.3; H, 5.2; N, 12.4.

Compound **5q**: colorless crystals; mp 303–304 °C. IR (KBr): 3250 (NH), 1585, 1550, 1426, 1360, 1250, 1211, 848, 704 cm^{-1}. ^{1}H NMR (300.1 MHz, DMSO-d_6): δ = 2.37, 2.47 (2 ×

s, 6 H, 2 × Me), 7.32 (d, *J* = 8.1 Hz, 2 H, 2 × CH), 7.48 (d, *J* = 8.2 Hz, 2 H, 2 × CH), 7.51 (d, *J* = 8.6 Hz, 1 H, CH), 7.61 (dd, *J* = 1.8, 8.6 Hz, 1 H, CH), 7.88 (d, *J* = 8.1 Hz, 2 H, 2 × CH), 7.89 (d, *J* = 1.8 Hz, 1 H, CH), 8.41 (d, *J* = 8.1 Hz, 2 H, 2 × CH), 12.62 (br s, 1 H, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 21.06, 21.14 (2 × Me), 107.77, 112.55 (2 × C), 113.90 (CH), 120.99 (C), 123.89, 127.94, 128.81, 129.21, 129.34, 129.73 (6 × CH), 135.23, 135.48, 137.83, 140.17, 140.18, 157.48, 159.82, 160.11 (8 × C). MS: *m*/*z* (%) = 429 (65) [M^{+81}Br], 427 (100) [M^{+79}Br], 413 (9), 273 (26), 192 (21), 107 (15), 91 (42), 78 (35). Anal. Calcd for $C_{24}H_{18}BrN_3$ (428.33): C, 67.30; H, 4.24; N, 9.81. Found: C, 67.2; H, 4.4; N, 9.7.

Compound **5r**: colorless crystals; mp 231–232 °C. IR (KBr): 3150 (NH), 1585, 1543, 1391, 1365, 1250, 760, 690 cm^{-1}. ^{1}H NMR (300.1 MHz, DMSO-d_6): δ = 7.42 (t, *J* = 7.8 Hz, 1 H, CH), 7.44 (d, *J* = 8.6 Hz, 1 H, CH), 7.56 (dd, *J* = 1.8, 8.6 Hz, 1 H, CH), 7.61 (t, *J* = 7.9 Hz, 1 H, CH), 7.63 (d, *J* = 7.9 Hz, 1 H, CH), 7.73 (d, *J* = 1.8 Hz, 1 H, CH), 7.85 (d, *J* = 7.7 Hz, 1 H, CH), 7.93 (d, *J* = 7.7 Hz, 1 H, CH), 8.09 (s, 1 H, CH), 8.39 (d, *J* = 7.9 Hz, 1 H, CH), 8.52 (s, 1 H, CH), 12.67 (br s, 1 H, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 108.50 (C), 112.83, 114.02, 120.26, 121.99, 122.08 (5 × CH), 124.02, 126.74 (2 × C), 127.84 (CH), 130.22, 130.23 (2 × C), 130.70, 130.96, 131.40 (3 × CH), 133.03, 133.10, 138.04, 139.80, 140.10, 157.02, 157.78, 158.18 (8 × C). MS: *m*/*z* (%) = 559 (95) [M^{+81}Br$_2$^{79}Br], 557 (100) [M^{+81}Br^{79}Br$_2$], 480 (13), 400(56), 192 (9), 181 (14), 155 (17), 79 (21), 57 (20). Anal. Calcd for $C_{22}H_{12}Br_3N_3$ (558.07): C, 47.35; H, 2.17; N, 7.53. Found: C, 47.3; H, 2.3; N, 7.5%.