Sequential three-component synthesis of 1,4-bis[6,9-dihydro-6-oxo-9-phenyl-1*H*-purin-2-yl]piperazines

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A simple one-pot efficient method for the synthesis of 1,4-bis[6,9-dihydro-6-oxo-9-phenyl-1*H*-purin-2-yl]piperazines by a domino three-component process involves an aza-Wittig reaction/heterocyclisation in the presence of sodium ethoxide as catalyst. Ethyl 1-phenyl-5-[(triphenylphosphoranylidene)amino]-1H-imidazole-4-carboxylate reacted with aromatic isocyanate to give carbodiimide intermediates, followed by addition of piperazines to give the corresponding guanidine intermediates. The guanidine intermediates were cyclised in the presence of a catalytic amount of sodium ethoxide to give 1,4-bis(6,9-dihydro-6-oxo-9-phenyl-1*H*-purin-2-yl)piperazine derivatives in good yields.

Keywords: multi-point reaction, purine, 1,4-bis[6,9-dihydro-6-oxo-9-phenyl-1*H*-purin-2-yl]piperazines, bioactive heterocycles

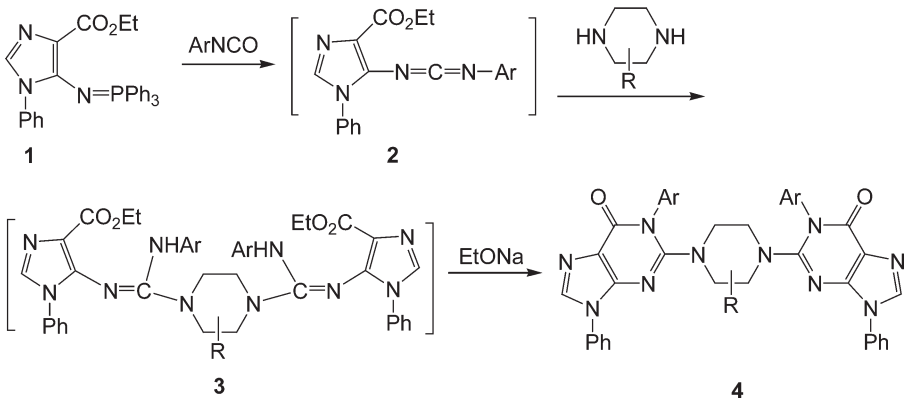
Substituted purines are widely used as potent inhibitors, antagonists, and receptors in living organisms[1–3]. The biological activities displayed by purines are conferred by a judicious choice of the nature of the substituents that can be combined on the N-1, C-2, N-3, C-6, N-7, C-8 and N-9 centres of the purine moiety[4,5]. Purines bearing C-substituents at position 2 are available by cyclisation reactions of 4-aminoimidazole-5-carboxamides or nitriles with derivatives of carboxylic acids (esters, orthoesters etc.)[6–8], while purines bearing C-substituents at position 8 are prepared by similar cyclisations from 5,6-diaminopyrimidines[9–10]. Other possible approaches to the C–C-purines are radical or nucleophilic substitutions or via generation of carbanions or organometallics (Li, Mg or Zn) on the purine skeleton followed by reaction with electrophiles[11–13]. However, the above mentioned synthesis methods were characterised by long reaction times and low yields. Recently, we have become interested in the synthesis of fused pyrimidinones via aza-Wittig reactions. As a continuation of our research for new bioactive heterocycles[14], we report here a sequential three-component synthesis of 1,4-bis[6-oxo-9-phenyl-1*H*-purin-2-yl]piperazines via multi-point reactions.

Results and discussion

The key iminophosphorane **1** was synthesised according to the literature[15], m.p.124–125 °C; IR (KBr): 1689 (C=O), 1542, 1502, 1438, 1417, 1137 cm^{-1}. Reaction of iminophosphorane **1** with aromatic isocyanates, followed by heterocyclisation with addition of nucleophilic piperazines in the presence of a base, resulting directly in the formation of the corresponding 1,4-bis[6-oxo-9-phenyl-1*H*-purin-2-yl]piperazines (Scheme 1). The results are listed in Table 1.

The iminophosphorane **1** reacted with aromatic isocyanates to give triphenylphosphine oxide and carbodiimides **2**. The reaction proceeded smoothly in THF at room temperature. The reaction of carbodiimides **2** with piperazine derivatives at room temperature gave intermediate guanidines **3** via initial double nucleophilic addition of piperazine to the carbodiimide. Even in refluxing toluene, **3** did not cyclise. However, in dry ethylene chloride and in the presence of a catalytic amount of EtONa, compounds **3** were converted smoothly to the 1,4-bis[6-oxo-9-phenyl-purin-2-yl]piperazines **4** in satisfactory yields at room temperature. We found that heterocyclisation occurred via nucleophilic displacement of the neighbouring ester ethoxide group to provide the target compounds **4** for intermolecular hetero conjugate addition annulations. No matter whether alkyl substituted piperazine or aryl substituted piperazines were used, the cyclisation proceeded very smoothly with the same regioselectivity. In position 2, whether the substituents on the benzene are electron-withdrawing or electron-donating groups, the cyclisation can be completed easily under mild conditions.

The structure of compounds **4** was confirmed by their analytical and spectral data (IR, ^{1}H NMR and MS). For example, the IR spectrum of **4a** showed a strong absorption at 1698 cm^{-1} assigned to the C=O group. In the ^{1}H NMR spectrum, the piperazine ring ($-CH_2$) proton appears at 2.67 ppm. The signals attributing to the imidazole proton and other aryl proton were found at 7.89 ppm and 7.22–7.65 ppm as a singlet and multiplet. The electrospray ionisation mass spectrum (ESI-MS) for **4a** showed the expected molecular ion peaks which showed *m/z* at 659.24 $(M+H)^+$ and the two-dimensional ionisation pattern is in accord with the proposed structure.



Scheme 1

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Table 1 Preparation of 1,4-bis[6-oxo-9-phenyl-1*H*-purin-2-yl]piperazines

Compd	Ar	R	Yield/%[a]
4a	Ph	H	83
4b	Ph	2-Me	80
4c	Ph	2,5-diMe	72
4d	Ph	Ph	71
4e	Ph		74
4f	4-MeC_6H_4	H	78
4g	4-MeC_6H_4	2-Me	73
4h	4-MeC_6H_4	2,5-diMe	68
4i	4-MeC_6H_4		71
4j	4-MeC_6H_4		70
4k	4-ClC_6H_4	H	87
4l	4-ClC_6H_4	2-Me	82
4m	4-ClC_6H_4	Ph	75
4n	4-ClC_6H_4		73

[a] Isolated yields based on iminophosphorane **1**.

Experimental

Melting points were determined using an X-4 model apparatus and were uncorrected. IR spectra were recorded on a Nicolet 7500 NXR IR spectrometer as KBr pellets with absorption given in cm^{-1}. ^1H NMR spectra were recorded in $CDCl_3$ on a Varian Mercury Plus 300 (300 MHz) spectrometer and chemical shifts (δ) were given in ppm using $(CH_3)_4Si$ as an internal reference ($\delta = 0$). Mass spectral (MS) data were obtained on a Finnigan LCQ Advantage MAX mass spectrometer. Elementary analyses were taken on a Perkin-Elmer CHN 2400 elemental analysis instrument. All reagents and solvents used in this work were available commercially and were used as received, unless otherwise indicated.

Synthesis of 1,4-bis[6-oxo-9-phenyl-1H-purin-2-yl]piperazines **4***; general procedure*

Aromatic isocyanate (0.006 mol) was added to the solution of iminophosphorane 1 (0.006 mol) in THF (10 mL) at 0–5 °C. When the resulting iminophosphorane 1 reacted with an aromatic isocyanate, triphenylphosphine oxide was formed. The reaction mixture was left unstirred for 5–6 h at 0–5 °C and then the solvent was removed under reduced pressure and Et_2O/petroleum ether (1:2, 12 mL) was added to precipitate triphenylphosphine oxide. Removal of the solvent gave carbodiimides 2, which were used directly without further purification. A piperazine derivative (0.003 mol) was added to the solution of **2** prepared as above in CH_2Cl_2 (10 mL) to give intermediate guanidines **3**. The reaction mixture was left unstirred for 2–3 h, the solvent was removed and EtONa in anhydrous EtOH (8 mL, 10%) was added. The mixture was stirred for 1–1.5 h at room temperature. The solution was condensed and the residue was recrystallised from EtOH to give the target compound **4**. TLC was used to follow the progress of all the above reactions.

1,4-Bis[6,9-dihydro-6-oxo-1,9-diphenyl-1H-purin-2-yl]piperazine (**4a**): White crystals; m.p. 231–233 °C; IR (KBr): 3327, 1698 (C=O), 1507, 1436, 1119 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 2.67 (t, J = 7.2 Hz, 8H, $4CH_2$), 7.03 (s, 2H, ArH), 7.22–7.65 (m, 18H, ArH), 7.89 (s, 2H, imidazole-H); ^{13}C NMR($CDCl_3$, 75 MHz): δ 45.3 (CH_2), 119.0 (N–C), 121.4, 122.1, 122.6, 124.8, 128.3, 129.0, 129.7, 132.4, 136.1(ArC), 137.8 (N–C), 148.9 (N=C), 151.2 (N=C), 160.2 (C=O); ESI-MS *m/z*: 659.24 $(M+H)^+$. Anal. Calcd for $C_{38}H_{30}N_{10}O_2$: C, 69.29; H, 4.59; N, 21.26. Found: C, 69.21; H, 4.73; N 21.37%.

1,4-Bis[6,9-dihydro-6-oxo-1,9-diphenyl-1H-purin-2-yl]-2-methylpiperazine (**4b**): White crystals; m.p. 255–256 °C; IR (KBr): 3342, 1709 (C=O), 1514, 1426, 1118 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.05 (d, J = 6.8 Hz, 3H, CH_3), 2.52 (d, J = 7.2 Hz, 2H, CH_2), 2.63 (t, J = 7.2 Hz, 2H, CH_2), 2.76 (t, J = 7.2 Hz, 2H, CH_2), 3.08 (m, 1H, CH), 7.00 (s, 2H, ArH), 7.24–7.64 (m, 18H, ArH), 7.97 (s, 2H, imidazole-H); ^{13}C NMR($CDCl_3$, 75 MHz): δ 16.3 (CH_3), 42.8 (CH_2), 44.2 (CH_2), 45.6 (CH_2), 46.6 (CH), 119.0 (N–C), 121.4, 122.4, 122.6, 124.8, 128.3, 129.0, 129.7, 132.4, 137.4 (ArC), 137.8 (N–C), 148.9 (N=C), 151.2 (N=C), 160.2 (C=O); ESI-MS *m/z*: 673.19 $(M+H)^+$. Anal. Calcd for $C_{39}H_{32}N_{10}O_2$: C, 69.63; H, 4.79; N, 20.82. Found: C, 69.76; H, 4.88; N, 20.69%.

1,4-Bis[6,9-dihydro-6-oxo-1,9-diphenyl-1H-purin-2-yl]-2,5-dimethylpiperazine (**4c**): White crystals; m.p. 288–289 °C; IR (KBr): 3305, 1687 (C=O), 1572, 1358, 1112 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.10 (d, J = 6.8 Hz, 6H, $2CH_3$), 2.52 (d, J = 7.2 Hz, 4H, $2CH_2$), 3.03 (m, 2H, 2CH), 7.01 (s, 2H, ArH), 7.23–7.65 (m, 18H, ArH), 7.95 (s, 2H, imidazole-H); ^{13}C NMR($CDCl_3$, 75 MHz): δ 16.3 (CH_3), 41.6 (CH_2), 46.9 (CH), 119.0 (N–C), 121.4, 122.4, 122.6, 124.8, 128.3, 129.0, 129.7, 132.4, 137.4 (ArC), 137.8 (N–C), 148.9 (N=C), 151.2 (N=C), 160.2 (C=O); ESI-MS *m/z*: 687.30 $(M+H)^+$. Anal. Calcd for $C_{40}H_{34}N_{10}O_2$: C, 69.96; H, 4.99; N, 20.40. Found: C, 69.82; H, 4.87; N, 20.34%.

1,4-Bis[6,9-dihydro-6-oxo-1,9-diphenyl-1H-purin-2-yl]-2-phenylpiperazine (**4d**): White crystals; m.p. > 300 °C; IR (KBr): 3342, 2943, 1688 (C=O), 1455, 1321 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 2.69 (t, J = 7.2 Hz, 4H, $2CH_2$), 2.87 (d, J = 7.2 Hz, 2H, CH_2), 4.12 (t, J = 6.8 Hz, 1H, CH), 7.00 (s, 2H, ArH), 7.16–7.48 (m, 23H, ArH), 7.96 (s, 2H, imidazole-H); ^{13}C NMR($CDCl_3$, 75 MHz): δ 36.6 (CH_2), 42.7 (CH_2), 45.6 (CH_2), 55.6 (CH), 119.0 (N–C), 121.4, 122.4, 122.6, 124.8, 127.1, 128.3, 128.6, 129.0, 129.7, 132.4, 137.4, 138.3 (ArC), 139.2 (N–C), 147.4 (N=C), 153.7 (N=C), 158.5 (C=O); ESI-MS *m/z*: 687.33 $(M+H)^+$. Anal. Calcd for $C_{44}H_{34}N_{10}O_2$: C, 71.92; H, 4.66; N, 19.06. Found: C, 71.87; H, 4.80; N, 19.13%.

1,4-Bis[6,9-dihydro-6-oxo-1,9-diphenyl-1H-purin-2-yl]-2-(thiophen-2-yl)-piperazine (**4e**): White crystals; m.p. 261–263 °C; IR (KBr): 3342, 2936, 1696 (C=O), 1576, 1374 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 2.68 (t, J = 7.2 Hz, 4H, CH_2), 2.97 (d, J = 7.2 Hz, 2H, CH_2), 4.13 (t, J = 7.2 Hz, 1H, CH), 6.56–6.97 (m, 3H, thiophene-H), 7. 3 (s, 2H, ArH), 7.24–7.65 (m, 18H, ArH), 7.96 (s, 2H, imidazole-H); ^{13}C NMR($CDCl_3$, 75 MHz): δ 37.5 (CH_2), 42.7 (CH_2), 45.6 (CH_2), 54.0 (CH), 119.0 (N–C), 121.4, 122.4, 122.6, 123.6, 124.8, 126.7, 126.9, 127.1, 127.8, 128.3, 128.6, 129.0, 129.7, 132.4, 137.4, 138.3 (ArC), 139.2 (N–C), 147.4 (N=C), 153.7 (N=C), 158.5 (C=O); ESI-MS *m/z*: 741.36 $(M+H)^+$. Anal. Calcd for $C_{42}H_{32}N_{10}O_2S$: C, 68.09; H, 4.35; N, 18.91. Found: C, 67.98; H, 4.38; N, 18.85%.

1,4-Bis[6,9-dihydro-6-oxo-1-(4-methylphenyl)-9-phenyl-1H-purin-2-yl]piperazine (**4f**): White crystals; m.p. 274–276 °C; IR (KBr): 3328, 2915, 1688 (C=O), 1508, 1119 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 2.33 (s, 6H, $2CH_3$), 2.65 (t, J = 7.2 Hz, 8H, $4CH_2$), 7.12–7.50 (m, 18H, ArH), 7.96 (s, 2H, imidazole-H); ^{13}C NMR($CDCl_3$, 75 MHz): δ 24.3 (CH_3), 45.3 (CH_2), 119.0 (N–C), 121.5, 122.4, 122.6, 128.3, 129.3, 129.6, 129.8, 134.0, 137.0 (ArC), 137.8 (N–C), 147.5 (N=C), 154.5 (N=C), 158.6 (C=O); ESI-MS *m/z*: 687.34 $(M+H)^+$. Anal. Calcd for $C_{40}H_{34}N_{10}O_2$: C, 69.96; H, 4.99; N, 20.40. Found: C, 69.81; H, 4.83; N, 20.28%.

1,4-Bis[6,9-dihydro-6-oxo-1-(4-methylphenyl)-9-phenyl-1H-purin-2-yl]-2-methylpiperazine (**4g**): White crystals; m.p. 287–2288 °C; IR (KBr): 3327, 2935, 1689 (C=O), 1486, 1138 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.11 (d, J = 6.4 Hz, 3H, CH_3), 2.35 (s, 6H, $2CH_3$), 2.62 (d, J = 7.2 Hz, 2H, CH_2), 2.76(t, J = 7.2 Hz, 4H, $2CH_2$), 3.03 (m, 1H, CH), 7.06–7.58 (m, 18H, ArH), 7.96 (s, 2H, imidazole-H); ^{13}C NMR($CDCl_3$, 75 MHz): δ 16.3 (CH_3), 24.3 (CH_3), 42.8 (CH_2), 44.1 (CH_2), 45.6 (CH_2), 46.6 (CH), 119.0 (N–C), 121.5, 122.4, 128.3, 129.3, 129.8, 134.0, 137.4 (ArC), 137.8 (N–C), 148.9 (N=C), 151.6 (N=C), 161.6 (C=O); ESI-MS *m/z*: 701.27 $(M+H)^+$. Anal. Calcd for $C_{41}H_{36}N_{10}O_2$: C, 70.27; H, 5.18; N, 19.99. Found: C, 70.13; H, 5.28; N, 20.06%.

1,4-Bis[6,9-dihydro-6-oxo-1-(4-methylphenyl)-9-phenyl-1H-purin-2-yl]-2,5-dimethylpiperazine (**4h**): White crystals; m.p. > 300 °C; IR (KBr): 3342, 1701 (C=O), 1557, 1423, 1118 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.11 (d, J = 7.0 Hz, 6H, $2CH_3$), 2.35 (s, 6H, $2CH_3$), 2.63 (d, J = 7.2 Hz, 4H, $2CH_2$), 3.04 (m, 2H, 2CH), 7.06–7.53 (m, 18H, ArH), 7.97 (s, 2H, imidazole-H); ^{13}C NMR($CDCl_3$, 75 MHz): δ 16.3 (CH_3), 24.3 (CH_3), 41.6 (CH_2), 46.9 (CH), 119.0 (N–C), 121.5, 122.4, 128.3, 129.3, 129.8, 134.0, 137.4 (ArC), 137.8 (N–C), 148.9 (N=C), 151.6 (N=C), 161.6 (C=O); ESI-MS *m/z*: 715.43 $(M+H)^+$. Anal. Calcd for $C_{42}H_{38}N_{10}O_2$: C, 70.57; H, 5.36; N, 19.59. Found: C, 70.63; H, 5.46; N, 19.71%.

1,4-Bis[6,9-dihydro-6-oxo-1-(4-methylphenyl)-9-phenyl-1H-purin-2-yl]-2-(thiophen-2-yl)-piperazine (**4i**): White crystals; m.p. 267–279 °C; IR (KBr): 3305, 1707 (C=O), 1517, 1465, 1118 cm^{-1}; ^1H

NMR ($CDCl_3$, 300 MHz): δ 2.35 (s, 6H, $2CH_3$), 2.67 (t, J = 7.2 Hz, 4H, $2CH_2$), 3.04 (d, J = 6.8 Hz, 2H, 2CH), 4.15 (t, J = 7.0 Hz, 1H, CH), 6.60–6.92 (m, 3H, thiophene-H), 7.06–7.52 (m, 18H, ArH), 7.97 (s, 2H, imidazole-H); ^{13}C NMR($CDCl_3$, 75 MHz): δ 24.3 (CH_3), 37.3 (CH_2), 42.6 (CH_2), 45.6 (CH_2), 54.3 (CH), 119.0 (N–C), 121.5, 122.4, 123.6, 126.7, 126.9, 127.8, 128.3, 129.3, 129.8, 134.0, 137.4 (ArC), 137.8 (N–C), 148.7 (N=C), 153.3 (N=C), 159.5 (C=O); ESI-MS *m/z*: 769.37 $(M+H)^+$. Anal. Calcd for $C_{44}H_{36}N_{10}O_2S$: C, 68.73; H, 4.72; N, 18.22. Found: C, 68.65; H, 4.66; N, 18.15%.

1,4-Bis[6,9-dihydro-6-oxo-1-(4-methylphenyl)-9-phenyl-1H-purin-2-yl]-2-(furan-2-yl)-piperazine (**4j**): White crystals; m.p.> 300 °C; IR (KBr): 3324, 2906, 1695 (C=O), 1443, 1324 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.35 (s, 6H, $2CH_3$), 2.68 (d, J = 7.2 Hz, 4H, $2CH_2$), 2.96 (d, J = 6.8 Hz, 2H, CH_2), 4.38 (t, J = 7.0 Hz, 1H, CH), 6.07–6.24 (m, 2H, furan-H), 7.04–7.52 (m, 19H, ArH and furan-H), 7.97 (s, 2H, imidazole-H); ^{13}C NMR($CDCl_3$, 75 MHz): δ 24.3 (CH_3), 34.8 (CH_2), 40.3 (CH_2), 45.1 (CH_2), 54.5 (CH), 119.0 (N–C), 105.8, 110.0, 121.5, 122.4, 123.6, 126.7, 126.9, 127.8, 128.3, 129.3, 129.8, 134.0, 137.4 (ArC), 137.8 (N–C), 148.5 (N=C), 155.9 (N=C), 161.3 (C=O); ESI-MS *m/z*: 753.34 $(M+H)^+$. Anal. Calcd for $C_{44}H_{36}N_{10}O_3$: C, 70.20; H, 4.82; N, 18.61. Found: C, 70.03; H, 4.75; N, 18.70%.

1,4-Bis[6,9-dihydro-6-oxo-1-(4-chlorophenyl)-9-phenyl-1H-purin-2-yl]piperazine (**4k**): White crystals; m.p. 255–256 °C; IR (KBr): 3302, 1688 (C=O), 1561, 1477, 1211 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.67 (t, J = 7.2 Hz, 8H, $4CH_2$), 7.25–7.57 (m, 18H, ArH), 7.97 (s, 2H, imidazole-H); ^{13}C NMR($CDCl_3$, 75 MHz): δ 45.3 (CH_2), 119.0 (N–C), 122.4, 123.0, 128.3, 129.1, 129.7, 129.9, 130.8, 137.3 (ArC), 137.8 (N–C), 148.5 (N=C), 152.7 (N=C), 158.6 (C=O); ESI-MS *m/z*: 727.39 $(M+H)^+$. Anal. Calcd for $C_{38}H_{28}N_{10}O_2Cl_2$: C, 62.73; H, 3.88; N, 19.25. Found: C, 62.64; H, 3.76; N, 19.19%.

1,4-Bis[6,9-dihydro-6-oxo-1-(4-chlorophenyl)-9-phenyl-1H-purin-2-yl]-2-methylpiperazine (**4l**): White crystals; m.p. 277–279 °C; IR (KBr): 3305, 1689 (C=O), 1557, 1434, 1118 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.06 (d, J = 6.8 Hz, 3H, CH_3), 2.63 (d, J = 7.2 Hz, 2H, CH_2), 2.72 (t, J = 7.2 Hz, 4H, $2CH_2$), 3.05 (m, 1H, CH), 7.26–7.58 (m, 18H, ArH), 7.97 (s, 2H, imidazole-H); ^{13}C NMR($CDCl_3$, 75 MHz): δ 16.3 (CH_3), 42.8 (CH_2), 44.1 (CH_2), 45.6 (CH_2), 46.6 (CH), 119.0 (N–C), 122.4, 123.0, 128.3, 129.1, 129.7, 129.9, 130.8, 137.3 (ArC), 137.8 (N–C), 144.3 (N–C), 147.8 (N=C), 153.3 (N=C), 159.2 (C=O); ESI-MS *m/z*: 741.25 $(M+H)^+$. Anal. Calcd for $C_{39}H_{30}N_{10}O_2Cl_2$: C, 63.16; H, 4.08; N, 18.89. Found: C, 63.08; H, 4.11; N, 18.85%.

1,4-Bis[6,9-dihydro-6-oxo-1-(4-chlorophenyl)-9-phenyl-1H-purin-2-yl]-2-phenylpiperazine (**4m**): White crystals; m.p. > 300 °C; IR (KBr): 3313, 1689 (C=O), 1453, 1212 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.66 (t, J = 7.2 Hz, 4H, $2CH_2$), 3.04 (d, J = 6.8 Hz, 2H, CH_2), 4.15 (t, J = 7.0 Hz, 1H, CH), 7.12–7.58 (m, 23H, ArH), 7.97 (s, 2H, imidazole-H); ^{13}C NMR($CDCl_3$, 75 MHz): δ 36.3 (CH_3), 42.7 (CH_2), 45.6 55.8 (CH), 119.0 (N–C), 122.4, 123.0, 127.1, 128.0, 128.3, 128.8, 129.1, 129.7, 129.9, 130.8, 137.3, 138.3 (ArC), 137.8 (N–C), 144.3 (N–C), 147.8 (N=C), 152.8 (N=C), 159.6 (C=O); ESI-MS *m/z*: 803.21 $(M+H)^+$. Anal. Calcd for $C_{44}H_{32}N_{10}O_2Cl_2$: C, 65.76; H, 4.01; N, 17.43. Found: C, 65.82; H, 3.91; N, 17.38%.

1,4-Bis[6,9-dihydro-6-oxo-1-(4-chlorophenyl)-9-phenyl-1H-purin-2-yl]-2-(thiophen-2-yl)-piperazine (**4n**): White crystals; m.p. 295–297 °C; IR (KBr): 3311, 2927, 1707 (C=O), 1540, 1438 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.75 (t, J = 7.2 Hz, 4H, $2CH_2$), 2.91 (d, J = 7.2 Hz, 2H, CH_2), 3.04 (t, J = 6.8 Hz, 1H, CH), 6.66–6.90 (m, 3H, thiophene-H), 7.25–7.58 (m, 18H, ArH), 7.97 (s, 2H, imidazole-H); ^{13}C NMR($CDCl_3$, 75 MHz): δ 37.5 (CH_3), 42.7 (CH_2), 45.6, 54.6 (CH), 119.0 (N–C), 122.4, 123.0, 123.6, 126.7, 126.9, 127.1, 127.8, 128.0, 128.3, 128.8, 129.1, 129.7, 129.9, 130.8, 137.3, 138.3 (ArC), 137.8 (N–C), 143.6 (N–C), 147.8 (N=C), 152.8 (N=C), 160.3 (C=O); ESI-MS *m/z*: 809.28 $(M+H)^+$. Anal. Calcd for $C_{42}H_{30}N_{10}O_2SCl_2$: C, 62.30; H, 3.73; N, 17.30. Found: C, 62.27; H, 3.62; N, 17.17.

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