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**An efficient synthesis of 2,4,7-trisubstituted  
pyrimido[1,2-a][1,3,5]triazin-6-ones**

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(Supplementary Information)

## Experimental Section

Melting points (uncorrected) were determined on a Gallenkamp melting point apparatus. NMR spectra were recorded on a Bruker DPX-300 or a Bruker Avance DRX-400 at 298K using Me<sub>2</sub>SO-*d*<sub>6</sub> as a solvent and TMS as an internal reference. <sup>1</sup>H 2DNOESY spectra were acquired using a 150 ms mixing time. The raw data were processed using Topspin 2.1 (Bruker Scientific Inc.). IR spectra were performed on a Perkin Elmer Spectrum 100 FT-IR spectrophotometer in potassium bromide pellets. Mass spectra were obtained using either a Finnigan MAT LCQ MS mass spectrometer or a QTRAP 2000 LC-MS mass spectrometer using atmospheric pressure chemical ionization (APCI) mode. The course of the reactions was monitored by TLC on Silica gel 60 F<sub>254</sub> plates (Merck, Germany). HPLC analysis was performed on an Agilent Eclipse XDB-C18 (4.6x250 mm, 5 μm) column at 30°C, with a flow rate of 1 mL/min. 5-90% Gradients of MeOH/MeCN (solvent A) and H<sub>2</sub>O (solvent B) were used as mobile phases. Microwave-assisted reactions were conducted using a Biotage Initiator microwave synthesizer at maximal power of 400W. Elemental analyses were performed on a Perkin Elmer 2400 Elemental Analyzer Series II.

### *General methods for the synthesis of 2-amino-8-methyl-4-(het)aryl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-ones (5a-5l)*

Procedure 1: A mixture of guanidine **4** (0.5 g, 2.5 mmol) and an appropriate aldehyde (5.0 mmol) in acetic acid (3 mL) was heated under reflux for 5-9 h. The excess solvent was removed under reduced pressure and the solid obtained was neutralized using sodium carbonate solution (50%). The precipitate formed was filtered and purified by either recrystallization (EtOH) or column chromatography (dichloromethane/methanol - 8.5/1.5).

Procedure 2: A mixture of guanidine **4** (1.5 mmol) and an appropriate aldehyde (1.8 mmol) in 0.2-0.3 mL of acetic acid was irradiated in a 10 mL vial using a Biotage microwave synthesizer at 150°C for 25 min. After cooling, the precipitated crude product was filtered, washed with cold ethyl acetate followed by aqueous sodium carbonate, dried under vacuum and recrystallized.

### *2-Amino-8-methyl-4-phenyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5a)*

mp 264-265°C; MS (APCI) *m/z* 256.3 (MH<sup>+</sup>); <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.05 (3H, s, 8-Me), 5.72 (1H, s, H-7), 6.86 (1H, s, H-4), 7.00 (2H, br s, NH<sub>2</sub>), 7.23 (2H, d, *J* = 7.9 Hz, H-2' and H-6'), 7.31-7.39 (3H, m, H-3', H-4' and H-5'), 8.28 (1H, s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 23.8 (8-Me), 59.8 (C-4), 102.2 (C-7), 125.2 (C-2' and C-6'), 128.4 (C-4'), 128.5 (C-3' and C-5'), 140.0 (C-1'), 154.1 (C-9a), 157.4 (C-2), 160.5 (C-6), 165.6 (C-8); IR (KBr): 3342 NH, 3057 CH, 1668 C=O, 1490, 1372. HPLC: purity 100%, *t<sub>R</sub>* 9.5 min (MeOH:H<sub>2</sub>O); purity 100%, *t<sub>R</sub>* 8.6 min (CH<sub>3</sub>CN:H<sub>2</sub>O).

### *2-Amino-8-methyl-4-(4-methylphenyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5b)*

mp 267-268°C; MS (APCI) *m/z* 270.1 (MH<sup>+</sup>); Anal. Calcd. C, 62.44; H, 5.61; N, 26.01; found C, 61.98; H, 5.36; N, 26.02. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.04 (3H, s, 8-Me), 2.26 (3H, s, 4'-Me), 5.69 (1H, s, H-7), 6.82 (1H, d, *J* = 2.6 Hz, H-4), 7.00 (2H, br s, NH<sub>2</sub>), 7.11 (2H, d, *J* = 8.3 Hz, H-3' and H-5'), 7.16 (2H, d, *J* = 8.3 Hz, H-2' and H-6'), 8.23 (1H, d, *J* = 3.0 Hz, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 20.5 (4'-Me), 23.8 (8-Me), 59.6 (C-4), 102.1 (C-7), 125.2 (C-2' and C-6'), 128.9 (C-3' and C-5'), 137.2 (C-1'), 137.7 (C-4'), 154.2 (C-9a), 157.4 (C-2), 160.5 (C-6), 165.6 (C-8); IR (KBr): ν 3331 NH, 3080 CH, 2922, 1688 C=O, 1663, 1592, 1487, 1366. HPLC: purity 98.5%, *t<sub>R</sub>* 11.4 min (MeOH:H<sub>2</sub>O); purity 100%, *t<sub>R</sub>* 7.7 min (CH<sub>3</sub>CN:H<sub>2</sub>O).

**2-Amino-4-(4-methoxyphenyl)-8-methyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5c)**

mp 252-253°C; MS (APCI)  $m/z$  289.1 (MH<sup>+</sup>); Anal. Calcd. C, 58.94; H, 5.30; N, 24.55; found C, 58.23; H, 5.09; N, 24.43. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.04 (3H, s, Me), 3.72 (3H, s, OMe), 5.69 (1H, s, H-7), 6.80 (1H, s, H-4), 6.91 (2H, d, *J* = 8.7 Hz, H-3' and H-5'), 7.00 (2H, br s, NH<sub>2</sub>), 7.16 (2H, d, *J* = 8.7 Hz, H-2' and H-6'), 8.20 (1H, s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 23.7 (8-Me), 55.1 (OMe), 59.6 (C-4), 102.2 (C-7), 113.8 (C-3' and C-5'), 126.6 (C-2' and C-6'), 132.2 (C-1'), 154.1 (C-9a), 157.4 (C-2), 159.2 (C-4'), 160.4 (C-6), 165.5 (C-8); IR (KBr); ν 3319 NH, 3083 CH, 2929 CH, 2837, 1687 C=O, 1661, 1612, 1585, 1487, 1395. HPLC: purity 100%, *t*<sub>R</sub> 12.6 min (MeOH:H<sub>2</sub>O); purity 100%, *t*<sub>R</sub> 7.1 min (CH<sub>3</sub>CN:H<sub>2</sub>O).

**2-Amino-4-(4-fluorophenyl)-8-methyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5d)**

mp 245-246°C; MS (APCI)  $m/z$  274.1 (MH<sup>+</sup>); <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 2.05 (3H, s, 8-Me), 5.71 (1H, s, H-7), 6.86 (1H, s, H-4), 7.02 (2H, br s, NH<sub>2</sub>), 7.18-7.29 (4H, m, H-2', H-6', H-3', H-5'), 8.28 (1H, s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 23.8 (8-Me), 59.3 (C-4), 102.2 (C-7), 115.4 (d, <sup>2</sup>*J*<sub>C-F</sub> = 21.8 Hz (C-3' and C-5')), 127.5 (d, <sup>3</sup>*J* = 8.8 Hz, C-2' and C-6'), 136.4 (C-1'), 154.1 (C-9a), 157.4 (C-2), 160.5 (C-6), 161.9 (d, <sup>1</sup>*J*<sub>C-F</sub> = 244.6 Hz, C-4'), 165.9 (C-8); IR (KBr); ν 3357 NH, 3070 CH, 1683 C=O, 1654, 1604, 1575, 1528, 1467, 1414, 1236 CF. HPLC: purity 100%, *t*<sub>R</sub> 17.9 min (MeOH:H<sub>2</sub>O).

**2-Amino-8-methyl-4-(4-(trifluoromethyl)phenyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5e)**

mp >300°C; MS (APCI)  $m/z$  324.1. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.03 (3H, s, 8-Me), 5.64 (1H, s, H-7), 6.83 (1H, s, H-4), 7.44 (2H, d, *J* = 8.3 Hz, H-2' and H-6'), 7.59 (2H, br s, NH<sub>2</sub>), 7.73 (2H, d, *J* = 7.9 Hz, H-3' and H-5'); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 23.9 (8-Me), 60.2 (C-4), 101.2 (C-7), 123.8 (q, <sup>1</sup>*J*<sub>C-F</sub> = 275.4 Hz, 4'-CF<sub>3</sub>), 125.4 (q, <sup>3</sup>*J*<sub>C-F</sub> = 3.3 Hz, C-3' and C-5'), 126.2 (C-2' and C-6'), 129.0 (q, <sup>2</sup>*J*<sub>C-F</sub> = 31.8 Hz, C-4'), 145.4 (C-1'), 154.5 (C-9a), 158.5 (C-2), 160.7 (C-6), 165.7 (C-8); IR (KBr); ν 3401 br NH, 1684 C=O, 1661, 1560, 1496, 1339. HPLC: purity 100%, *t*<sub>R</sub> 18.9 min (MeOH:H<sub>2</sub>O).

**2-Amino-4,8-dimethyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5f)**

mp >300°C (EtOH); MS (APCI)  $m/z$  194.3 (MH<sup>+</sup>); <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 1.21 (3H, d, *J* = 6.0 Hz, CH<sub>3</sub>), 2.01 (3H, s, 8-Me), 5.64 (1H, s, H-7), 5.83 (1H, q, *J* = 5.8 Hz, H-4), 6.88 (2H, s, NH<sub>2</sub>), 7.65 (1H, s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 20.3 (4-Me), 23.7 (8-Me), 56.2 (C-4), 102.1 (C-7), 153.7 (C-9a), 156.8 (C-2), 160.2 (C-6), 165.2 (C-8). HPLC: purity 96.7%, *t*<sub>R</sub> 6.4 min (MeOH:H<sub>2</sub>O).

**2-Amino-4-isopropyl-8-methyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5g)**

mp 226-227°C (EtOH); MS (APCI)  $m/z$  222.3 (MH<sup>+</sup>); <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 0.78 (3H, d, *J* = 9.0 Hz, Me), 0.79 (3H, d, *J* = 9.0 Hz, Me), 1.91 (1H, m, CHMe<sub>2</sub>), 2.01 (3H, s, 8-Me), 5.53 (1H, d, *J* = 5.0 Hz, H-4), 5.62 (1H, s, H-7), 7.10 (2H, br s, NH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 15.7 (Me), 17.5 (Me), 23.7 (8-Me), 33.0 (CH), 63.6 (C-4), 101.9 (C-7), 154.5 (C-9a), 157.8 (C-2), 160.7 (C-6), 165.1 (C-8); IR (KBr); ν 3334 br NH, 3111, 2966 (CH), 1670 C=O, 1489, 1400, 1290, 1222, 1136, 815, 790. HPLC: purity 99.1%, *t*<sub>R</sub> 10.3 min (MeOH:H<sub>2</sub>O).

**2-Amino-8-methyl-4-cyclohexyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5h)**

mp 221-222°C dec. (EtOH); MS (APCI)  $m/z$  262.3; <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 0.81-1.20 (5H, m, H<sub>cyclohex</sub>), 1.36 (1H, s, H<sub>cyclohex</sub>), 1.60-1.78 (5H, m, H<sub>cyclohex</sub>), 2.02 (3H, s, 8-Me), 5.56 (1H, br s, H-4), 5.64 (1H, s, H-7), 6.84 (2H, s, NH<sub>2</sub>), 7.94 (1H, s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 23.7 (8-Me), 25.0, 25.1, 25.6, 26.1, 27.4, 42.5 (C-4'), 62.6 (C-4), 102.1 (C-7), 154.6 (C-9a), 157.5 (C-2), 160.6 (C-6), 165.1 (C-8); IR (KBr); ν 3292 br NH, 3132, 2927 (CH), 2848, 1645 C=O, 1483, 1400, 1288, 1220, 1132, 817. HPLC: purity 97.8%, *t*<sub>R</sub> 16.5 min (MeOH:H<sub>2</sub>O).

*2-Amino-8-methyl-4-phenylethyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5i)*

mp 243-244°C (EtOH); MS (APCI) *m/z* 284.1. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 1.68-1.95 (2H, m, CH<sub>2</sub>), 2.03 (3H, s, 8-Me), 2.53-2.75 (2H, m, CH<sub>2</sub>), 5.66 (1H, s, H-7), 5.80 (1H, br s, H-4), 6.97 (2H, br s, NH<sub>2</sub>), 7.12-7.32 (5H, m, H-2' H-6', H-3', H-5' and H-4'), 8.02 (1H, s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 23.8 (8-Me), 29.4 (CH<sub>2</sub>), 35.2 (CH<sub>2</sub>), 58.8 (C-4), 102.2 (C-7), 125.9 (C-4'), 128.0 (C-2' and C-6'), 128.3 (C-3' and C-5'), 140.5 (C-1'), 154.1 (C-9a), 157.4 (C-2), 160.3 (C-6), 165.3 (C-8); IR (KBr); ν 3356 br NH, 3084, 1678 C=O, 1647, 1489, 1404, 1294, 1134, 786. HPLC: purity 99.3%, *t<sub>R</sub>* 17.1 min (MeOH:H<sub>2</sub>O); purity 100%, *t<sub>R</sub>* 10.2 min (CH<sub>3</sub>CN:H<sub>2</sub>O).

*2-Amino-4-(furan-2-yl)-8-methyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5j)*

mp >300°C; MS (APCI) *m/z* 246.2 (MH<sup>+</sup>); <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.02 (3H, s, Me), 5.64 (1H, s, H-7), 6.19 (1H, d, *J* = 3.0 Hz, H-3'), 6.38 (1H, dd, *J* = 3.5, 1.6 Hz, H-4'), 6.87 (1H, s, H-4), 7.10 (2H, br s, NH<sub>2</sub>), 7.58 (1H, d, *J* = 1.0 Hz, H-5'), 8.25 (1H, s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 23.8 (8-Me), 55.4 (C-4), 101.8 (C-7), 106.9 (C-3'), 110.3 (C-4'), 142.8 (C-5'), 152.0 (C-2'), 153.9 (C-9a), 157.7 (C-2), 160.0 (C-6), 165.5 (C-8); IR (KBr); ν 3344 NH, 3066 CH, 2804, 2697, 1669 br C=O, 1490. HPLC: purity 97.5%, *t<sub>R</sub>* 15.9 min (MeOH:H<sub>2</sub>O); purity 100%, *t<sub>R</sub>* 7.9 min (CH<sub>3</sub>CN:H<sub>2</sub>O).

*2-Amino-8-methyl-4-(thiophen-2-yl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5k)*

mp 275-276°C; LC-MS (APCI) MS *m/z*: 262.6 (MH<sup>+</sup>); <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.03 (3H, s, 8-Me), 5.71 (1H, s, H-7), 6.94-6.98 (2H, m, H-4 and H-4'), 7.06 (1H, s, H-3'), 7.13 (2H, br s, NH<sub>2</sub>), 7.45 (1H, d, *J* = 4.5 Hz, H-5'), 8.30 (1H, br s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 23.8 (8-Me), 56.9 (C-4), 102.2 (C-7), 125.2 (C-3'), 126.3 (C-5'), 126.4 (C-4'), 143.0 (C-2'), 153.4 (C-9a), 157.5 (C-2), 160.1 (C-6), 165.7 (C-8) IR (KBr); ν 3466 NH, 3020 CH, 1679 C=O, 1651, 1628, 1610, 1570, 1533, 1518, 1468, 1414. HPLC: purity 98.9%, *t<sub>R</sub>* 11.5 min (MeOH:H<sub>2</sub>O).

*2-Amino-8-methyl-4-(pyridin-2-yl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5l)*

mp >300°C (EtOH); MS (APCI) *m/z* 257.1. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.04 (3H, s, 8-Me), 5.63 (1H, s, H-7), 6.75 (1H, s, H-4), 7.21 (2H, br s, NH<sub>2</sub>), 7.27-7.39 (2H, m, H-5' and H-3'), 7.79 (1H, t, *J* = 7.5 Hz, H-4'), 8.48 (1H, d, *J* = 4.1 Hz, H-6'); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 23.8 (8-Me), 61.6 (C-4), 101.8 (C-7), 120.5 (C-3' and C-5'), 123.5 (C-4'), 137.0 (C-2'), 149.0 (C-6'), 154.4 (C-9a), 157.8 (C-2), 160.7 (C-6), 165.5 (C-8); IR (KBr); ν 3401 br NH, 1684 C=O, 1661, 1560, 1496, 1339. HPLC: purity 98.5%, *t<sub>R</sub>* 10.7 min (MeOH:H<sub>2</sub>O).

*General methods for the synthesis of 2-amino-4-(het)aryl-8-trifluoromethyl-3,4-dihydro-pyrimido[1,2-a][1,3,5]triazin-6-one (5m-5v)*

Procedure 1: A mixture of **4** (0.5 g, 2.5 mmol) and an appropriate aldehyde (3.0 mmol) in DMF (5 mL) was heated under reflux for 3-8 h. After 2 hours, more amount (up to 0.5 equivalent) of the aldehyde was added to facilitate the completion of reaction. The reaction mixture was concentrated under vacuum, filtered, washed with diethyl ether and recrystallized from DMF.

Procedure 2: A mixture of guanidine **4** (1.5 mmol) and an appropriate aldehyde (2.0 mmol) in DMF (1.0 mL) was irradiated in a 10mL vial using a Biotage initiator microwave synthesizer at 165 °C for 20 min. After cooling, the precipitated product was filtered, washed with diethyl ether and recrystallized.

**2-Amino-4-phenyl-8-trifluoromethyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5m)**

mp 255-256°C (DMF); TLC (silica gel, 8.5:1.5 DCM:MeOH):  $R_f$  0.90; MS (ESI)  $m/z$ : 310.047 [MH]<sup>+</sup>; Anal. Calcd. for C<sub>13</sub>H<sub>10</sub>F<sub>3</sub>N<sub>5</sub>O: C, 50.49; H, 3.26; N, 22.65; found C, 50.16; H 4.43; N 22.04. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 6.24 (1H, s, H-7), 6.92 (1H, s, H-4), 7.26 (2H, d,  $J$  = 7.5 Hz, H-2' and H-6'), 7.29 (2H, br s, NH<sub>2</sub>), 7.35-7.43 (3H, m, H-3', H-4' and H-5'), 8.53 (1H, br s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 60.4 (C-4), 100.9 (q, <sup>3</sup> $J_{C-F}$  = 3.5 Hz, C-7), 122.6 (q, <sup>1</sup> $J_{C-F}$  = 274.6 Hz, CF<sub>3</sub>), 125.2 (C-2' and C-6'), 128.7 (C-3', C-4' and C-5'), 139.3 (C-1'), 153.4 (q, <sup>2</sup> $J_{C-F}$  = 33.5 Hz, C-8), 155.9 (C-9a), 157.6 (C-2), 160.4 (C-6); IR (KBr); ν 3333 NH, 3144, 2951 CH, 2802, 1663 C=O, 1492, 1278. HPLC: purity 100%,  $t_R$  4.84 min (MeOH:H<sub>2</sub>O).

**2-Amino-4-(4-methylphenyl)-8-(trifluoromethyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5n)**

mp 251-252°C (DMF); TLC (silica gel, 8.5:1.5 DCM:MeOH):  $R_f$  0.5; MS  $m/z$ : 324.060 [MH]<sup>+</sup>; Anal. Calcd. for C<sub>14</sub>H<sub>12</sub>F<sub>3</sub>N<sub>5</sub>O: C, 52.01; H, 3.74; N, 21.66; found: C, 51.87; H, 3.50; N, 21.63. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.27 (3H, s, Me), 6.22 (1H, s, H-7), 6.88 (1H, d,  $J$  = 2.3 Hz, H-4), 7.14 (2H, d,  $J$  = 7.9 Hz, H-3' and H-5'), 7.19 (2H, d,  $J$  = 7.9 Hz, H-2' and H-6'), 7.40 (2H, br s, NH<sub>2</sub>), 8.49 (1H, d,  $J$  = 2.3 Hz, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 20.6 (4'-Me), 60.2 (C-4), 100.8 (q, <sup>3</sup> $J_{C-F}$  = 3.1 Hz, C-7), 120.8 (q, <sup>1</sup> $J_{C-F}$  = 275.0 Hz, CF<sub>3</sub>), 125.2 (C-2' and C-6'), 129.2 (C-3' and C-5'), 136.4 (C-4'), 138.3 (C-1'), 153.3 (q, <sup>2</sup> $J_{C-F}$  = 33.5 Hz, C-8), 155.9, 157.6, 160.3; IR (KBr); ν 3419 NH, 3345, 3154, 2954 CH, 2821, 1684, 1658 C=O, 1552, 1491, 1424, 1298, 1276. HPLC: purity 100%,  $t_R$  4.90 min (MeOH:H<sub>2</sub>O).

**2-Amino-4-(4-methoxyphenyl)-8-(trifluoromethyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5o)**

mp 225-226°C (DMF); TLC (silica gel, 8.5:1.5 DCM:MeOH):  $R_f$  0.40; Anal. Calcd. for C<sub>14</sub>H<sub>12</sub>F<sub>3</sub>N<sub>5</sub>O<sub>2</sub>: C, 49.56; H, 3.57; N, 20.64; found: C, 49.31; H, 4.09; N, 19.83. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 3.73 (3H, s, OMe), 6.22 (1H, s, H-7), 6.86 (1H, s, H-4), 6.95 (2H, d,  $J$  = 8.7 Hz, H-3' and H-5'), 7.20 (2H, d,  $J$  = 8.7 Hz, H-2' and H-6'), 7.36 (2H, br s, NH<sub>2</sub>), 8.49 (1H, s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 55.1 (OMe), 60.1 (C-4), 100.9 (q, <sup>3</sup> $J_{C-F}$  = 3.5 Hz, C-7), 114.0 (C-3' and C-5'), 120.8 (q, <sup>1</sup> $J_{C-F}$  = 275.6 Hz, CF<sub>3</sub>), 126.6 (C-2' and C-6'), 131.4 (C-1'), 153.3 (q, <sup>2</sup> $J_{C-F}$  = 33.0 Hz, C-8), 155.7, 157.5, 159.5 (C-4'), 160.3. HPLC: purity 96.5%,  $t_R$  4.95 min (MeOH:H<sub>2</sub>O).

**2-Amino-4-(4-fluorophenyl)-8-(trifluoromethyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5p)**

mp 260-261°C (MeOH); TLC (silica gel, 8.5:1.5 DCM:MeOH):  $R_f$  0.7; MS (ESI)  $m/z$ : 328.034 [MH]<sup>+</sup>; Anal. Calcd. for C<sub>13</sub>H<sub>9</sub>F<sub>4</sub>N<sub>5</sub>O: C, 47.71; H, 2.77; N, 21.40; found: C, 47.38; H, 2.81; N, 21.24. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 6.23 (1H, s, H-7), 6.91 (1H, d,  $J$  = 3.8 Hz, H-4), 7.21-7.34 (4H, m, H2', H6', H3' and H5'), 7.46 (2H, br s, NH<sub>2</sub>), 8.50 (1H, d,  $J$  = 3.8 Hz, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 59.9 (C-4), 100.9 (q, <sup>3</sup> $J_{C-F}$  = 2.7 Hz, C-7), 115.7 (d, <sup>2</sup> $J_{C-F}$  = 21.8 Hz, C-3' and C-5'), 120.8 (q, <sup>1</sup> $J_{C-F}$  = 275.6 Hz, CF<sub>3</sub>), 127.5 (d, <sup>3</sup> $J_{C-F}$  = 8.8 Hz, C-2' and C-6'), 135.6 (d, <sup>4</sup> $J_{C-F}$  = 2.8 Hz, C-1'), 153.4 (q, <sup>2</sup> $J_{C-F}$  = 33.3 Hz, C-8), 155.8, 157.5, 160.3, 162.1 (d, <sup>1</sup> $J_{C-F}$  = 245.2 Hz, C-4').

**2-Amino-8-(trifluoromethyl)-4-[4-(trifluoromethyl)phenyl]-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5q)**

mp 150-151°C (DMF); TLC (silica gel, 8.5:1.5 DCM:MeOH):  $R_f$  0.7; MS  $m/z$ : 378.021 [MH]<sup>+</sup>; Anal. Calcd. for C<sub>14</sub>H<sub>9</sub>F<sub>6</sub>N<sub>5</sub>O: C, 44.57; H, 2.40; N, 18.56; found: C, 44.30; H, 2.37; N, 18.48. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 6.27 (1H, s, H-7), 7.00 (1H, d,  $J$  = 2.2 Hz, H-4), 7.48 (2H, d,  $J$  = 8.3 Hz, H-2' and H-6'), 7.38 (2H, br s, NH<sub>2</sub>), 7.81 (2H, d,  $J$  = 8.3 Hz, H-3' and H-5'), 8.62 (1H,  $J$  = 2.2 Hz, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 60.2 (C-4), 100.9 (q, <sup>3</sup> $J_{C-F}$  = 3.4 Hz, C-7), 120.8 (q, <sup>1</sup> $J_{C-F}$  = 275.4 Hz, 8-CF<sub>3</sub>), 123.9 (q, <sup>1</sup> $J_{C-F}$  = 275.4 Hz, 4'-CF<sub>3</sub>), 125.9 (q, <sup>3</sup> $J_{C-F}$  = 3.5 Hz, C-3' and C-5'), 126.2 (C-2' and 6'), 129.3 (q, <sup>2</sup> $J_{C-F}$  = 31.8 Hz, C-4'), 143.7 (d, <sup>4</sup> $J_{C-F}$  = 1.2 Hz, C-1'), 153.5 (q, <sup>2</sup> $J_{C-F}$  = 33.7 Hz, C-8), 155.8, 157.5,

160.4; IR (KBr);  $\nu$  3336 br NH, 3166 br, 2949, 1684, 1550, 1496, 1419, 1329, 1278, 1219. HPLC: purity 99.4%,  $t_R$  6.03 min (MeOH:H<sub>2</sub>O).

**2-Amino-4-(furan-2-yl)-8-(trifluoromethyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5r)**

mp 226-227°C (DMF); TLC (silica gel, 8.5:1.5 DCM:MeOH):  $R_f$  0.5; MS  $m/z$ : 300.025 [MH]<sup>+</sup>; Anal. Calcd. for C<sub>11</sub>H<sub>8</sub>F<sub>3</sub>N<sub>5</sub>O<sub>2</sub>: C, 44.16; H, 2.69; N, 23.41; found: C, 43.21; H, 3.04; N, 22.81. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>):  $\delta$  6.21 (1H, s, H-7), 6.33 (1H, d,  $J = 3.0$  Hz, H-3'), 6.44 (1H, dd,  $J = 3.0$  Hz,  $J = 1.9$  Hz, H-4'), 6.95 (1H, s, H-4), 7.19 (2H, br s, NH<sub>2</sub>), 7.65 (1H, d,  $J = 0.8$  Hz, H-5'), 8.45 (1H, s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 55.3 (C-4), 100.8 (q, <sup>3</sup> $J_{C-F} = 3.2$  Hz, C-7), 107.8 (C-3'), 110.5 (C-4'), 120.8 (q, <sup>1</sup> $J_{C-F} = 275.2$  Hz, CF<sub>3</sub>), 143.5 (C-5'), 150.7 (C-2'), 153.4 (q, <sup>2</sup> $J_{C-F} = 33.5$  Hz, C-8), 155.6, 157.8, 159.9; IR (KBr);  $\nu$  3294 NH, 3153, 2941, 2817, 1697, 1664 C=O, 1496, 1410, 1299, 1277, 1229. HPLC: purity 100%,  $t_R$  4.03 min (MeOH:H<sub>2</sub>O).

**2-Amino-4-(thiophen-2-yl)-8-(trifluoromethyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5s)**

mp 174-175°C (DMF); TLC (silica gel, 8.5:1.5 DCM:MeOH):  $R_f$  0.5; MS  $m/z$ : 316.002 [MH]<sup>+</sup>; Anal. Calcd. for C<sub>11</sub>H<sub>8</sub>F<sub>3</sub>N<sub>5</sub>OS: C, 41.91; H, 2.56; N, 22.21; found: C, 41.61; H, 3.17; N, 22.00. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>):  $\delta$  6.30 (1H, s, H-7), 6.99-7.02 (1H, m, H-4'), 7.06 (1H, d,  $J = 3.0$  Hz, H-3'), 7.15 (1H, s, H-4), 7.51 (1H, dd,  $J = 4.9$  Hz, 1.1 Hz, H-5'), 7.58 (2H, br s, NH<sub>2</sub>), 8.73 (1H, br s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 57.4 (C-4), 101.4 (q, <sup>3</sup> $J_{C-F} = 3.2$  Hz, C-7), 120.7 (q, <sup>1</sup> $J_{C-F} = 275.2$  Hz, CF<sub>3</sub>), 125.7 (C-3'), 126.6 (C-5'), 126.8 (C-4'), 141.7 (C-2'), 153.2 (q, <sup>2</sup> $J_{C-F} = 33.5$  Hz, C-8), 154.5, 157.2, 159.8; IR (KBr);  $\nu$  3290 NH, 3106, 1669 C=O, 1489, 1277. HPLC: purity 100%,  $t_R$  4.54 min (MeOH:H<sub>2</sub>O).

**2-Amino-4-(pyridin-2-yl)-8-(trifluoromethyl)-3,4-dihydropyrimido[1,2-a][1,3,5] triazin-6-one (5t)**

mp 253-254°C (DMF); TLC (silica gel, 8.5:1.5 DCM:MeOH):  $R_f$  0.6; MS (ESI)  $m/z$ : 311.043 [MH]<sup>+</sup>; Anal. Calcd. for C<sub>12</sub>H<sub>9</sub>F<sub>3</sub>N<sub>6</sub>O: C, 46.46; H, 2.92; N, 27.09; found: C, 46.18; H, 3.11; N, 26.98. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>):  $\delta$  6.18 (1H, s, H-7), 6.87 (1H, s, H-4), 7.18 (2H, br s, NH<sub>2</sub>), 7.35-7.42 (2H, m, H-3' and H-5'), 7.86 (1H, dt, H-4', <sup>3</sup> $J = 7.9$  Hz, <sup>4</sup> $J = 1.5$  Hz), 8.48-8.52 (2H, m, NH and H-6'); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 61.6 (C-4), 100.6 (q, <sup>3</sup> $J_{C-F} = 3.3$  Hz, C-7), 120.7 (C-5'), 120.9 (q, <sup>1</sup> $J_{C-F} = 275.2$  Hz, CF<sub>3</sub>), 124.0 (C-3'), 137.3 (C-4'), 149.2 (C-6'), 153.4 (q, <sup>2</sup> $J_{C-F} = 33.5$  Hz, C-8), 156.3, 156.7 (C-2'), 157.5, 160.5; IR (KBr);  $\nu$  3391 NH, 3139, 2944, 2802, 1696, 1656 C=O, 1486, 1278. HPLC: purity 98.7%,  $t_R$  4.02 min (MeOH:H<sub>2</sub>O).

**2-Amino-4-(4-chlorophenyl)-8-(trifluoromethyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5u)**

mp 256-257°C (DMF); TLC (silica gel, 8.5:1.5 DCM:MeOH):  $R_f$  0.6; MS (ESI)  $m/z$ : 344.000, 346.000 [MH]<sup>+</sup>; Anal. Calcd. for C<sub>13</sub>H<sub>9</sub>ClF<sub>3</sub>N<sub>5</sub>O: C, 45.43; H, 2.64; N, 20.38; found: C, 45.46; H, 2.52; N, 20.39. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>):  $\delta$  6.25 (1H, s, H-7), 6.92 (1H, s, H-4), 7.28 (2H, d,  $J = 8.3$  Hz, H-2' and H-6'), 7.38 (2H, br s, NH<sub>2</sub>), 7.49 (2H, d,  $J = 8.3$  Hz, H-3' and H-5'), 8.54 (1H, br s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 60.0 (C-4), 101.0 (q, <sup>3</sup> $J_{C-F} = 3.5$  Hz, C-7), 120.8 (q, <sup>1</sup> $J_{C-F} = 275.6$  Hz, CF<sub>3</sub>), 127.2 (C-3' and C-5'), 128.8 (C-2' and C-6'), 133.5 (C-4'), 138.2 (C-1'), 153.4 (q, <sup>2</sup> $J_{C-F} = 33.5$  Hz, C-8), 155.7, 157.4, 160.3; Calcd. for C<sub>13</sub>H<sub>9</sub>ClF<sub>3</sub>N<sub>5</sub>O: 343.045, 345.042; IR (KBr);  $\nu$  3333 NH, 3152, 2951, 2822, 1685, 1657 C=O, 1551, 1491, 1415, 1276, 1225, 1096 (C-Cl). HPLC: purity 100%,  $t_R$  6.40 min (MeOH:H<sub>2</sub>O).

**2-Amino-4-(4-bromophenyl)-8-(trifluoromethyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5v)**

mp 242-243°C (DMF); TLC (silica gel, 8.5:1.5 DCM:MeOH):  $R_f$  0.6; MS  $m/z$ : 387.943, 389.941 [MH]<sup>+</sup>; Anal. Calcd. for C<sub>13</sub>H<sub>9</sub>BrF<sub>3</sub>N<sub>5</sub>O: C, 40.23; H, 2.34; N, 18.04; found: C, 40.01; H, 2.19; N, 18.03. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>):  $\delta$  6.24 (1H, s, H-7), 6.90 (1H, s, H-4), 7.22 (2H, d,  $J = 8.7$  Hz, H-2' and

H-6'), 7.38 (2H, br s, NH<sub>2</sub>), 7.62 (2H, d,  $J = 8.3$  Hz, H-3' and H-5'), 8.52 (1H, br s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 60.0 (C-4), 100.9 (q, <sup>3</sup> $J_{C-F} = 3.5$  Hz, C-7), 120.8 (q, <sup>1</sup> $J_{C-F} = 274.6$  Hz, CF<sub>3</sub>), 122.1 (C-4'), 127.5 (C-3' and C-5), 131.7 (C-2' and C-6'), 138.6 (C-1'), 153.4 (q, <sup>2</sup> $J_{C-F} = 33.5$  Hz, C-8), 155.8, 157.5, 160.3; IR (KBr)  $\nu$  3485 and 3464 NH<sub>2</sub>, 3331 NH, 2980 CH, 2823, 1711 C=O, 1674, 1662, 1613, 1558, 1489, 1456, 1411, 1295, 1273, 1235, 1217, 1205, 618(C-Br). HPLC: purity 100%,  $t_R$  6.58 min (MeOH:H<sub>2</sub>O).

*General methods for the synthesis of 4-substituted 2-amino-8-phenyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5w-5af)*

Procedure 1: A mixture of **4** (0.5 g, 2.5 mmol) and an appropriate aldehyde (3.0 mmol) in DMF (5 mL) was heated under reflux for 3-8 h. After 2 hours, more amount (up to 0.5 equivalent) of the aldehyde was added to facilitate the completion of reaction. The reaction mixture was concentrated under vacuum, filtered, washed with diethyl ether and recrystallized from suitable solvent.

Procedure 2: A mixture of guanidine **4** (1.5 mmol) and an appropriate aldehyde (2.0 mmol) in DMF (1.0 mL) was irradiated in a 10mL vial using a Biotage initiator microwave synthesizer at 170°C for 20 min. After cooling, the precipitated product was filtered, washed with diethyl ether and recrystallized.

*2-Amino-4,8-diphenyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5w)*

mp 260-261°C (MeOH-AcOEt); TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:6):  $R_f$  0.43; MS (ESI)  $m/z = 318.1$  (MH<sup>+</sup>). <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>):  $\delta$  6.44 (1H, s, H-7), 6.93 (1H, s, H-4), 7.11 (2H, br s, NH<sub>2</sub>), 7.24-7.55 (8H, m, H<sub>Ar</sub>), 8.00 (2H, dd,  $J = 7.0$  Hz, 3.2 Hz, H-2'' and H-6''), 8.36 (1H, br s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>):  $\delta$  60.0 (C-4), 99.1 (C-7), 125.3, 126.6 (C-7), 128.3 (C-2' and C-6'), 128.5, 128.6, 130.0, 137.1 (C-4'), 140.0 (C-1'), 151.2, 154.5 (br, C-2), 157.5 (C-9a), 161.2 (C-6), 161.8 (C-8). HPLC: purity 100%,  $t_R$  11.0 min (MeOH:H<sub>2</sub>O).

*2-Amino-4-(4-methylphenyl)-8-phenyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5x)*

mp 241-242°C (MeOH-AcOEt); <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>):  $\delta$  2.26 (3H, s, Me), 6.42 (1H, s, H-7), 6.90 (1H, s, H-4), 7.08-7.15 (6H, m, NH<sub>2</sub>, H-2', H-6', H-3' and H-5'), 7.51-7.62 (3H, m, H-3'', H-4'' and H-5''), 8.01 (2H, dd,  $J = 7.0$  Hz, 3.2 Hz, H-2'' and H-6''), 8.29 (1H, d,  $J = 3.4$  Hz, NH). HPLC: purity 99.2%,  $t_R$  12.3 min (MeOH:H<sub>2</sub>O).

*2-Amino-4-(4-methoxyphenyl)-8-phenyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5y)*

mp 249-250°C (MeOH-AcOEt); TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:6):  $R_f$  0.43; MS (ESI)  $m/z = 348.1$  (MH<sup>+</sup>); Anal. Calcd. C, 65.69; H, 4.93; N, 20.16; found C, 65.20; H, 4.83; N, 20.09. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>):  $\delta$  3.72 (3H, s, OMe), 6.41 (1H, s, H-7), 6.87 (1H, d,  $J = 3.4$  Hz, H-4), 6.93 (2H, d, = 8.7 Hz, H-2' and H-6'), 7.07 (2H, br s, NH<sub>2</sub>), 7.23 (2H, d, = 8.7 Hz, H-3' and H-5'), 7.51-7.62 (3H, m, H-3'', H-4'' and H-5''), 8.00 (2H, dd,  $J = 7.0$  Hz, 3.2 Hz, H-2'' and H-6''), 8.27 (1H, d,  $J = 3.4$  Hz, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>):  $\delta$  55.1 (OMe), 59.8 (C-4), 99.1 (C-7), 113.9, 126.6, 126.7, 128.3 (C-2' and C-6'), 129.3, 129.9, 132.2, 137.1 (C-4'), 154.5 (br, C-2), 157.5 (C-9a), 159.3 (C-1'), 161.1 (C-6), 161.7 (C-8). HPLC: purity 100%,  $t_R$  16.5 min (MeOH:H<sub>2</sub>O).

*2-Amino-4-(4-fluorophenyl)-8-phenyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5z)*

mp 268-269°C (MeOH-AcOEt); TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:6):  $R_f$  0.31; MS (ESI)  $m/z = 336.1$  (MH<sup>+</sup>). <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>):  $\delta$  6.44 (1H, s, H-7), 6.94 (1H, s, H-4), 7.01 (2H, br s, NH<sub>2</sub>), 7.10-7.59 (7H, m, H-3'', H-4'', H-5'', H-2', H-6', H-3', H-5'), 7.90-8.11 (2H, m, H-2'' and H-6''), 8.36

(1H, br s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 59.6 (C-4), 99.1 (C-7), 115.5 (d, <sup>2</sup>*J* = 21.2 Hz, C-3' and C-5'), 126.6, 127.5 (d, <sup>3</sup>*J* = 7.5 Hz, C-2' and C-6'), 128.3, 130.01, 136.3, 137.0, 154.3 (C-2), 157.4 (C-9a), 161.0 (C-6), 161.8 (C-8), 162.0 (d, <sup>1</sup>*J* = 240.3 Hz, C-4'). HPLC: purity 99.6%, *t*<sub>R</sub> 17.7 min (MeOH:H<sub>2</sub>O).

**2-Amino-8-phenyl-4-(4-(trifluoromethyl)phenyl)-3,4-dihydropyrimido[1,2-*a*][1,3,5]triazin-6-one (5aa)**

mp 239-240 °C (MeOH-AcOEt); TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:6): *R*<sub>f</sub> 0.55. MS (ESI) *m/z* = 304.0 (MH<sup>+</sup>). <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 6.49 (1H, s, H-7), 7.05 (1H, s, H-4), 7.24 (2H, br s, NH<sub>2</sub>), 7.38-7.49 (3H, m, H-3'', H-4'' and H-5''), 7.53 (2H, d, <sup>3</sup>*J* = 7.9 Hz, H-2' and H-6'), 7.80 (2H, d, <sup>3</sup>*J* = 7.9 Hz, H-3' and H-5'), 8.04 (2H, dd, *J* = 7.0 Hz, 3.2 Hz, H-2'' and H-6''), 8.46 (1H, s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 59.8 (C-4), 99.2 (C-7), 123.9 (q, <sup>1</sup>*J* = 271.5 Hz, CF<sub>3</sub>), 125.8 (q, <sup>3</sup>*J* = 3.9 Hz, C-3'' and C-5''), 126.3, 126.7, 128.4, 128.9, 129.1 (d, <sup>2</sup>*J* = 32 Hz, C-4''), 137.0 (C-4'), 144.4 (C-1'), 154.4 (br, C-2), 157.4 (C-9a), 161.2 (C-6), 162.0 (C-8). HPLC: purity 99.4%, *t*<sub>R</sub> 24.0 min (MeOH:H<sub>2</sub>O).

**General methods for the synthesis of 2,8-disubstituted-4-aryl-3,4-dihydropyrimido[1,2-*a*][1,3,5]triazin-6-ones (5af-5az)**

Procedure 1: To a stirred suspension of **4** (1.05-1.20 mmol) in ethanol (5 ml), an appropriate amount of aldehyde (1.26-1.44 mmol) and piperidine (0.48-0.60 mmol) was added. The reaction mixture was heated under reflux. After 2 hours, more amount (up to 0.5 equivalent) of the aldehyde was added to facilitate the completion of reaction. The reaction mixture was refluxed until the TLC showed no spot for the starting material (4-12 h). The reaction mixture was concentrated under vacuum, filtered, and washed with diethyl ether. The product was then recrystallized from appropriate solvent.

Procedure 2: A mixture of guanidine **4** (1.2 mmol), piperidine (0.25 mmol) and appropriate aldehyde (1.5 mmol) in 1.5 mL of absolute ethanol was irradiated in a 10mL vial using a Biotage microwave synthesizer for 20 min at 140°C. After removing solvent under vacuum the crude product was washed with diethyl ether and filtered.

**2-(*N,N*-Dimethylamino)-8-methyl-4-phenyl-3,4-dihydropyrimido[1,2-*a*][1,3,5]triazin-6-one (5af)**

mp 290-291°C (MeOH); TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:6): *R*<sub>f</sub> 0.45; MS (ESI) *m/z* 284.1 (MH<sup>+</sup>); Anal. Calcd. C, 63.59; H, 6.05; N, 24.72; found C, 63.48; H, 5.78; N, 24.66. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.07 (3H, s, Me) 3.02 (6H, s, N(Me)<sub>2</sub>), 5.74 (1H, s, H-7), 6.84 (1H, d, <sup>3</sup>*J* = 3.4 Hz, H-4), 7.17 (2H, d, <sup>3</sup>*J* = 6.8 Hz, H-2' and H-6'), 7.43 (3H, m, H-3', H-4' and H-5'), 8.74 (1H, d, <sup>3</sup>*J* = 3.4 Hz, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 23.7 (Me), 36.6 (N(Me)<sub>2</sub>), 59.6 (C-4), 102.1 (C-7), 125.1 (C-2' and C-6'), 128.5 (C-4'), 128.6 (C-3' and C-5'), 139.5 (C-1'), 153.5 (C-2), 155.6 (C-9a), 160.4 (C-6), 165.7 (C-8). HPLC: purity 100%, *t*<sub>R</sub> 14.8 min (MeOH:H<sub>2</sub>O).

**2-(*N,N*-Dimethylamino)-8-methyl-4-(4-methylphenyl)-3,4-dihydropyrimido[1,2-*a*][1,3,5]triazin-6-one (5ag)**

mp 288-289°C (AcOEt); TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:6): *R*<sub>f</sub> 0.49; MS (ESI) *m/z* 298.1 (MH<sup>+</sup>); Anal. Calcd. C, 64.63; H, 6.44; N, 23.55; found C, 64.44; H, 6.81; N, 21.35. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.06 (3H, s, 8-Me), 2.26 (3H, s, *p*-Me) 3.01 (6H, s, N(Me)<sub>2</sub>), 5.73 (1H, s, H-7), 6.80 (1H, s, H-4), 7.06 (2H, d, <sup>3</sup>*J* = 7.9 Hz, H-2' and H-6'), 7.16 (2H, d, <sup>3</sup>*J* = 7.9 Hz, H-3' and H-5'), 8.68 (1H, s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 20.5 (Me), 23.8 (8-Me), 36.6 (N(Me)<sub>2</sub>), 59.5 (C-4), 102.1 (C-7), 125.1 (C-2' and C-6'), 129.0 (C-3' and C-5'), 136.6 (C-1'), 137.8 (C-4'), 153.5 (C-2), 155.7 (C-9a), 160.4 (C-6), 165.8 (C-8). HPLC: purity 100%, *t*<sub>R</sub> 16.6 min (MeOH:H<sub>2</sub>O).

*2-(N,N-Dimethylamino)-4-(4-methoxyphenyl)-8-methyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one*  
**(5ah)**

mp 280-281°C (AcOEt:EtOH); TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:6): *R<sub>f</sub>* 0.48; MS (ESI) *m/z* 314.0 (MH<sup>+</sup>); Anal. Calcd. C, 61.33; H, 6.11; N, 22.35; found C, 61.32; H, 5.65; N, 22.44. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.06 (3H, s, Me), 3.02 (6H, s, N(Me)<sub>2</sub>), 3.71 (3H, s, OMe), 5.72 (1H, s, H-7), 6.79 (1H, d, <sup>3</sup>*J* = 3.4 Hz, H-4), 6.90 (2H, d, <sup>3</sup>*J* = 8.7 Hz, H-3' and H-5'), 7.10 (2H, d, <sup>3</sup>*J* = 8.7 Hz, H-2' and H-6'), 8.67 (1H, d, <sup>3</sup>*J* = 3.4 Hz, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 23.7 (Me), 36.6 (N(Me)<sub>2</sub>), 55.1 (OMe), 59.4 (C-4), 102.1 (C-7), 113.9 (C-3' and C-5'), 126.5 (C-2' and C-6'), 131.6 (C-1'), 153.5 (C-2), 155.7 (C-9a), 159.2 (C-4'), 160.4 (C-6), 165.7 (C-8). HPLC: purity 100% *t<sub>R</sub>* 15.0 min (MeOH:H<sub>2</sub>O); purity 100%, *t<sub>R</sub>* 8.0 min (CH<sub>3</sub>CN:H<sub>2</sub>O).

*2-(N,N-Dimethylamino)-4-(4-fluorophenyl)-8-methyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one*  
**(5ai)**

mp 287-288°C (AcOEt:EtOH), TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:9): *R<sub>f</sub>* 0.70; MS (ESI) *m/z* 302.1 (MH<sup>+</sup>); Anal. Calcd. C, 59.79; H, 5.35; N, 23.24; found C, 59.67; H, 5.29; N, 23.12. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.07 (3H, s, Me), 3.03 (6H, s, N(Me)<sub>2</sub>), 5.74 (1H, s, H-7), 6.83 (1H, s, H-4), 7.11-7.33 (4H, m, H-2', H-3', H-5' and H-6'), 8.72 (1H, br s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 23.1 (Me), 36.0 (N(Me)<sub>2</sub>), 58.6 (C-4), 101.5 (C-7), 114.8 (d, <sup>2</sup>*J*<sub>C-F</sub> = 21.8 Hz, C-3' and C-5'), 126.8 (d, <sup>3</sup>*J*<sub>C-F</sub> = 8.2 Hz, C-2' and C-6'), 135.6 (d, <sup>4</sup>*J*<sub>C-F</sub> = 3.5 Hz, C-1'), 152.7 (C-2), 154.9 (C-9a), 159.8 (C-6), 162.1 (d, <sup>1</sup>*J*<sub>C-F</sub> = 245.1 Hz, C-4'), 165.3 (C-8). HPLC: purity 100%, *t<sub>R</sub>* 16.1 min (MeOH:H<sub>2</sub>O).

*2-(N,N-Dimethylamino)-8-methyl-4-(4-trifluoromethylphenyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one*  
**(5aj)**

mp 270-271°C (AcOEt); TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:6): *R<sub>f</sub>* 0.54; MS (ESI) *m/z* 352.1 (MH<sup>+</sup>); <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.08 (3H, s, Me), 3.03 (6H, s, N(Me)<sub>2</sub>), 5.77 (1H, s, H-7), 6.90 (1H, d, <sup>3</sup>*J* = 4.9 Hz, H-4), 7.40 (2H, d, <sup>3</sup>*J* = 7.9 Hz, H-2' and H-6'), 7.77 (2H, d, <sup>3</sup>*J* = 7.9 Hz, H-3' and H-5'), 8.81 (1H, d, <sup>3</sup>*J* = 4.9 Hz, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 23.9 (Me), 36.8 (N(Me)<sub>2</sub>), 59.4 (C-4), 102.2 (C-7), 124.0 (q, <sup>1</sup>*J*<sub>C-F</sub> = 274.0 Hz, CF<sub>3</sub>), 125.8 (q, <sup>3</sup>*J*<sub>C-F</sub> = 3.7 Hz, C-3' and C-5'), 126.3 (C-2' and C-6'), 129.1 (q, <sup>2</sup>*J*<sub>C-F</sub> = 31.8 Hz, C-4'), 144.0 (C-1'), 153.5 (C-2), 155.6 (C-9a), 160.6 (C-6), 166.3 (C-8). HPLC: purity 99.5%, *t<sub>R</sub>* 20.3 min (MeOH:H<sub>2</sub>O).

*4-(4-Cyanophenyl)-2-(N,N-dimethylamino)-8-methyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one*  
**(5ak)**

mp 243-244°C (CH<sub>2</sub>Cl<sub>2</sub>-MeOH); TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:6): *R<sub>f</sub>* 0.41; MS (ESI) *m/z* 309.0 (MH<sup>+</sup>). <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.09 (3H, s, Me), 3.03 (6H, s, N(Me)<sub>2</sub>), 5.78 (1H, s, H-7), 6.90 (1H, s, H-4), 7.36 (2H, d, <sup>3</sup>*J* = 8.2 Hz, H-2' and H-6'), 7.86 (2H, d, <sup>3</sup>*J* = 8.2 Hz, H-3' and H-5'), 8.82 (1H, s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 23.8 (Me), 36.7 (N(Me)<sub>2</sub>), 59.4 (C-4), 102.1 (C-7), 111.3 (C-4'), 118.3 (CN), 126.3 (C-2' and C-6'), 132.8 (C-3' and C-5'), 144.6 (C-1'), 153.3 (C-2), 155.5 (C-9a), 160.4 (C-6), 166.1 (C-8). HPLC: purity 100%, *t<sub>R</sub>* 13.1 min (MeOH:H<sub>2</sub>O).

*2-(N,N-Dimethylamino)-4-(furan-2-yl)-8-methyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one*  
**(5al)**

mp 249-250°C, TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:6): *R<sub>f</sub>* 0.39; MS (ESI) *m/z* 274.1 (MH<sup>+</sup>); Anal. Calcd. C, 57.13; H, 5.53; N, 25.63; found C, 57.19; H, 5.57; N, 25.57. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.05 (3H, s, Me), 3.03 (6H, s, N(Me)<sub>2</sub>), 5.70 (1H, s, H-7), 6.18 (1H, d, *J* = 3.0 Hz, H-3'), 6.33-6.44 (1H, m, H-4'), 6.85 (1H, s, H-4), 7.59-7.61 (1H, m, H-5'), 8.64 (1H, s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 23.8 (Me), 36.7 (N(Me)<sub>2</sub>), 55.9 (C-4), 102.1 (C-7), 107.3 (C-3'), 110.4 (C-4'), 143.2 (C-5'), 151.1 (C-2'), 153.1 (C-2), 155.7 (C-9a), 159.9 (C-6), 165.9 (C-8). HPLC: purity 100%, *t<sub>R</sub>* 11.9 min (MeOH:H<sub>2</sub>O).

*2-(N,N-Dimethylamino)-8-methyl-4-(pyridin-2-yl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5am)*

mp 288-289°C (MeOH), TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:6): *R<sub>f</sub>* 0.61; MS (ESI) *m/z* 285.1 (MH<sup>+</sup>); Anal. Calcd. C, 59.14; H, 5.67; N, 29.56; found C, 58.73; H, 5.49; N, 29.53. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.06 (3H, s, 8-Me), 2.99 (6H, s, N(Me)<sub>2</sub>), 5.69 (1H, s, H-7), 6.79 (1H, s, H-4), 7.24-7.41 (2H, m, H-3' 5'), 7.81 (1H, dt, *J* = 7.7 Hz, 1.51 Hz, H-4'), 8.49 (1H, d, *J* = 4.1 Hz, H-6'), 8.75 (1H, br s., NH). HPLC: purity 100%, *t<sub>R</sub>* 12.7 min (MeOH:H<sub>2</sub>O); purity 100%, *t<sub>R</sub>* min (CH<sub>3</sub>CN:H<sub>2</sub>O).

*4-(4-Chlorophenyl)-2-(N,N-dimethylamino)-8-methyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5an)*

mp 289-290°C (AcOEt:EtOH); TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:6): *R<sub>f</sub>* 0.52; MS (ESI) *m/z* 317.9 (MH<sup>+</sup>); Anal. Calcd. C, 56.69; H, 5.08; N, 22.04; found C, 56.46; H, 5.19; N, 21.86. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.07 (3H, s, Me), 3.02 (6H, s, N(Me)<sub>2</sub>), 5.75 (1H, s, H-7), 6.82 (1H, s, H-4), 7.18 (2H, d, <sup>3</sup>*J* = 8.7 Hz, H-2' and H-6'), 7.44 (2H, d, <sup>3</sup>*J* = 8.7 Hz, H-3' and H-5'), 8.74 (1H, s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 23.6 (Me), 36.6 (N(Me)<sub>2</sub>), 59.3 (C-4), 102.1 (C-7), 127.1 (C-2' and C-6'), 128.7 (C-3' and C-5'), 133.1 (C-4'), 138.5 (C-1'), 153.3 (C-2), 155.5 (C-9a), 160.3 (C-6), 165.7 (C-8). HPLC: purity 100%, *t<sub>R</sub>* 19.0 min (MeOH:H<sub>2</sub>O); purity 100%, *t<sub>R</sub>* 12.8 min (CH<sub>3</sub>CN:H<sub>2</sub>O).

*4-(4-Bromophenyl)-2-(N,N-dimethylamino)-8-methyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5ao)*

mp 296-297°C (AcOEt:EtOH), TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:9): *R<sub>f</sub>* 0.71; MS (ESI) *m/z* 363.1 (MH<sup>+</sup>); Anal. Calcd. C, 49.74; H, 4.45; N, 19.33; found C, 49.93; H, 4.53; N, 19.28. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.07 (3H, s, Me), 3.02 (6H, s, N(Me)<sub>2</sub>), 5.75 (1H, s, H-7), 6.81 (1H, s, H-4), 7.13 (2H, d, <sup>3</sup>*J* = 8.3 Hz, H-2' and H-6'), 7.58 (2H, d, <sup>3</sup>*J* = 7.9 Hz, H-3' and H-5'), 8.73 (1H, br s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 23.9 (Me), 36.7 (N(Me)<sub>2</sub>), 59.4 (C-4), 102.1 (C-7), 121.7, 127.5, 131.6 (C-4'), 139.0 (C-1'), 153.4 (C-2), 155.6 (C-9a), 160.4 (C-6), 166.1 (C-8). HPLC: purity 100%, *t<sub>R</sub>* 18.8 min (MeOH:H<sub>2</sub>O).

*2-(N,N-Dimethylamino)-8-methyl-4-(4-hydroxyphenyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5ap)*

mp 271-272°C (MeOH), TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:6): *R<sub>f</sub>* 0.28; MS (ESI) *m/z* 300.0 (MH<sup>+</sup>); Anal. Calcd. C, 60.19; H, 5.72; N, 23.40; found C, 59.71; H, 5.81; N, 23.19. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.05 (3H, s, 8-Me), 3.02 (6H, s, N(Me)<sub>2</sub>), 5.70 (1H, s, H-7), 6.71 (2H, d, *J* = 8.3 Hz, H-3' and H-5'), 6.74 (1H, d, *J* = 4.9 Hz, H-4), 6.98 (2H, d, *J* = 8.3 Hz, H-2' and H-6'), 8.61 (1H, d, *J* = 4.9 Hz, NH), 9.54 (1H, s, OH).

*8-Methyl-2-morpholino-4-phenyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5aq)*

mp 272-273°C (EtOH); TLC (silica gel, MeOH:CH<sub>2</sub>Cl<sub>2</sub>, 1:9): *R<sub>f</sub>* 0.48; MS (ESI) *m/z* 326.1 (MH<sup>+</sup>); Anal. Calcd. C, 62.75; H, 5.89; N, 21.52; found C, 62.51; H, 5.80; N, 21.35. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 2.08 (3H, s, Me), 3.36-3.71 (8H, m, morpholino), 5.79 (1H, s, H-7), 6.87 (1H, br s, H-4), 7.18 (2H, d, *J* = 7.5 Hz, H-2' and H-6'), 7.30-7.40 (3H, m, H-3', H-4' and H-5'), 8.91 (1H, br s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 23.8 (8-Me), 44.5 (C-2'' and C-6''), 59.6 (C-4), 65.6 (C-3'' and C-5''), 102.6 (C-7), 125.1 (C-2' and C-6'), 128.5 (C-4'), 128.6 (C-3' and C-5'), 139.3 (C-1'), 153.5 (C-2), 155.1 (C-9a), 160.4 (C-6), 165.8 (C-8); IR (KBr); ν 3390 br NH, 2980 (CH), 1670 C=O, 1616, 1481, 1388, 1296, 1203, 966. HPLC: purity 98.4%, *t<sub>R</sub>* 15.2 min (MeOH:H<sub>2</sub>O).

**2-Morpholino-4-(methylphenyl)-8-methyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5ar)**

mp 211-212°C (AcOEt:EtOH); TLC (silica gel, MeOH:DCM, 1:9):  $R_f$  0.49; MS (ESI)  $m/z$  340.1 (MH<sup>+</sup>); Anal. Calcd. C, 63.70; H, 6.24; N, 20.64; found C, 61.88; H, 6.05; N, 19.87. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.07 (3H, s, 8-Me), 2.26 (3H, s, 4'-Me) 3.48-3.69 (8H, m, morpholino), 5.78 (1H, s, H-7), 6.83 (1H, s, H-4), 7.06 (2H, d, <sup>3</sup>*J* = 7.9 Hz, H-2' and H-6'), 7.16 (2H, d, <sup>3</sup>*J* = 7.9 Hz, H-3' and H-5'), 8.94 (1H, br s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 20.5 (4'-Me), 23.7 (8-Me), 44.5 (C-3'' and C-5''), 59.7 (C-4), 65.6 (C-2'' and C-6''), 102.6 (C-7), 125.1 (C-2' and C-6'), 129.1 (C-3' and C-5'), 136.5 (C-1'), 137.8 (C-4'), 153.5 (C-2), 155.0 (C-9a), 160.4 (C-6), 165.4 (C-8); IR (KBr); ν 3398 br NH, 2988 (CH), 1672 C=O, 1620, 1418, 1308, 1211, 967. HPLC: purity 99.6%,  $t_R$  17.6 min (MeOH:H<sub>2</sub>O).

**4-(4-Methoxyphenyl)-8-methyl-2-morpholino-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5as)**

mp 203-204°C (Ether); TLC (silica gel, MeOH:DCM, 1:9):  $R_f$  0.53; MS (ESI)  $m/z$  356.1 (MH<sup>+</sup>); Anal. Calcd. C, 60.83; H, 5.96; N, 19.71; found C, 60.26; H, 5.86; N, 19.39. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.07 (3H, s, Me), 3.46-3.67 (8H, m, morpholino), 3.72 (3H, s, OMe), 5.78 (1H, s, H-7), 6.83 (1H, s, H-4), 6.91 (2H, d, <sup>3</sup>*J* = 8.7 Hz, H-3' and H-5'), 7.12 (2H, d, <sup>3</sup>*J* = 8.7 Hz, H-2' and H-6'), 8.89 (1H, s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 23.7 (Me) 44.7 (C-3'' and C-5''), 55.1 (OMe), 59.4 (C-4), 65.7 (C-2'' and C-6''), 102.7 (C-7), 113.9 (C-3' and 5'), 126.5 (C-2' and C-6'), 131.4 (C-1'), 153.5 (C-2), 155.1 (C-9a), 159.3 (C-4'), 160.4 (C-6), 165.7 (C-8). HPLC: purity 100%,  $t_R$  15.3 min (MeOH:H<sub>2</sub>O).

**4-(4-Fluorophenyl)-8-methyl-2-morpholin-4-yl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5at)**

mp 269-270°C (EtOH); TLC (silica gel, MeOH:DCM, 1:9):  $R_f$  0.51; MS (ESI)  $m/z$  344.1 (MH<sup>+</sup>); Anal. Calcd. C, 59.47; H, 5.28; N, 20.40; found C, 59.45; H, 5.26; N, 20.15. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.08 (3H, s, 8-Me), 3.49-3.70 (8H, m, morpholino), 5.79 (1H, s, H-7), 6.86 (1H, s, H-4), 7.15-7.30 (4H, m, H-2', H-3', H-5' and H-6'), 8.90 (1H, s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 23.7 (Me), 44.5 (C-3'' and C-5''), 59.2 (C-4), 65.6 (C-2'' and C-6''), 102.7 (C-7), 115.5 (d, <sup>2</sup>*J*<sub>C-F</sub> = 21.8 Hz, C-3' and C-5'), 127.4 (d, <sup>3</sup>*J*<sub>C-F</sub> = 8.8 Hz, C-2' and C-6'), 135.6 (d, <sup>4</sup>*J*<sub>C-F</sub> = 2.4 Hz, C-1'), 153.4 (C-2), 155.0 (C-9a), 160.3 (C-6), 161.9 (d, <sup>1</sup>*J*<sub>C-F</sub> = 245.2, C-4'), 165.9 (C-8). HPLC: purity 94.7%,  $t_R$  16.1 min (MeOH:H<sub>2</sub>O).

**8-Methyl-2-morpholino-(4-trifluoromethylphenyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5au)**

mp 233-234°C (AcOEt); TLC (silica gel, MeOH:DCM, 1:9):  $R_f$  0.52; MS (ESI)  $m/z$  394.1 (MH<sup>+</sup>); Anal. Calcd. C, 54.96; H, 4.61; N, 17.80; found C, 54.80; H, 4.58; N, 17.73. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.10 (1H, s, Me) 3.48-3.71 (8H, m morpholino), 5.83 (1H, s, H-7), 6.94, (1H, s, H-4), 7.41 (2H, d, <sup>3</sup>*J* = 7.9 Hz, H-2' and H-6'), 7.77 (2H, d, <sup>3</sup>*J* = 7.9 Hz, H-3' and H-5'), 9.02 (1H, br s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 44.7 (C-3'' and C-5''), 60.1 (C-4), 65.6 (C-2'' and C-6''), 102.8 (C-7), 123.9 (q, <sup>1</sup>*J*<sub>C-F</sub> = 272.1 Hz, *p*-CF<sub>3</sub>), 125.8(q, <sup>3</sup>*J*<sub>C-F</sub> = 3.5 Hz, C-3' and C-5'), 126.2 (C-2' and C-6'), 129.1 (q, <sup>2</sup>*J*<sub>C-F</sub> = 31.8 Hz, C-4'), 143.9 (C-1'), 153.5 (C-2), 154.8 (C-9a), 160.3 (C-6), 165.9 (C-8). HPLC: purity 100%,  $t_R$  20.3 min (MeOH:H<sub>2</sub>O).

**4-(8-Methyl-2-morpholino-6-oxo-4,6-dihydro-3H-pyrimido[1,2-a][1,3,5]triazin-4-yl)benzotrile (5av)**

mp 269-270°C (MeOH); TLC (silica gel, AcOEt:Hexane, 8:2):  $R_f$  0.18; MS (ESI)  $m/z$  351.1 (MH<sup>+</sup>); Anal. Calcd. C, 61.70; H, 5.18; N, 23.99; found C, 61.60; H, 5.13; N, 23.72. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.09 (3H, s, Me), 3.48-3.69 (8H, m, morpholino), 5.82 (1H, s, H-7), 6.92 (1H, s, H-4), 7.35 (2H, d, <sup>3</sup>*J* = 8.3 Hz, H-2' and H-6'), 7.86 (2H, d, <sup>3</sup>*J* = 8.3 Hz, H-3' and H-5'), 8.99 (1H, s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 23.7 (Me), 44.7 (C-3'' and C-5''), 59.5 (C-4), 65.6 (C-2'' and C-6''), 102.7 (C-7), 111.4 (C-4'), 118.3 (CN), 126.3 (C-2' and C-6'), 132.8 (C-3' and C-5'), 144.5 (C-1'), 153.3 (C-2), 154.9 (C-9a), 160.3 (C-6), 166.1 (C-8). HPLC: purity 100%,  $t_R$  19.1 min (MeOH:H<sub>2</sub>O).

*4-(Furan-2-yl)-8-methyl-2-morpholino-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5aw)*

mp 262-263°C (EtOH); TLC (silica gel, MeOH:DCM, 1:9):  $R_f$  0.56; MS (ESI)  $m/z$  316.1 (MH<sup>+</sup>); Anal. Calcd. C, 57.13; H, 5.43; N, 22.21; found C, 56.88; H, 5.34; N, 21.80. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.05 (Me), 3.47-3.71 (8H, m, morpholino), 5.75 (1H, s, H-7), 6.21 (1H, d,  $J = 3.4$  Hz, H-3'), 6.36-6.44 (1H, m, H-4'), 6.88 (1H, s, H-4), 7.61 (1H, s, H-5'), 8.81 (1H, s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 23.7 (Me), 44.6 (C-3'' and C-5''), 54.9 (C-4), 65.6 (C-2'' and C-6''), 102.7 (C-7), 107.3 (C-3'), 110.5 (C-4'), 143.3 (C-2'), 150.9 (C-2'), 153.1 (C-2), 155.1 (C-9a), 159.8 (C-6), 165.8 (C-8); IR (KBr); ν 3420 br NH, 3176, 3138, 3116, 2993 (CH), 1670 C=O, 1616, 1525, 1479, 1384, 1286, 1199, 1149, 1111, 1008, 881, 761. HPLC: purity 99.8%,  $t_R$  12.1 min (MeOH:H<sub>2</sub>O).

*8-Methyl-2-morpholino-4-(thiophen-2-yl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5ax)*

mp 267-268°C (decomposed) (EtOH); TLC (silica gel, MeOH:DCM, 1:9):  $R_f$  0.41; MS (ESI)  $m/z$  332.1 (MH<sup>+</sup>); Anal. Calcd. C, 54.36; H, 5.17; N, 21.13, S, 9.68; found C, 54.23; H, 5.05; N, 21.09, S, 9.60. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.05 (3H, s, Me), 3.49-3.78 (8H, m, morpholino), 5.79 (1H, s, H-7), 6.89-7.00 (2H, m, H-4, H-4'), 7.06 (1H, m, H-3'), 7.45 (1H, dd,  $J = 4.9$  Hz,  $J = 1.1$  Hz, H-5'), 8.97 (1H, s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 23.6 (Me), 44.6 (C-3'' and C-5''), 56.9 (C-4), 65.7 (C-2'' and C-6''), 102.8 (C-7), 125.1, 126.3, 126.7, 142.8 (C-2'), 152.7 (C-2), 154.9 (C-9a), 160.0 (C-6), 165.8 (C-8); IR (KBr); ν 3400 br NH, 3097, 2991 (CH), 1674 C=O, 1620, 1530, 1477, 881, 760. HPLC: purity 99.4%,  $t_R$  14.1 min (MeOH:H<sub>2</sub>O).

*8-Methyl-2-morpholino-4-(pyridin-2-yl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5ay)*

mp 272-273°C (EtOH); 2.07 (Me), 3.43-3.71 (8H, m, morpholino), 5.75 (1H, s, H-7), 6.81 (1H, s, H-4), 7.30 (1H, d,  $J = 7.5$  Hz, H-3'), 7.35 (1H, m, H-5'), 7.82 (1H, t,  $J = 7.5$  Hz, H-4'), 8.50 (1H, d,  $J = 3.8$  Hz, H-6'), 8.86 (1H, s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 23.8 (Me), 44.6 (C-3'' and C-5''), 60.9 (C-4), 65.6 (C-2'' and C-6''), 102.5 (C-7), 120.4, 123.7, 137.2, 149.1 (C-2'), 153.7 (C-2), 155.2 (C-9a), 156.9, 160.5 (C-6), 165.7 (C-8). HPLC: purity 100%,  $t_R$  12.4 min (MeOH:H<sub>2</sub>O).

*4-(4-Bromophenyl)-8-methyl-2-morpholino-3,4-dihydro-pyrimido[1,2-a][1,3,5]triazin-6-one (5az)*

mp 245-246°C (MeOH); TLC (silica gel, MeOH:DCM, 1:9):  $R_f$  0.60; MS (ESI)  $m/z$  404.1, 406.1 (MH<sup>+</sup>); Anal. Calcd. C, 50.51; H, 4.49; N, 17.32; found C, 50.50; H, 4.27; N, 17.32. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.08 (3H, s, Me), 3.60 (8H, s, morpholino), 5.80 (1H, s, H-7), 6.83 (1H, s, H-4), 7.12 (2H, d,  $^3J = 8.7$  Hz, H-2' and H-6'), 7.58 (2H, d,  $^3J = 8.3$  Hz, H-3' and H-5'), 8.92 (1H, s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 23.8 (Me), 44.5 (C-3'' and C-5''), 59.3 (C-4), 65.6 (C-2'' and C-6''), 102.6 (C-7), 121.7 (C-4'), 127.4 (C-2' and C-6'), 131.6 (C-3' and C-5'), 138.7 (C-1'), 153.4 (C-2), 154.9 (C-9a), 160.3 (C-6), 165.9 (C-8). HPLC: purity 100%,  $t_R$  19.9 min (MeOH:H<sub>2</sub>O).

*General methods for the synthesis of 4-substituted 2-morpholino-8-trifluoromethyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-ones (5ba-5bn)*

Procedure 1: The solution of *N*-(6-oxo-4-trifluoromethyl-1,6-dihydro-pyrimidin-2-yl)-morpholine-4-carboxamide **4** (0.50 g, 1.7 mmol), aldehydes (2.0 mmol) and piperidine (0.05 ml, 0.5 mmol) in ethanol (10 ml) was heated under reflux for 12-18 h. During halfway through the reaction period, additional aldehyde (up to 0.5 mmol) was added. The precipitate formed is filtered, washed with diethyl ether, dried and recrystallized from suitable solvents.

Procedure 2: A mixture of guanidine **4** (1.2 mmol), piperidine (0.25 mmol) and appropriate aldehyde (1.5 mmol) in 1.5 mL of absolute ethanol was irradiated in a 10 mL vial at 150°C for 20 min using a

Biotage microwave synthesizer. After removing solvent under vacuum the crude product was washed with diethyl ether and filtered.

*2-Morpholino-4-phenyl-8-trifluoromethyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5ba)*

mp 269-270°C (AcOEt); MS (APCI) *m/z*: 380.1 (MH<sup>+</sup>); Anal. Calcd. for C<sub>18</sub>H<sub>18</sub>F<sub>3</sub>N<sub>5</sub>O<sub>2</sub>: C, 53.83; H, 4.25; N, 18.46; found: C, 53.99; H, 3.90; N, 18.46. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 3.54-3.69 (8H, m, morpholino) 6.33 (1H, s, H-7), 6.91 (1H, br s, H-4), 7.22 (2H, d, *J* = 7.5 Hz, H-2' and H-6'), 7.35-7.43 (3H, m, H-3', H-4' and H-5'), 9.16 (1H, br s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 44.7 (C-2'' and C-6''), 60.3 (C-4), 65.6 (C-3'' and C-5''), 101.5 (q, <sup>3</sup>*J*<sub>C-F</sub> = 3.5 Hz, C-7), 120.8 (q, <sup>1</sup>*J*<sub>C-F</sub> = 275.4 Hz, CF<sub>3</sub>), 125.1 (C-3' and C-5'), 128.9 (C-2' and C-6'), 138.6 (C-1'), 153.4 (q, <sup>2</sup>*J*<sub>C-F</sub> = 33.7 Hz, C-8), 155.0, 155.3, 160.2 (C-6); IR (KBr); ν 3385 NH, 3014, 1675 C=O, 1499, 1307. HPLC: purity 100%, *t*<sub>R</sub> 11.9 min (MeOH:H<sub>2</sub>O).

*2-Morpholino-4-(4-methylphenyl)-8-trifluoromethyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5bb)*

mp 251-252°C (Diethyl ether); Anal. Calcd. for C<sub>18</sub>H<sub>18</sub>F<sub>3</sub>N<sub>5</sub>O<sub>2</sub>: C, 54.96; H, 4.61; N, 17.80. Found: C, 54.86; H, 4.17; N, 17.81. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 2.27 (1H, s, Me), 3.51-3.69 (8H, m, morpholino), 6.31 (1H, s, H-7), 6.87 (1H, s, H-4), 7.09 (2H, d, *J* = 7.5 Hz, H-3' and H-5'), 7.19 (2H, d, *J* = 7.5 Hz, H-2' and H-6'), 9.12 (1H, s, NH); <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 44.6 (C-2'' and C-6''), 60.2 (C-4), 65.6 (C-3'' and C-5''), 101.4 (q, <sup>3</sup>*J*<sub>C-F</sub> = 2.5 Hz, C-7), 120.8 (q, <sup>1</sup>*J*<sub>C-F</sub> = 275.2 Hz, CF<sub>3</sub>), 125.0 (C-3' and C-5'), 129.3 (C-2' and C-6'), 135.7 (C-1'), 138.3 (C-4'), 153.3 (q, <sup>2</sup>*J*<sub>C-F</sub> = 33.0 Hz, C-8), 155.0, 155.3, 160.2 (C-6); IR (KBr); ν 3411 br NH, 2981 (CH), 2924, 2868, 1693 C=O, 1600, 1579, 1447, 1363, 1276, 906, 840, 790. HPLC: purity 100%, *t*<sub>R</sub> 13.7 min (MeOH:H<sub>2</sub>O).

*4-(4-Methoxyphenyl)-2-morpholino-8-trifluoromethyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5bc)*

mp 229-230°C (Diethyl ether); Anal. Calcd. for C<sub>18</sub>H<sub>18</sub>F<sub>3</sub>N<sub>5</sub>O<sub>3</sub>: C, 52.81; H, 4.43; N, 17.11; found: C, 52.96; H, 4.05; N, 17.10. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 3.54-3.69 (8H, m, morpholino), 3.73 (3H, s, OMe), 6.30 (1H, s, H-7), 6.86 (1H, s, H-4), 6.94 (2H, d, *J* = 8.7 Hz, H-3' and H-5'), 7.15 (2H, d, *J* = 8.7 Hz, H-2' and H-6'), 9.08 (1H, br s, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 44.6 (C-2'' and C-6''), 55.1 (OMe), 60.1 (C-4), 65.6 (C-3'' and C-5''), 101.4 (q, <sup>3</sup>*J*<sub>C-F</sub> = 3.5 Hz, C-7), 114.2 (C-3' and C-5'), 120.8 (q, <sup>1</sup>*J*<sub>C-F</sub> = 275.4 Hz, CF<sub>3</sub>), 126.5 (C-2' and C-6'), 130.7 (C-1'), 153.3 (q, <sup>2</sup>*J*<sub>C-F</sub> = 33.5 Hz, C-8), 155.0, 155.2, 159.5 (C-4'), 160.2 (C-6). HPLC: purity 100%, *t*<sub>R</sub> 12.9 min (MeOH:H<sub>2</sub>O).

*4-(4-Fluorophenyl)-2-morpholino-8-trifluoromethyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5bd)*

mp 270-271°C (AcOEt:diethylether); Anal. Calcd. for C<sub>17</sub>H<sub>15</sub>F<sub>4</sub>N<sub>5</sub>O<sub>2</sub>: C, 51.39; H, 3.81; N, 17.63; found: C, 51.34; H, 3.41; N, 17.65. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): δ 3.54-3.74 (8H, m, morpholino), 6.33 (1H, s, H-7), 6.90 (1H, d, *J* = 4.9 Hz, H-4), 7.20-7.30 (4H, m, H<sub>2'</sub>, H<sub>6'</sub>, H<sub>3'</sub> and H<sub>5'</sub>), 9.15 (1H, d, *J* = 4.9 Hz, NH). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 44.6 (C-2'' and C-6''), 59.8 (C-4), 65.5 (C-3'' and C-5''), 101.4 (q, <sup>3</sup>*J*<sub>C-F</sub> = 2.4 Hz, C-7), 115.7 (d, <sup>2</sup>*J*<sub>C-F</sub> = 21.8 Hz, C-3' and C-5'), 120.8 (q, <sup>1</sup>*J*<sub>C-F</sub> = 278.1 Hz, CF<sub>3</sub>), 127.4 (d, <sup>3</sup>*J*<sub>C-F</sub> = 8.8 Hz, C-2' and C-6'), 134.8 (d, <sup>4</sup>*J*<sub>C-F</sub> = 2.9 Hz, C-1'), 153.3 (q, <sup>2</sup>*J*<sub>C-F</sub> = 33.3 Hz, C-8), 154.8, 155.1, 160.2 (C-6), 162.0 (d, <sup>1</sup>*J*<sub>C-F</sub> = 245.2 Hz, C-4'). HPLC: purity 100%, *t*<sub>R</sub> 12.6 min (MeOH:H<sub>2</sub>O).

*2-Morpholino-8-trifluoromethyl-4-(4-trifluoromethylphenyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5be)*

mp 288-289°C (AcOEt); Anal. Calcd. for C<sub>18</sub>H<sub>15</sub>F<sub>6</sub>N<sub>5</sub>O<sub>2</sub>: C, 48.33; H, 3.38; N, 15.66. Found: C, 48.57; H, 3.14; N, 15.79. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>SO-*d*<sub>6</sub>): 3.52-3.75 (8H, m, morpholino), 6.36 (1H, s, H-7),

6.99 (2H, d,  $J = 4.2$  Hz, H-4), 7.45 (2H, d,  $J = 8.3$  Hz, H-3' and H-5'), 7.80 (2H, d,  $J = 8.3$  Hz, H-2' and H-6'), 9.23 (d,  $J = 4.2$  Hz, NH).  $^{13}\text{C}$  NMR (75 MHz,  $\text{Me}_2\text{SO}-d_6$ ): 44.7 (C-2'' and C-6''), 60.1 (C-4), 65.6 (C-3'' and C-5''), 101.6 (q,  $^3J_{\text{C-F}} = 2.4$  Hz, C-7), 120.8 (q,  $^1J_{\text{C-F}} = 275.8$  Hz, 8-CF<sub>3</sub>), 123.8 (q,  $^1J_{\text{C-F}} = 272.3$  Hz, 4'-CF<sub>3</sub>), 126.0 (q,  $^3J_{\text{C-F}} = 3.3$  Hz, C-3' and C-5'), 126.2 (C-2' and C-6'), 129.4 (q,  $^2J_{\text{C-F}} = 31.8$  Hz, C-4'), 143.0 (C-1'), 153.5 (q,  $^2J_{\text{C-F}} = 33.7$  Hz, C-8), 154.9, 155.2, 160.3 (C-6); IR (KBr);  $\nu$  3396 br NH, 2982 (CH), 1693 C=O, 1604, 1581, 1417, 1336, 1278. HPLC: purity 98.3%,  $t_{\text{R}}$  20.4 min ( $\text{MeOH}:\text{H}_2\text{O}$ ); purity 100%,  $t_{\text{R}}$  7.4 min ( $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ ).

*2-Morpholino-4-(furan-2-yl)-8-trifluoromethyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5bf)*

mp 255-256°C ( $\text{CH}_2\text{Cl}_2$ ); Anal. Calcd. for  $\text{C}_{15}\text{H}_{14}\text{F}_3\text{N}_5\text{O}_3$ : C, 48.78; H, 3.82; N, 18.96; found: C, 48.79; H, 3.92; N, 18.63.  $^1\text{H}$  NMR (300 MHz,  $\text{Me}_2\text{SO}-d_6$ ):  $\delta$  3.57-3.70 (8H, m, morpholino), 6.24 (1H, s, H-7), 6.31 (1H, d,  $J = 3.4$  Hz, H-3'), 6.43 (1H, dd,  $J = 3.0$  Hz, 1.9 Hz, H-4'), 6.93 (1H, s, H-4), 7.64 (1H, d,  $J = 1.1$  Hz, H-5'), 9.09 (1H, d,  $J = 4.9$  Hz, NH); IR (KBr);  $\nu$  3253 NH, 3147, 2970, 2843, 1657 br C=O, 1490, 1209, 1114, 1006, 958, 904, 819. HPLC: purity 95.4%,  $t_{\text{R}}$  8.6 min ( $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ ).

*2-Morpholino-4-(4-nitrophenyl)-8-trifluoromethyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5bg)*

mp 294-295°C (AcOEt); TLC (silica gel, AeOEt:Hexane, 8:2):  $R_f$  0.3.  $^1\text{H}$  NMR (300 MHz,  $\text{Me}_2\text{SO}-d_6$ ):  $\delta$  3.64-3.70 (8H, m, morpholino), 6.37 (1H, s, H-7), 7.02 (1H, d,  $^3J = 4.5$  Hz, H-4), 7.51 (2H, d,  $^3J = 8.7$  Hz, H-2' and H-6'), 8.27 (2H, d,  $^3J = 8.7$  Hz, H-3' and H-5'), 9.25 (1H, d,  $^3J = 4.5$  Hz, NH).  $^{13}\text{C}$  NMR (75 MHz,  $\text{Me}_2\text{SO}-d_6$ ): 44.7 (C-3'' and C-5''), 60.0 (C-4), 65.6 (C-2'' and C-6''), 101.7 (q,  $^3J_{\text{C-F}} = 2.9$  Hz, C-7), 120.8 (q,  $^1J_{\text{C-F}} = 275.8$  Hz, CF<sub>3</sub>), 124.2 (C-2' and C-6'), 126.8 (C-3' and C-5'), 145.4 (C-1'), 147.7 (C-4'), 153.5 (q,  $^2J_{\text{C-F}} = 33.5$  Hz, C-8), 154.8, 155.2, 160.3 (C-6).

*2-Morpholino-4-(pyridin-2-yl)-8-(trifluoromethyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5bh)*

mp 260-261°C ( $\text{CH}_2\text{Cl}_2$ ); MS (APCI)  $m/z$ : 381.5 ( $\text{MH}^+$ ); Anal. Calcd. for  $\text{C}_{16}\text{H}_{15}\text{F}_3\text{N}_6\text{O}_2$ : C, 50.53; H, 3.98; N, 22.10; found: C, 50.29; H, 3.83; N, 21.93.  $^1\text{H}$  NMR (300 MHz,  $\text{Me}_2\text{SO}-d_6$ ):  $\delta$  3.50-3.71 (8H, m, morpholino), 6.27 (1H, s, H-7), 6.88 (1H, d,  $J = 4.5$  Hz, H-4), 7.34-7.46 (2H, m, H-4' and H-5'), 7.88 (1H, dt,  $J = 7.9$  Hz, 1.5 Hz, H-4'), 8.50 (1H, d,  $J = 4.5$  Hz, H-3'), 9.08 (1H, d,  $J = 4.9$  Hz, NH).  $^{13}\text{C}$  NMR (75 MHz,  $\text{Me}_2\text{SO}-d_6$ ): 44.7 (C-2'' and C-6''), 61.4 (C-4), 65.6 (C-3'' and C-5''), 101.3 (q,  $^4J_{\text{C-F}} = 1.7$  Hz, C-7), 120.8, 120.9 (q,  $^1J_{\text{C-F}} = 275.1$  Hz, CF<sub>3</sub>), 124.1, 137.5, 149.2 (C-1'), 153.3 (q,  $^2J_{\text{C-F}} = 33.2$  Hz, C-8), 155.1 (C-2), 155.6 (C-2'), 156.1 (C-9a), 160.4 (C-6); IR (KBr);  $\nu$  3357 NH, 3068, 2970, 2845, 1656 C=O, 1208, 1070, 908. HPLC: purity 99.2%,  $t_{\text{R}}$  6.2 min ( $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ ).

*4-(4-Bromophenyl)-2-morpholino-8-trifluoromethyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5bi)*

mp 270-271°C (AcOEt); MS (APCI)  $m/z$ : 458.2 ( $\text{MH}^+$ ); Anal. Calcd. for  $\text{C}_{17}\text{H}_{15}\text{BrF}_3\text{N}_5\text{O}_2$ : C, 44.56; H, 3.30; N, 15.28; found: C, 44.84; H, 3.48; N, 15.33.  $^1\text{H}$  NMR (300 MHz,  $\text{Me}_2\text{SO}-d_6$ ):  $\delta$  3.54-3.69 (8H, m, morpholino), 6.34 (1H, s, H-7), 6.88 (1H, s, H-4), 7.18 (2H, d,  $J = 8.3$  Hz, H-3' and H-5'), 7.61 (2H, d,  $J = 8.3$  Hz, H-2' and H-6'), 9.16 (1H, br s, NH).  $^{13}\text{C}$  NMR (75 MHz,  $\text{Me}_2\text{SO}-d_6$ ): 44.7 (C-2'' and C-6''), 60.0 (C-4), 65.6 (C-3'' and C-5''), 101.5 (q,  $^3J_{\text{C-F}} = 2.4$  Hz, C-7), 120.8 (q,  $^1J_{\text{C-F}} = 275.2$  Hz, CF<sub>3</sub>), 122.2, 127.5 (C-3' and C-5'), 131.9 (C-2' and C-6'), 138.0 (C-1'), 153.3 (q,  $^2J_{\text{C-F}} = 33.5$  Hz, C-8), 154.9, 155.2, 160.2 (C-6); IR (KBr)  $\nu$  3333 NH, 2991 CH, 1674 C=O, 1660, 1613. HPLC: purity 100%,  $t_{\text{R}}$  17.9 min ( $\text{MeOH}:\text{H}_2\text{O}$ ); purity 100%,  $t_{\text{R}}$  7.9 min ( $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ ).

*4-(2-Morpholino-6-oxo-8-trifluoromethyl-4,6-dihydro-3H-pyrimido[1,2-a][1,3,5]triazin-4-yl)benzotrile (5bj)*

mp 269-270°C (AcOEt); Anal. Calcd. for  $\text{C}_{18}\text{H}_{15}\text{F}_3\text{N}_6\text{O}_2$ : C, 53.47; H, 3.74; N, 20.78. Found: C, 53.59; H, 3.91; N, 20.89.  $^1\text{H}$  NMR (300 MHz,  $\text{Me}_2\text{SO}-d_6$ ):  $\delta$  3.54-3.73 (8H, m, morpholino), 6.36 (1H, s, H-7), 6.97 (1H, s, H-4), 7.41 (2H, d,  $J = 8.3$  Hz, H-3' and H-5'), 7.89 (2H, d,  $J = 8.3$  Hz, H-2' and H-6'), 9.23

(1H, br s, NH);  $^{13}\text{C}$  NMR (75 MHz,  $\text{Me}_2\text{SO}-d_6$ ): 44.7 (C-2'' and C-6''), 60.1 (C-4), 65.6 (C-3'' and C-5''), 101.6 (q,  $^4J_{\text{C-F}} = 2.4$  Hz, C-7), 111.8 (C-4'), 118.2 (CN), 120.8 (q,  $^1J_{\text{C-F}} = 275.6$  Hz,  $\text{CF}_3$ ), 126.3 (C-2' and C-6'), 133.0 (C-3' and C-5'), 143.6 (C-1'), 153.5 (q,  $^2J_{\text{C-F}} = 33.5$  Hz, C-8), 154.8, 155.1, 160.3 (C-6). HPLC: purity 98.9%,  $t_{\text{R}}$  12.2 min (MeOH:H<sub>2</sub>O).

**8-Methyl-2-pyrrolidino-4-(4-methylphenyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5bk)**

mp 202-203°C (AcOEt+EtOH); Anal. Calcd. for  $\text{C}_{18}\text{H}_{21}\text{N}_5\text{O}$ : C, 66.85; H, 6.55; N, 21.66. Found: C, 66.76; H, 6.71; N, 21.59.  $^1\text{H}$  NMR (300 MHz,  $\text{Me}_2\text{SO}-d_6$ ): 1.86 (8H, br s, pyrrolidino), 2.05 (3H, s, 8-Me), 2.26 (3H, s, 4'-Me), 5.70 (1H, s, H-7), 6.79 (1H, d,  $J = 3.4$  Hz, H-4), 7.08 (2H, d,  $J = 8.3$  Hz, H-3' and H-5'), 7.15 (2H, d,  $J = 8.3$  Hz, H-2' and H-6'), 8.59 (1H, d,  $J = 3.7$  Hz, NH);  $^{13}\text{C}$  NMR (75 MHz,  $\text{Me}_2\text{SO}-d_6$ ): 20.5 (4'-Me), 23.8 (8-Me), 59.6 (C-4), 101.9 (C-7), 125.2 (C-2' and C-6'), 129.1 (C-3' and C-5'), 136.9 (C-1'), 137.7 (C-4'), 153.6 (C-9a), 160.5 (C-6), 165.7 (C-8).

**8-Methyl-2-(4-methylpiperazino)-4-(4-methylphenyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5bl)**

mp 208-209°C (AcOEt); Anal. Calcd. for  $\text{C}_{19}\text{H}_{24}\text{N}_6\text{O}$ : C, 64.75; H, 6.86; N, 23.85. Found: C, 64.90; H, 6.92; N, 23.95.  $^1\text{H}$  NMR (300 MHz,  $\text{Me}_2\text{SO}-d_6$ ): 2.07 (3H, s, 8-Me), 2.18 (3H, s, N-Me), 2.26 (3H, s, 4'-Me), 3.46-3.67 (4H, s, piperazino), 5.76 (1H, s, H-7), 6.80 (1H, s, H-4), 7.05 (2H, d,  $J = 8.0$  Hz, H-3' and H-5'), 7.18 (2H, d,  $J = 7.9$  Hz, H-2' and H-6'), 8.85 (1H, br s, NH);  $^{13}\text{C}$  NMR (75 MHz,  $\text{Me}_2\text{SO}-d_6$ ): 20.5 (4'-Me), 23.7 (8-Me), 44.0, 45.4, 54.0, 59.5 (C-4), 102.5 (C-7), 125.0 (C-2' and C-6'), 129.1 (C-3' and C-5'), 136.5 (C-1'), 137.8 (C-4'), 153.5 (C-9a), 154.7 (C-2), 160.4 (C-6), 165.7 (C-8).

**2-(3-Chlorophenylamino)-8-methyl-4-(4-methylphenyl)-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5bm)**

Mp 259-260°C Anal. Calcd. for  $\text{C}_{20}\text{H}_{18}\text{N}_5\text{OCl}$ : C, 63.24; H, 4.78; N, 18.44. Found: 63.31; H, 4.86; N 18.55.  $^1\text{H}$  NMR (300 MHz,  $\text{Me}_2\text{SO}-d_6$ ): 2.13 (3H, s, 8-Me), 2.26 (3H, s, 4'-Me), 5.87 (1H, s, H-7), 6.92 (1H, s, H-4), 7.03-7.22 (5H, m, H-3', H-5', H-2', H-6' and H-4''), 7.30-7.42 (2H, m, H-5'' and H-6''), 7.81 (1H, s, H-2''), 8.38 (1H, br s, NH), 9.70 (1H, br s, NH).

**2-(3-Chlorophenylamino)-4-(5-(hydroxymethyl)furan-2-yl)-8-methyl-3,4-dihydropyrimido[1,2-a][1,3,5]triazin-6-one (5bn)**

mp 237-238°C; Anal. Calcd. for  $\text{C}_{18}\text{H}_{16}\text{N}_5\text{O}_3\text{Cl}$ : C, 56.04; H, 4.18; N, 18.15. Found: C, 56.44; H, 4.50; N, 18.01.  $^1\text{H}$  NMR (300 MHz,  $\text{Me}_2\text{SO}-d_6$ ): 2.12 (3H, s, 8-Me), 4.32 (2H, d,  $J = 5.6$  Hz,  $\text{CH}_2$ ), 5.22 (1H, t,  $J = 5.3$  Hz, OH), 5.85 (1H, s, H-7), 6.11-6.28 (2H, m, H-3' and 4'), 6.93 (1H, s, H-4), 7.13 (1H, d,  $J = 7.2$  Hz, H-4''), 7.35 (1H, t,  $J = 8.1$  Hz, H-5''), 7.43 (1H, d,  $J = 7.9$  Hz, H-6''), 7.79 (1H, s, H-2''), 8.53 (1H, s, NH), 9.82 (1H, s, NH);  $^{13}\text{C}$  NMR (75 MHz,  $\text{Me}_2\text{SO}-d_6$ ): 21.0, 23.2, 55.5 ( $\text{CH}_2$ ), 64.8 (C-4), 104.1 ( $\text{CH}_{\text{Ar}}$ ), 107.7 ( $\text{CH}_{\text{Ar}}$ ), 108.1 ( $\text{CH}_{\text{Ar}}$ ), 130.3 ( $\text{CH}_{\text{Ar}}$ ), 133.0, 140.2, 150.3, 152.5 (C-9a), 155.8 (C-2), 159.4 (C-6), 165.7 (C-8).