Preliminary Communication

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A facile one-pot synthesis of aryl-substituted fused pyrimidinones

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Abstract: The convenient synthesis of a series of 3-phenylpyrido[1,2-*a*]pyrimidinones **4**, 3-phenylpyrimido-[1,2-*c*]quinazolinones **7** and 3-phenylpyrazino[1,2-*a*]pyrimidinones **10** with promising biological activity is presented.

Keywords: cyclization; pyrazino[1,2-*a*]pyrimidinones; pyrido[1,2-*a*]pyrimidinones; pyrimido[1,2-*c*]quinazolinones.

Fused pyrimidinone systems have been important in drug design over many years due to diverse biological properties including antimicrobial, antiviral, antioxidant and antitumor activities [1–4]. In particular, C3-arylated pyrido[1,2-*a*]pyrimidin-4-ones have been exploited in the design of pharmaceutically active compounds such as phosphoinositide 3-kinase (pi3k) inhibitors, endothelial cell dysfunction inhibitors, and CXCR3 antagonists [5–7]. The conventional methods previously reported for the synthesis (Gould-Jacob type reaction) [8–10] and the functionalization (Suzuki-Miyaura reaction) [11] of fused pyrimidinones have limitations in that they are multi-step reactions and require harsh reaction conditions. Recently, Guchhait showed a novel method for the synthesis of 3-aryl-pyrido[1,2-*a*]pyrimidin-4-ones by Pd-catalyzed Ag(I)-promoted activation-arylation of pyrido[1,2-*a*]pyrimidin-4-one [12]. We have also reported convenient synthesis of novel 3-phenylpyrimido[1,2-*c*] thienopyrimidinones as potent inhibitors of interlukin-6/signal transducer and activator of transcription 3 (IL-6/STAT3) by the one-pot reaction of formamidine derivatives of 4-aminothienopyrimidine with phenylacetyl chlorides [13]. Since STAT3 is frequently over-expressed or persistently activated in most tumors [14], effective IL-6/STAT3 inhibitors could be useful candidates for development of new anticancer and anti-inflammatory drugs [15].

In this communication we report synthesis new fused pyrimidinone compounds, 3-phenylpyrido[1,2-*a*]pyrimidinones **4**, 3-phenylpyrimido[1,2-*c*]quinazolinones **7** and 3-phenylpyrazino[1,2-*a*]pyrimidinones **10** by reactions of heteroaryl formamidines with phenylacetyl chlorides (Scheme 1).

The heterocyclic substrates **2a–b** [16], **6** [17] and **9** [18] were easily prepared in quantitative yield by treatment of fused heterocyclic amines **1a–b**, **5** and **8** with dimethylformamide dimethyl acetal (DMF-DMA), and they were used without isolation for the next reaction. The cyclization of **2a–b** with various 2-phenylacetyl chlorides **3** in dichloromethane in the presence of a catalytic amount of triethylamine at room temperature gave **4a–f** within 3 h in good to excellent yields. The reaction of **6** or **9** with **3** under similar conditions was also successfully carried out to afford corresponding **7a–e** or **10a–e** in good yields. The crude solid products obtained were easily isolated by filtration, washing and drying, and then purified by crystallization from ethanol. All products were fully characterized by spectral data and elemental analysis. The preliminary biological tests of IL-6/STAT3 inhibition for some synthesized compounds (**4b**, **7c**, **10d**) exhibited IC_{50} values ranging from 1.5 μM to 5.8 μM [19], and further pharmacological studies are still in progress.

Experimental

Melting points were measured using capillary tubes on a Büchi apparatus and are uncorrected. The reactions were monitored by thin-layer chromatography on Merck kieselgel $60F_{254}$ plates and the products were purified by column chromatography using Merck silica gel (70–230 mesh). The ^{1}H NMR spectra were recorded on a Unity Inova 400NB FT NMR spectrometer at 400 MHz in DMSO-d_6. Mass spectra were recorded on a HP 59580 B spectrometer with electrospray ionization in a positive ion mode. Elemental analyses were performed on a Carlo Erba 1106 elemental analyzer.

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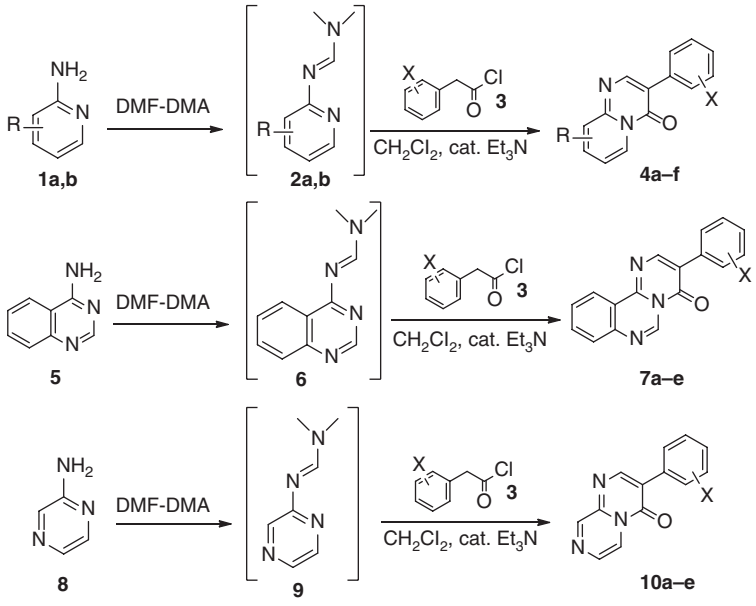

1a, **2a**: R = H; **1b**, **2b**: R = 5-Cl; **4a**: X = 3-Cl, R = H; **4b**: X = 4-Cl, R = H; **4c**: X = 4-Br, R = H; **4d**: X = 4-NO_2, R = H; **4e**: X = 4-OMe, R = H; **4f**: X = 4-Cl, R = 7-Cl; **7a**: X = 2-Cl; **7b**: X = 3-Cl; **7c**: X = 4-Cl; **7d**: X = 4-Br; **7e**: X = 4-NO_2; **10a**: X = H; **10b**: X = 2-Cl; **10c**: X = 3-Cl; **10d**: X = 4-Cl; **10e**: X = 4-OMe

Scheme 1 One-pot synthesis of compounds **4a–f, 7a–e** and **10a–e.**

General procedure for the preparation of compounds 4a–f, 7a–e and 10a–e

A mixture of heterocyclic amine **1a**,**b**, **5** or **8** (5 mmol) and DMF-DMA (6 mmol) was heated under reflux for 3 h and then stirred at room temperature for 10 h and concentrated. The residue was treated with a solution of the appropriate acyl chloride **3** (5 mmol) in dichloromethane (10 mL) containing a catalytic amount of triethylamine. The resulting solution was stirred at room temperature for 3 h and the precipitated crude product was filtered, washed with ethyl acetate, and crystallized from ethanol.

3-(3-Chlorophenyl)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (4a) This compound was obtained from **1a** and 2-(3-chlorophenyl)acetyl chloride; yield 80%; mp 177–179°C; ^{1}H NMR: δ 9.09 (d, 1H, *J* = 7.6 Hz), 8.66 (s, 1H), 8.00 (t, 1H, *J* = 7.6 Hz), 7.94 (s, 1H), 7.79 (d, 1H, *J* = 7.6 Hz), 7.75 (d, 1H, *J* = 7.6 Hz), 7.45 (m, 2H), 7.38 (d, 1H, *J* = 7.6 Hz); MS: *m/z* 256.67 (M^+). Anal. Calcd for $C_{14}H_9ClN_2O$: C, 65.51; H, 3.53; N, 10.91. Found: C, 65.82; H, 3.80; N, 10.60.

3-(4-Chlorophenyl)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (4b) This compound was obtained from **1a** and 2-(4-chlorophenyl)acetyl chloride; yield 85%; mp 198–199°C (Lit. [12] mp 198–200°C); ^{1}H NMR: δ 9.07 (d, 1H, *J* = 7.6 Hz), 8.61 (s, 1H), 7.97 (t, 1H, *J* = 7.6 Hz), 7.85 (d, 2H, *J* = 8.0 Hz), 7.72 (d, 1H, *J* = 7.6 Hz), 7.46 (d, 2H, *J* = 8.0 Hz), 7.41 (t, 1H, *J* = 7.6 Hz); MS: *m/z* 256.80 (M^+). Anal. Calcd for $C_{14}H_9ClN_2O$: C, 65.51; H, 3.53; N, 10.91. Found: C, 65.77; H, 3.20; N, 10.69.

3-(4-Bromophenyl)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (4c) This compound was obtained from **1a** and 2-(4-bromophenyl)acetyl chloride; yield: 82%; mp 200–202°C; ^{1}H NMR: δ 9.07 (d, 1H, *J* = 7.5 Hz), 8.57 (s, 1H), 7.98 (t, 1H, *J* = 7.5 Hz), 7.79 (d, 2H, *J* = 8.0 Hz), 7.73 (d, 1H, *J* = 7.5 Hz), 7.60 (d, 2H, *J* = 8.0 Hz), 7.41 (t, 1H, *J* = 7.5 Hz), MS (ESI): *m/z* 301.22 (M^+). Anal. Calcd for $C_{14}H_9BrN_2O$: C, 55.84; H, 3.01; N, 9.30. Found: C, 55.70; H, 3.18; N, 9.18.

3-(4-Nitrophenyl)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (4d) This compound was obtained from **1a** and 2-(4-nitrophenyl)acetyl chloride; yield 88%; mp 166–168°C; ^{1}H NMR: δ 9.14 (d, 1H, *J* = 7.5 Hz), 8.78 (s, 1H), 8.27 (d, 2H, *J* = 8.0 Hz), 8.18 (d, 2H, *J* = 8.0 Hz), 8.06 (t, 1H, *J* = 7.5 Hz), 7.80 (d, 1H, *J* = 7.5 Hz), 7.66 (t, 1H, *J* = 7.5 Hz); MS: *m/z* 267.80 (M^+). Anal. Calcd for $C_{14}H_9N_3O_3$: C, 62.92; H, 3.39; N, 15.72. Found: C, 62.80; H, 3.49; N, 15.88.

3-(4-Methoxyphenyl)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (4e) This compound was obtained from **1a** and 2-(4-methoxyphenyl)acetyl chloride; yield: 65%; mp 142–143°C (Lit. [11] mp 142–144°C); ^{1}H NMR: δ 9.06 (d, 1H, *J* = 7.5 Hz), 8.54 (s, 1H), 7.93 (t, 1H, *J* = 7.5 Hz), 7.76 (d, 2H, *J* = 7.5 Hz), 7.69 (d, 1H, *J* = 7.5 Hz), 7.38 (t, 1H, *J* = 7.5 Hz), 6.98 (d, 2H, *J* = 7.5 Hz), 3.75 (s, 3H); MS: *m/z* 252.69 (M^+). Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.66; H, 4.88; N, 10.91.

7-Chloro-3-(4-chlorophenyl)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (4f) This compound was obtained from **1b** and 2-(4-chlorophenyl) acetyl chloride; yield: 68%; mp 198–200°C; ^{1}H NMR: δ 9.04 (s, 1H), 8.62 (s, 1H), 8.02 (d, 1H, *J* = 7.5 Hz), 7.85 (d, 2H, *J* = 7.5 Hz), 7.75 (d, 1H, *J* = 7.5 Hz), 7.48 (d, 2H, *J* = 7.5 Hz); MS: *m/z* 291.45 (M^+). Anal. Calcd for $C_{14}H_8Cl_2N_2O$: C, 57.76; H, 2.77; N, 9.62. Found: C, 57.90; H, 2.69; N, 9.77.

3-(2-Chlorophenyl)-4*H*-pyrimido[1,2-*c*]quinazolin-4-one (7a) This compounds was obtained from **5** and 2-(2-chlorophenyl) acetyl chloride; yield 85%; mp 237–239°C; ^{1}H NMR: δ 9.46 (s, 1H), 8.75 (d, 1H, *J* = 7.6 Hz), 8.41 (s, 1H), 8.00 (t, 1H, *J* = 7.6 Hz), 7.96 (d, 1H, *J* = 7.6 Hz), 7.82 (t, 1H, *J* = 7.6 Hz), 7.76 (d, 1H, *J* = 7.6 Hz), 7.45 (m, 3H); MS: *m/z* 307.44 (M^+). Anal. Calcd for $C_{17}H_{10}ClN_3O$: C, 66.35; H, 3.28; N, 13.65. Found: C, 66.74; H, 3.39; N, 13.40.

3-(3-Chlorophenyl)-4*H*-pyrimido[1,2-*c*]quinazolin-4-one (7b) This compounds was obtained from **5** and 2-(3-chlorophenyl) acetyl chloride; yield 80%; mp 259–261°C; ^{1}H NMR: δ 9.64 (s, 1H), 8.75 (d, 1H, *J* = 7.5 Hz), 8.68 (s, 1H), 8.00 (m, 2H), 7.92 (s, 1H), 7.83 (d, 1H, *J* = 7.5 Hz), 7.79 (d, 1H, *J* = 7.5 Hz), 7.49 (t, 1H, *J* = 7.5 Hz), 7.45 (d, 1H, *J* = 7.5 Hz); MS: *m/z* 307.60 (M^+). Anal. Calcd for $C_{17}H_{10}ClN_3O$: C, 66.35; H, 3.28; N, 13.65. Found: C, 66.58; H, 3.11; N, 13.72.

3-(4-Chlorophenyl)-4*H*-pyrimido[1,2-*c*]quinazolin-4-one (7c) This compound was obtained from **5** and 2-(4-chlorophenyl) acetyl chloride; yield: 90%; mp 262–264°C; ^{1}H NMR: δ 9.50 (s, 1H), 8.74 (d, 1H, *J* = 7.5 Hz), 8.65 (s, 1H), 7.98 (m, 2H), 7.87 (d, 2H, *J* = 8.0 Hz), 7.82 (d, 1H, *J* = 7.5 Hz), 7.53 (d, 2H, *J* = 8.0 Hz); MS: *m/z* 307.90 (M^+). Anal. Calcd for $C_{17}H_{10}ClN_3O$: C, 66.35; H, 3.28; N, 13.65. Found: C, 66.50; H, 3.39; N, 13.80.

3-(4-Bromophenyl)-4*H*-pyrimido[1,2-*c*]quinazolin-4-one (7d) This compound was obtained from **5** and 2-(4-bromophenyl) acetyl chloride; yield 80%; mp 268–270°C; ^{1}H NMR: δ 9.50 (s, 1H), 8.74 (d, 1H, *J* = 7.5 Hz), 8.66 (s, 1H), 7.98 (m, 2H), 7.80 (d, 2H, *J* = 8.0 Hz), 7.80 (d, 1H, *J* = 7.5 Hz), 7.67 (d, 2H, *J* = 8.0 Hz); MS: *m/z* 352.44 (M^+). Anal. Calcd for $C_{17}H_{10}BrN_3O$: C, 57.98; H, 2.86; N, 11.93. Found: C, 58.22; H, 2.77; N, 11.77.

3-(4-Nitrophenyl)-4*H*-pyrimido[1,2-*c*]quinazolin-4-one (7e) This compound was obtained from **5** and 2-(4-nitrophenyl)acetyl chloride; yield 85%; mp 231–233°C; ^{1}H NMR: δ 9.50 (s, 1H), 8.75 (d, 1H, *J* = 7.6 Hz), 8.65 (s, 1H), 8.00–7.98 (m, 2H), 7.87 (d, 2H, *J* = 8.0 Hz), 7.82 (d, 1H, *J* = 7.6 Hz), 7.53 (d, 2H, *J* = 8.0 Hz); MS: *m/z* 318.53 (M^+). Anal. Calcd for $C_{17}H_{10}N_4O_3$: C, 64.15; H, 3.17; N, 17.60. Found: C, 63.90; H, 3.28; N, 17.88.

3-Phenyl-4*H*-pyrazino[1,2-*a*]pyrimidin-4-one (10a) This compound was obtained from **8** and 2-phenylacetyl chloride; yield 77%; mp 221–223°C; ^{1}H NMR: δ 9.13 (s, 1H), 8.76 (d, 1H, *J* = 7.6 Hz), 8.70 (s, 1H), 8.23 (d, 1H, *J* = 7.6 Hz), 7.82 (d, 2H, *J* = 7.6 Hz), 7.46–7.42 (m, 3H); MS: *m/z* 223.44 (M^+). Anal. Calcd for $C_{13}H_9N_3O$: C, 69.95; H, 4.06; N, 18.82. Found: C, 69.72; H, 3.90; N, 19.03.

3-(2-Chlorophenyl)-4*H*-pyrazino[1,2-*a*]pyrimidin-4-one (10b) This compound was obtained from **8** and 2-(2-chlorophenyl) acetyl chloride; yield 84%; mp 173–175°C; ^{1}H NMR: δ 9.17 (s, 1H), 8.74 (d, 1H, *J* = 7.6 Hz), 8.47 (s, 1H), 8.25 (d, 1H, *J* = 7.6 Hz), 7.56 (d, 1H, *J* = 7.6 Hz), 7.45–7.42 (m, 3H); MS: *m/z* 257.60 (M^+). Anal. Calcd for $C_{13}H_8ClN_3O$: C, 60.60; H, 3.13; N, 16.31. Found: C, 60.48; H, 3.01; N, 16.50.

3-(3-Chlorophenyl)-4*H*-pyrazino[1,2-*a*]pyrimidin-4-one (10c) This compound was obtained from **8** and 2-(3-chlorophenyl) acetyl chloride; yield 79%; mp 252–254°C; ^{1}H NMR: δ 9.16 (s, 1H), 8.79 (s, 1H), 8.76 (d, 1H, *J* = 7.6 Hz), 8.27 (d, 1H, *J* = 7.6 Hz), 7.95 (s, 1H), 7.81 (d, 1H, *J* = 7.6 Hz), 7.50 (t, 1H, *J* = 7.6 Hz), 7.44 (d, 1H, *J* = 7.6 Hz); MS: *m/z* 257.66 (M^+). Anal. Calcd for $C_{13}H_8ClN_3O$: C, 60.60; H, 3.13; N, 16.31. Found: C, 60.85; H, 3.19; N, 16.48.

3-(4-Chlorophenyl)-4*H*-pyrazino[1,2-*a*]pyrimidin-4-one (10d) This compound was obtained from **8** and 2-(4-chlorophenyl) acetyl chloride; yield 81%; mp 224–226°C; ^{1}H NMR: δ 9.16 (s, 1H), 8.77 (d, 1H, *J* = 7.6 Hz), 8.75 (s, 1H), 8.26 (d, 1H, *J* = 7.6 Hz), 7.90 (d, 2H, *J* = 8.0 Hz), 7.52 (d, 1H, *J* = 8.0 Hz); MS: *m/z* 257.64 (M^+). Anal. Calcd for $C_{13}H_8ClN_3O$: C, 60.60; H, 3.13; N, 16.31. Found: C, 60.44; H, 3.01; N, 16.22.

3-(4-Methoxyphenyl)-4*H*-pyrazino[1,2-*a*]pyrimidin-4-one (10e) This compound was obtained from **8** and 2-(4-methoxyphenyl)acetyl chloride; yield 62%; mp 233–235°C; ^{1}H NMR: δ 9.12 (s, 1H), 8.75 (d, 1H, *J* = 7.3 Hz), 8.69 (s, 1H), 8.21 (d, 1H, *J* = 7.3 Hz), 7.83 (d, 2H, *J* = 8.0 Hz), 7.02 (d, 2H, *J* = 8.0 Hz), 3.77 (s, 3H); MS: *m/z* 253.38 (M^+). Anal. Calcd for $C_{14}H_{11}N_3O_2$: C, 60.40; H, 4.38; N, 16.59. Found: C, 60.65; H, 4.22; N, 16.47.

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References

[1] Guo, C.; Linton, A.; Jalaie, M.; Kephart, S.; Ornelas, M.; Pairish, M.; Greasley, S.; Richardson, P.; Maegley, K.; Hickey, M.; et al. Discovery of 2-((1*H*-benzo[*d*]imidazole-1-yl)methyl)-4*H*-pyrido[1,2-*a*]pyrimidi-4-one as novel PKM2 activators. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 3358–3363.

[2] Bakavoli, M.; Bagherzadeh, G.; Vaseghifar, M.; Shiri, A.; Pordel, M.; Mashreghi, M.; Pordeli, P.; Araghi, M. Molecular iodine promoted synthesis of new pyrazolo[3,4-*d*]pyrimidine derivatives as potential antibacterial agent. *Eur. J. Med. Chem.* **2010**, *45*, 647–650.

[3] Januszczyk, P.; Fogt, J.; Boryski, J.; Izawa, K.; Onishi, T.; Neyts, J.; De Crercq, E. Synthesis and antiviral evalution of 2′-C-methyl analogues of 5-alkynyl- and 6-alkylfurano- and pyrrolo[2,3-*d*] pyrimidine ribonucleosides. *Nucleos. Nucleot. Nucl. Acid.* **2009**, *28*, 713–723.

[4] Gouda, M. A. Synthesis and antioxidant activity of a novel series of pyrazolotriazine, coumarin, oxaazinone and pyrazinopyrimidine derivatives. *Arch. Pharm.* (*Weinheim*), **2013**, *346*, 623–634.

[5] Li, Y.-L.; Metcalf, B. W.; Combs, A. P. Pyrimidinones as pi3k inhibitors. EP2448938, June 10, 2015.

[6] Del Turco, S.; Sartini, S.; Sentieri, C.; Saponaro, C.; Navarra, T.; Dario, B.; Settimo, F. D.; Motta, C. L.; Basta, G. A novel 2,3-diphenyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one derivative inhibits endothelial cell dysfunction and smooth muscle cell proliferation/activation. *Eur. J. Med. Chem.* **2014**, *72*, 102–109.

[7] Li, A.-R.; John, M. G.; Liu, J.; Chen, X.; Du, X.; Mihalic, J. T.; Deignan, J.; Gustin, D. J.; Duquette, J.; Fu, Z.; et al. Optimization of the heterocyclic core of the quinazolinone-derived CXCR3 antagonists. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 688–693.

[8] Dennin, F.; Blondeau, D.; Sliwa, H. Synthesis of new heterocyclic phenols: 9-hydroxy-pyrido[1,2-*a*]pyrimidine-4-one and 9-hydroxy-pyrimidio[1,6-*a*]pyrimidine-4-one. *Tetrahedron Lett.* **1989**, *30*, 1529–1530.

[9] Cassis, R.; Tapia, R.; Valderrama, J. A. Synthesis of 4(1*H*)-quinolones by thermolysis of arylaminoethylene Meldrum's acid derivatives. *Synth. Commun.* **1985**, *15*, 125–133.

[10] Smith, R. B.; Faki, H.; Lesli, R. Limitations of the Jacob-Gould reaction using microwave irradiation. *Synth. Commun*. **2011**, *41*, 1492–1499.
[11] Molnar, A.; Kapros, A.; Parkanyi, L.; Mucsi, Z.; Vlad, G.; Hermecz, I. Suzuki-Miyaura cross-coupling reactions of halo derivatives of 4*H*-pyrido[1,2-*a*]pyrimidin-4-ones. *Org. Biomol. Chem.* **2011**, *9*, 6559–6565.
[12] Guchhait, S.; Priyadarshani, G. Pd-catalyzed Ag(I)-promoted C3-arylation of pyrido[1,2-*a*]pyrimidin-4-ones with bromo/iodo-arenes. *J. Org. Chem.* **2015**, *80*, 8482–8488.
[13] Park, J. H.; Hong, S. Y.; Kim, J.; Lee, H. J.; Lee, H. H.; Kim, K. Y.; Lee, S. W.; Oh, H.-M.; Rho, M.-C.; Lee, B.-G.; et al. Convenient synthesis of novel phenylpyrimido[1,2-*c*]thienopyrimidinones as IL-6/STAT3 inhibitors. *Heterocycles* **2015**, *91*, 833–848.
[14] Yu, H.; Pardoll, D.; Jove, R. S. STATs in cancer inflammation and immunity: a leading role for STAT3. *Nat. Rev. Cancer* **2009**, *9*, 798–809.
[15] Zhang, M.; Zhu, W.; Li, Y. Discovery of novel inhibitors of signal transducer and activator of transcription 3 (STAT3) signaling pathway by virtual screening. *Eur. J. Med. Chem.* **2013**, *62*, 301–310.
[16] Cunningham, I. D.; Blanden, J. S.; Llor, J.; Munoz, L.; Sharratt, A. P. Chemistry of amidines. Part 1. Determination of the site of initial protonation in *N′*-pyridylformamidines. *J. Chem. Soc. Perkin Trans*. **1991**, *2*, 1747–1750.
[17] Okuda, K.; Zhang, Y.-X.; Ohtomo, H.; Hirota, T.; Sakai, K. Polycyclic *N*-heterocyclic Compounds. Part 62: Reaction of (*N*-quinazolin-4-yl)amidine derivatives with hydroxylamine hydrochloride and anti-platelet aggregation activity of the products. *Chem. Pharm. Bull.* **2010**, *58*, 369–374.
[18] Stanovnik, B.; Stimac, A.; Tisler, M.; Vercek, B. Reaction of *N*-heteroarylformamide oxime and *N*-heteroarylactamide oxime with *N,N*-dimethylformamide dimethyl acetal. Synthesis of 2-methyl-*s*-triazolo[1,5-*x*]azines and *N*-methylcyanoaminoazines. *J. Heterocycl. Chem*. **1982**, *19*, 577–583.
[19] Li, H. C.; Zhang, G. Y. Inhibitory effect of genistein on activation of STAT3 induced by brain ischemia/reperfusion in rat hippocampus. *Acta Pharmacol. Sin*. **2003**, *24*, 1131–1136.