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Practical one-pot protocol for the syntheses of 2-chloro-pyrrolo[3,2-*d*]pyrimidines

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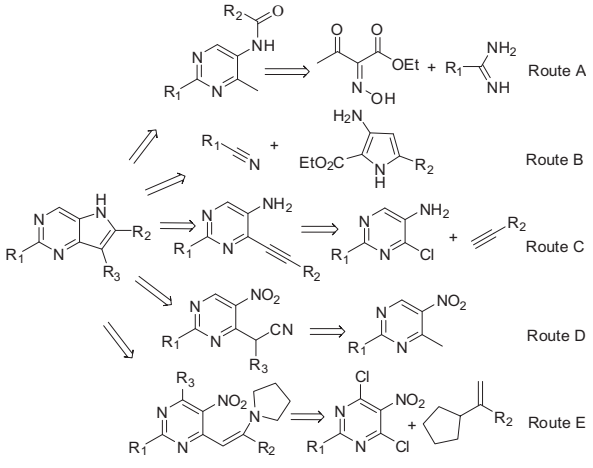
ABSTRACT

A novel one-pot protocol for the syntheses of 2-chloro-pyrrolo[3,2-*d*]pyrimidines was described. A series of 2-chloro-pyrrolo[3,2-*d*]pyrimidines were prepared from readily available starting materials in moderate to good yields using this methodology.

1. Introduction

Construction of privileged chemical structures is an important strategy in medicinal chemistry. Pyrimidine nucleus fused with another heterocycle has shown diverse biological activities.[1,2] In 1964, Imai reported preparation of pyrrolo[3,2-*d*]pyrimidines and their activities against bacteria and protozoa.[3,4] Recently, pyrrolo [3,2-*d*]pyrimidines have attracted considerable interest due to their remarkable pharmacological properties.[5–11] However, there are only a few reported literature examples for the synthesis of pyrrolo [3,2-*d*]pyrimidines.[12,13] Among these reports, Imai and Sokolova published a series of papers describing the syntheses of pyrrolo [3,2-*d*]pyrimidines by employing the Madelung cyclization as a key step in the synthesis (Scheme 1, route A).[3,7,14,15] The general method involving the use of 3-amino-2-carboxylpyrroles proved to be very useful and provided synthetic entries into several pyrrolopyrimidine analogues with various substitution patterns (route B).[7,16] The pyrrolo[3,2-*d*]pyrimidine ring system was also prepared via a Sonogashira reaction followed by a copper (I) iodide catalyzed cyclization (route C).[7,17] The fourth method developed for the syntheses of pyrrolo[3,2-*d*]pyrimidine derivatives by Otmar, used benzyl as the arylmethyl substituent, which was introduced by prior alkylation of the 5-nitro-4(6)-(cyanomethyl)pyrimidines followed by reductive cyclization (route D).[11,18,19] The last method is based on the work of Montgomery, wherein the key step involved the addition of an enamine to a chloropyrimidine intermediate (route E).[7,20] However, these methods suffered from either multiple steps, harsh reaction conditions, expensive reagents, or tedious workup procedures, and thus there is a need to develop a more simple and direct method.



Scheme 1. Reported routes for the syntheses of pyrrolo[3,2-*d*]pyrimidines.

Herein, we report a new method for the syntheses of 2-chloro-pyrrolo[3,2-*d*]pyrimidines from readily available 2,4-dichloro-5-nitropyrimidine.[21] These compounds can be further converted to 2-amino-pyrrolo[3,2-*d*]pyrimidines or 2-aryl-pyrrolo[3,2-*d*] pyrimidines as depicted in Scheme 2.

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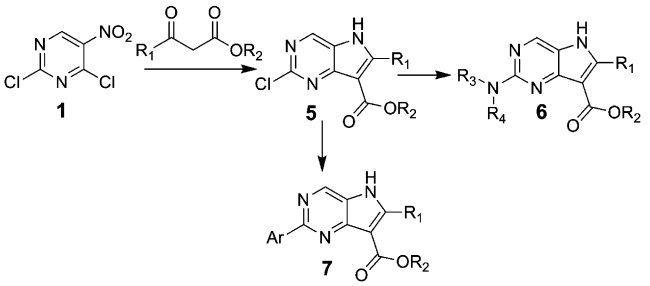
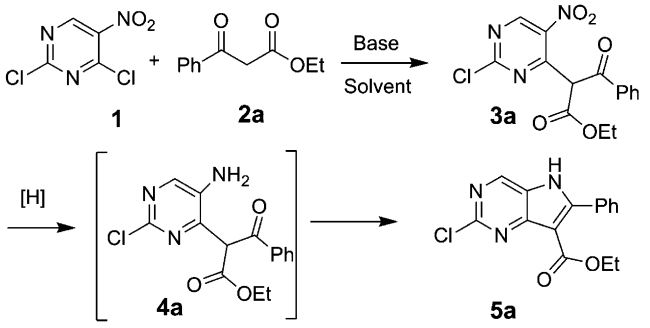


Scheme 2. Our route for the syntheses of pyrrolo[3,2-*d*]pyrimidine derivatives.

2. Results and discussion

Initially, 2,4-dichloro-5-nitropyrimidine (**1**) and ethyl benzoylacetate (**2a**) were chosen as the model substrates to survey the reaction conditions of nucleophilic substitution including bases, solvents, and reaction temperatures (Scheme 3). When a weak base, such as potassium carbonate or Et_3N, was used, the nucleophilic substitution did not complete overnight at rt in THF or ethanol. If the reaction conducted at the elevated temperatures at 50 °C, the reaction system became complicated perhaps due to the instability of 2,4-dichloro-5-nitropyrimidine. In contrast, when NaH was used as the base, the reaction was completed in about 3 h at −50 °C in dry THF in 81% yield. Under this condition, the substitution reaction was region-selective to react mainly at the 4-chloro position and only minor 2-subtituted product was formed. HPLC analysis indicated that the ratio of isomers was 10:1, but the desired major regio-isomer was not readily isolated by the column chromatography. Without further purification, the compound **3** was converted into the 2-chloro-pyrrolo[3,2-*d*]pyrimidine through a reductive cyclization process. A few reaction conditions including $SnCl_2$/HCl, Fe/HCl, Fe/NH_4Cl, and Fe/AcOH were explored, and iron powder in AcOH was found to be the optimal reductive cyclization condition at 70 °C, with up to 83% yield, as shown in Table 1.



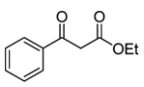
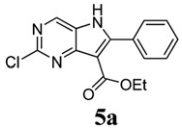
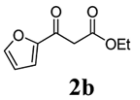
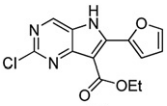
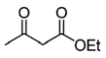
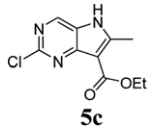
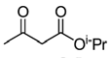
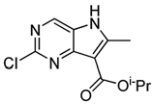
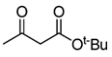
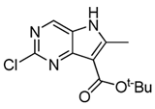
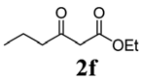
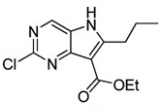
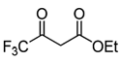
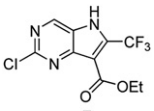
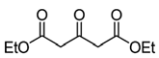
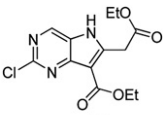
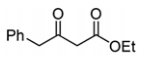
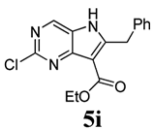
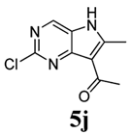
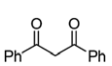
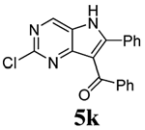
Scheme 3.

Table 1
Reductive cyclization of nitropyrimide **3a**

Entry	Reductive cyclization conditions	Yield of **5a** (%)
1	$SnCl_2$/HCl/rt/12 h	11
2	Fe/HCl/EtOH/rt/12 h	68
3	Fe/NH_4Cl/EtOH/rt/12 h	35
4	Fe/AcOH/rt/12 h	75
5	Fe/AcOH/70 °C/3 h	83

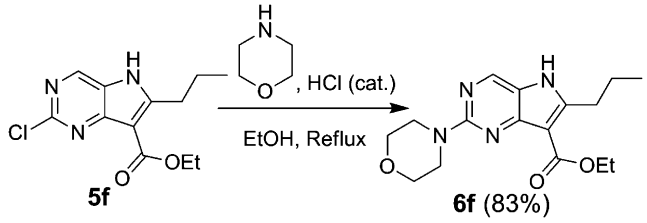
Under the optimized condition (1.1 equiv of NaH as the base, 3.0 equiv of Fe–AcOH as the reductive cyclization reagents), the scope of this one-pot protocol for the synthesis of 2-chloro-pyrrolo[3,2-*d*]pyrimidines was investigated. As shown in Table 2, most of the β-ketoesters examined afforded moderate to good yields (Table 2, entries 1–9). This protocol can be extended to the 1,3-dicarbonyl compounds as well (Table 2, entries 10 and 11).

Table 2
Preparation of 2-chloro-pyrrolo[3,2-*d*]pyrimidines

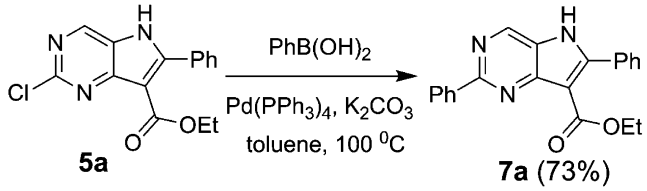
Entry	Substrate	Product	Yield (%)
1	 **2a**	 **5a**	61
2	 **2b**	 **5b**	46
3	 **2c**	 **5c**	41
4	 **2d**	 **5d**	46
5	 **2e**	 **5e**	35
6	 **2f**	 **5f**	52
7	 **2g**	 **5g**	49
8	 **2h**	 **5h**	63
9	 **2i**	 **5i**	53
10	 **2j**	 **5j**	55
11	 **2k**	 **5k**	58

This one-pot reaction sequence is presumably involved first the selective nucleophilic aromatic substitution at 4-Cl of the pyrimidines, followed by reduction of nitro group by Fe/AcOH, and further cyclization of the resulting amino group with the ketone group.

To test the reactivity of the 2-Cl group in 2-chloro-pyrrolo[3,2-*d*] pyrimidines, a nucleophilic substitution was performed by an amine as shown in Scheme 4. The desired amine-substituted product **6f** was obtained in a good yield (83%). A Suzuki coupling reaction was also feasible for C-functionalization of pyrrolo[3,2-*d*]-pyrimidine scaffold in position 2 (Scheme 5). These further modifications allow the ready access of various important frameworks with diverse substitutions.



Scheme 4.



Scheme 5.

3. Conclusions

In summary, we have developed a novel one-pot procedure for the syntheses of 2-chloro-pyrrolo[3,2-*d*]pyrimidines starting from readily available 2,4-dichloro-5-nitropyrimidine. The resulting 2-chloro-pyrrolo[3,2-*d*]pyrimidines can be subjected to further nucleophilic substitution or metal catalyzed cross-coupling to provide chemical structures with more diversity. This strategy provides an efficient method to access a library of compounds based on pharmacologically privileged substructures.

4. Experimental

4.1. General

All reagents were commercially available and used without any further purification. Anhydrous tetrahydrofuran used was freshly distilled from sodium benzophenone. Melting points were uncorrected. NMR spectra were recorded on a Bruker AV400 or Bruker AV500 instrument. Low resolution mass spectra were recorded on an Agilent1200/MSD LC–MS spectrometer. High-resolution mass spectra were performed on Kompact Axima-CFR MALDI mass spectrometers. The reactions were monitored by TLC, and visualized with UV light. All yields refer to isolated products.

4.2. Typical procedure for the preparation of 2-chloro-pyrrolo[3,2-*d*]pyrimidines 5

*4.2.1. Ethyl 2-chloro-6-phenyl-5H-pyrrolo[3,2-d]pyrimidine-7-carboxylate (**5a**).* A 10 mL round-bottom flask was charged with a magnetic stirrer, THF (2 mL), ethyl benzoylacetate (192 mg, 1 mmol), and NaH (26 mg, 1.1 mmol), after stirring of the mixture for 15 min at rt, the mixture was cooled down to −50 °C. Then 2,4-dichloro-5-nitropyrimidine (194 mg, 1 mmol) in 1 mL of THF was added. The mixture was stirred at −50 °C for 3 h (TLC determination), then when warmed to rt, Fe powder (3.0 equiv) and 3 mL of AcOH were added. The mixture reacted for 3 h at 70 °C. The resulting mixture was cooled to rt and filtered. The solid was washed with methanol two times (2×3 mL), and the combined filtrate was concentrated on the rotary evaporator, and the residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (3:1, v/v)as the eluent to give the desired product **5a** (pale yellow solid, 184 mg, 61%). Mp 176–177 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.04 (s, 1H), 8.84 (s, 1H), 7.68–7.70 (m, 2H), 7.52–7.56 (m, 3H), 4.19 (q, 2H, J=7.2 Hz), 1.14 (t, 3H, J=7.2 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.0, 153.2, 151.8, 151.4, 143.2, 130.7, 130.6, 130.0, 128.7, 126.8, 104.1, 60.3, 14.3; ESI-MS: m/z=302.1 (M+H$^+$); HRMS: m/z 302.0693 (M+H$^+$, $C_{15}H_{13}ClN_3O_2^+$ requires 302.0691), m/z 324.0507(M+Na$^+$, $C_{15}H_{12}ClN_3NaO_2^+$ requires 324.0510).

*4.2.2. Ethyl 2-chloro-6-(furan-2-yl)-5H-pyrrolo[3,2-d]pyramidine-7-carboxylate (**5b**).* Following the general procedure, the reaction was performed with **1b** (182 mg, 1.0 mmol) to afford **5b** as a brown solid (134 mg, 46%). Mp 204–205 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.10 (s, 1H), 8.78 (s, 1H), 8.09 (d, 1H, J=1.2 Hz), 7.81 (d, 1H, J=3.2 Hz), 6.82 (dd, 1H, J=1.2, 3.2 Hz), 4.37 (q, 2H, J=7.2 Hz), 1.34 (t, 3H, J=7.2 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.1, 153.5, 151.3, 146.4, 144.4, 143.1, 139.6, 126.8, 117.7, 113.6, 102.2, 60.5, 14.8; ESI-MS: m/z=292.1 (M+H$^+$); HRMS: m/z 292.0487 (M+H$^+$, $C_{13}H_{11}ClN_3O_3^+$ requires 292.0483).

*4.2.3. Ethyl 2-chloro-6-methyl-5H-pyrrolo[3,2-d]pyrimidine-7-carboxylate (**5c**).* Following the general procedure, the reaction was performed with **1c** (130 mg, 1.0 mmol) to afford **5c** as a brown solid (98 mg, 41%). Mp 142–143 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.55 (s, 1H, broad), 8.89 (1H, s), 4.30 (q, 2H, J=3.2 Hz), 2.73 (s, 3H), 1.31 (t, 3H, J=3.2 Hz); ^{13}C NMR (125 MHz, DMSO-d_6): δ 162.9, 153.7, 150.0, 146.0, 140.4, 124.3, 99.9, 60.0, 14.8, 11.3; ESI-MS: m/z=240.1 (M+H$^+$); HRMS: m/z 240.0536 (M+H$^+$, $C_{10}H_{11}ClN_3O_2^+$ requires 240.0534).

*4.2.4. Isopropyl 2-chloro-6-methyl-5H-pyrrolo[3,2-d]pyrimidine-7-carboxylate (**5d**).* Following the general procedure, the reaction was performed with **1d** (144 mg, 1.0 mmol) to afford **5d** as a yellow solid (117 mg, 46%). Mp 155–156 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.46 (s, 1H, br), 8.97 (1H, s), 5.12 (m, 1H), 2.72 (s, 3H), 1.33 (d, 6H, J=6 Hz); ^{13}C NMR (125 MHz, DMSO-d_6): δ 161.8, 153.1, 149.2, 145.6, 140.0, 123.8, 99.5, 66.9, 21.9, 11.0; ESI-MS: m/z=254.1 (M+H$^+$); HRMS: m/z 254.0694 (M+H$^+$, $C_{11}H_{13}ClN_3O_2^+$ requires 254.0691).

*4.2.5. tert-Butyl 2-chloro-6-methyl-5H-pyrrolo[3,2-d]pyrimidine-7-carboxylate (**5e**).* Following the general procedure, the reaction was performed with **1e** (158 mg, 1.0 mmol) to afford **5e** as a brown solid (94 mg, 35%). Mp 202–203 °C; ^{1}H NMR (400 MHz, methanol-d_4): δ 8.61 (s, 1H), 2.76 (s, 3H), 1.63 (s, 9H); ^{13}C NMR (100 MHz, methanol-d_4): δ 164.3, 154.5, 153.4, 141.8, 127.1, 106.5, 82.2, 28.8, 15.3; ESI-MS: m/z=268.0 (M+H$^+$); HRMS: m/z 268.0848 (M+H$^+$, $C_{12}H_{15}ClN_3O_2^+$ requires 268.0847).

*4.2.6. Ethyl 2-chloro-6-propyl-5H-pyrrolo[3,2-d]pyrimidine-7-carboxylate (**5f**).* Following the general procedure, the reaction was performed with **1f** (158 mg, 1.0 mmol) to afford **5f** as a deep brown solid (139 mg, 52%). Mp 182–183 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.48 (s, 1H, br), 8.92 (s, 1H), 4.30 (q, 2H, J=7.2 Hz), 3.15 (t, 2H, J=7.6 Hz), 1.70 (m, 2H), 1.32 (t, 3H, J=7.2 Hz), 0.96 (t, 3H, J=7.2 Hz); ^{13}C NMR (125 MHz, DMSO-d_6): δ 162.7, 153.7, 153.2, 146.1, 140.7,

124.3, 99.6, 60.0, 26.5, 21.9, 14.8, 14.2; ESI-MS: m/z=268.1 ($M+H^+$); HRMS: m/z 268.0849 ($M+H^+$, $C_{12}H_{15}ClN_3O_2^+$ requires 268.0847).

*4.2.7. Ethyl 2-chloro-6-(trifluoromethyl)-5H-pyrrolo[3,2-d]pyrimidine-7-carboxylate (**5g**).* Following the general procedure, the reaction was performed with **1g** (184 mg, 1.0 mmol) to afford **5g** as a brown solid (144 mg, 49%). Mp 164–165 °C; ^1H NMR (400 MHz, methanol-d_4): δ 8.96 (s, 1H), 4.41 (q, 2H, J=7.2 Hz), 1.40 (t, 3H, J=7.2 Hz); ^{13}C NMR (125 MHz, methanol-d_4): δ 162.2, 155.9, 150.6, 146.8, 137.2 (d, $^2J_{CF}$=40 Hz), 126.9, 121.1 (d, $^1J_{CF}$=271 Hz), 108.2, 62.3, 14.4; ESI-MS: m/z=294.1 ($M+H^+$); HRMS: m/z 294.0256 ($M+H^+$, $C_{10}H_8ClF_3N_3O_2^+$ requires: 294.0252).

*4.2.8. Ethyl 2-chloro-6-(2-ethoxy-2-oxoethyl)-5H-pyrrolo[3,2-d]pyrimidine-7-carboxylate (**5h**).* Following the general procedure, the reaction was performed with **1h** (202 mg, 1.0 mmol) to afford **5h** as a deep brown solid (196 mg, 63%). Mp 89–90 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 12.91 (s, 1H, br), 8.91 (s, 1H), 4.25–4.30 (m, 4H), 4.14 (q, 2H, J=7.2 Hz), 1.29 (t, 3H, J=7.2 Hz), 1.19 (t, 3H, J=7.2 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.6, 162.9, 153.5, 150.7, 148.8, 143.3, 126.2, 104.8, 61.4, 60.1, 34.6, 14.7, 14.4; ESI-MS: m/z=312.1 ($M+H^+$); HRMS: m/z 312.0751 ($M+H^+$, $C_{13}H_{15}ClN_3O_4^+$ requires: 312.0746).

*4.2.9. Ethyl 6-benzyl-2-chloro-5H-pyrrolo[3,2-d]pyrimidine-7-carboxylate (**5i**).* Following the general procedure, the reaction was performed with **1i** (206 mg, 1.0 mmol) to afford **5i** as a brown solid (167 mg, 53%). Mp 115–117 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 12.68 (s, 1H, br), 8.93 (s, 1H), 7.19–7.31 (m, 5H), 4.59 (s, 2H), 4.30 (q, 2H, J=7.2 Hz), 1.27 (t, 3H, J=7.2 Hz); ^{13}C NMR (125 MHz, DMSO-d_6): δ 162.3, 153.3, 150.3, 145.3, 140.8, 136.7, 128.5, 128.5, 126.6, 123.8, 99.3, 59.7, 29.7, 14.3; ESI-MS: m/z=316.0 ($M+H^+$); HRMS: m/z 316.0850 ($M+H^+$, $C_{16}H_{15}ClN_3O_2^+$ requires: 316.0847).

*4.2.10. 1-(2-Chloro-6-methyl-5H-pyrrolo[3,2-d]pyrimidine-7-yl) ethanone (**5j**).* Following the general procedure, the reaction was performed with **1j** (100 mg, 1.0 mmol) to afford **5j** as a brown solid (115 mg, 55%). Mp 110–111 °C; ^1H NMR (400 MHz, methanol-d_4): δ 8.73(s, 1H), 2.78 (s, 3H), 2.77 (s, 3H); ^{13}C NMR (100 MHz, methanol-d_4): δ 194.5, 153.5, 150.4, 146.7, 138.9, 123.9, 108.3, 29.7, 9.9; ESI-MS: m/z=210.1 ($M+H^+$); HRMS: m/z 210.0430 ($M+H^+$, $C_9H_9ClN_3O^+$ requires: 210.0429).

*4.2.11. (2-Chloro-6-phenyl-5H-pyrrolo[3,2-d]pyrimidine-7-yl)(phenyl)methanone (**5k**).* Following the general procedure, the reaction was performed with **1k** (224 mg, 1.0 mmol) to afford **5 k** as a brown solid (193 mg, 58%). Mp 147–148 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 12.12 (s, 1H, br), 8.93 (s, 1H), 7.76–7.78 (m, 2H), 7.57–7.60 (m, 3H), 7.40–7.45 (m, 5H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 190.7, 152.2, 151.0, 149.2, 142.9, 138.0, 133.2, 130.2, 129.8, 129.8, 129.1, 128.8, 128.4, 126.2, 111.8; ESI-MS: m/z=334.1 ($M+H^+$); HRMS: m/z 334.0744 ($M+H^+$, $C_{19}H_{13}ClN_3O^+$ requires: 334.0742).

4.3. Procedure for the preparation of ethyl 2-morpholino-6-propyl-5*H*-pyrrolo[3,2-*d*]pyrimidine-7-carboxylate (6f)

Ethyl 2-chloro-6-propyl-5*H*-pyrrolo[3,2-*d*]pyrimidine-7-carboxylate **5f** (98 mg, 0.37 mmol) was dissolved in ethanol (5 mL), morpholine (70 mg, 2.2 mmol) and three drops of HCl (concd) was added at rt. After being stirred for 6 h at reflux, the reaction mixture was concentrated in vacuo and purified by flash chromatography with petroleum/EtOAc (1:1, v/v) as the eluent to afford 97 mg (83%) of **6f** as a pale yellow solid. Mp 186–187 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 9.59 (s, br, 1H). 8.31 (s, 1H), 4.37(q, 2H, J=7.2 Hz), 3.79 (d, 4H, J=4.0 Hz), 3.74 (d, 4H, J=4.0 Hz), 3.06 (t, 2H, J=7.6 Hz), 1.71 (q, 2H, J=7.6 Hz), 1.41 (t, 3H, J=7.2 Hz), 0.93 (t, 3H, J=7.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.6, 159.2, 154.2, 151.6, 140.0, 121.3, 103.0, 67.0, 59.8, 45.0, 30.6, 22.3, 14.4, 13.8; ESI-MS: m/z=319.1 ($M+H^+$); HRMS: m/z 319.1768 ($M+H^+$, $C_{16}H_{23}N_4O_3^+$ requires: 319.1765).

4.4. Procedure for the preparation of ethyl 2,6-diphenyl-5*H*-pyrrolo[3,2-*d*]pyrimidine-7-carboxylate (7a)

A mixture of compound **6a** (61 mg, 0.20 mmol), phenyl-boronic acid (99 mg, 0.80 mmol), potassium carbonate (112 mg, 0.80 mmol), and $Pd(PPh_3)_4$ (46 mg, 0.04 mmol) in toluene (5 mL) was heated to 100 °C under argon for 5 h, then was taken into ethyl acetate, washed with water, and evaporated. Chromatography on a silica gel column (petroleum ether/ethyl acetate, 3:1) afforded compound **7a** (51 mg, 73%) as a white solid. Mp 205–206 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 9.58 (s, br, 1H), 8.85 (s, 1H), 8.51 (d, 2H, J=6.4 Hz), 7.63 (d, 2H, J=6.4 Hz), 7.42–7.45 (m, 6H), 4.37(q, 2H, J=7.2 Hz), 1.37 (t, 3H, J=7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.8, 159.1, 150.4, 150.1, 140.1, 138.6, 130.7, 130.2, 129.7, 129.4, 128.4, 128.3, 128.1, 125.7, 105.5, 60.4, 14.2; ESI-MS: m/z=344.1 ($M+H^+$); HRMS: m/z 344.1396 ($M+H^+$, $C_{21}H_{18}N_3O_2^+$ requires: 344.1394).

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Supplementary data

Copies of ^1H NMR, ^{13}C NMR spectra of **5a**–**k**, **6f**, and **7a** are provided. Supplementary data associated with this article can be found in online version, at doi:10.1016/j.tet.2010.01.089. These data include MOL files and InChiKeys of the most important compounds described in this article.

References and notes

1. Brown, D. J. Pyrimidines and their Benzo Derivatives. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 3, p 443.
2. Roth, B.; Cheng, C. In *Progress in Medicinal Chemistry*; Ellis, G. P., West, G. B., Eds.; Elsevier Biomedical: New York, NY, 1982; Vol. 19, p 267.
3. Tanaka, K.; Sugawa, T.; Nakamori, R.; Sanno, Y.; Ando, Y.; Imai, K. *Chem. Pharm. Bull.* **1964**, *12*, 1024.
4. Imai, K. *Chem. Pharm. Bull.* **1964**, *12*, 1030.
5. McGuire, J. J.; Bergoltz, V. V.; Heitzman, K. J.; Haile, W. H.; Russell, C. A.; Bolanowska, W. E.; Kotake, Y.; Haneda, T.; Nomura, H. *Cancer Res.* **1994**, *54*, 2673.
6. Norman, M. H.; Chen, N.; Chen, Z. D.; Fotsch, C.; Hale, C.; Han, N. H.; Hurt, R.; Jenkins, T.; Kincaid, J.; Liu, L. B.; Lu, Y. L.; Moreno, O.; Santora, V. J.; Sonnenberg, J. D.; Karbon, W. *J. Med. Chem.* **2000**, *43*, 4288.
7. Trejo, A.; Arzeno, H.; Browner, M.; Chanda, S.; Cheng, S.; Comer, D. D.; Dalrymple, S. A.; Dunten, P.; Lafargue, J.; Lovejoy, B.; Freire-Moar, J.; Lim, J.; Mcintosh, J.; Miller, J.; Papp, E.; Reuter, D.; Roberts, R.; Sanpablo, F.; Saunders, J.; Song, K.; Villasenor, A.; Warren, S. D.; Welch, M.; Weller, P.; Whiteley, P. E.; Zeng, L.; Goldstein, D. M. *J. Med. Chem.* **2003**, *46*, 4702.
8. Evans, G. B.; Furneaux, R. H.; Hausler, H.; Larsen, J. S.; Tyler, P. C. *J. Org. Chem.* **2004**, *69*, 2217.
9. Gomtsyan, A.; Didomenico, S.; Lee, C.; Stewart, A. O.; Bhagwat, S. S.; Kowaluk, E. A.; Jarvis, M. F. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 4165.
10. Otmar, M.; Masojídková, M.; Votruba, I.; Holý, A. *Bioorg. Med. Chem.* **2004**, *12*, 3187.
11. Bambuch, V.; Otmar, M.; Pohl, R.; Masojídková, M.; Holý, A. *Tetrahedron* **2007**, *63*, 1589.
12. Amarnath, V.; Madhav, R. *Synthesis* **1974**, 837.
13. Glushkov, R. G.; Sizova, O. S. *Pharm. Chem. J. (Eng. Ed.)* **1986**, *20*, 415.
14. Sokolova, V. N.; Modnikova, G. A.; Novitskii, K.; Shcherbakova, L. I.; Pershchin, G. N.; Zykova, T. N. *Pharm. Chem. J. (Eng. Ed.)* **1974**, *8*, 13.
15. Modnikova, G. A.; Titkova, R. M.; Glushkov, R. G.; Sokolova, A. S.; Silin, V. A.; Chernov, V. A. *Pharm. Chem. J. (Eng. Ed.)* **1988**, *22*, 135.
16. Lim, M. I.; Ren, W. Y.; Otter, B. A.; Klein, R. S. *J. Org. Chem.* **1983**, *48*, 780.
17. Xu, L.; Lewis, I. R.; Davidson, S. K.; Summers, J. B. *Tetrahedron Lett.* **1998**, *39*, 5159.
18. Otmar, M.; Masojídková, M.; Holý, A. *Tetrahedron* **1997**, *53*, 391.
19. Otmar, M.; Masojídková, M.; Buděšínský, M.; Holý, A. *Tetrahedron* **1998**, *54*, 2931.
20. Montgomery, J. A.; Laseter, A. G. *J. Heterocycl. Chem.* **1972**, *9*, 1077.
21. Whittaker, N.; Jones, T. S. G. *J. Chem. Soc.* **1951**, 1565.