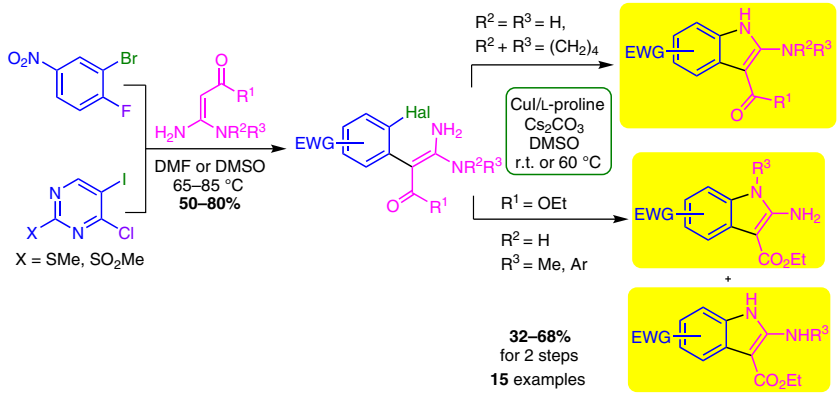
Synthesis M. S. Mishina et al. Paper

A New Synthesis of 2-Aminoindoles and 6-Aminopyrrolo[3,2-*d*]pyrimidines from π-Deficient 1,2-Dihaloarenes and Geminal Enediamines

Maria S. Mishina
Alexander Yu. Ivanov
Pavel S. Lobanov
Dmitrii V. Dar'in*

St. Petersburg State University, 198504 St. Petersburg, Russian Federation
d.dariin@spbu.ru



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Abstract An efficient approach for the synthesis of fused 2-aminopyrroles via geminal enediamines and π-deficient 1,2-dihaloarenes is presented. The two-step methodology includes aromatic nucleophilic substitution of the activated halogen of dihaloarene with enediamine *C*-nucleophilic center followed by Cu-catalyzed intramolecular *N*-arylation. This approach allows access to a variety of 2-amino-6-nitroindoles and 6-aminopyrrolo[3,2-*d*]pyrimidines (including *N*-mono- and *N*,*N*-disubstituted) in moderate and good yields under mild conditions.

Keywords 2-aminoindoles, pyrrolo[3,2-*d*]pyrimidines, geminal enediamines, cyclization, copper catalyst, *N*-arylation

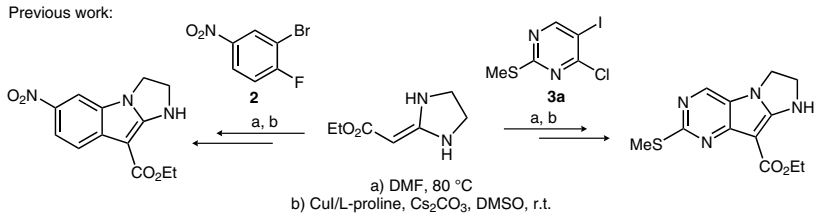
Indoles always attracted the interest of synthetic chemists, which continues to grow in recent years.[1] This is due to the fact that the indole ring is found in many naturally occurring compounds (tryptamine, serotonin, melatonin, etc., and indole alkaloids and terpenoids).[2] Wide range of compounds containing indole fragment in their structure demonstrate various type of biological activity and are important from the pharmacological point of view.[3] Moreover, indole derivatives are widely used in agrochemistry, dyes and pigments, and essential oils.[4] In this connection, the development of new effective approaches to the synthesis of functionalized indole derivatives is strongly desired.

Heterocyclic systems with heteroatoms in the six-membered ring of the indole are also attractive for chemists and biologists due to their remarkable pharmacological properties.[5] However, there are only a few reported literature examples of the synthesis of such heterocyclic systems.[6]

Currently known methods for the synthesis of 2-aminoindoles cannot be considered as universal and are often quite laborious,[7] therefore the development of new approaches to the synthesis of the functional derivatives of 2-aminoindoles and their aza-analogues is an important synthetic task. One of the most effective and rapidly growing strategies of the construction of the indole ring is the cyclization of β-(aryl)enamines, occurring as intramolecular *N*-arylation.[8] These concepts inspired us to develop a new synthetic approach to the fused 2-aminopyrroles using geminal enediamines.

Not only are geminal enediamines **1**, also called ketene aminals, effective precursors for 2-aminopyridines and 2-aminopyrroles,[9a] but they are also widely used in the synthesis of various fused α-aminoazaheterocyclic systems.[9b] In our previous work, we demonstrated the possibility of producing fused α-aminopyrroles via the interaction of cyclic ketene aminal – ethyl 2-(imidazolidin-2-ylidene)acetate – with π-deficient *ortho*-dihaloarenes (Scheme 1).[10] In the present work, we report on our investigation on this synthetic approach extended to a number of acyclic enediamines. The synthesis starting from geminal enediamines **1** and dihaloarenes **2** and **3a**,**b** includes two steps. The first step is the noncatalyzed aromatic nucleophilic substitution of the activated halogen atom leading to intermediate compounds **4**, **7**, and **8**. The second step is the Cu(I)-catalyzed cyclization resulting in the corresponding 2-aminoindoles **5**, **6**, and 6-aminopyrrolo[3,2-*d*]pyrimidines **9**, **10**, and **11** (Scheme 2).

The choice of starting dihaloarenes **2** and **3a**,**b** was mainly determined by the possibility of the first step of the synthesis – aromatic nucleophilic substitution of the acti-



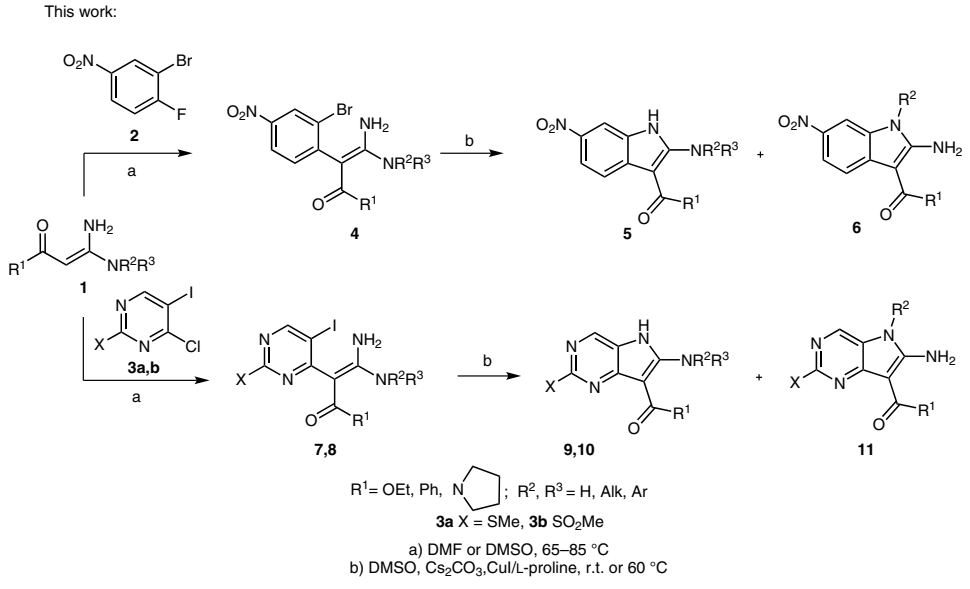
Scheme 1 A new synthetic approach to fused imidazolinopyrroles via ethyl 2-(imidazolidin-2-ylidene)acetate

vated halogen atom. The progress of this reaction is provided by the high π-deficiency of selected dihaloarenes. Enediamines are known as moderate *C*-nucleophiles. In the reactions with the active haloarenes, the products of halogen atom substitution by the carbon nucleophilic center are formed.[11] Bromofluorobenzene **2** and iodochloropyrimidine **3b** are sufficiently reactive and react smoothly with all studied enediamines. At the same time 1,2-dichloro-4-nitrobenzene and 3-bromo-4-fluorobenzonitrile (similar to arene **2**) were not active enough and did not react with enediamine **1a**. Iodochloropyrimidine **3a** reacted with more active enediamines **1a**,**c**, but its reactivity was not enough for the reaction with less active enediamine **1b**. Oxidation of methylsulfanyl group in the pyrimidine **3a** led to the expected increase in the π-deficit and the reactivity of the resulting chloropyrimidine **3b**.

Enediamines **1a**,**b** were used in the reaction as a free base, whereas enediamines **1e**–**h** were used as hydrochlorides. In the case of enediamines **1c** and **1d**, hydrochlorides as well as free base gave good results. In order to transfer hydrochloride to the free base form, diisopropylethylamine (DIPEA) or K_2CO_3 were used as a base.

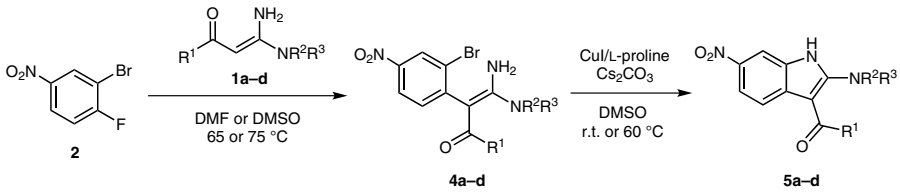
Reactions of enediamines **1a**–**h** with bromofluorobenzene **2** leading to the formation of the compounds **4** were performed in DMF or DMSO under moderate heating. In most cases reactions occurred smoothly in moderate to good yields (Tables 1 and 2). Generally compounds **4** were isolated in pure form and fully characterized. However, thorough purification prior to the cyclization step usually was not required, only fairly rough treatment of the reaction mixture was sufficient, as was done in the case of compound **4d** (Table 1, entry 4). Synthesis of indole **5c** was performed as a one-pot procedure, without any workup of the reaction mixture after the first step (Table 1, entry 3). However, it must be realized that such an approach cannot be extended to all syntheses. In some cases, the attempts to perform the both steps of synthesis consecutively without workup after first reaction led to a significantly lower yield of the target product.

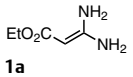
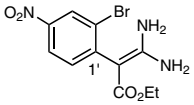
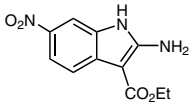
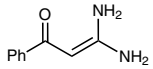
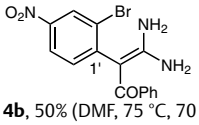
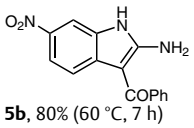
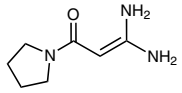
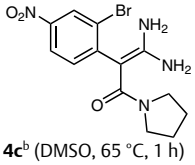
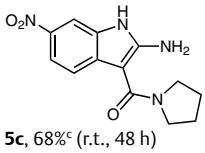
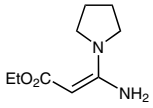
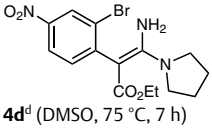
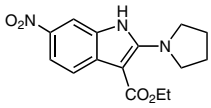
The cyclization step was performed under conditions we had developed previously,[9] namely using the catalyst



Scheme 2 A new synthetic approach to fused 2-aminopyrroles via geminal enediamines

Table 1 Synthesis of 2-Aminoindoles **5** from Bromofluorobenzene **2** and *N*,*N*′-Unsubstituted **1a–c** or *N*,*N*-Disubstituted Enediamines **1d**



Entry	Enediamine **1**	Compound **4**[a]	Product **5**[a]
1	 **1a**	 **4a**, 52% (DMF, 75 °C, 20 h)	 **5a**, 81% (60 °C, 3 h)
2	 **1b**	 **4b**, 50% (DMF, 75 °C, 70 h)	 **5b**, 80% (60 °C, 7 h)
3	 **1c**	 **4c**[b] (DMSO, 65 °C, 1 h)	 **5c**, 68%[c] (r.t., 48 h)
4	 **1d**	 **4d**[d] (DMSO, 75 °C, 7 h)	 **5d**, 52%[c] (60 °C, 15 h)

[a] Yields are indicated for isolated compounds.
[b] Compound **4c** was not isolated. Synthesis of **5c** was performed under 'one pot' conditions.
[c] Yield is given for 2 steps.
[d] Compound **4d** was used in the 2nd step without purification.

system CuI/L-proline (0.1 equiv/0.2 equiv), base Cs_2CO_3 (3 equiv), and solvent DMSO. The cyclization of compounds **4** occurs under mild conditions (ambient temperature or 60 °C) and in high yields.

Cyclization of *N*-monosubstituted compounds **4e–h** resulted in the mixtures of two isomeric indoles **5e–h** and **6e–h** (Table 2). As expected, in the reaction of *N*-methyl-substituted derivative **4e**, the major product turned out to be indole **5e** resulting from the intramolecular *N*-arylation of unsubstituted sterically more accessible nitrogen atom of enediamine moiety (Table 2, entry 1). Isomeric indole **6e** was formed in trace amounts, and the main product **5e** was purified and isolated in an individual form via crystallization. At the same time cyclization of *N*-aryl-substituted derivatives **4f–h** led to the mixtures with comparable amounts of isomeric indoles **5** and **6**. In two of three cases, cyclization took place mainly involving substituted nitrogen atom, giving 1-aryl-2-aminoindoles **6** as major products. Even though, quality correlation of the product mixture composition (isomers **5** and **6**) with electronic influence of substituents in the phenyl ring was not observed. One can only assume that since the *N*-arylation process occurring in the basic media includes NH-deprotonation step the formation of considerable amount of 1-arylindoles **6** may result from higher acidity of NH bearing aryl group compared to NH_2. This factor would be especially significant in the case of NH-deprotonation (stabilized anion formation) taking place prior to N–Cu bonding.

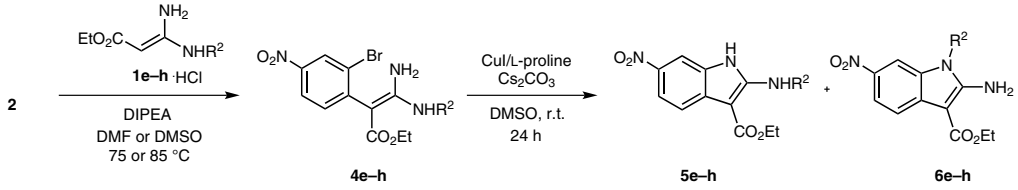
Iodochloropyrimidine **3a** has proved to be less active than bromofluorobenzene **2** in the first step of the synthesis. In the case of enediamine **1a**, substitution of active halogen occurs at a higher temperature and requires longer time. Nevertheless, the product **7a** was obtained in good yield (Table 3, entry 1). However, our attempts to obtain the substitution reaction product in the case of less reactive enediamine **1b** failed. The reaction did not take place at low temperatures, and heating up to 100 °C led to an unidentifiable mixture. In the case of more active enediamine **1c**, the reaction occurred rapidly, but was accompanied by the formation of considerable amounts of by-products.[12] Even car-

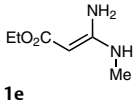
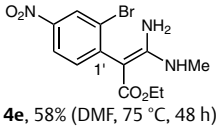
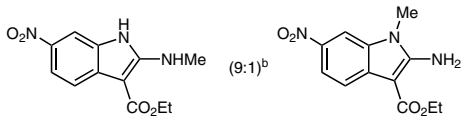
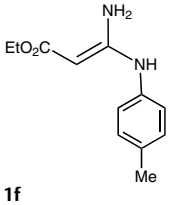
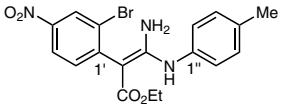
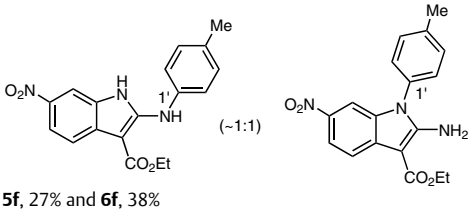
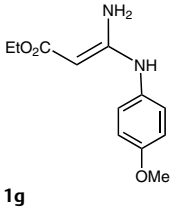
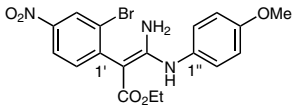
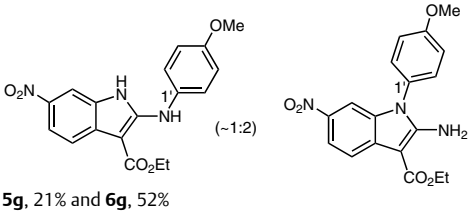
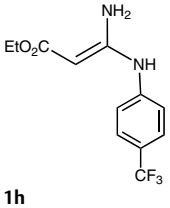
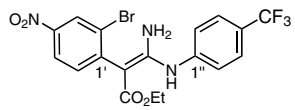
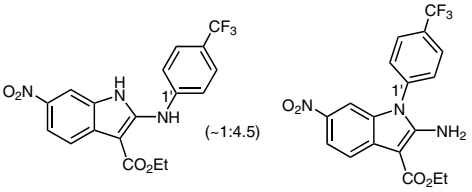
rying out the reaction without heating did not prevent side reactions to increase the yield of compound **7c**. Thus, the target product **9c** was synthesized without isolation of pure intermediate compound **7c** in an overall yield of 37% (entry 3). In the same manner, starting from enediamine **1d** pyrrolopyrimidine **9d** was isolated in relatively low yield (entry 4). This was probably caused by the problems with the first step.

Oxidation of methylsulfanyl group of iodochloropyrimidine **3a** afforded pyrimidine **3b**, which, as expected, was more reactive in reactions with enediamines than its synthetic precursor. Use of more active substrate allowed to obtain compound **8b** in the reaction with enediamine **1b** and carry out its cyclization to pyrrolopyrimidine **10b** (Table 3, entry 2). The reaction of iodochloropyrimidine **3b** with enediamine **1d** and subsequent cyclization also gave significantly better results compared with use of **3a** affording compounds **8d** and **10d** in high yields (entry 5).

In the case of compounds **7** and **8**, cyclization occurs very easily at room temperature, probably due to the higher activity of iodine atom compared to bromine atom in Cu-catalyzed *N*-arylation. Similarly, in the case of compounds **4**, thorough purification of intermediates **7** and **8** prior to the cyclization step was not usually required.

Table 2 Synthesis of 2-Aminoindoles **5** and **6** from Bromofluorobenzene **2** and *N*-Monosubstituted Enediamines **1e–h**[a]

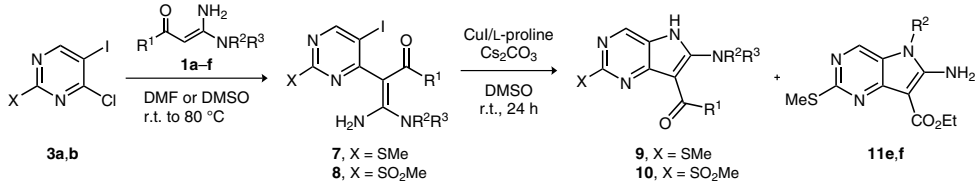


Entry	Enediamine **1**	Compound **4**	Products **5** and **6**
1	 **1e**	 **4e**, 58% (DMF, 75 °C, 48 h)	 **5e**, 61% and **6e** (not isolated)
2	 **1f**	 **4f**, 88% (DMSO, 75 °C, 48 h)	 **5f**, 27% and **6f**, 38%
3	 **1g**	 **4g**, 49% (DMF, 75 °C, 48 h)	 **5g**, 21% and **6g**, 52%
4	 **1h**	 **4h**, 61% (DMSO, 85 °C, 72 h)	 **5h**, 20% and **6h**, 58%

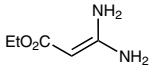
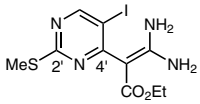
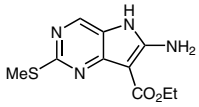
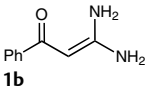
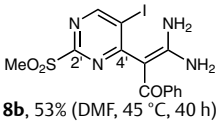
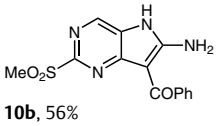
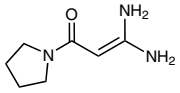
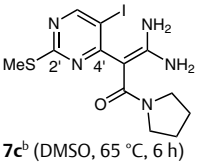
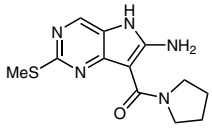
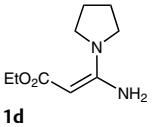
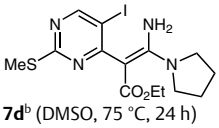
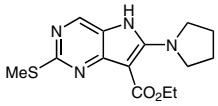
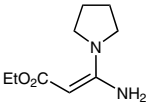
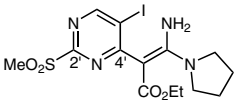
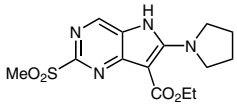
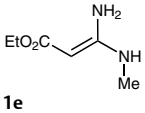
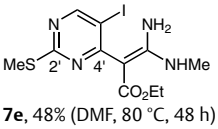
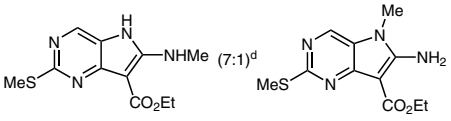
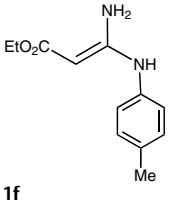
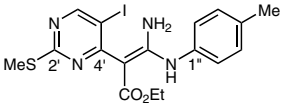
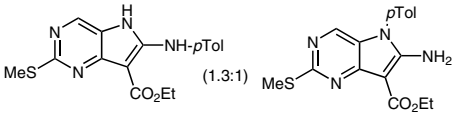
[a] The indicated yields are of isolated products.
[b] Ratio of regioisomers **5**/**6** in the reaction mixture, estimated by ^{1}H NMR spectroscopy, is given in parentheses.

The use of pyrimidine **3a** in the synthesis of *N*-monosubstituted enediamines **1e** and **1f** led to similar results as for bromofluorobenzene **2**. The cyclization of compound **7e** mainly afforded pyrrolopyrimidine **9e**, which was isolated in the individual form in good yield (Table 3, entry 6). *N*-Tolyl-

Table 3 Synthesis of 6-Aminopyrrolo[3,2-*d*]pyrimidines **9** and **10** from Iodochloropyrimidines **3a**,**b** and Enediamines **1a**–**f**[a]



3a,**b** **7**, X = SMe; **8**, X = SO_2Me **9**, X = SMe; **10**, X = SO_2Me **11e**,**f**

Entry	Enediamine **1**	Pyrimidine **3**	Compounds **7**, **8**	Products **9**, **10**, and **11**
1	 **1a**	**3a**, X = SMe	 **7a**, 75% (DMF, 80 °C, 24 h)	 **9a**, 71%
2	 **1b**	**3b**, X = SO_2Me	 **8b**, 53% (DMF, 45 °C, 40 h)	 **10b**, 56%
3	 **1c**	**3a**, X = SMe	 **7c**[b] (DMSO, 65 °C, 6 h)	 **9c**, 37%[c]
4	 **1d**	**3a**, X = SMe	 **7d**[b] (DMSO, 75 °C, 24 h)	 **9d**, 32%[c]
5	 **1d**	**3b**, X = SO_2Me	 **8d**, 78% (DMF, r.t., 2 h)	 **10d**, 72% (56% over 2 steps)
6	 **1e**	**3a**, X = SMe	 **7e**, 48% (DMF, 80 °C, 48 h)	 **9e**, 61% and **11e** (not isolated)
7	 **1f**	**3a**, X = SMe	 **7f**, 54% (DMSO, 75 °C, 48 h)	 **9f** + **11f**, 92%

[a] The indicated yields are of isolated products.
[b] Compound was used in cyclization step without purification.
[c] Yield is given for 2 steps.
[d] Ratio of regioisomers **9**/**11** in the reaction mixture.

substituted derivative **7f** gave comparable amounts of the isomeric cyclization products (entry 7).

In summary, we have developed a new synthetic approach to fused 2-aminopyrroles from electron-deficient *ortho*-dihaloarenes and geminal enediamines. This methodology can be considered as very efficient due to the synthetic availability and variety of the starting enediamines, the mild reaction conditions, the low cost of the *N*-arylation catalyst, and the procedural ease. It should be also noted that the proposed synthetic strategy may be used to produce structures containing a 2-aminopyrrole cycle fused with other cyclic π-deficient systems.

All commercial reagents and solvents were used without further purification, unless otherwise noted. DMF for the synthesis was distilled over CaH_2 and stored over freshly activated molecular sieves 4Å. NMR spectra were recorded on a Bruker Avance III 400 spectrometer [^{1}H: 400.13 MHz; ^{13}C: 100.61 MHz; chemical shifts are reported as parts per million (δ, ppm)]; the residual solvent peaks were used as internal standards: 7.28 ($CHCl_3$) and 2.50 (DMSO-d_5) ppm for ^{1}H in $CDCl_3$ and DMSO-d_6 respectively, 40.01 and 77.02 ppm for ^{13}C in DMSO-d_6 and $CDCl_3$ respectively. Standard abbreviations for multiplicities were used; coupling constants, *J*, are reported in Hz. Mass spectra were recorded on a Bruker micrOTOF spectrometer (ESI ionization). Elemental analysis was performed on a Hewlett-Packard HP-185B CHN analyzer. Melting points were determined in open capillary tubes on a Stuart SMP30 melting point apparatus.

Ethyl 3,3-Diamino-2-(2-bromo-4-nitrophenyl)acrylate (4a)

A mixture of compound **2** (0.8 g, 3.6 mmol) and enediamine **1a** (0.59 g, 4.5 mmol) in anhyd DMF (3 mL) was stirred at 75 °C for 20 h and concentrated in vacuo. The oily residue was treated with H_2O (20 mL), the crystals formed were filtered, dried in air, and recrystallized from MeCN to yield 0.62 g (52%) of the title compound as an orange solid; mp 233–235 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.35 (d, *J* = 2.0 Hz, 1 H, 3′-H), 8.02 (dd, *J* = 8.0, 2.0 Hz, 1 H, 5′-H), 7.41 (d, *J* = 8.0 Hz, 1 H, 6′-H), 6.30–7.70 (br s, 2 H, NH_2), 4.95 (br s, 2 H, NH_2), 3.80–4.00 (m, 2 H, CH_2), 1.02 (t, *J* = 7.0 Hz, 3 H, CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 167.2 (C=O), 160.4 (C=*C*–NH), 147.0, 146.4 (2′-C, 4′-C), 136.2 (6′-C), 129.6 (1′-C), 127.4 (3′-C), 122.8 (5′-C), 78.1 (*C*=C–NH), 57.7 (CH_2CH_3), 15.3 (CH_3).

Anal. Calcd for $C_{11}H_{12}BrN_3O_4$: C, 40.02; H, 3.66; N, 12.73. Found: C, 40.31; H, 3.74; N, 13.00.

3,3-Diamino-2-(2-bromo-4-nitrophenyl)-1-phenylprop-2-en-1-one (4b)

A mixture of compound **2** (1.05 g, 4.8 mmol) and enediamine **1b** (1.0 g, 6.2 mmol) in anhyd DMF (5 mL) was stirred at 75 °C for 70 h and concentrated in vacuo. The oily residue was treated with H_2O (30 mL) and extracted with EtOAc (2 × 50 mL). The combined organic phases were washed with brine, dried ($MgSO_4$), and evaporated. The residue was purified by flash chromatography (EtOAc) to yield 0.87 g (50%) of the title compound as an orange solid; mp 234–235 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.70 (br s, 1 H, NH), 8.27 (d, *J* = 2.0 Hz, 1 H, 3′-H), 7.83 (dd, *J* = 8.0, 2.0 Hz, 1 H, 5′-H), 7.23 (d, *J* = 8.0 Hz, 1 H, 6′-H), 6.90–7.10 (m, 5 H, C_6H_5), 6.60 (br s, 1 H, NH), 5.11 (br s, 2 H, NH_2).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 185.7 (*C*OPh), 162.4 (C=*C*–NH_2), 148.4, 147.0 (2′-C, 4′-C), 144.5 (*i*-C, C_6H_5), 137.9 (6′-C), 130.2, 128.4, 128.0 (1′-C, 3′-C, *p*-CH, C_6H_5), 127.9, 127.7 (*o*-CH, *m*-CH, C_6H_5), 123.0 (5′-C), 94.5 (*C*=C–NH_2).

Anal. Calcd for $C_{15}H_{12}BrN_3O_3$: C, 49.74; H, 3.34; N, 11.60. Found: C, 49.89; H, 3.60; N, 11.72.

Ethyl 3-Amino-2-(2-bromo-4-nitrophenyl)-3-(methylamino)acrylate (4e)

A mixture of compound **2** (374 mg, 1.7 mmol), enediamine **1e** hydrochloride (354 mg, 2.0 mmol), and DIPEA (348 mg, 2.7 mmol) in anhyd DMF (3.5 mL) was stirred at 75 °C for 48 h and concentrated in vacuo. The oily residue was treated with H_2O (30 mL) and extracted with EtOAc (2 × 40 mL). The combined organic phases were washed with brine, dried ($MgSO_4$), and evaporated. The residue was purified by flash chromatography (EtOAc) to yield 340 mg (58%) of the title compound as a red solid; mp 149–151 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.36 (d, *J* = 2.4 Hz, 1 H, 3′-H), 8.10 (dd, *J* = 8.5, 2.5 Hz, 1 H, 5′-H), 7.47 (d, *J* = 8.5 Hz, 1 H, 6′-H), 7.20–6.50 (br s, 3 H, NH, NH_2), 3.90 (q, *J* = 7.0 Hz, 2 H, CH_2CH_3), 2.75 (d, *J* = 5.0 Hz, 3 H, $NHCH_3$), 1.03 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 167.2 (C=O), 160.8 (C=*C*–NH_2), 147.0, 146.4 (2′-C, 4′-C), 136.6 (6′-C), 129.9 (1′-C), 127.5 (3′-C), 122.8 (5′-C), 77.4 (*C*=C–NH_2), 57.6 (CH_2CH_3), 28.4 ($NHCH_3$), 15.3 (CH_2CH_3).

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{14}BrN_3O_4$: 344.0240/346.0220; found: 344.0243/346.0224.

Ethyl 3-Amino-2-(2-bromo-4-nitrophenyl)-3-(*p*-tolylamino)acrylate (4f)

A mixture of compound **2** (600 mg, 2.7 mmol), enediamine **1f** hydrochloride (821 mg, 3.2 mmol), and DIPEA (555 mg, 4.3 mmol) in anhyd DMSO (4 mL) was stirred at 75 °C for 48 h and concentrated in vacuo. The residue was treated with H_2O (30 mL), the crystals formed were filtered, and dried in air to yield 1.01 g (88%) of the title compound as a red solid; mp 151–153 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6, 80 °C): δ = 8.80 (br s, 1 H, NH), 8.38 (d, *J* = 2.4 Hz, 1 H, 3′-H), 8.13 (dd, *J* = 8.5, 2.4 Hz, 1 H, 5′-H), 7.56 (d, *J* = 8.5 Hz, 1 H, 6′-H), 7.17 (d, *J* = 7.9 Hz, 2 H, 2″-H, 6″-H), 7.07 (d, *J* = 7.9 Hz, 2 H, 3″-H, 5″-H), 6.50 (br s, 2 H, NH_2), 3.94 (q, *J* = 7.0 Hz, 2 H, CH_2CH_3), 2.28 (s, 3 H, 4″-CH_3), 1.04 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6, 80 °C): δ = 167.5 (C=O), 157.9 (C=*C*–NH_2), 146.2, 146.1 (2′-C, 4′-C), 136.3 (6′-C), 135.3, 134.1 (1″-C, 4″-C), 129.8 (2″-C, 6″-C), 129.3 (1′-C), 124.3 (3″-C, 5″-C), 127.3 (3′-C), 122.5 (5′-C), 79.4 (*C*=C–NH_2), 57.9 (CH_2CH_3), 20.6 (4″-CH_3), 14.9 (CH_2CH_3).

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{18}BrN_3O_4$: 420.0553/422.0534; found: 420.0565/422.0548.

Ethyl 3-Amino-2-(2-bromo-4-nitrophenyl)-3-[(4-methoxyphenyl)amino]acrylate (4g)

A mixture of compound **2** (330 mg, 1.5 mmol), enediamine **1g** hydrochloride (354 mg, 2.0 mmol), and DIPEA (310 mg, 2.4 mmol) in anhyd DMF (3 mL) was stirred at 75 °C for 48 h and concentrated in vacuo. The oily residue was treated with H_2O (25 mL) and extracted with EtOAc (2 × 40 mL). The combined organic phases were washed with brine, dried ($MgSO_4$), and evaporated. The residue was purified by flash chromatography (*n*-hexane–EtOAc, 4:1) to yield 323 mg (49%) of the title compound as a red solid; mp 177–178 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.38 (d, J = 2.4 Hz, 1 H, 3′-H), 8.13 (dd, J = 8.5, 2.4 Hz, 1 H, 5′-H), 7.60 (br s, 1 H, NH), 7.57 (d, J = 8.5 Hz, 1 H, 6′-H), 7.11 (d, J = 8.3 Hz, 2 H, 2″-H, 6″-H), 6.93 (d, J = 8.3 Hz, 2 H, 3″-H, 5″-H), 6.40 (br s, 2 H, NH_2), 3.93 (q, J = 7.0 Hz, 2 H, CH_2CH_3), 3.75 (s, 3 H, 4″-OCH_3), 1.04 (t, J = 7.0 Hz, 3 H, CH_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 167.8 (C=O), 158.6 (C=C–NH_2), 157.4 (4″-C), 146.5, 146.4 (2′-C, 4′-C), 136.7 (6′-C), 130.6 (1″-C), 129.6 (1′-C), 127.5 (2″-C, 6″-C), 127.0 (3′-C), 122.8 (5′-C), 114.9 (3″,5″-C), 79.1 (C=C–NH_2), 58.1 (CH_2CH_3), 55.7 (4″-OCH_3), 15.2 (CH_2CH_3).

HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{18}H_{18}BrN_3O_5$: 458.0323/460.0302; found: 458.0320/460.0301.

Ethyl 3-Amino-2-(2-bromo-4-nitrophenyl)-3-{[4-(trifluoromethyl)phenyl]amino}acrylate (4h)

A mixture of compound **2** (270 mg, 1.2 mmol), enediamine **1h** hydrochloride (435 mg, 1.4 mmol), and DIPEA (245 mg, 1.9 mmol) in anhyd DMSO (3 mL) was stirred at 85 °C for 72 h and concentrated in vacuo. The oily residue was treated with H_2O (30 mL) and extracted with EtOAc (2 × 40 mL). The combined organic phases were washed with brine, dried ($MgSO_4$), and evaporated. The residue was purified by flash chromatography (*n*-hexane–EtOAc, 4:1) to yield 350 mg (61%) of the title compound as an orange solid; mp 168–170 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.50–7.00 (br s, 3 H, NH, NH_2), 8.37 (d, J = 2.3 Hz, 1 H, 3′-H), 8.12 (dd, J = 8.5, 2.3 Hz, 1 H, 5′-H), 7.62 (d, J = 7.8 Hz, 2 H, 3″-H, 5″-H), 7.55 (d, J = 8.5 Hz, 1 H, 6′-H), 7.33 (d, J = 7.3 Hz, 2 H, 2″-H, 6″-H), 3.97 (q, J = 7.0 Hz, 2 H, CH_2CH_3), 1.06 (t, J = 7.0 Hz, 3 H, CH_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 168.1 (C=O), 157.3 (C=C–NH_2), 146.5, 146.0 (2′-C, 4′-C), 143.6 (1″-C), 136.4 (6′-C), 131.4 (4″-C), 129.2 (1′-C), 127.4 (3′-C), 126.5 (3″-C, 5″-C), 124.9 (q, J = 271.0 Hz, CF_3), 122.6 (5′-C), 122.0 (2″-C, 6″-C), 82.7 (C=C–NH_2), 58.6 (CH_2CH_3), 15.0 (CH_2CH_3).

HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{18}H_{15}BrF_3N_3O_5$: 474.0271/476.0250; found: 474.0288/476.0271.

Ethyl 3,3-Diamino-2-[5-iodo-2-(methylsulfanyl)pyrimidin-4-yl]acrylate (7a)

A mixture of compound **3a** (0.6 g, 2.1 mmol) and enediamine **1a** (0.6 g, 4.6 mmol) in anhyd DMF (3 mL) was stirred at 80 °C for 24 h and concentrated in vacuo. The residue was treated with H_2O (20 mL), the crystals formed were filtered and dried in air to yield 598 mg (75%) of the title compound as a colorless solid; mp 187–189 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.69 (s, 1 H, 6′-H), 7.80–5.30 (br s, 4 H, 2 × NH_2), 3.94 (q, J = 7.0 Hz, 2 H, CH_2CH_3), 2.45 (s, 3 H, SCH_3), 1.08 (t, J = 7.0 Hz, 3 H, CH_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 170.0, 168.9, 167.8, 164.4 (C=O, 2′-C, C=C–NH_2), 161.4 (6′-C), 97.2 (5′-C), 81.6 (C=C–NH_2), 58.8 (CH_2CH_3), 15.4, 14.5 (CH_2CH_3, SCH_3).

Anal. Calcd for $C_{10}H_{13}IN_4O_2S$: C, 31.59; H, 3.45; N, 14.74. Found: C, 31.66; H, 3.29; N, 14.77.

3,3-Diamino-2-[5-iodo-2-(methylsulfanyl)pyrimidin-4-yl]-1-(pyrrolidin-1-yl)prop-2-en-1-one (7c)

A mixture of compound **3a** (250 mg, 0.87 mmol) and enediamine **1c** (310 mg, 2.0 mmol) in anhyd DMSO (2 mL) was stirred at 65 °C for 6 h and concentrated in vacuo. The residue was treated with H_2O (20 mL) and extracted with EtOAc (2 × 40 mL). The combined organic phases were washed with brine, dried ($MgSO_4$), and evaporated. The residue was purified by flash chromatography (EtOAc–MeOH, from 20:1 to 5:1) to yield 25 mg (7%) of the title compound as a beige solid; mp 184–186 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.43 (s, 1 H, 6′-H), 7.80–7.10 (br s, 4 H, 2 × NH_2), 3.14–2.97 (m, 4 H, NCH_2CH_2), 2.43 (s, 3 H, SCH_3), 1.75–1.67 (m, 4 H, NCH_2CH_2).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 168.0 (C=O), 167.8 (2′-C), 164.8, 164.2 (4′-C, 6′-C), 160.9 (C=C–NH_2), 86.4 (5′-C), 84.8 (C=C–NH_2), 47.3 (NCH_2CH_2), 25.3 (NCH_2CH_2), 14.0 (SCH_3).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{12}H_{16}IN_5OSNa$: 428.0012; found: 428.0014.

Ethyl 3-Amino-2-[5-iodo-2-(methylsulfanyl)pyrimidin-4-yl]-3-(methylamino)acrylate (7e)

A mixture of compound **3a** (487 mg, 1.7 mmol), enediamine **1e** hydrochloride (365 mg, 2.0 mmol), and DIPEA (555 mg, 4.3 mmol) in anhyd DMF (4 mL) was stirred at 80 °C for 48 h and concentrated in vacuo. The residue was treated with H_2O (30 mL) and extracted with EtOAc (2 × 40 mL). The combined organic phases were washed with brine, dried ($MgSO_4$), and evaporated. The residue was purified by flash chromatography (*n*-hexane–EtOAc, 5:2) to yield 220 mg (48%) of the title compound as a colorless solid; mp 203–205 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.69 (s, 1 H, 6′-H), 7.95 (br s, 1 H, NH), 7.25 (br s, 2 H, NH_2), 3.94 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 2.77 (d, J = 5.0 Hz, 3 H, $NHCH_3$), 2.45 (s, 3 H, SCH_3), 1.09 (t, J = 7.1 Hz, 3 H, CH_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 169.6 (C=O), 168.5, 167.6, 164.0 (2′-C, 4′-C, 6′-C), 161.0 (C=C–NH_2), 97.1 (5′-C), 80.7 (C=C–NH_2), 58.3 (CH_2CH_3), 28.3 ($NHCH_3$), 15.0 (CH_2CH_3), 14.1 (SCH_3).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{11}H_{15}IN_4O_2SNa$: 395.0034; found: 395.0036.

Ethyl 3-Amino-2-[5-iodo-2-(methylsulfanyl)pyrimidin-4-yl]-3-(*p*-tolylamino)acrylate (7f)

A mixture of compound **3a** (0.8 g, 2.8 mmol), enediamine **1f** hydrochloride (872 mg, 3.4 mmol), and DIPEA (774 mg, 6.0 mmol) in anhyd DMSO (3 mL) was stirred at 75 °C for 48 h and concentrated in vacuo. The residue was treated with H_2O (30 mL), the crystals formed were collected, dried in air, and recrystallized from MTBE to yield 712 mg (54%) of the title compound as a colorless solid; mp 132–134 °C (MTBE).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.25 (br s, 1 H, NH), 8.73 (s, 1 H, 6′-H), 7.20 (d, J = 8.1 Hz, 2 H, 2″,6″-H), 7.10 (d, J = 8.1 Hz, 2 H, 3″-H, 5″-H), 6.95 (br s, 2 H, NH_2), 3.99 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 2.45 (s, 3 H, SCH_3), 2.30 (s, 3 H, 4″-CH_3), 1.11 (t, J = 7.1 Hz, 3 H, CH_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 169.8 (C=O), 168.0, 167.9, 164.1 (2′-C, 4′-C, 6′-C), 158.4 (C=C–NH_2), 135.0, 134.9 (1″-C, 4″-C), 130.3 (2″-C, 6″-C), 124.7 (3″-C, 5″-C), 97.1 (5′-C), 82.4 (C=C–NH_2), 58.7 (CH_2CH_3), 20.9 (4″-CH_3), 15.0 (CH_2CH_3), 14.2 (SCH_3).

HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{17}H_{18}IN_4O_2S$: 471.0346; found: 471.0345.

3,3-Diamino-2-[5-iodo-2-(methylsulfonyl)pyrimidin-4-yl]-1-phenylprop-2-en-1-one (8b)

A mixture of compound **3b** (255 mg, 0.8 mmol) and enediamine **1b** (292 mg, 1.8 mmol) in anhyd DMF (2.5 mL) was stirred at 45 °C for 40 h and concentrated in vacuo. The residue was treated with H_2O (25

mL), the crystals formed were collected and purified by flash chromatography (CH_2Cl_2–MeOH, 15:1) to yield 188 mg (53%) of the title compound as a pale brown solid; mp 140–142 °C (dec.).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.02 (s, 1 H, 6′-H), 7.50 (br s, 4 H, 2 × NH_2), 7.18 (t, J = 7.3 Hz, 1 H, p-CH, C_6H_5), 7.11 (t, J = 7.3 Hz, 2 H, m-CH, C_6H_5), 7.02 (d, J = 7.3 Hz, 2 H, o-CH, C_6H_5), 3.07 (s, 3 H, SO_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 186.7 (C=O), 166.2 (6′-C), 171.3, 164.5 (2′-C, 4′-C), 161.9 (C=*C*–NH_2), 143.7 (*i*-C, C_6H_5), 129.0 (*p*-CH, C_6H_5), 128.1 (*m*-CH, C_6H_5), 127.6 (*o*-CH, C_6H_5), 107.4 (5′-C), 96.2 (*C*=C–NH_2), 39.5 (SO_2CH_3).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{14}H_{13}IN_4O_3SNa$: 466.9646; found: 466.9653.

Ethyl 3-Amino-2-[5-iodo-2-(methylsulfonyl)pyrimidin-4-yl]-3-(pyrrolidin-1-yl)acrylate (8d)

A mixture of compound **3b** (382 mg, 1.2 mmol), enediamine **1d** hydrochloride (287 mg, 1.3 mmol), and K_2CO_3 (360 mg, 2.6 mmol) in anhyd DMF (3 mL) was stirred at r.t. for 2 h and concentrated in vacuo. The residue was treated with H_2O (15 mL) and extracted with EtOAc (2 × 40 mL). The combined organic phases were washed with brine (2 ×), dried ($MgSO_4$), and evaporated to yield 440 mg (78%) of the title compound as a colorless solid; mp 98–100 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.81 (s, 1 H, 6′-H), 7.60 (br s, 2 H, NH_2), 3.99 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 3.25 (s, 3 H, SO_2CH_3), 1.86–1.77 (m, 4 H, NCH_2CH_2), 3.16–3.05 (m, 4 H, NCH_2CH_2), 1.14 (t, J = 7.1 Hz, 3 H, CH_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 169.8 (C=O), 164.4 (6′-C), 166.0, 163.8, 162.0 (2′-C, 4′-C, C=*C*–NH_2), 100.4 (5′-C), 84.5 (*C*=C–NH_2), 58.4 (CH_2CH_3), 49.4 (NCH_2CH_2), 39.3 (SO_2CH_3), 25.3 (NCH_2CH_2), 15.0 (CH_2CH_3).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{14}H_{19}IN_4O_4SNa$: 489.0064; found: 489.0073.

Ethyl 2-Amino-6-nitro-1*H*-indole-3-carboxylate (5a)

A mixture of compound **4a** (400 mg, 1.2 mmol), Cs_2CO_3 (1.17 g, 3.6 mmol), CuI (23 mg, 0.12 mmol), and L-proline (28 mg, 0.24 mmol) in DMSO (3 mL) was stirred at 60 °C for 3 h and then concentrated in vacuo. H_2O (20 mL) and EtOAc (50 mL) were added, the mixture was shaken, and filtered through a pad of Celite. The organic layer was separated, washed with H_2O and brine, dried ($MgSO_4$), and evaporated. The crystalline residue was washed with *n*-hexane and filtered to yield 242 mg (81%) of the title compound as a pale orange solid; mp 276–280 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.10 (s, 1 H, 1-NH), 8.01 (d, J = 2.2 Hz, 1 H, 7-H), 7.91 (dd, J = 8.6, 2.2 Hz, 1 H, 5-H), 7.62 (d, J = 8.6 Hz, 1 H, 4-H), 7.31 (br s, 2 H, NH_2), 4.27 (q, J = 7.0 Hz, 2 H, CH_2CH_3), 1.33 (t, J = 7.0 Hz, 3 H, CH_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 165.9 (C=O), 157.2 (2-C), 140.7 (6-C), 134.1 (7a-C), 132.7 (3a-C), 117.9, 117.4 (4-C, 5-C), 106.5 (7-C), 86.4 (3-C), 59.5 (CH_2CH_3), 15.5 (CH_2CH_3).

Anal. Calcd for $C_{11}H_{11}N_3O_4$: C, 53.01; H, 4.45; N, 16.86. Found: C, 52.81; H, 4.42; N, 16.61.

(2-Amino-6-nitro-1*H*-indol-3-yl)(phenyl)methanone (5b)

A mixture of compound **4b** (695 mg, 1.9 mmol), Cs_2CO_3 (1.86 g, 5.7 mmol), CuI (36 mg, 0.19 mmol), and L-proline (44 mg, 0.38 mmol) in DMSO (4.5 mL) was stirred at 60 °C for 7 h and then concentrated in vacuo. H_2O (40 mL) and EtOAc (120 mL) were added, the mixture was shaken, and filtered through a pad of Celite. The organic layer was separated, washed with H_2O and brine, dried ($MgSO_4$), and evaporated. The crystalline residue was washed with *n*-hexane and filtered to yield 425 mg (80%) of the title compound as a pale orange solid; mp 293–294 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.34 (s, 1 H, 1-NH), 8.10 (s, 2 H, NH_2), 8.02 (d, J = 2.0 Hz, 1 H, 7-H), 7.66 (dd, J = 8.0, 2.0 Hz, 1 H, 5-H), 7.65–7.45 (m, 5 H, C_6H_5), 6.47 (d, J = 8.0 Hz, 1 H, 4-H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 190.4 (C=O), 158.5 (2-C), 142.7, 141.0, 133.5, 133.4 (3a-C, 6-C, 7a-C, *i*-C, C_6H_5), 131.2 (*p*-CH, C_6H_5), 129.4, 127.8 (*o*-CH, *m*-CH, C_6H_5), 117.5, 116.8 (4-C, 5-C), 106.8 (7-C), 97.3 (3-C).

HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{15}H_{11}N_3O_3$: 282.0873; found: 282.0870.

(2-Amino-6-nitro-1*H*-indol-3-yl)(pyrrolidin-1-yl)methanone (5c)

A mixture of compound **2** (330 mg, 1.55 mmol) and enediamine **1c** (300 mg, 1.9 mmol) in anhyd DMSO (2 mL) was stirred at 65 °C for 1 h. After cooling to r.t., Cs_2CO_3 (1.96 g, 6.0 mmol), CuI (29 mg, 0.15 mmol), and L-proline (35 mg, 0.3 mmol) were added and the mixture was stirred for 48 h. The solvent was partially removed in vacuo and H_2O (20 mL) was added to the residue. The crystals formed were filtered and purified by flash chromatography (CH_2Cl_2–MeOH, 20:1) to yield 280 mg (68%) of the title compound as an orange solid; mp 280–283 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.01 (s, 1 H, 1-NH), 8.01 (d, J = 2.0 Hz, 1 H, 7-H), 7.85 (dd, J = 8.7, 2.0 Hz, 1 H, 5-H), 7.17 (d, J = 8.7 Hz, 1 H, 4-H), 6.81 (br s, 2 H, NH_2), 3.52–3.38 (m, 4 H, NCH_2CH_2), 1.78–1.87 (m, 4 H, NCH_2CH_2).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 166.5 (C=O), 154.5 (2-C), 138.6 (6-C), 133.2 (7a-C), 131.5 (3a-C), 116.9 (5-C), 115.8 (4-C), 106.0 (7-C), 91.6 (3-C), 47.3 (NCH_2CH_2), 25.4 (NCH_2CH_2).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{13}H_{14}N_4O_3Na$: 297.0958; found: 297.0954.

Ethyl 6-Nitro-2-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (5d)

A mixture of compound **2** (250 mg, 1.1 mmol), enediamine **1d** hydrochloride (265 mg, 1.2 mmol), and K_2CO_3 (331 mg, 1.2 mmol) in DMSO (2 mL) was stirred at 75 °C for 7 h and then concentrated in vacuo. The residue was treated with H_2O (15 mL) and extracted with EtOAc (2 × 35 mL). The combined organic layers were dried ($MgSO_4$) and passed through a pad of silica gel. After evaporation of solvent, the oily residue was dissolved in anhyd DMSO (4 mL). Cs_2CO_3 (1.08 g, 3.3 mmol), CuI (21 mg, 0.11 mmol), and L-proline (25 mg, 0.22 mmol) were added and the mixture was stirred at 60 °C for 12 h. The solvent was partially removed in vacuo and the residue was partitioned between H_2O (20 mL) and EtOAc (100 mL). The organic layer was separated, washed with brine, and evaporated. The crude product was purified by flash chromatography (EtOAc) to yield 175 mg (52%) of the title compound as a pale orange solid; mp 208–210 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.09 (br s, 1 H, NH), 7.97 (d, J = 2.1 Hz, 1 H, 7-H), 7.92 (dd, J = 8.7, 2.1 Hz, 1 H, 5-H), 7.76 (d, J = 8.7 Hz, 1 H, 4-H), 4.25 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 3.72–3.56 (m, 4 H, NCH_2CH_2), 2.06–1.92 (m, 4 H, NCH_2CH_2), 1.34 (t, J = 7.1 Hz, 3 H, CH_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 163.8 (C=O), 154.0 (2-C), 140.0 (6-C), 135.5 (7a-C), 132.1 (3a-C), 117.7 (5-C), 117.3 (4-C), 105.4 (7-C), 88.3 (3-C), 59.2 (CH_2CH_3), 51.3 (NCH_2CH_2), 25.7 (NCH_2CH_2), 15.0 (CH_2CH_3).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{15}H_{17}N_3O_4Na$: 326.1112; found: 326.1108.

Ethyl 2-(Methylamino)-6-nitro-1*H*-indole-3-carboxylate (5e)

A mixture of compound **4e** (340 mg, 1.3 mmol), Cs_2CO_3 (1.27 g, 3.9 mmol), CuI (19 mg, 0.1 mmol), and L-proline (23 mg, 0.2 mmol) in DMSO (3 mL) was stirred at r.t. for 24 h and then concentrated in vacuo. The residue was treated with H_2O (20 mL), the crystals formed were filtered, and recrystallized from MeCN to yield 162 mg (61%) of the title compound as an orange solid; mp 266–268 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.61 (br s, 1 H, 1-NH), 7.97–7.90 (m, 2 H, 5-H, 7-H), 7.64–7.59 (m, 1 H, 4-H), 7.51–7.59 (m, 1 H, N*H*CH_3), 4.27 (q, *J* = 7.1 Hz, 2 H, C*H*$_2$CH$_3$), 3.05 (d, *J* = 5.1 Hz, 3 H, NHC*H*$_3$), 1.34 (t, *J* = 7.1 Hz, 3 H, CH_2C*H*$_3$).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 165.5 (C=O), 157.3 (2-C), 139.8 (6-C), 134.1 (7a-C), 132.5 (3a-C), 117.9 (5-C), 116.8 (4-C), 105.8 (7-C), 85.7 (3-C), 59.1 (*C*H$_2$CH$_3$), 30.2 (NH*C*H$_3$), 15.1 (CH_2*C*H$_3$).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{13}N_3O_4Na$: 286.0799; found: 286.0798.

Ethyl 6-Nitro-2-(*p*-tolylamino)-1*H*-indole-3-carboxylate (5f) and Ethyl 2-Amino-6-nitro-1-*p*-tolyl-1*H*-indole-3-carboxylate (6f)

A mixture of compound **4f** (250 mg, 0.6 mmol), Cs_2CO_3 (587 g, 1.8 mmol), CuI (12 mg, 0.06 mmol), and L-proline (14 mg, 0.12 mmol) in DMSO (3 mL) was stirred at r.t. for 48 h and then concentrated in vacuo. The residue was treated with H_2O (20 mL), the crystals formed were filtered, dried in air, and subjected to column chromatography on silica gel (*n*-hexane–EtOAc, 3:2) to yield 55 mg (27%) of compound **5f** and 77 mg (38%) of compound **6f**.

5f

Pale orange solid; mp 243–245 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.66 (s, 1 H, 1-NH), 9.26 (s, 1 H, 2-NH) 8.04 (d, *J* = 2.0 Hz, 1 H, 7-H), 7.98 (dd, *J* = 8.7, 2.0 Hz, 1 H, 5-H), 7.73 (d, *J* = 8.7 Hz, 1 H, 4-H), 7.34 (d, *J* = 8.5 Hz, 2 H, 3′-H, 5′-H), 7.30 (d, *J* = 8.5 Hz, 2 H, 2′-H, 6′-H), 4.35 (q, *J* = 7.1 Hz, 2 H, C*H*$_2$CH$_3$), 2.36 (s, 3 H, 4′-CH_3), 1.38 (t, *J* = 7.1 Hz, 3 H, CH_2C*H*$_3$).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 165.8 (C=O), 153.0 (2-C), 140.8 (6-C), 135.6, 135.1, 132.9, 132.3 (3a-C, 7a-C, 1′-C, 4′-C), 130.7 (2′-C, 6′-C), 123. 2 (3′-C, 5′-C), 117.8 (5-C), 117.7 (4-C), 107.0 (7-C), 87.4 (3-C), 59.6 (*C*H$_2$CH$_3$), 21.0 (4′-CH_3), 15.0 (CH_2*C*H$_3$).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{17}N_3O_4Na$: 362.1111; found: 326.1120.

6f

Pale orange solid; mp 206–208 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.02 (dd, *J* = 8.7, 2.2 Hz, 1 H, 5-H), 7.77 (d, *J* = 8.7 Hz, 1 H, 4-H), 7.51 (d, *J* = 8.1 Hz, 2 H, 2′-H, 6′-H), 7.47–7.42 (m, 3 H, 7-H, 3′-H, 5′-H), 7.18 (br s, 2 H, NH_2), 4.34 (q, *J* = 7.1 Hz, 2 H, C*H*$_2$CH$_3$), 2.47 (s, 3 H, 4′-CH_3), 1.37 (t, *J* = 7.1 Hz, 3 H, CH_2C*H*$_3$).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 165.6 (C=O), 156.5 (2-C), 140.6, 140.0, 134.5, 133.0 (3a-C, 6-C, 7a-C, 1′-C), 131.5 (2′-C, 6′-C), 130.8 (4′-C), 128. 3 (3′-C, 5′-C), 118.5 (5-C), 117.6 (4-C), 104.5 (7-C), 85.7 (3-C), 59.5 (*C*H$_2$CH$_3$), 21.3 (4′-CH_3), 15.1 (CH_2*C*H$_3$).

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{17}N_3O_4$: 340.1292; found: 340.1303.

Ethyl 2-(4-Methoxyphenylamino)-6-nitro-1*H*-indole-3-carboxylate (5g) and Ethyl 2-Amino-1-(4-methoxyphenyl)-6-nitro-1*H*-indole-3-carboxylate (6g)

A mixture of compound **4g** (166 mg, 0.38 mmol), Cs_2CO_3 (359 g, 1.1 mmol), CuI (8 mg, 0.04 mmol), and L-proline (9 mg, 0.08 mmol) in DMSO (2 mL) was stirred at r.t. for 48 h and then concentrated in vacuo. The residue was treated with H_2O (15 mL), the crystals formed were filtered, dried in air, and subjected to column chromatography on silica gel (*n*-hexane–EtOAc, 3:2) to yield 28 mg (21%) of compound **5g** and 70 mg (52%) of compound **6g**.

5g

Orange solid; mp 221–223 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.52 (br s, 1 H, 1-NH), 9.15 (s, 1 H, 2-NH) 8.00 (d, *J* = 2.0 Hz, 1 H, 7-H), 7.95 (dd, *J* = 8.7, 2.0 Hz, 1 H, 5-H), 7.70 (d, *J* = 8.7 Hz, 1 H, 4-H), 7.37 (d, *J* = 8.6 Hz, 2 H, 2′-H, 6′-H), 7.06 (d, *J* = 8.6 Hz, 2 H, 3′-H, 5′-H), 4.34 (q, *J* = 7.0 Hz, 2 H, C*H*$_2$CH$_3$), 3.81 (s, 3 H, OCH_3), 1.38 (t, *J* = 7.0 Hz, 3 H, CH_2C*H*$_3$).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 165.7 (C=O), 157.8 (4′-C), 153.9 (2-C), 140.6 (6-C), 133.2 (3a-C), 132.3 (7a-C), 130.8 (1′-C), 125.8 (2′-C, 6′-C), 117.8 (5-C), 117.5 (4-C), 115.4 (3′-C, 5′-C), 106.8 (7-C), 87.0 (3-C), 59.5 (*C*H$_2$CH$_3$), 55.9 (OCH_3), 15.1 (CH_2*C*H$_3$).

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{17}N_3O_5$: 356.1241; found: 356.1243.

6g

Orange solid; mp 228–230 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.01 (dd, *J* = 8.7, 2.1 Hz, 1 H, 5-H), 7.77 (d, *J* = 8.7 Hz, 1 H, 4-H), 7.48 (d, *J* = 8.8 Hz, 2 H, 2′-H, 6′-H), 7.43 (d, *J* = 2.1 Hz, 1 H, 7-H), 7.23 (d, *J* = 8.8 Hz, 2 H, 3′-H, 5′-H), 7.19 (br s, 2 H, NH_2), 4.33 (q, *J* = 7.1 Hz, 2 H, C*H*$_2$CH$_3$), 3.89 (s, 3 H, OCH_3), 1.37 (t, *J* = 7.1 Hz, 3 H, CH_2C*H*$_3$).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 165.6 (C=O), 160.5 (4′-C), 156.7 (2-C), 140.6 (6-C), 134.8 (7a-C), 132.9 (3a-C), 130.0 (2′-C, 6′-C), 125.7 (1′-C), 118.4 (5-C), 117.6 (4-C), 116.1 (3′-C, 5′-C), 104.5 (7-C), 85.6 (3-C), 59.5 (*C*H$_2$CH$_3$), 56.0 (OCH_3), 15.1 (CH_2*C*H$_3$).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{17}N_3O_4Na$: 378.1061; found: 378.1061.

Ethyl 6-Nitro-2-[4-(trifluoromethyl)phenylamino]-1*H*-indole-3-carboxylate (5h) and Ethyl 2-Amino-6-nitro-1-[4-(trifluoromethyl)phenyl]-1*H*-indole-3-carboxylate (6h)

A mixture of compound **4h** (217 mg, 0.46 mmol), Cs_2CO_3 (456 mg, 1.4 mmol), CuI (10 mg, 0.05 mmol), and L-proline (11 mg, 0.1 mmol) in DMSO (2.5 mL) was stirred at r.t. for 24 h and then concentrated in vacuo. The residue was treated with H_2O (15 mL), the crystals formed were filtered, dried in air, and subjected to column chromatography on silica gel (*n*-hexane–EtOAc, 5:2) to yield 36 mg (20%) of compound **5h** and 105 mg (58%) of compound **6h**.

5h

Orange solid; mp 228–230 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.12 (s, 1 H, 1-NH), 9.61 (s, 1 H, 2-NH) 8.09 (d, *J* = 2.0 Hz, 1 H, 7-H), 8.02 (dd, *J* = 8.7, 2.0 Hz, 1 H, 5-H), 7.86–7,75 (m, 3 H, 4-H, 2′-H, 6′-H), 7.66 (d, *J* = 8.2 Hz, 2 H, 3′-H, 5′-H), 4.36 (q, *J* = 7.0 Hz, 2 H, C*H*$_2$CH$_3$), 1.39 (t, *J* = 7.0 Hz, 3 H, CH_2C*H*$_3$).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 165.5 (C=O), 153.9 (2-C), 151.2 (1′-C), 142.8 (7a-C), 141.2 (6-C), 132.6 (3a-C), 127.2 (q, J = 3.6 Hz, 3′-C, 5′-C), 124.8 (q, J = 268.1 Hz, CF_3), 124.3 (q, J = 32.1 Hz, 4′-C), 121.3 (2′-C, 6′-C), 118.3 (5-C), 117.7 (4-C), 107.4 (7-C), 89.6 (3-C), 59.8 (CH_2CH_3), 15.0 (CH_2CH_3).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{18}H_{14}F_3N_3O_5Na$: 416.0829; found: 416.0842.

6h

Orange solid; mp 211–213 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.08 (d, J = 8.3 Hz, 2 H, 2′-H, 6′-H), 8.05 (dd, J = 8.7, 2.0 Hz, 1 H, 5-H), 7.84 (d, J = 8.3 Hz, 2 H, 3′-H, 5′-H), 7.80 (d, J = 8.7 Hz, 1 H, 4-H), 7.52 (d, J = 2.0 Hz, 1 H, 7-H), 7.39 (s, 2 H, NH_2), 4.35 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 1.38 (t, J = 7.1 Hz, 3 H, CH_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 165.5 (C=O), 156.4 (2-C), 140.7 (6-C), 137.3 (7a-C), 133.9 (3a-C), 133.2 (1′-C), 130.3 (q, J = 32.2 Hz, 4′-C), 129.7 (2′-C, 6′-C), 128.1 (q, J = 3.7 Hz, 3′-C, 5′-C), 124.4 (q, J = 272.5 Hz, CF_3), 118.8 (5-C), 117.7 (4-C), 104.6 (7-C), 86.0 (3-C), 59.6 (CH_2CH_3), 15.1 (CH_2CH_3).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{18}H_{14}F_3N_3O_4Na$: 416.0829; found: 416.0840.

Ethyl 6-Amino-2-(methylsulfanyl)-5*H*-pyrrolo[3,2-*d*]pyrimidine-7-carboxylate (9a)

A mixture of compound **7a** (515 mg, 1.4 mmol), Cs_2CO_3 (1.37 g, 4.2 mmol), CuI (27 mg, 0.14 mmol), and L-proline (32 mg, 0.28 mmol) in DMSO (3 mL) was stirred at r.t. for 6 h and then concentrated in vacuo. The residue was treated with H_2O (15 mL), the crystals formed were filtered, dissolved in warm *i*-PrOH (100 mL), and passed through a pad of silica gel. The solvent was evaporated to yield 252 mg (71%) of the title compound as a colorless solid; mp 296–298 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.83 (s, 1 H, 5-NH), 8.15 (s, 1 H, 4-H), 7.42 (s, 2 H, NH_2), 4.22 (q, J = 7.0 Hz, 2 H, CH_2CH_3), 2.49 (s, 3 H, SCH_3), 1.29 (t, J = 7.0 Hz, 3 H, CH_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 165.5, 162.4 (C=O, 2-C), 157.3 (6-C), 151.9 (7a-C), 135.3 (4-C), 123.5 (4a-C), 84.9 (7-C), 59.3 (CH_2CH_3), 15.4, 14.7 (CH_2CH_3, SCH_3).

Anal. Calcd for $C_{10}H_{12}N_4O_2S$: C, 47.61; H, 4.79; N, 22.21. Found: C, 47.60; H, 4.80; N, 22.25.

{6-Amino-2-(methylsulfanyl)-5*H*-pyrrolo[3,2-*d*]pyrimidin-7-yl}(pyrrolidin-1-yl)methanone (9c)

A mixture of compound **3a** (600 mg, 2.1 mmol) and enediamine **1c** (714 mg, 4.6 mmol) in anhyd DMSO (4 mL) was stirred at 65 °C for 2 h and then concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (20 mL) and passed through silica gel, washing out with EtOAc–MeOH (8:1). After evaporation of solvents, the residue was dissolved in DMSO (4 mL); Cs_2CO_3 (2.05 g, 6.3 mmol), CuI (40 mg, 0.21 mmol), and L-proline (48 mg, 0.42 mmol) were added and the mixture was stirred at r.t. for 24 h. The solvent was partially removed in vacuo, the residue was dissolved in *i*-PrOH (20 mL), and passed through a pad of silica gel. After evaporation of solvent, the crude product was purified by flash chromatography (CH_2Cl_2–acetone, 1:1) and crystallized from MeCN to yield 216 mg (37%) of the title compound as a colorless solid; mp 230–231 °C (dec.).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.82 (s, 1 H, 5-NH), 8.11 (s, 1 H, 4-H), 7.16 (s, 2 H, NH_2), 3.65–3.96 (m, 2 H, NCH_2CH_2), 3.35–3.65 (m, 2 H, NCH_2CH_2), 2.47 (s, 3 H, SCH_3), 1.74–1.89 (m, 4 H, NCH_2CH_2).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 165.4 (C=O), 160.9 (2-C), 156.6 (6-C), 149.8 (7a-C), 134.2 (4-C), 122.4 (4a-C), 88.7 (7-C), 46.4, 48.2 (br s, NCH_2CH_2), 24.4, 26.2 (br s, NCH_2CH_2), 14.2 (SCH_3).

HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{12}H_{15}N_5OS$: 278.1071; found: 278.1079.

Ethyl 2-(Methylsulfanyl)-6-(pyrrolidin-1-yl)-5*H*-pyrrolo[3,2-*d*]pyrimidine-7-carboxylate (9d)

A mixture of compound **3a** (350 mg, 1.2 mmol), enediamine **1d** hydrochloride (331 mg, 1.5 mmol), and DIPEA (361 mg, 2.8 mmol) in anhyd DMSO (3 mL) was stirred at 75 °C for 24 h and then concentrated in vacuo. The residue was treated with H_2O (30 mL) and extracted with CH_2Cl_2 (2 × 50 mL). The combined organic phases were dried ($MgSO_4$) and evaporated. The oily residue was dissolved in anhyd DMSO (5 mL); Cs_2CO_3 (1.17 g, 3.6 mmol), CuI (23 mg, 0.12 mmol), and L-proline (28 mg, 0.24 mmol) were added and the mixture was stirred at r.t. for 24 h. The solvent was partially removed in vacuo, H_2O (25 mL) was added followed by extraction with EtOAc (3 × 30 mL). The organic phase was washed with brine and evaporated to yield 116 mg (32%) of the title compound as a colorless solid; mp 227–228 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.05 (br s, 1 H, NH), 8.15 (s, 1 H, 4-H), 4.20 (q, J = 7.0 Hz, 2 H, CH_2CH_3), 3.59–3.45 (m, 4 H, NCH_2CH_2), 2.51 (s, 3 H, SCH_3), 2.03–1.90 (m, 4 H, NCH_2CH_2), 1.31 (t, J = 7.0 Hz, 3 H, CH_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 163.5 (C=O), 161.8 (2-C), 153.3 (6-C), 152.9 (7a-C), 134.6 (4-C), 122.9 (4a-C), 87.2 (7-C), 59.2 (CH_2CH_3), 50.8 (NCH_2CH_2), 25.6 (NCH_2CH_2), 15.0 (CH_2CH_3), 14.1 (SCH_3).

HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{14}H_{18}N_4O_2S$: 307.1224; found: 307.1226.

Ethyl 6-(Methylamino)-2-(methylsulfanyl)-5*H*-pyrrolo[3,2-*d*]pyrimidine-7-carboxylate (9e)

A mixture of compound **7e** (311 mg, 0.79 mmol), Cs_2CO_3 (782 mg, 2.4 mmol), CuI (15 mg, 0.08 mmol), and L-proline (18 mg, 0.16 mmol) in DMSO (3 mL) was stirred at r.t. for 24 h and then concentrated in vacuo. The residue was treated with *i*-PrOH (30 mL) and passed through a pad of silica gel. Evaporation of solvent afforded a mixture of isomers **9e** and **11e** (~7:1), which was recrystallized from MeCN to yield 121 mg (57%) of the title compound as a beige solid; mp 253–255 °C (MeCN).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.20 (br s, 1 H, 5-NH), 8.15 (s, 1 H, 4-H), 7.72 (q, J = 5.1 Hz, 1 H, $NHCH_3$), 4.26 (q, J = 7.0 Hz, 2 H, CH_2CH_3), 3.06 (d, J = 5.2 Hz, 3 H, $NHCH_3$), 2.51 (s, 3 H, SCH_3), 1.32 (t, J = 7.0 Hz, 3 H, CH_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 165.2 (C=O), 162.3 (2-C), 157.3 (6-C), 151.7 (7a-C), 134.5 (4-C), 123.4 (4a-C), 84.2 (7-C), 58.9 (CH_2CH_3), 29.9 ($NHCH_3$), 15.0 (CH_2CH_3), 14.1 (SCH_3).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{11}H_{14}N_4O_2SNa$: 267.0910; found: 267.0911.

Ethyl 6-Amino-5-methyl-2-(methylsulfanyl)-5*H*-pyrrolo[3,2-*d*]pyrimidine-7-carboxylate (11e)

This compound was not isolated.

^{1}H NMR (400 MHz, DMSO-d_6): δ (isomeric mixture) = 8.31 (s, 1 H, 4-H), 7.63 (br s, 2 H, NH_2), 4.24 (q, J = 7.0 Hz, 2 H, CH_2CH_3), 3.55 (s, 1 H, NCH_3), 2.55 (s, 3 H, SCH_3), 1.31 (t, J = 7.0 Hz, 3 H, CH_2CH_3).

Mixture of Ethyl 2-(Methylsulfanyl)-6-(*p*-tolylamino)-5*H*-pyrrolo[3,2-*d*]pyrimidine-7-carboxylate (9f) and Ethyl 6-Amino-2-(methylsulfanyl)-5-(*p*-tolyl)-5*H*-pyrrolo[3,2-*d*]pyrimidine-7-carboxylate (11f)

A mixture of compound **7f** (126 mg, 0.27 mmol), Cs_2CO_3 (264 mg, 0.81 mmol), CuI (6 mg, 0.03 mmol), and L-proline (6 mg, 0.06 mmol) in DMSO (2 mL) was stirred at r.t. for 24 h and then concentrated in vacuo. The residue was treated with H_2O (15 mL), the crystals formed were filtered, and dried in air to yield 86 mg (92%) of a mixture of isomers **9f** and **11f** (~1.3:1).

^{1}H NMR (400 MHz, DMSO-d_6): δ (signals of **9f**) = 11.96 (s, 1 H, 5-H), 9.44 (s, 1 H, 6-NH), 8.18 (s, 1 H, H-4), 7.33 (d, *J* = 8.4 Hz, 2 H, 2′-H, 6′-H), 7.29 (d, *J* = 8.4 Hz, 2 H, 3′-H, 5′-H), 4.30 (q, *J* = 7.0 Hz, 2 H, CH_2CH_3), 2.53 (s, 3 H, SCH_3), 2.44 (s, 3 H, 4′-CH_3), 1.34 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3); δ (signals of **11f**) = 7.82 (s, 1 H, H-4), 7.46 (d, *J* = 8.2 Hz, 2 H, 2′-H, 6′-H), 7.42 (d, *J* = 8.2 Hz, 2 H, 3′-H, 5′-H), 7.36 (s, 2 H, NH_2), 4.28 (q, *J* = 7.0 Hz, 2 H, CH_2CH_3), 2.55 (s, 3 H, SCH_3), 2.35 (s, 3 H, 4′-CH_3), 1.33 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3).

{6-Amino-2-(methylsulfonyl)-5*H*-pyrrolo[3,2-*d*]pyrimidin-7-yl}(phenyl)methanone (10b)

A mixture of compound **8b** (550 mg, 1.24 mmol), Cs_2CO_3 (1.21 g, 3.72 mmol), CuI (24 mg, 0.124 mmol), and L-proline (29 mg, 0.25 mmol) in DMSO (6 mL) was stirred at r.t. for 24 h and then concentrated in vacuo. The residue was dissolved in acetone (70 mL) and passed through a pad of silica gel. After evaporation of solvent, the residue was treated with H_2O (25 mL), the crystals were filtered, and dried in air to yield 223 mg (56%) of the title compound as a beige solid; mp 180–183 °C (dec.).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.70 (br s, 1 H, 5-NH), 8.47 (s, 1 H, 4-H), 8.43 (s, 2 H, NH_2), 7.78 (d, *J* = 7.2 Hz, 2 H, *o*-CH, C_6H_5), 7.54 (t, *J* = 7.0 Hz, 1 H, *p*-CH, C_6H_5), 7.46 (t, *J* = 7.2 Hz, 2 H, *m*-CH, C_6H_5), 3.05 (s, 3 H, SO_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 189.8 (C=O), 159.6 (6-C), 158.7 (2-C), 150.0 (7a-C), 140.7 (*i*-C, C_6H_5), 134.7 (4-C), 131.1 (*p*-CH, C_6H_5), 129.0 (*o*-CH, C_6H_5), 127.8 (*m*-CH, C_6H_5), 126.5 (4a-C), 95.7 (7-C), 39.7 (SO_2CH_3).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{12}N_4O_3SNa$: 339.0523; found: 339.0534.

Ethyl 2-(Methylsulfonyl)-6-(pyrrolidin-1-yl)-5*H*-pyrrolo[3,2-*d*]pyrimidine-7-carboxylate (10d)

A mixture of compound **8d** (300 mg, 0.64 mmol), Cs_2CO_3 (626 g, 1.92 mmol), CuI (12 mg, 0.064 mmol), and L-proline (15 mg, 0.13 mmol) in DMSO (3 mL) was stirred at r.t. for 24 h and then concentrated in vacuo. The residue was treated with H_2O (30 mL) and extracted with EtOAc (2 × 30 mL). The residue after evaporation of solvent was crystallized from MeCN to yield 157 mg (72%) of the title compound as a colorless solid; mp 233–235 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.75 (br s, 1 H, NH), 8.40 (s, 1 H, 4-H), 4.24 (q, *J* = 7.1 Hz, 2 H, CH_2CH_3), 3.66–3.53 (m, 4 H, NCH_2CH_2), 3.35 (s, 3 H, SO_2CH_3), 2.05–1.94 (m, 4 H, NCH_2CH_2), 1.32 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 163.0 (C=O), 158.8 (6-C), 154.2 (2-C), 151.9 (7a-C), 133.3 (4-C), 126.4 (4a-C), 88.2 (7-C), 59.6 (CH_2CH_3), 51.1 (NCH_2CH_2), 39.7 (SO_2CH_3), 25.6 (NCH_2CH_2), 14.9 (CH_2CH_3).

HRMS (ESI-TOF): *m*/*z* [M + K]$^+$ calcd for $C_{14}H_{18}N_4O_4SK$: 377.0680; found: 377.0688.

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Supporting Information

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