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Graphical Abstract

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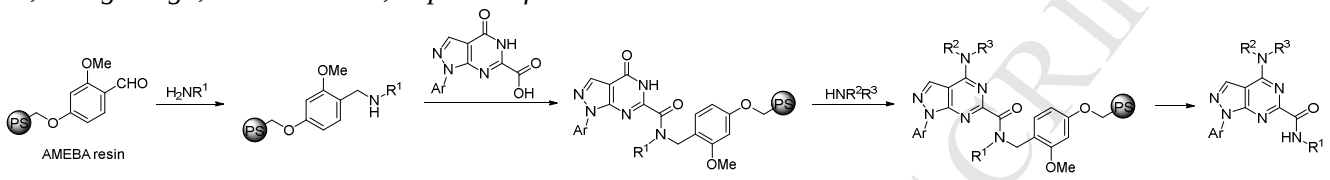

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ABSTRACT

This work describes a solid-phase synthetic method for building a compound library of *N*-alkyl-4-alkylamino-1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide derivatives, that are based on the biologically active 1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine scaffold. In the first step of this synthetic sequence, condensation reactions of ethyl 5-amino-1-aryl-1*H*-pyrazole-4-carboxylates with methyl cyanoformate resulted in the formation of esters that underwent hydrolysis to give 1-aryl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acids. The coupling reaction of these carboxylic acids with primary alkylamine-loaded acid-sensitive methoxybenzaldehyde (AMEBA) resins was followed by amination reactions mediated by benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (BOP). Subsequent cleavage from the solid support resulted in the formation of the target *N*-alkyl-4-alkylamino-1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide derivatives. The reaction conditions for solid-phase transformations were optimized using a solution-phase model study with 2,4-dimethoxybenzyl-protected isobutylamine as a reactant in place of the AMEBA resin-loaded isobutylamine. The progress of the solid-phase reactions was monitored by on-bead ATR-FTIR spectroscopy. Diversification experiments were performed by using 1-aryl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acids and a variety of primary and secondary amine building blocks to build the target compound library.

1. Introduction

Small organic molecule screening libraries, including diverse and target-focused libraries, serve as important sources for hit and lead generation in the drug discovery process.[1,2] Solid-phase organic synthesis (SPOS) provides an efficient synthetic route to small organic molecule libraries when its operational procedures are set up appropriately.[3] This reaction methodology involves the attachment of a synthetic intermediate onto a solid polymeric support via a linker, followed by repeated reactions on the solid phase with filtration and washing steps, and finally cleavage from the solid support to afford the desired product. Reactions on the solid phase can be driven to completion by the use of excess reagents and supported intermediates can be purified by simple filtration and washing steps. Therefore, SPOS can be automated and mix-and-split synthesis is also made possible.

The privileged structure concept has been a stepping stone towards enhancing small organic molecule screening libraries.[4-6] A privileged structure can be defined as a structural motif that possesses different biological activities depending on its substitution pattern. Despite its conceptual ambiguity,[5] this ~~concept~~ has prevailed since its first introduction by Evans and co-workers[4] two and a half decades ago as one of the most common approaches towards scaffold selection for the production of both diversity and focused screening libraries.[6]

As shown in Figure 1 (together with values for some of its physicochemical properties),[7] 1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine derivatives are biologically active and exhibit A_1/A_{2A} antagonistic,[8a-b] GPR119 agonistic,[8c] p38α inhibitory,[8d] anticancer/radioprotective,[8e] CRF-1 receptor antagonistic,[8f] glucokinase activating,[8g] GLUT1 inhibitory,[8h] and COX-2 inhibitory[8i] effects. These properties arise from the difference in the substituents around the 1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine scaffold. Therefore, this scaffold can be regarded as a privileged structure that exhibits a broad range of biological activities, and one that can yield promising libraries when appropriately modified. A few reports have been published regarding the synthesis of 1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine derivatives in a high-throughput manner.[9] Lindsley and co-workers have reported the microwave-assisted organic synthesis (MAOS) of 4-amino-1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine derivatives via 4-cyano-5-aminopyrazole precursors, which in turn were prepared from ethoxymethylenemalononitrile and hydrazines.[9a] Slavish et al.

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described a sequential introduction of the aniline and hydrazine building blocks onto 2,4,6-trichloropyrimidine-5-carboxaldehyde to form a 4,6-bis(anilino)-1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine library.[9b] Morrill and co-workers have reported the synthesis of 4-substituted 1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine derivatives via condensation reactions of 4,6-dichloropyrimidine-5-carboxaldehyde with hydrazines and subsequent substitution reactions with various nucleophiles at the 4-position.[9c] Liao et al. have developed a solid-phase synthetic route for pyrazolo[3,4-*d*]pyrimidine derivatives via Aza-Wittig/electrocyclic ring closure reaction.[9d] There is a continuing interest in high-throughput chemistry within the scientific community for hit- and lead-finding heterocyclic compound screening libraries. Therefore, in this work, the biologically active 1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine scaffold was chosen as a candidate. Herein, a novel solid-phase synthetic method has been reported for the development of an *N*-alkyl-4-alkylamino-1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide library. This procedure involves loading of 1-aryl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid templates onto aminated acid-sensitive methoxybenzaldehyde (AMEBA) resins,[10] followed by benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (BOP)-mediated direct amination reactions at the 4-position, and final cleavage reactions to obtain the target compounds, as illustrated in Figure 2. This work describes the synthesis of 1-aryl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acids, a solution-phase model study and its adaptation to develop the solid-phase synthetic method, on-bead monitoring of solid-phase reactions by ATR (attenuated total reflectance)-FTIR spectroscopy, and the effect of varying substituents.

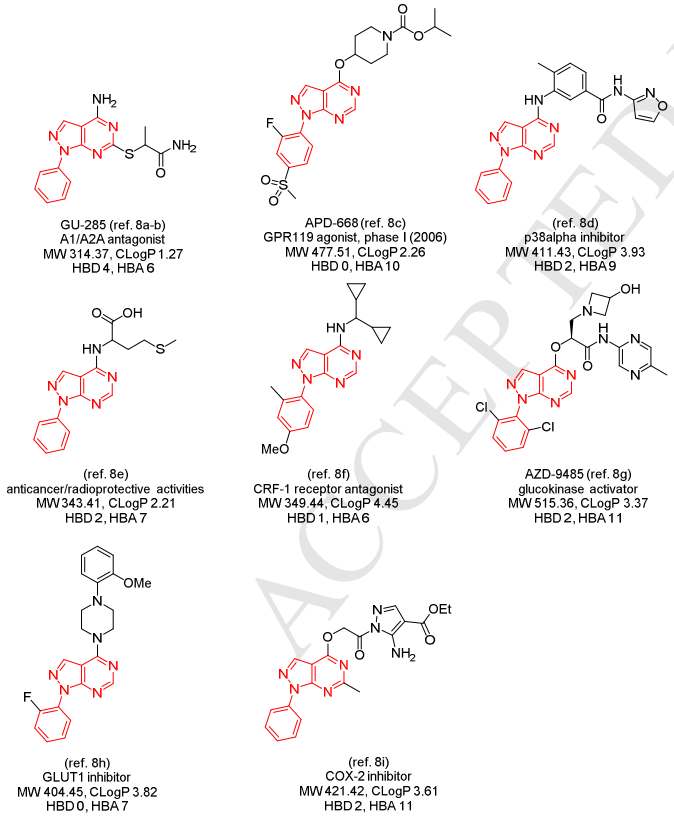


Figure 1. Representative biologically active 1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine derivatives.

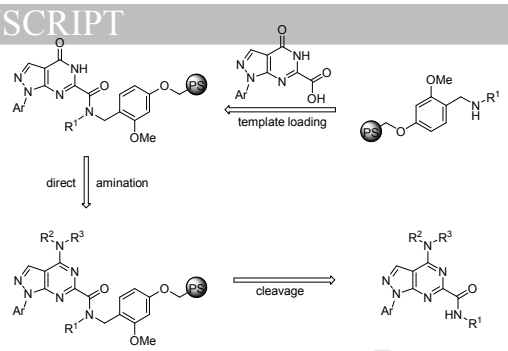
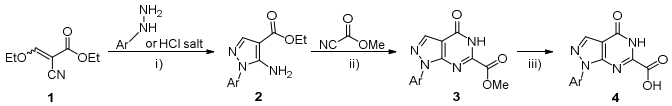


Figure 2. Solid-phase synthetic strategy for *N*-alkyl-4-alkylamino-1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide derivatives.

2. Results and discussion

The synthesis of 1-aryl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acids (**4**) started from preparation of ethyl 5-amino-1-aryl-1*H*-pyrazole-4-carboxylates (**2**). The latter compounds were synthesized by condensation reactions between ethyl 2-cyano-3-ethoxyacrylate (**1**) and aryl hydrazines that were present either as a free form (for Ar = C_6H_5) or HCl salt form (for Ar = 4-MeOC_6H_4, 4-MeC_6H_4, 4-FC_6H_4, and 4-NCC_6H_4) in EtOH at 80 °C, as shown in Scheme 1. The pyrazole intermediates (**2**) underwent cyclization with methyl cyanoformate in the presence of 4 N HCl in 1,4-dioxane at 100 °C to give the ester intermediates **3**. These esters (**3**) were readily hydrolyzed on treatment with lithium hydroxide in MeOH/H_2O at room temperature to afford the desired 4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acids (**4**). The overall results are summarized in Table 1. The known compounds **2a**,[11a] **2b**,[11a] **2c**,[11b] **2d**,[11c] and **2e**[11d] were characterized by ^{1}H NMR and MS. Both compounds **3** and **4** except **3a**[11e] have been reported in this work for the first time and were completely characterized by their melting point, ^{1}H and ^{13}C NMR, IR, MS, and HRMS.



Scheme 1. i) (Et_3N,) EtOH, 80 °C; ii) 4N HCl in 1,4-dioxane, 100 °C; iii) LiOH·H_2O, MeOH/H_2O, rt.

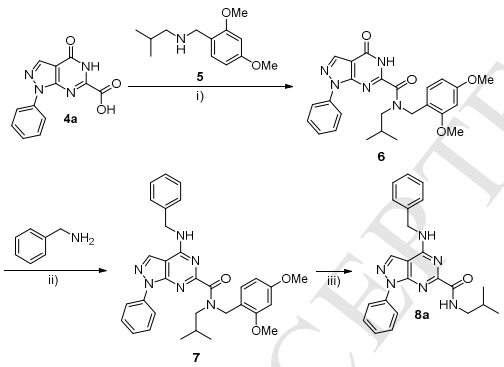
Table 1. Yields of compounds **2a-e**, **3a-e**, and **4a-e**

Compound	Ar	Yield (%)
2a	C_6H_5	90
2b	4-MeO-C_6H_4	78
2c	4-Me-C_6H_4	85
2d	4-F-C_6H_4	65
2e	4-NC-C_6H_4	80
3a	C_6H_5	78
3b	4-MeO-C_6H_4	72
3c	4-Me-C_6H_4	43
3d	4-F-C_6H_4	71
3e	4-NC-C_6H_4	88
4a	C_6H_5	90
4b	4-MeO-C_6H_4	81
4c	4-Me-C_6H_4	90

4d	4-F-C_6H_4	81	8	proton sponge	rt	9 h	71
4e	4-NC-C_6H_4	90	9	TMG	rt	20 h	12

[a]Each reaction was run for **6** (50 mg, 0.11 mmol) in the presence of BOP (62 mg, 0.22 mmol) and a base (1.5 molar eq.) in DMF (3 mL).

A solution-phase model study for optimization of reaction conditions was performed using the synthesized carboxylic acid **4a** (Scheme 2) and 2,4-dimethoxybenzyl-protected isobutylamine **5**[12] as a substitute for the AMEBA resin-loaded isobutylamine in an amide coupling reaction. The reaction was carried out in the presence of EDC and HOAt in DMF at room temperature and the carboxamide derivative **6** was obtained in 85% yield. No significant side reactions were observed during this transformation. BOP-mediated direct amination reaction[13] of **6** with benzylamine was optimized by varying the base and reaction temperature as shown in Table 2. DMF was selected as the reaction solvent instead of acetonitrile because it assists in resin-swelling during the solid-phase reactions.[14] Typical coupling reaction conditions such as the combination of BOP and DBU did not provide satisfactory results at ambient or elevated temperature (entry 1-3). Using DBN as a base at room temperature resulted in no formation of the desired product (entry 4) but when DIPEA was used under identical reaction conditions, the product yield considerably improved to 84% (entry 5). Elevating the reaction temperature to 60 °C gave only a slightly higher product yield of 87% (entry 6). Other bases such as TEA, proton sponge, and TMG at room temperature afforded the benzylaminated product **7** in 49, 71, and 12% yields respectively. From the above results, the combination of BOP/DIPEA was selected as standard conditions for subsequent reactions. After the deprotection of compound **7** using TFA in DCM, the final target compound **8a** was obtained in 91% yield. Compounds **6**, **7**, and **8a** have not been reported before and were therefore characterized by their melting points, ^{1}H and ^{13}C NMR, IR, MS, and HRMS.

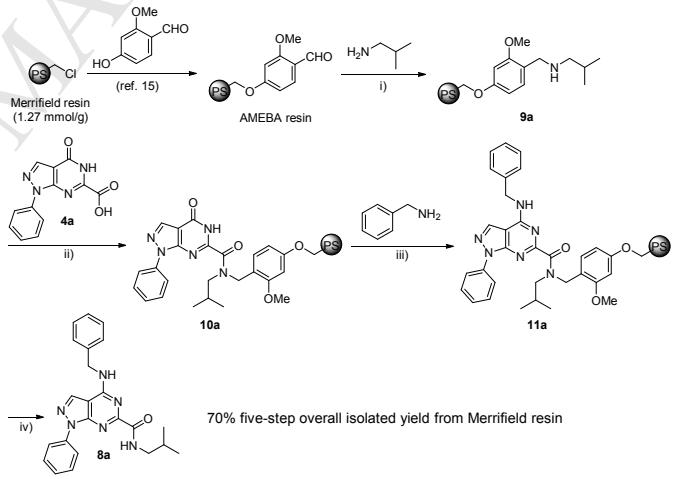


Scheme 2. i) EDC, HOAt, DMF, rt, 8 h, 85% for **6**; ii) BOP, DIPEA, DMF, rt, 7 h, 84% for **7**; iii) 25% TFA in DCM, rt, 3 h, 91% for **8a**.

Table 2. Variation experiments of reaction conditions for direct amination of intermediate **6** to **7**[a]

Entry	Base	Reaction temp.	Reaction time	Yield (%) for **7**
1	DBU	rt	14 h	22
2	DBU	60 °C	13 h	40
3	DBU	100 °C	14 h	46
4	DBN	rt	12 h	-
5	DIPEA	rt	7 h	84
6	DIPEA	60 °C	14 h	87
7	TEA	rt	7 h	49

In the next step, the optimized reaction parameters determined from the solution-phase model study were utilized for solid-phase synthesis, as shown in Scheme 3. Isobutylamine loaded onto AMEBA resin (**9a)** was prepared by reductive amination of AMEBA resin[15] with isobutylamine **16a** under typical conditions. The reaction conditions set for the solution model study were applied to **9a** to give a template-loaded intermediate resin **10a** and a benzylaminated intermediate resin **11a**. The final product **8a** was then obtained by cleavage from the resin **11a** under the same conditions as those used for compound **7**. Subsequent purification by silica gel column chromatography gave **8a** in a 70% five-step overall isolated yield from the Merrifield resin. The progress of the solid-phase reactions was monitored by ATR-FTIR spectroscopy of resin samples withdrawn during the course of the reactions. The IR spectra of the Merrifield and AMEBA resins, compounds **9a**, **10a**, and **11a** are given in Figure 3, together with those of the corresponding compounds **5**, **6**, and **7** obtained from the above solution-phase model study for comparison. In the transformations of AMEBA resin to **9a** and **10a** to **11a**, the characteristic carbonyl bands at 1671 cm^{-1} and 1709 cm^{-1}, respectively, disappeared from the IR spectra of the products. Furthermore, the IR spectra for resins **10a** and **11a** were comparable to those of compounds **6** and **7**, respectively.



Scheme 3. i) $NaBH(OAc)_3$, DCE, rt, 21 h; ii) EDC, HOAt, DMF, rt, 19 h; iii) BOP, DIPEA, DMF, rt, 13 h; iv) 25% TFA in DCM, rt, 1 h.

The effect of different substituents on these reactions was also studied (Scheme 4). The building blocks used in these experiments are shown in Figure 4. Isobutyl and benzylamino groups were chosen as R^1 and NR^2R^3 groups respectively, and the aryl group was varied by using 1-aryl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acids (**4b**−**e**). These transformations resulted in the formation of the corresponding products **8b**−**e** in 50−71% overall yields from Merrifield resin, as summarized in Table 3. The primary amines shown in Figure 4 were utilized for the diversity point R^1 and the NR^2R^3 group was fixed with the cyclopropylamino group. In these transformations, 1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide derivatives **8f**−**o** were formed with overall isolated yields of 31−77% after a five-step sequence. With R^1 group as cyclopropyl, the NR^2R^3 group was varied by using primary and secondary amines (illustrated in Figure 4) and the final products

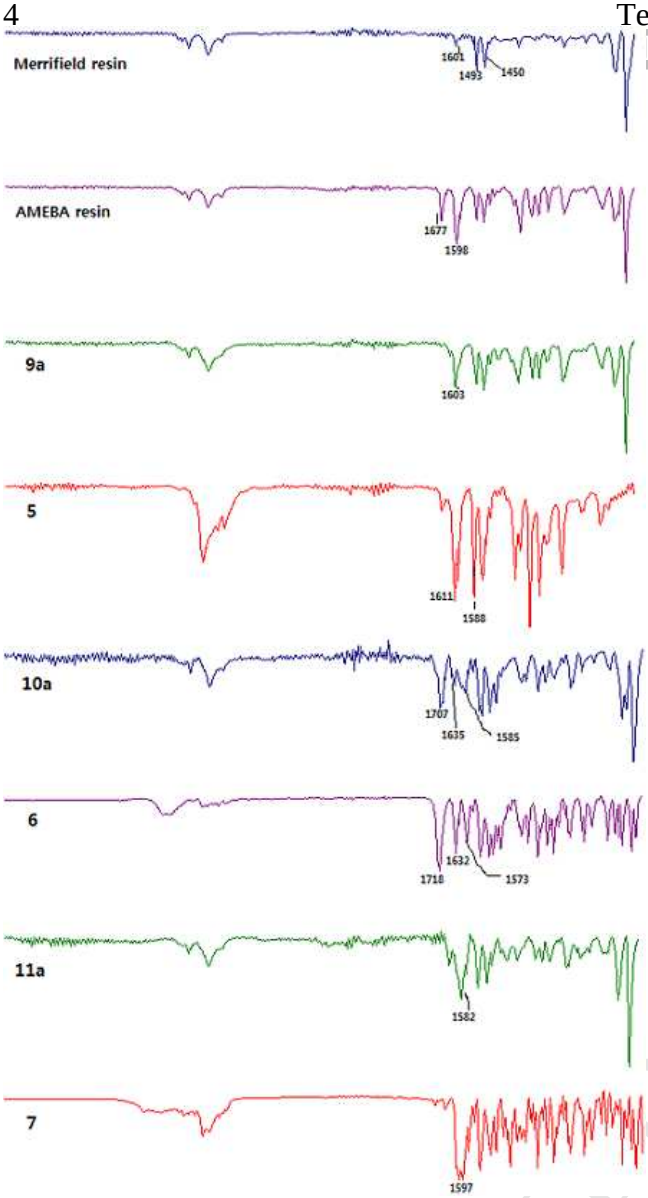
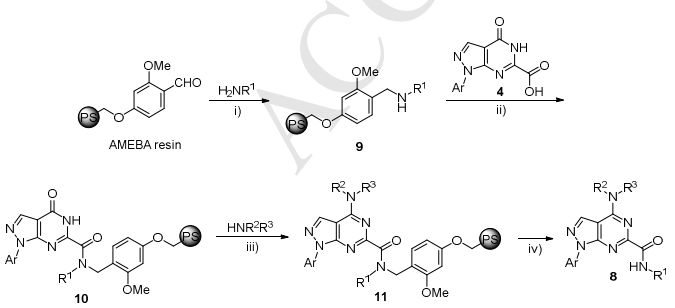


Figure 3. Stacked IR spectra of resins (Merrifield resin, AMEBA resin, **9a**, **10a**, and **11a**) and compounds (**5**, **6** and **7**).

8p−**y** were obtained in 34−71% yields. The *N*-Alkyl-4-alkylamino-1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide derivatives **8b**−**y** have not been synthesized before and were characterized in this work by their melting points, ^{1}H and ^{13}C NMR, IR, MS, and HRMS. ATR-FTIR data were recorded for the intermediate resins **9**, **10**, and **11**.



Scheme 4. i) $NaBH(OAc)_3$, DCE, rt; ii) EDC, HOAt, DMF, rt; iii) BOP, DIPEA, DMF, rt; iv) 25% TFA in DCM, rt.

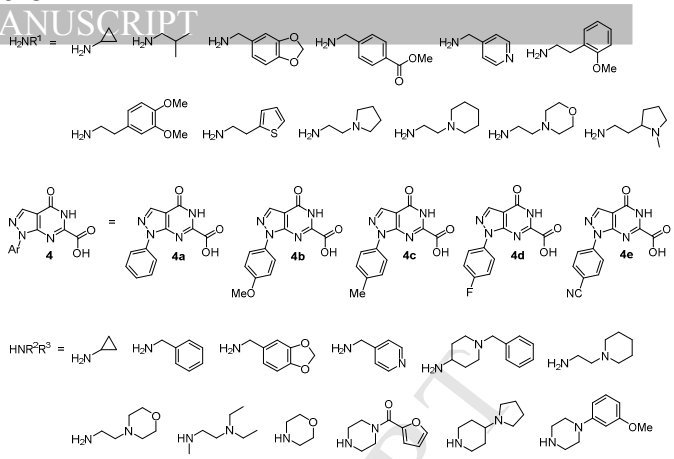


Figure 4. Building blocks used in variation experiments of substituents.

Table 3. Yields of compounds **8b-y**

Compd	Ar	R^1	NR^2R^3	Yield (%)[a]
8b	4-MeO-C_6H_4	*i*-Bu	benzylamino	71
8c	4-Me-C_6H_4	*i*-Bu	benzylamino	50
8d	4-F-C_6H_4	*i*-Bu	benzylamino	61
8e	4-NC-C_6H_4	*i*-Bu	benzylamino	63
8f	C_6H_5	piperonyl	cyclopropylamino	72
8g	C_6H_5	(4-methoxycarbonyl)benzyl	cyclopropylamino	77
8h	4-MeO-C_6H_4	pyridin-4-ylmethyl	cyclopropylamino	76
8i	4-MeO-C_6H_4	2-methoxyphenethyl	cyclopropylamino	51
8j	4-Me-C_6H_4	3,4-dimethoxyphenethyl	cyclopropylamino	55
8k	4-Me-C_6H_4	2-(thiophen-2-yl)ethyl	cyclopropylamino	31
8l	4-F-C_6H_4	2-(pyrrolidin-1-yl)ethyl	cyclopropylamino	45
8m	4-F-C_6H_4	2-(piperidin-1-yl)ethyl	cyclopropylamino	50
8n	4-NC-C_6H_4	2-morpholinoethyl	cyclopropylamino	48
8o	4-NC-C_6H_4	2-(1-methylpyrrolidin-2-yl)ethyl	cyclopropylamino	53
8p	C_6H_5	cyclopropyl	piperonylamino	69
8q	C_6H_5	cyclopropyl	(pyridin-4-ylmethyl)amino	60
8r	4-MeO-C_6H_4	cyclopropyl	(1-benzylpiperidin-4-yl)amino	71
8s	4-MeO-C_6H_4	cyclopropyl	(2-(piperidin-1-yl)ethyl)amino	61
8t	4-Me-C_6H_4	cyclopropyl	(2-morpholinoethyl)amino	49

8u	4-Me-C_6H_4	cyclopropyl	(2-(diethylamino)ethyl)(methyl)amino	34
8v	4-F-C_6H_4	cyclopropyl	morpholino	56
8w	4-F-C_6H_4	cyclopropyl	4-(2-furoyl)piperazin-1-yl	69
8x	4-NC-C_6H_4	cyclopropyl	4-(pyrrolidin-1-yl)piperidin-1-yl	50
8y	4-NC-C_6H_4	cyclopropyl	4-(3-methoxyphenyl)piperazin-1-yl	49

[a]Five-step overall isolated yield from Merrifield resin (loading capacity 1.27 mmol/g).

3. Conclusion

In this work, a solid-phase synthetic method for *N*-alkyl-4-alkylamino-1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide derivatives has been developed. Coupling of 1-aryl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acids with primary alkylamine-loaded AMEBA resins was followed by BOP-mediated amination reactions and subsequent cleavage from the solid support afforded the desired compounds. 1-Aryl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acids were prepared from the condensation reactions of ethyl 5-amino-1-aryl-1*H*-pyrazole-4-carboxylates with methyl cyanoformate, followed by hydrolysis of the resulting esters with lithium hydroxide. The reaction conditions for solid-phase synthesis were optimized by a solution-phase model study using 2,4-dimethoxybenzyl-protected isobutylamine, which was used as a surrogate for the AMEBA resin-loaded isobutylamine. The progress of the solid-phase reactions was monitored by on-bead ATR-FTIR spectroscopy. Diversification experiments were performed by using 1-aryl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acids and a variety of primary and secondary amine building blocks to validate the utility of the established solid-phase synthetic method for the construction of the *N*-alkyl-4-alkylamino-1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide library. The abovementioned results suggest that the synthetic method would be a viable route towards creating structurally more diverse *N*-alkyl-4-alkylamino-1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide derivatives in a high-throughput fashion.

4. Experimental section

4.1. General

Triethylamine was purchased from Junsei. Lithium hydroxide monohydrate was purchased from Fluka. Potassium iodide was purchased from Oriental Chemical Industries. Potassium carbonate was purchased from Duksan Pure Chemical. Merrifield resin was purchased from Bead Tech. Trifluoroacetic acid was purchased from Daejung Chemicals. Sodium chloridee and sodium carbonate anhydrous were purchased from Samchun Chemicals. *p*-Tolyl hydrazine hydrochloride, 4-fluorophenyl hydrazine hydrochloride, (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate, 3*H*-1,2,3-triazolo[4,5-*b*]pyridin-3-ol, 2-(2-methoxyphenyl)ethylamine, 4-(2-aminoethyl)morpholine and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride were purchased from Tokyo Chemical Industry. Benzylamine and sodium triacetoxyborohydride were purchased from Acros Organics. The rest of reagents used were purchased from Sigma-Aldrich. All reagents were used without further purification. Compound **5**[12] was prepared on the basis of previous literature method and were obtained in ^{1}H NMR spectroscopically pure form. AMEBA resin was prepared using a literature method.[15] Most of solvents were purchased from Burdick & Jackson and were HPLC grade. Melting points were measured using a Mettler Toledo FP900 Thermo System. ATR-FTIR spectra were recorded on a IdentifyIR (Smiths Scientific) spectrophotometer. ^{1}H NMR spectra were recorded on a Varian VNMRS 300 or a Bruker Avance 500 spectrophotometer at rt. ^{13}C NMR spectra were recorded on a Bruker Avance 500 spectrophotometer at rt. NMR solvents such as $CDCl_3$ and DMSO-d_6 were purchased from Cambridge Isotope Laboratories, Inc. MS analyses were performed on a Micromass Quattro micro mass spectrometer equipped with PDA (200-400 nm) detection using Acquity UPLC BEH column (C_{18}, 1.7 μm, 2.1 × 50 mm) and typical gradient was 5-95% CH_3CN/H_2O containing 0.1% trifluoroacetic acid. HRMS analyses were performed on a JEOL MStation JMS-700 spectrometer.

4.2. Synthetic procedures

Ethyl 5-amino-1-phenyl-1*H*-pyrazole-4-carboxylate (2a): A mixture of ethyl 2-cyano-3-ethoxyacrylate (3.00 g, 17.7 mmol) and phenyl hydrazine (1.75 mL, 17.7 mmol) in ethanol (75 mL) was stirred at 0 °C for 1 h. Then, the mixture was stirred at 80 °C for 5 h. After cooling the reaction mixture to room temperature, ethanol was removed *in vacuo* and the residue was partitioned between ethyl acetate and water. The organic layer was dried over magnesium sulfate. The solvent was evaporated *in vacuo* and the residue was chromatographed on a silica gel column with a mixture of *n*-hexane and ethyl acetate (6:1) to give the desired product **2a** (3.71 g, 90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.79 (s, 1H), 7.52 (m, 4H), 7.40 (m, 1H), 5.30 (br s, 2H), 4.30 (q, *J*=7.1 Hz, 2H), 1.36 (t, *J*=7.1 Hz, 3H) ppm; MS (ESI): *m/z*: 232 [M+H$^+$].

Ethyl 5-amino-1-(4-methoxyphenyl)-1*H*-pyrazole-4-carboxylate (2b): To ethyl 2-cyano-3-ethoxyacrylate (2.00 g, 11.8 mmol) and 4-methoxyphenyl hydrazine hydrochloride (2.06 g, 11.8 mmol) in ethanol (75 mL) at room temperature was added triethylamine (1.65 mL, 11.8 mmol). The mixture was stirred at 80 °C for 8 h. After cooling the reaction mixture to room temperature, ethanol was removed *in vacuo* and the residue was partitioned between ethyl acetate and water. The organic layer was dried over magnesium sulfate. The solvent was evaporated *in vacuo* and the residue was chromatographed on a silica gel column with a mixture of *n*-hexane and ethyl acetate (3:1) to give the desired product **2b** (2.42 g, 78%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.76 (s, 1H), 7.42 (d, *J*=6.9 Hz, 2H), 7.01 (d, *J*=6.9 Hz, 2H), 5.19 (br s, 2H), 4.30 (q, *J*=7.1 Hz, 2H), 3.82 (s, 3H), 1.36 (t, *J*=7.1 Hz, 3H) ppm; MS (ESI): *m/z*: 262 [M+H$^+$].

Ethyl 5-amino-1-(*p*-tolyl)-1*H*-pyrazole-4-carboxylate (2c): The procedure for **2b** was applied to ethyl 2-cyano-3-ethoxyacrylate (3.00 g, 17.7 mmol) and *p*-tolyl hydrazine hydrochloride (2.81 g, 17.7 mmol). Silica gel column chromatography (a mixture of *n*-hexane and ethyl acetate (2:1)) gave the desired product **2c** (3.69 g, 85 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.77 (s, 1H), 7.40 (d, *J*=8.0 Hz, 2H), 7.30 (d, *J*=8.0 Hz, 2H), 5.25 (br s, 2H), 4.30 (q, *J*=7.1 Hz, 2H), 2.41 (s, 3H), 1.36 (t, *J*=7.1 Hz, 3H) ppm; MS (ESI): *m/z*: 246 [M+H$^+$].

Ethyl 5-amino-1-(4-fluorophenyl)-1*H*-pyrazole-4-carboxylate (2d): The procedure for **2b** was applied to ethyl 2-cyano-3-ethoxyacrylate (3.00 g, 17.7 mmol) and 4-fluorophenyl hydrazine hydrochloride (2.88 g, 17.7 mmol). Silica gel column chromatography (a mixture of *n*-hexane and ethyl acetate (2:1)) gave the desired product **2d** (2.89 g, 65%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.78 (s, 1H), 7.52 (m, 2H), 7.20 (m, 2H), 5.25 (br s,

2H), 4.30 (q, *J*=7.1 Hz, 2H), 1.36 (t, *J*=7.1 Hz, 3H) ppm; MS (ESI): *m/z*: 250 [*M*+H$^+$].

Ethyl 5-amino-1-(4-cyanophenyl)-1*H*-pyrazole-4-carboxylate (2e): The procedure for **2b** was applied to ethyl 2-cyano-3-ethoxyacrylate (3.00 g, 17.7 mmol) and 4-cyanophenyl hydrazine hydrochloride (3.01 g, 17.7 mmol). Silica gel column chromatography (a mixture of *n*-hexane and ethyl acetate (1:1)) gave the desired product **2e** (3.64 g, 80%)**.** ^{1}H NMR (300 MHz, DMSO-d_6): δ=8.01 (d, *J*=6.9 Hz, 2H), 7.80 (d, *J*=6.9 Hz, 2H), 7.78 (s, 1H), 6.60 (br s, 2H), 4.23 (q, *J*=7.1 Hz, 2H), 1.27 (t, *J*=7.1 Hz, 3H) ppm; MS (ESI): *m/z*: 257 [*M*+H$^+$].

Methyl 1-phenyl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylate (3a): To ethyl 5-amino-1-phenyl-1*H*-pyrazole-4-carboxylate (**2a**, 1.60 g, 6.92 mmol) in 4N HCl in 1,4-dioxane (35 mL) at room temperature was added methyl cyanoformate (1.77 g, 20.8 mmol). The mixture was stirred at 100 °C for 14 h and was cooled to room temperature. After 1,4-dioxane was removed *in vacuo* and the residue was partitioned between methylene chloride and water. The organic layer was dried over magnesium sulfate and was evaporated *in vacuo*. The residue was chromatographed on a silica gel column with a mixture of methylene chloride and ethyl acetate (7:1) to give the desired product **3a (**1.47 g, 78%). m.p. 235.9 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=10.40 (br s, 1H), 8.35 (s, 1H), 8.06 (d, *J*= 7.7Hz, 2H), 7.55 (t, *J*= 7.5 Hz, 2H), 7.40 (t, *J*=7.5 Hz, 1H), 4.09 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=160.6, 157.1, 150.9, 144.1, 138.2, 136.4, 129.3, 127.8, 122.3, 108.9, 54.5 ppm; IR (ATR, neat): ν=3071, 2943, 1732, 1670, 1597, 1576, 1508, 1492, 1444, 1399, 1294, 1205, 1114, 1111, 1093, 1007, 967, 869, 778, 688 cm^{-1} ; MS (ESI): *m/z*: 271 [*M*+H$^+$]; HRMS (EI): *m/z* calcd for $C_{13}H_{10}N_4O_3$: 270.0753 [*M*$^+$]; found: 270.0753.

Methyl 1-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylate (3b): The procedure for **3a** was applied to ethyl 5-amino-1-(4-methoxyphenyl)-1*H*-pyrazole-4-carboxylate (**2b**, 2.36 g, 9.03 mmol). Silica gel column chromatography (a mixture of methylene chloride and ethyl acetate (7:1)) gave the desired product **3b** (1.97 g, 72%). m.p. 184.7 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=10.01 (br s, 1H), 8.31 (s, 1H), 7.92 (d, *J*=8.9 Hz, 2H), 7.05 (d, *J*=8.9 Hz, 2H), 4.07 (s, 3H), 3.87 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ= 160.6, 159.1, 157.2, 150.5, 144.0, 136.0, 131.3, 123.9, 114.4, 108.5, 55.6, 54.4 ppm; IR (ATR, neat): ν=3383, 3236, 2959, 1734,1708, 1678, 1578, 1535, 1511, 1443, 1431, 1305, 1256, 1206, 1084, 972, 830, 774, 659 cm^{-1}; MS (ESI): *m/z*: 301 [*M*+H$^+$]; HRMS (EI): *m/z* calcd for $C_{14}H_{12}N_4O_4$: 300.0859 [*M*$^+$]; found: 300.0828.

Methyl 1-(*p*-tolyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylate (3c): The procedure for **3a** was applied to ethyl 5-amino-1-(*p*-tolyl)-1*H*-pyrazole-4-carboxylate (**2c**, 2.90 g, 11.8 mmol). Silica gel column chromatography (a mixture of *n*-hexane and ethyl acetate (2:1)) gave the desired product **3c** (1.43 g, 43%). m.p. > 375 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6): δ=10.02-9.93 (br s, 1H), 8.32 (s, 1H), 7.91 (d, *J*=8.4 Hz, 2H), 7.34 (d, *J*=8.4 Hz, 2H), 4.08 (s, 3H), 2.42 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=160.6, 156.8, 150.6, 143.8, 137.9, 136.2, 135.6, 129.9, 122.3, 108.7, 54.5, 21.1 ppm; IR (ATR, neat): ν=3355, 3267, 2957, 1758, 1742, 1674, 1577, 1534, 1509, 1428, 1400, 1288, 1212, 1150, 1123, 1081, 1002, 968, 891, 810, 774, 677 cm^{-1}; MS (ESI): *m/z*: 285 [*M*+H$^+$]; HRMS (EI): *m/z* calcd for $C_{14}H_{12}N_4O_3$: 284.0909 [*M*$^+$]; found: 284.0904.

Methyl 1-(4-fluorophenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylate (3d): The procedure for **3a** was applied to ethyl 5-amino-1-(4-fluorophenyl)-1*H*-pyrazole-4-carboxylate carboxylate (**2d**, 3.00 g, 12.1 mmol). Silica gel column chromatography (a mixture of methylene chloride and ethyl acetate (7:1)) gave the desired product **3d** (2.45 g, 71%). m.p. 247.5 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6): δ=12.86 (br s, 1H), 8.43 (s, 1H), 8.03 (dd, *J*=4.9, 9.1 Hz, 2H), 7.44 (m, 2H), 3.93 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ=161.4 (d, *J*=230.1 Hz), 157.5, 151.3, 149.4, 146.8, 136.7, 134.8, 124.7 (d, *J*=8.6 Hz), 116.7 (d, *J*=23.1 Hz), 108.8, 54.2 ppm; IR (ATR, neat): ν=3066, 2953, 1735, 1677, 1577, 1507, 1448, 1401, 1304, 1215, 1159, 1147, 1110, 1178, 1007, 968, 884, 837, 776, 686 cm^{-1}; MS (ESI): *m/z*: 289 [*M*+H$^+$]; HRMS (EI): *m/z* calcd for $C_{13}H_9FN_4O_3$: 288.0659 [*M*$^+$]; found: 288.0658.

Methyl 1-(4-cyanophenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylate (3e): The procedure for **3a** was applied to ethyl 5-amino-1-(4-cyanophenyl)-1*H*-pyrazole-4-carboxylate (**2e**, 3.50 g, 13.658 mmol). Silica gel column chromatography (a mixture of methylene chloride and ethyl acetate (6:1)) gave the desired product **3e** (3.58 g, 88%). m.p. 280.7 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6): δ=13.03 (br s, 1H), 8.52 (s, 1H), 8.34 (d, *J*=8.8 Hz, 2H), 8.09 (d, *J*=8.8 Hz, 2H), 3.96 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ=160.5, 157.2, 152.5, 149.6, 147.8, 142.1, 137.6, 134.1, 122.6, 118.5, 110.1, 54.0 ppm; IR (ATR, neat): ν= 3055, 1752, 1692, 1604, 1579, 1509, 1438, 1397, 1303, 997, 879, 835, 774, 738, 674, 584, 548 cm^{-1}; MS (ESI): *m/z*: 296 [*M*+H$^+$]; HRMS (EI): *m/z* calcd for $C_{14}H_9N_5O_3$: 295.0705 [*M*$^+$]; found: 295.0706.

1-Phenyl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (4a): To methyl 1-phenyl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylate (**3a**, 2.30 g, 8.51 mmol) in MeOH/water (75 mL/75 mL) at room temperature was added lithium hydroxide monohydrate (893 mg, 21.3 mmol) and the mixture was stirred for 3.5 h at the same temperature. After completion of the reaction, the reaction mixture was adjusted to pH 3-4 by adding 1N hydrochloric acid. The precipitated solid was filtered and washed with water to give the desired product **4a** (1.96 g, 90%). m.p. 326.3 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6): δ=12.59 (br s, 1H), 8.41 (s, 1H), 8.06 (d, *J*=7.6 Hz, 2H), 7.60 (t, *J*=7.6 Hz, 2H), 7.44 (t, *J*=7.6 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ= 161.6, 157.7, 151.6, 148.3, 138.7, 136.6, 129.7, 127.6, 122.4, 108.8 ppm; IR (ATR, neat): ν=3119, 1717, 1635, 1586, 1560, 1540, 1498, 1473, 1459, 1425, 1389, 1337, 1306, 1285, 1198, 1063, 1024, 999, 963, 837, 820, 775, 757, 682 cm^{-1}; MS (ESI): *m/z*: 257 [*M*+H$^+$]; HRMS (EI): *m/z* calcd for $C_{12}H_8N_4O_3$: 256.0596 [*M*$^+$]; found: 256.0594.

1-(4-Methoxyphenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (4b): The procedure for **4a** was applied to methyl 1-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylate (**3b**, 1.91 g, 6.37 mmol) to give the desired product **4b** (1.48 g, 81%). m.p. 301.3 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6): δ=12.51 (br s, 1H), 8.36 (s, 1H), 7.90 (d, *J*=9.1 Hz, 2H), 7.14 (d, *J*=9.1 Hz, 2H), 3.83 (s, 4H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ= 161.6, 158.9, 157.5, 151.1, 147.9, 136.2, 131.6, 124.2, 114.9, 108.4, 55.9 ppm; IR (ATR, neat): ν= 3288, 3116, 3014, 2837, 1694, 1636, 1578, 1540, 1509, 1443, 1301, 1275, 1244, 1198, 1183, 1024, 993, 964, 819, 774, 692, 667 cm^{-1}; MS (ESI): *m/z*: 287 [*M*+H$^+$]; HRMS (EI): *m/z* calcd for $C_{13}H_{10}N_4O_4$: 286.0702 [*M*$^+$]; found: 286.0753.

1-(*p*-Tolyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (4c): The procedure for **4a** was applied to methyl 1-(*p*-tolyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylate (**3c**, 1.39 g, 4.89 mmol) to give the desired product **4c** (1.19 g, 90%). m.p. 301.3 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6): δ=12.56 (br s, 1H), 8.39 (s, 1H), 7.90 (d, *J*= 8.3 Hz, 2H), 7.39 (d, *J*= 8.3 Hz, 2H), 2.39 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ=161.4, 157.5, 151.2, 147.7, 137.4, 136.2,

135.8, 130.0, 122.3, 108.4, 20.9 ppm; IR (ATR, neat): ν=3230, 3111, 2913, 1718, 1537, 1510,1457, 1401, 1300, 1265, 1231, 1196, 1185, 1084, 1027, 997, 965, 946, 879, 827, 813, 790, 776, 671 cm^{-1}; MS (ESI): *m/z*: 271 [*M*+H^+]; HRMS (EI): *m/z* calcd for $C_{13}H_{10}N_4O_4$: 270.0753 [M^+]; found: 270.0754.

1-(4-Fluorophenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (4d): The procedure for **4a** was applied to methyl 1-(4-fluorophenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylate (**3d**, 2.91 g, 1.10 mmol) to give the desired product **4d** (2.24 g, 81%). m.p. 111.2 ^oC; ^1H NMR (300 MHz, DMSO-d_6): δ=12.05 (br s, 1H), 8.37 (s, 1H), 8.11 (dd, *J*=4.9, 9.1 Hz, 2H), 7.44 (m, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ=165.9 (d, *J*= 242.9 Hz), 166.2, 162.2, 156.9, 155.4, 141.3 (d, *J*= 9.3 Hz), 139.8, 129.2, 121.3 (d, *J*= 22.8 Hz), 113.0 ppm; IR (ATR, neat): ν=3152, 3120, 3061, 1700, 1618, 1575, 1506, 1443, 1399, 1381, 1362, 1311, 1278, 1222, 1199, 1160, 1117, 1080, 1013, 997, 964, 876, 835, 805, 776, 728, 692, 673 cm^{-1}; MS (ESI): *m/z*: 275 [*M*+H^+]; HRMS (EI): *m/z* calcd for $C_{12}H_7FN_4O_3$: 274.0502 [M^+]; found: 274.0502.

1-(4-Cyanophenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (4e): The procedure for **4a** was applied to methyl 1-(4-cyanophenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylate (**3e**, 3.10 g, 10.4 mmol) to give the desired product **4e** (2.65 g, 90%). m.p. >375^oC; ^1H NMR (300 MHz, DMSO-d_6): δ=12.62 (br s, 1H), 8.49 (s, 1H), 8.40 (d, *J*= 8.8 Hz, 2H), 8.08 (d, *J*= 8.8 Hz, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ=161.4, 157.3, 152.5, 149.0, 142.0, 137.8, 134.1, 121.7, 121.4, 118.8, 109.5 ppm; IR (ATR, neat): ν= 3102, 3009, 2226, 1707, 1606, 1574, 1537, 1502, 1429, 1397, 1258, 1210, 1186, 1077, 1021, 990, 955, 927, 845, 832, 816, 774, 710, 679 cm^{-1}; MS (ESI): *m/z*: 282 [*M*+H^+]; HRMS (EI): *m/z* calcd for $C_{13}H_7N_5O_3$: 281.0549 [M^+]; found: 281.0550.

***N*-(2,4-Dimethoxybenzyl)-*N*-isobutyl-1-phenyl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxamide (6):** To 1-phenyl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4a**, 650 mg, 0.254 mmol), 3*H*-1,2,3-triazolo[4,5-*b*]pyridin-3-ol (38 mg, 0.28 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (79 mg, 0.51 mmol) in DMF (2 mL) at room temperature was added *N*-(2,4-dimethoxybenzyl)-2-methylpropan-1-amine (57 mg, 0.25 mmol) in DMF (0.5 mL). The resulting mixture was stirred for 8 h at the same temperature. The mixture was partitioned between ethyl acetate and distilled water. The organic layer was dried over magnesium sulfate and was evaporated *in vacuo*. The residue was chromatographed on a silica gel column with a mixture of *n*-hexane and ethyl acetate (1:1) to give the desired product **6** (100 mg, 85%). m.p. 119.2 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ=10.37 and 10.14 (2 br s, 0.3 H and 0.7 H), 8.30(s, 1H), 7.89-7.84 (m, 2H), 7.50 (m, 1H), 7.41-7.33 (m, 2H), 7.22 and 7.01 (2d, *J*= 8.1 Hz, 0.3 H and 0.7 H), 6.47-6.41 (m, 2H), 5.17 and 4.74 (2s, 1.4 H and 0.6 H), 3.93 and 3.28 (2d, *J*= 7.3 Hz, 0.7 H and 1.3 H), 3.82, 3.78 and 3.68 (3s, 6H), 2.14 and 2.04 (2m, 0.7 H and 0.3 H), 0.96 and 0.80 (2d, *J*= 6.5 Hz, 4H and 2H) ppm ; ^{13}C NMR (125 MHz, $CDCl_3$): δ=161.6, 160.8, 158.6, 157.2, 150.8, 149.2, 138.2, 136.4, 130.7, 129.2, 127.8, 127.2, 122.9, 122.0, 116.5, 108.1, 104.2, 98.7, 55.4, 54.8, 53.6, 48.1, 45.8, 27.7, 16.6, 20.2 ppm; IR (ATR, neat): ν=3126, 2961, 2935, 1718, 1632, 1573, 1499, 1459, 1437, 1396, 1289, 1252, 1201, 1154, 1118, 1031, 958, 916, 834, 796, 789, 687 $cm^{-1;}$ MS (ESI): *m/z*: 462 [*M*+H^+]; HRMS (EI): *m/z* calcd for $C_{25}H_{27}N_5O_4$: 461.2063 [M^+]; found: 461.2063.

4-Benzylamino-*N*-(2,4-dimethoxybenzyl)-*N*-isobutyl-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (7): To *N*-(2,4-dimethoxybenzyl)-*N*-isobutyl-1-phenyl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxamide (**6**, 30 mg, 0.065 mmol), in DMF (3 mL) at room temperature were added (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate (38 mg, 0.085 mmol) and *N*,*N*-diisopropylethylamine(43 mg, 0.98 mmol). The mixture was stirred for 15 min at room temperature and benzylamine (14 mg, 0.13 mmol) was added to the mixture. The resulting mixture was stirred for 7 h at the same temperature. The mixture was partitioned between methylene chloride and distilled water. The organic layer was evaporated *in vacuo* and the residue was chromatographed on a silica gel column with a mixture of *n*-hexane and ethyl acetate (1:1) to give the desired product **7** (30 mg, 84%). m.p. 235.8 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ=8.23 and 8.10 (2d, *J*= 8.3 Hz, 0.6H and 1.4H), 8.03 (m, 1H), 7.47-7.35 (m, 2H), 7.32- 7.27 (m, 3H), 7.26-7.23 (m, 3H), 6.46, 6.36 and 6.33 (m,3H), 4.75 (m, 2H), 4.35 (m, 2H), 3.82, 3.80, 3.72 and 3.66 (4s, 6H), 3.28 and 2.91 (2d, *J*= 7.6 Hz, 1.3H and 0.7H), 2.16 and 1.91 (2m, 0.7H and 0.3H), 1.0 and 0.72 (2d, *J*= 6.6 Hz, 4H and 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=168.9, 161.1, 160.2, 160.1, 158.6, 158.1, 138.8,137.6, 129.7, 128.9, 128.8, 128.7, 127.8, 127.7, 127.3, 126.2, 121.3, 117.2, 104.3, 104.1, 98.3, 55.3, 51.0, 46.3, 42.2, 41.9, 29.7, 26.7, 20.1 ppm; IR (ATR, neat): ν=3265, 2956, 2925, 2870, 1683, 1625, 1610, 1597, 1585, 1560, 1502, 1451, 1419, 1345, 1308, 1288, 1285, 1204, 1155, 1031, 958, 917, 838, 801, 755, 509, 682 cm^{-1}; MS (ESI): *m/z*: 551 [*M*+H^+]; HRMS (EI): *m/z* calcd for $C_{32}H_{34}N_6O_3$: 550.2692 [M^+]; found: 550.2686.

4-Benzylamino-*N*-isobutyl-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8a): To 4-benzylamino-*N*-(2,4-dimethoxybenzyl)-*N*-isobutyl-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (50 mg, 0.091 mmol) in methylene chloride (3 mL) at room temperature was added TFA (1 mL) and the reaction mixture was stirred for 3 h. The mixture was evaporated *in vacuo*, was treated with an excess amount of triethylamine in methylene chloride, and was adsorbed on a suitable amount of silica gel. The adsorbate was chromatographed on a silica gel column with a mixture of *n*-hexane and ethyl acetate (1:2) to give the desired product **8a** (33 mg, 91%). m.p. 158.4 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ=8.15 (m, 2H), 8.04 (m, 1H), 7.50 (m, 2H), 7.39-7.31 (m, 6H), 6.34 (br, 1H), 4.91 (d, *J*=5.7 Hz, 2H), 3.32 (t, *J*=6.6 Hz, 2H), 1.96-1.87 (m, 1H), 0.98 (d, *J*=6.7 Hz, 6H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6)): δ=163.5, 157.0, 156.7, 153.9, 139.5, 139.2, 134.3, 129.6, 128.9, 128.3, 127.6, 126.9, 121.4, 102.3, 46.9, 44.1, 28.6, 20.5 ppm; IR (ATR, neat): ν=3499, 3363, 3265, 3205, 3111, 3050, 2954, 2923, 2866, 1659, 1619, 1595, 1561, 1528, 1496, 1452, 1414, 1381, 1350, 1312, 1293, 1263, 1218, 1183, 1139, 1109, 1098, 960, 912, 897, 878, 755, 731, 698 cm^{-1}; MS (ESI): *m/z*: 401 [*M*+H^+]; HRMS (EI): *m/z* calcd for $C_{23}H_{24}N_6O$: 400.2012 [M^+]; found: 400.2007.

Resin 9a (R^1 = isobutyl): To AMEBA resin (200 mg, theoretically 0.221 mmol) in 1,2-dichloroethane (5 mL) at room temperature were added isobutylamine (49 mg, 0.66 mmol) and sodium triacetoxyborohydride (141 mg, 0.663 mmol). The resulting mixture was shaked for 21 h at the same temperature. The resin was filtered and washed with MC (3×10 mL), DMF (3×10 mL), MeOH (3×10 mL), H_2O (3×10 mL), MeOH (3×10 mL), DMF (3×10 mL) and MC (3×10 mL). Drying the resin in a vacuum oven gave the desired resin **9a** (161 mg). IR (ATR, neat): *ν*=3024, 2919, 1603, 1492, 1451, 1419, 1373, 1267, 1195, 1158, 1029, 822, 756, 697 cm^{-1}.

Resin 10a (Ar = C_6H_5, R^1 = isobutyl): To resin **9a** (130 mg, theoretically 0.135 mmol) in DMF (1 mL) at room temperature were added 1-phenyl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4a**, 69 mg, 0.27 mmol), 3*H*-1,2,3-

triazolo[4,5-*b*]pyridin-3-ol (37 mg, 0.27 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (46 mg, 0.30 mmol) in DMF (3 mL**).** The resulting mixture was shaked for 19 h at the same temperature. The resin was filtered and washed with DMF (3×10 mL), MC (3×10 mL) DMF (3×10 mL) and MC (3×10 mL). Drying the resin in a vacuum oven gave the desired resin **10a** (161 mg). IR (ATR, neat): *v*=3025, 2920, 1707, 1685, 1636, 1585, 1559, 1540, 1506, 1492, 1450, 1420, 1287, 1263, 1196, 1159, 1111, 1028, 972, 907, 819, 757, 735, 637 cm^{-1}.

Resin 10b (Ar = 4-MeO-C_6H_4, R^1 = isobutyl): The procedure for **10a** was applied to resin **9a** (170 mg, theoretically 0.177 mmol) using 1-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4b**, 478 mg, 1.58 mmol) to give the desired resin **10b** (182 mg). IR (ATR, neat): *v*=3024, 2921, 1707, 1653, 1636, 1604, 1559, 1541, 1508, 1491, 1449, 1419, 1288, 1248, 1195, 1158, 1113, 1082, 1029, 974, 830, 756, 696 cm^{-1}.

Resin 10c (Ar = 4-Me-C_6H_4, R^1 = isobutyl): The procedure for **10a** was applied to resin **9a** (170 mg, theoretically 0.177 mmol) using 1-(*p*-tolyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4c**, 96 mg, 0.35 mmol) to give the desired resin **10c** (178 mg). IR (ATR, neat): *v*=2919, 1700, 1641, 1584, 1540, 1507, 1491, 1449, 1287, 1195, 1154, 1107, 834, 755, 696 cm^{-1}.

Resin 10d (Ar = 4-F-C_6H_4, R^1 = isobutyl): The procedure for **10a** was applied to resin **9a** (170 mg, theoretically 0.177 mmol) using 1–(4-fluorophenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4d**, 97 mg, 0.35 mmol) to give the desired resin **10d** (183 mg). IR (ATR, neat): *v*=3022, 2920, 1709, 1646, 1606, 1583, 1507, 1491, 1449, 1286, 1195, 1158, 1113, 1028, 838, 757, 696 cm^{-1}.

Resin 10e (Ar = 4-NC-C_6H_4, R^1 = isobutyl): The procedure for **10a** was applied to resin **9a** (170 mg, theoretically 0.177 mmol) using 1-(4-cyanophenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4e**, 100 mg, 0.35 mmol) to give the desired resin **10e** (192 mg). IR (ATR, neat): *v*=3022, 2919, 1701, 1649, 1584, 1507, 1491, 1450, 1287, 1196, 1158, 1113, 1028, 817, 753, 696 cm^{-1}.

Resin 11a (Ar = C_6H_5, R^1 = isobutyl, NR^2R^3 = benzylamino): A mixture of resin **10a** (150 mg, theoretically 0.125 mmol), (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate (111 mg, 0.250 mmol) and *N*,*N*-diisopropylethylamine (138 mg, 0.313 mmol) in DMF (3 mL) was shaked at room temperature, followed by the addition of benzylamine (48 mg, 0.45 mmol) after 1 h. The resulting mixture was shaked for 13 h at the same temperature. The resin was filtered and washed with DMF (3 x 5mL), MC (3 x 5mL) DMF (3 x 5mL) and MC (3 x 10mL). Drying the resin in a vacuum oven to give the desired resin **11a** (132 mg). IR (ATR, neat): *v*=3109, 2922, 1647, 1582, 1560, 1502, 1491, 1450, 1419, 1341, 1286, 1195, 1157, 1112, 1028, 1017, 955, 818, 807, 754, 696 cm^{-1}.

Resin 11b (Ar = 4-MeO-C_6H_4, R^1 = isobutyl, NR^2R^3 = benzylamino): The procedure for **11a** was applied to resin **10b** (160 mg, theoretically 0.130 mmol) using benzylamine (42 mg, 0.37 mmol) to give the desired resin **11b** (163 mg). IR (ATR, neat): *v*=3024, 2921, 1653, 1608, 1565, 1508, 1492, 1450, 1341, 1287, 1196, 1155, 1110, 1082, 1028, 1017, 956, 834, 755, 686 cm^{-1}.

Resin 11c (Ar = 4-Me-C_6H_4, R^1 = isobutyl, NR^2R^3 = benzylamino): The procedure for **11a** was applied to resin **10c** (155 mg, theoretically 0.128 mmol) using benzylamine (41 mg, 0.38 mmol) to give the desired resin **11c** (161 mg). IR (ATR, neat): *v*=3023, 2921, 1602, 1586, 1560, 1507, 1492, 1450, 1340, 1285, 1195, 1157, 1115, 1028, 956, 817, 755, 696 cm^{-1}.

Resin 11d (Ar = 4-F-C_6H_4, R^1 = isobutyl, NR^2R^3 = benzylamino)**:** The procedure for **11a** was applied to resin **10d** (155 mg, theoretically 0.127 mmol) using benzylamine (41 mg, 0.38 mmol) to give the desired resin **11d** (122 mg). IR (ATR, neat): *v*=3023, 2919, 1644, 1601, 1567, 1508, 1492, 1450, 1286, 1195, 1155, 1110, 956, 834, 755, 696 cm^{-1}.

Resin 11e (Ar = 4-NC-C_6H_4, R^1 = isobutyl, NR^2R^3 = benzylamino): The procedure for **11a** was applied to resin **10e** (100 mg, theoretically 0.0659 mmol) using benzylamine (42 mg, 0.39 mmol) to give the desired resin **11e** (102 mg). IR (ATR, neat): *v*=3027, 2927, 1591, 1578, 1507, 1493, 1452, 1380, 1279, 1198, 1159, 1119, 1068, 1025, 951,841, 821, 752, 690 cm^{-1}.

4-(Benzylamino)-*N*-isobutyl-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8a): To resin **11a** (132 mg, theoretically 0.103 mmol) in methylene chloride (3 mL) at room temperature was added TFA (1 mL) and the reaction mixture was shaked for 3 h. The mixture was filtered and washed with methylene chloride. The filtrate was evaporated *in vacuo*, was treated with an excess amount of triethylamine in methylene chloride, and was adsorbed on a suitable amount of silica gel. The adsorbate was chromatographed on a silica gel column with a mixture of *n*-hexane and ethyl acetate (1:2) to give the desired product **8a** (29 mg, 70%).

4-Benzylamino-*N*-isobutyl-1-(4-methoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8b): The procedure for **8a** was applied to resin **11b** (120 mg, theoretically 0.091 mmol). Silica gel column chromatography (a mixture of methylene chloride and ethyl acetate (5:1)) gave the desired product **8b** (28 mg, 71%). m.p. 149.3 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ=8.15 (br s, 1H), 8.04 (t, *J*=5.9 Hz, 2H), 7.97 (d, *J*=8.7 Hz, 2H), 7.33 (m, 4H), 6.96 (d, *J*=8.1 Hz, 2H), 6.76 (br s,1H), 4.86 (d, *J*=5.5 Hz, 2H), 3.83 (s, 3H), 3.30 (t, *J*=6.4 Hz, 2H), 1.90 (m, 1H), 0.97 (d, *J*=6.8 Hz, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=163.7, 158.0, 156.5, 155.2, 153.2, 138.5, 133.2, 132.1, 128.6, 127.5, 123.7, 114.0, 102.3, 55.4, 47.0, 45.0, 29.6, 28.5, 20.3 ppm; IR (ATR, neat): *v*=3352, 3263, 2955, 2919, 2867, 1659, 1608, 1555, 1442, 1385, 1341,1299, 1251, 1211, 1175, 1138, 1087, 961, 908, 835, 812, 777, 718, 689 cm^{-1}; MS (ESI): *m/z*: 431 [M+H^+]; HRMS (EI): *m/z* calcd for $C_{24}H_{26}N_6O_2$: 430.2117 [M^+]; found: 430.2119.

4-Benzylamino-*N*-isobutyl-1-(*p*-tolyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8c): The procedure for **8a** was applied to resin **11c** (95 mg, theoretically 0.073 mmol). Silica gel column chromatography (a mixture of methylene chloride and ethyl acetate (5:1)) gave the desired product **8c** (15 mg, 50%). m.p. 175.6 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ=8.27 (br s, 1H), 8.07 (m, 2H), 7.97 (d, *J*=8.1 Hz, 3H), 7.34 (m, 2H), 7.14 (m, 3H), 6.42 (br s, 1H), 4.85 (d, *J*=5.5 Hz, 2H), 3.31 (q, *J*=6.5 Hz, 2H), 2.38 (s, 3H), 1.90 (m, 1H), 1.00 (d, *J*=6.8 Hz, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=163.6, 157.6, 155.3, 154.8, 153.4, 136.6, 134.3, 133.2, 129.9, 128.5, 127.5, 121.8, 102.2, 47.1, 45.0, 30.9, 28.9, 21.0, 20.2 ppm; IR (ATR, neat): *v*=3379, 3251, 3024, 2956, 2867, 166, 1603, 1554, 1513, 1463, 1428, 1380, 1340, 1248, 1210, 1155, 1139, 1120, 1085, 1019 958, 934, 910, 849, 815, 778, 737, 723, 695 cm^{-1}; MS (ESI): *m/z*: 415 [M+H^+]; HRMS (EI): *m/z* calcd for $C_{24}H_{26}N_6O$: 414.2168 [M^+]; found: 414.2168.

4-Benzylamino-*N*-isobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8d): The procedure

for **8a** was applied to resin **11d** (90 mg, theoretically 0.069 mmol). Silica gel column chromatography (a mixture of methylene chloride and ethyl acetate (3:1)) gave the desired product **8d** (18 mg, 61%). m.p. 160.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.34 (br s, 1H), 8.11 (m, 5H), 7.35 (t, *J*= 6.9 Hz, 1H), 7.15 (m, 4H), 6.47 (br s, 1H), 4.85 (d, *J*= 5.1 Hz, 2H), 3.33 (t, *J*= 6.6 Hz, 2H), 1.95 (m, 1H), 1.00 (d, *J*= 6.7Hz, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=163.4, 161.1 (d, *J*= 243.2 Hz), 158.2, 156.3, 155.6, 153.6, 135.1, 133.9, 132.9, 128.7, 127.4, 123.5 (d, *J*= 7.9 Hz), 115.8 (d, *J*= 22.7 Hz), 102.4, 47.1, 29.7, 28.6, 20.2 ppm; IR (ATR, neat): *v*=3282, 2953, 2921, 2867, 1675, 1613, 1560, 1508, 1463, 1436, 1382, 1346, 1293, 1265, 1217, 1184, 1152, 1105, 1080, 1029, 1012, 959, 903, 833, 777, 698, 670 cm^{-1}; MS (ESI): *m/z*: 419 [*M*+H$^+$]; HRMS (EI): *m/z* calcd for $C_{23}H_{23}FN_6O$: 418.1917 [*M*$^+$]; found: 418.1920.

4-Benzylamino-1-(4-cyanophenyl)-*N*-isobutyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8e): The procedure for **8a** was applied to resin **11e** (88 mg, theoretically 0.067 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (30:1)) gave the desired product **8e** (18 mg, 63%). m.p. 132.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.51, (d, *J*= 6.7 Hz, 3H), 8.34 (d, *J*= 8.6 Hz, 1H), 8.11 (m, 2H), 7.76 (d, *J*= 8.3 Hz, 3H), 7.32 (m, 2H), 6.48 (br s, 1H), 4.87 (d, *J*= 5.5 Hz, 2H), 3.35 (m, 2H), 1.97 (m, 1H), 1.02 (d, *J*= 6.7 Hz, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=163.1, 159.1, 156.0, 154.7, 142.4, 135.1, 133.2, 130.6, 128.7, 127.5, 121.1, 118.6, 109.4, 102.9, 51.5, 47.2, 29.7, 28.6, 20.3 ppm; IR (ATR, neat): *v*=3286, 2955, 2868, 2224, 1675, 1617, 1602, 1557, 1512, 1450, 1431, 1381, 1344, 1317, 1216,1184, 1126, 1115, 1086, 1028, 960, 899, 837, 773, 723, 694, 665 cm^{-1}; MS (ESI): *m/z*: 426 [*M*+H$^+$]; HRMS (EI): *m/z* calcd for $C_{24}H_{23}N_7O$: 425.1964 [*M*$^+$]; found: 425.1962.

Resin 9b (R^1 = piperonyl): The procedure for **9a** was applied to AMEBA resin (200 mg, theoretically 0.221 mmol) using piperonylamine (100 mg, 0.663 mmol) to give the desired resin **9b** (182 mg). IR (ATR, neat): *v*=3022, 2918, 1586, 1489, 1449, 1378, 1283, 1245, 1194, 1156, 1128, 1035, 928, 815, 755, 696 cm^{-1}.

Resin 9c (R^1 = (4-methoxycarbonyl)benzyl): The procedure for **9a** was applied to AMEBA resin (200 mg, theoretically 0.221 mmol) using methyl 4-(aminomethyl)benzoate hydrochloride (134 mg, 0.663 mmol), sodium triacetoxyborohydride (141 mg, 0.663 mmol) and triethylamine (67 mg, 0.66 mmol) to give the desired resin **9c** (172 mg). IR (ATR, neat): *v*=3023, 2918, 1717, 1608, 1504, 1491, 1449, 1275, 1191, 1156, 1107, 1017, 814, 752, 696 cm^{-1}.

Resin 9d (R^1 = pyridine-4-ylmethyl): The procedure for **9a** was applied to AMEBA resin (200 mg, theoretically 0.221 mmol) using 4-(aminomethyl)pyridine (72 mg, 0.66 mmol) to give the desired resin **9d** (174 mg). IR (ATR, neat): *v*=3022, 2916, 1599, 1558, 1504, 1491, 1449, 1412, 1373, 1363, 1283, 1194, 1156, 1128, 1114, 1028, 1017, 907, 918, 754, 695, 669 cm^{-1}.

Resin 9e (R^1 = 2-methoxyphenethyl): The procedure for **9a** was applied to AMEBA resin (200 mg, theoretically 0.221 mmol) using 2-(2-methoxyphenyl)ethanamine (100 mg, 0.663 mmol) to give the desired resin **9e** (173 mg). IR (ATR, neat): *v*=3023, 2921, 1602, 1587, 1507, 1491, 1450, 1418, 1374, 1259, 1235, 1194, 1154, 1028, 818, 756, 696 cm^{-1}.

Resin 9f (R^1 = 3,4-dimethoxyphenethyl): The procedure for **9a** was applied to AMEBA resin (200 mg, theoretically 0.221 mmol) using 3,4-dimethoxyphenethylamine (120 mg, 0.663 mmol) to give the desired resin **9f** (168 mg). IR (ATR, neat): *v*=3022, 2917, 1602, 1586, 1507, 1491, 1449, 1418, 1373, 1259, 1235, 1194, 1154, 1027, 818, 756, 696 cm^{-1}.

Resin 9g (R^1 = 2-(thiophen-2-yl)ethyl): The procedure for **9a** was applied to AMEBA resin (200 mg, theoretically 0.221 mmol) using 2-thiopheneethylamine (84 mg, 0.66 mmol) to give the desired resin **9g** (182 mg). IR (ATR, neat): *v*=3023, 2916, 1603, 1586, 1491, 1449, 1361, 1283, 1255, 1194, 1155, 1028, 819, 754, 695 cm^{-1}.

Resin 9h (R^1 = 2-(pyrrolidin-1-yl)ethyl): The procedure for **9a** was applied to AMEBA resin (200 mg, theoretically 0.221 mmol) using 1-(2-aminoethyl)pyrrolidine (76 mg, 0.66 mmol) to give the desired resin **9h** (176 mg). IR (ATR, neat): *v*=3023, 2919, 1602, 1586, 1491, 1450, 1419, 1368, 1283, 1194, 1154, 1208, 818, 755, 696 cm^{-1}.

Resin 9i (R^1 = 2-(piperidin-1-yl)ethyl): The procedure for **9a** was applied to AMEBA resin (200 mg, theoretically 0.221 mmol) using 1-(2-aminoethyl)piperidine (85 mg, 0.66 mmol) to give the desired resin **9i** (186 mg). IR (ATR, neat): *v*=3022, 2919, 1605, 1586, 1504, 1491, 1450, 1282, 1194, 1155, 1133, 1028, 817, 755, 696 cm^{-1}.

Resin 9j (R^1 = 2-morpholinoethyl): The procedure for **9a** was applied to AMEBA resin (200 mg, theoretically 0.221 mmol) using 4-(2-aminoethyl)morpholine (86 mg, 0.66 mmol) to give the desired resin **9j** (174 mg). IR (ATR, neat): *v*=3022, 2919, 1602, 1586, 1491, 1450, 1369, 1283, 1194, 1155, 1116, 1023, 912, 820, 755, 696 cm^{-1}.

Resin 9k (R^1 = 2-(1-methylpyrrolidin-2-yl)ethyl): The procedure for **9a** was applied to AMEBA resin (200 mg, theoretically 0.221 mmol) using 2-(2-aminoethyl)-1-methylpyrrolidine (85 mg, 0.66 mmol) to give the desired resin **9k** (181 mg). IR (ATR, neat): *v*=3023, 2918, 1602, 1586, 1505, 1491, 1450, 1419, 1368, 1283, 1194, 1155, 1130, 1028, 819, 755, 696 cm^{-1}.

Resin 10f (Ar = C_6H_5, R^1 = piperonyl): The procedure for **10a** was applied to resin **9b** (145 mg, theoretically 0.14 mmol) using 1-phenyl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4a**, 38 mg, 0.28 mmol) to give the desired resin **10f** (161 mg). IR (ATR, neat): *v*=3022, 2920, 1710, 1644, 1589, 1541, 1500, 1490, 1448, 1420, 1286, 1242, 1195, 1158, 1111, 1032, 976, 957, 927, 817, 755, 696 cm^{-1}.

Resin 10g (Ar = C_6H_5, R^1 = (4-methoxycarbonyl)benzyl): The procedure for **10a** was applied to resin **9c** (140 mg, theoretically 0.133 mmol) using 1-phenyl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4a**, 60 mg, 0.266 mmol) to give the desired resin **10g** (159 mg). IR (ATR, neat): *v*=3024, 2919, 1714, 1644, 1584, 1492, 1450, 1419, 1276, 1194, 1158, 1106, 1018, 976, 946, 824, 753, 696 cm^{-1}.

Resin 10h (Ar = 4-MeO-C_6H_4, R^1 = pyridine-4-ylmethyl): The procedure for **10a** was applied to resin **9d** (140 mg, theoretically 0.141 mmol) using 1-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4b**, 81 mg, 0.28 mmol) to give the desired resin **10h** (149 mg). IR (ATR, neat): *v*=3023, 2913, 1704, 1639, 1585, 1507, 1491, 1448, 1412, 1288, 1248, 1195, 1159, 1113, 1028, 977, 829, 755, 696 cm^{-1}.

Resin 10i (Ar = 4-MeO-C_6H_4, R^1 = 2-methoxyphenethyl): The procedure for **10a** was applied to resin **9e** (140 mg, theoretically 0.135 mmol) using 1-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4b**, 77 mg, 0.27 mmol) to give the desired resin **12i** (1.22 g). IR (ATR, neat): *v*=3023, 2918, 1709, 1636, 1584, 1508, 1491, 1449, 1287, 1244, 1194, 1157, 1113, 1028, 970, 829, 751, 696 cm^{-1}.

Resin 10j (Ar = 4-Me-C_6H_4, R^1 = 3,4-dimethoxyphenethyl): The procedure for **10a** was applied to resin **9f** (136 mg, theoretically 0.127 mmol) using 1-(*p*-tolyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4c**, 69 mg, 0.25 mmol) to give the desired resin **10j** (138 mg). IR (ATR, neat): *v*=3022, 2919, 1706, 1639, 1584, 1508, 1491, 1449, 1419, 1261, 1236, 1195, 1156, 1027, 817, 750, 696 cm^{-1}.

Resin 10k (Ar = 4-Me-C_6H_4, R^1 = 2-(thiophen-2-yl)ethyl): The procedure for **10a** was applied to resin **9g** (142 mg, theoretically 0.140 mmol) using 1-(*p*-tolyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4c**, 76 mg, 0.28 mmol) to give the desired resin **10k** (151 mg). IR (ATR, neat): *v*=3022, 2918, 1706, 1636, 1610, 1583, 1507, 1491, 1449, 1286, 1261, 1194, 1158, 1113, 1028, 959, 917, 756, 695 cm^{-1}.

Resin 10l (Ar = 4-F-C_6H_4, R^1 = 2-(pyrrolidin-1-yl)ethyl): The procedure for **10a** was applied to resin **9h** (140 mg, theoretically 0.140 mmol) using 1-(4-fluorophenyl)-4,5-dihydro-1*H*-pyrazolo[3,4,-*d*]pyrimidin-4-one-6-carboxylic acid (**4d**, 77 mg, 0.27 mmol) to give the desired resin **10l** (158 mg). IR (ATR, neat): *v*=3022, 2919, 2162, 1701, 1649, 1584, 1541, 1508, 1491, 1449, 1288, 1221, 1195, 1155, 118, 1028, 834, 756, 696 cm^{-1}.

Resin 10m (Ar= 4-F-C_6H_4, R^1 = 2-(piperidin-1-yl)ethyl): The procedure for **10a** was applied to resin **9i** (150 mg, theoretically 0.148 mmol) using 1-(4-fluorophenyl)-4,5-dihydro-1*H*-pyrazolo[3,4,-*d*]pyrimidin-4-one-6-carboxylic acid (**4d**, 81 mg, 0.30 mmol) to give the desired resin **10m** (161 mg). IR (ATR, neat): *v*=3023, 2921, 1697, 1644, 1584, 1508, 1491, 1450, 1289, 1222, 1196, 1155, 1109, 1028, 834, 755, 696 cm^{-1}.

Resin 10n (Ar = 4-NC-C_6H_4, R^1 = 2-morpholinoethyl): The procedure for **10a** was applied to resin **9j** (140 mg, theoretically 0.138 mmol) using 1-(4-cyanophenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4e**, 72 mg, 0.28 mmol) to give the desired resin **10n** (157 mg). IR (ATR, neat): *v*=3022, 2920, 2225, 1702, 1649, 1606, 1583, 1507, 1492, 1450, 1430, 1395, 1286, 1196, 1158, 1114, 1028, 970, 907, 834, 757, 696 cm^{-1}.

Resin 10o (Ar = 4-NC-C_6H_4, R^1 = 2-(1-methylpyrrolidin-2-yl)ethyl): The procedure for **10a** was applied to resin **9k** (145 mg, theoretically 0.143 mmol) using 1-(4-cyanophenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4e**, 80 mg, 0.29 mmol) to give the desired resin **10o** (136 mg). IR (ATR, neat): *v*=3022, 2917, 2225, 1701, 1639, 1605, 1584, 1507, 1491, 1449, 1431, 1286, 1196, 1158, 1114, 1028, 961, 837, 756, 696 cm^{-1}.

Resin 11f (Ar = C_6H_5, R^1 = piperonyl, NR^2R^3 = cyclopropylamino): The procedure for **11a** was applied to resin **10f** (130 mg, theoretically 0.102 mmol) using cyclopropylamine (18 mg, 0.31 mmol) to give the desired resin **11f** (112 mg). IR (ATR, neat): *v*=3022, 2919, 1583, 1560, 1500, 1489, 1448, 1420, 134, 1242, 1194, 1157, 1114, 1031, 927, 805, 754, 696 cm^{-1}.

Resin 11g (Ar = C_6H_5, R^1 = (4-methoxycarbonyl)benzyl, NR^2R^3 = cyclopropylamino): The procedure for **11a** was applied to resin **10g** (130 mg, theoretically 0.101 mmol) using cyclopropylamine (17 mg, 0.30 mmol) to give the desired resin **11g** (117 mg). IR (ATR, neat): *v*=3022, 2923, 1718, 1591, 1560, 1502, 1491, 1450, 1419, 1347, 1276, 1194, 1159, 1107, 1018, 945, 754, 696 cm^{-1}.

Resin 11h (Ar = 4-MeO-C_6H_4, R^1 = pyridine-4-ylmethyl, NR^2R^3 = cyclopropylamino): The procedure for **11a** was applied to resin **10h** (120 mg, theoretically 0.0949 mmol) using cyclopropylamine (16 mg, 0.29 mmol) to give the desired resin **11h** (115 mg). IR (ATR, neat): *v*=3023, 2919, 1639, 1584, 1560, 1509, 1491, 1450, 1414, 1341, 1247, 1194, 1161, 1114, 1080, 1028, 977, 942, 830, 755, 696 cm^{-1}.

Resin 11i (Ar = 4-MeO-C_6H_4, R^1 = 2-methoxyphenethyl, NR^2R^3 = cyclopropylamino): The procedure for **11a** was applied to resin **10i** (117 mg, theoretically 0.0896 mmol) using cyclopropylamine (15 mg, 0.27 mmol) to give the desired resin **11i** (108 mg). IR (ATR, neat): *v*=3023, 2917, 1641, 1584, 1560, 158, 1491, 145, 1339, 1288, 1243, 1157, 1114, 1080, 1028, 953, 829, 750, 696 cm^{-1}.

Resin 11j (Ar = 4-Me-C_6H_4, R^1 = 3,4-dimethoxyphenethyl, NR^2R^3 = cyclopropylamino): The procedure for **11a** was applied to resin **10j** (110 mg, theoretically 0.0833 mmol) using cyclopropylamine (14 mg, 0.25 mmol) to give the desired resin **11j** (111 mg). IR (ATR, neat): *v*=3023, 2918, 1646, 1585, 1560, 158, 1491, 1449, 1419, 1340, 1260, 1235, 1194, 1154, 1121, 1027, 954, 817,755, 696 cm^{-1}.

Resin 11k (Ar = 4-Me-C_6H_4, R^1 = 2-(thiophen-2-yl)ethyl, NR^2R^3 = cyclopropylamino): The procedure for **11a** was applied to resin **10k** (130 mg, theoretically 0.103 mmol) using cyclopropylamine (18 mg, 0.31 mmol) to give the desired resin **11k** (119 mg). IR (ATR, neat): *v*=3023, 2919, 1644, 1583, 1559, 1507, 1491, 1449, 1419, 1340, 1286, 1194, 1157, 1113, 1028, 817, 755, 695 cm^{-1}.

Resin 11l (Ar = 4-F-C_6H_4, R^1 = 2-(pyrrolidin-1-yl)ethyl, NR^2R^3 = cyclopropylamino): The procedure for **11a** was applied to resin **10l** (130 mg, theoretically 0.103 mmol) using cyclopropylamine (18 mg, 0.31 mmol) to give the desired resin **11l** (125 mg). IR (ATR, neat): *v*=3022, 2917, 1641, 1583, 1507, 1491, 1449, 1340, 1287, 1194, 1154, 1114, 1018, 937, 834, 753, 696 cm^{-1}.

Resin 11m (Ar= 4-F-C_6H_4, R^1 = 2-(piperidin-1-yl)ethyl, NR^2R^3 = cyclopropylamino): The procedure for **11a** was applied to resin **10m** (135 mg, theoretically 0.106 mmol) using cyclopropylamine (18 mg, 0.31 mmol) to give the desired resin **11m** (128 mg). IR (ATR, neat): *v*=3025, 2923, 1639, 1584, 1508, 1491, 1449, 1340, 1287, 1195, 1154, 1115, 1028, 834, 754, 696 cm^{-1}.

Resin 11n (Ar = 4-NC-C_6H_4, R^1 = 2-morpholinoethyl, NR^2R^3 = cyclopropylamino): The procedure for **11a** was applied to resin **10n** (130 mg, theoretically 0.102 mmol) using cyclopropylamine (17 mg, 0.31 mmol) to give the desired resin **11n** (129 mg). IR (ATR, neat): *v*=3022, 2915, 2222, 1641, 1584, 1560, 1507, 1491, 1449, 1340, 1284, 1194, 1156, 1114, 1069, 1028, 839, 755, 696 cm^{-1}.

Resin 11o (Ar = 4-NC-C_6H_4, R^1 = 2-(1-methylpyrrolidin-2-yl)ethyl, NR^2R^3 = cyclopropylamino): The procedure for **11a** was applied to resin **10o** (130 mg, theoretically 0.102 mmol) using cyclopropylamine (17 mg, 0.31 mmol) to give the desired resin **11o** (128 mg). IR (ATR, neat): *v*=3022, 2922, 2225, 1600, 1586, 1507, 1491, 1449, 1343, 1280, 1195, 1157, 1114, 1023, 937, 838, 755, 696 cm^{-1}.

4-Cyclopropylamino-1-phenyl-*N*-piperonyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8f): The procedure for **8a** was applied to resin **11f** (90 mg, theoretically 0.068 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (30:1)) gave the desired product **8f** (21 mg, 72%). m.p. 358.6 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ=8.43 (s, 1H), 8.19 (br s, 1H), 8.12 (d, *J*=8.0 Hz, 2H), 7.52 (t, *J*=7.7 Hz, 2H), 7.35 (t, *J*=7.3 Hz, 1H), 6.81 (m, 3H), 6.36 (s, 1H), 5.94 (s, 2H), 4.59 (d, *J*=6.1 Hz, 2H), 3.03 (m, 1H), 1.07 (d, *J*=6.0 Hz, 2H), 0.80 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=163.0, 155.2, 154.1, 147.9, 147.0, 138.7, 134.8, 132.1, 129.2, 128.8, 126.8, 121.9, 121.0, 108.4, 108.3, 101.7, 101.1, 43.6, 25.2, 9.2 ppm; IR (ATR, neat): *v*=3383, 3263, 3071, 2952, 2911, 2979,1725, 1670, 1559, 1517, 1450, 1487, 1441, 1412, 1363, 1335, 1313, 1245, 1213,

1190, 1130, 1103, 1093, 1034, 972, 957, 926, 860, 824, 780, 755, 812, 685 cm^{-1}; MS (ESI): *m/z*: 429 [*M*+H^+]; HRMS (EI): *m/z* calcd for $C_{23}H_{20}N_6O_3$: 428.1597 [M^+]; found: 428.1596.

4-Cyclopropylamino-*N*-((4-methoxycarbonyl)benzyl)-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8g): The procedure for **8a** was applied to resin **11g** (90 mg, theoretically 0.068 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (30:1)) gave the desired product **8g** (23 mg, 77%). m.p. 228.3 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ=8.44 (s, 1H), 8.31 (s, 1H), 8.12 (d, *J*=8.1 2H), 8.00 (d, *J*=8.1 Hz, 2H),7.51 (t, *J*=7.8 Hz, 2H), 7.43 (d, *J*=8.1 Hz, 2H), 7.35 (t, *J*=7.4 Hz, 1H), 6.38 (s, 1H), 4.75 (d, *J*=6.2 Hz, 2H), 3.91 (s, 3H), 1.27 (m, 1H), 1.08 (m, 2H), 0.82 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=166.8, 166.6, 163.2, 155.0, 154.0, 150.7, 150.2, 143.4, 138.7, 130.0, 129.2, 127.5, 127.0, 122.0, 101.9, 52.1, 43.4, 25.2, 9.3 ppm; IR (ATR, neat): *v*=3305, 3118, 2999, 2949, 2098, 1704, 1664, 1586, 1572, 1540, 1501, 1460, 1418, 1405, 1363, 1343, 1295, 1280, 1225, 1195, 1177, 1114, 1093, 1062, 1031, 975, 941, 907, 749, 712, 695 cm^{-1}; MS (ESI): *m/z*: 443 [*M*+H^+]; HRMS (EI): *m/z* calcd for $C_{24}H_{22}N_6O_3$: 442.1753 [M^+]; found: 442.1754.

4-Cyclopropylamino-1-(4-methoxyphenyl)-*N*-(pyridine-4-ylmethyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8h): The procedure for **8a** was applied to resin **11h** (86 mg, theoretically 0.066 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (20:1)) gave the desired product **8h** (21 mg, 76%). m.p. 118.8 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ=8.56 (d, *J*=4.7 Hz, 2H), 8.41 (s, 1H), 8.34 (m, 2H), 7.95 (d, *J*=8.6 Hz, 2H), 7.04 (d, *J*=8.6 Hz, 2H), 6.39 (s, 1H), 4.70 (d, *J*=6.3 Hz, 2H), 3.87 (s, 3H), 3.04 (s, 1H), 1.26 (m, 1H), 1.08 (m, 2H), 0.85 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=163.6, 159.8, 158.5, 154.7, 153.6, 150.0, 147.3, 134.5, 131.8, 123.7, 122.3, 114.4, 101.5, 55.6, 42.6, 25.2, 9.2 ppm; IR (ATR, neat): *v*=3269, 2923, 1734, 1672, 1586, 1560, 1509, 1455, 1440, 1413, 1342, 1299, 1244, 1171, 1112, 1084, 1024, 973, 952, 940, 828, 777, 731, 684 cm^{-1}; MS (ESI): *m/z*: 416 [*M*+H^+]; HRMS (EI): *m/z* calcd for $C_{22}H_{21}N_7O_2$: 415.1757 [M^+]; found: 415.1755.

4-Cyclopropylamino-*N*-(2-methoxyphenethyl)-1-(4-methoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8i): The procedure for **8a** was applied to resin **11i** (73 mg, theoretically 0.056 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (20:1)) gave the desired product **8i** (12 mg, 51%). m.p. 147.2 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ=8.13 (s, 1H), 7.98 (d, *J*=8.9 Hz, 3H), 7.52 (br s, 1H), 7.20 (t, *J*=7.6 Hz, 2H), 7.01 (d, *J*=9.0 Hz, 2H), 6.87 (t, *J*=8.0 Hz, 2H), 3.88 (s, 3H), 3.77 (s, 3H), 3.72 (t, *J*=6.7 Hz, 2H), 2.95 (t, *J*=6.6 Hz, 2H), 1.66 (m, 1H), 1.25 (m, 2H), 0.85 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=163.1, 159.8, 158.3, 157.6, 155.4, 153.6, 134.4, 132.0, 130.6, 127.8, 127.4, 123.5, 120.5, 114.3, 110.3, 101.4, 55.6, 39.7, 34.5, 30.3, 22.7, 14.9 ppm; IR (ATR, neat): *v*=3267, 2922, 1734, 1670, 1610, 1586, 1560, 1509, 1458, 1438, 1379, 1342, 1299, 1241, 1171, 1118, 1085, 1027, 954, 875, 854, 829, 777, 751, 684, 660 cm^{-1}; MS (ESI): *m/z*: 459 [*M*+H^+]; HRMS (EI): *m/z* calcd for $C_{25}H_{26}N_6O_3$: 458.2066 [M^+]; found: 458.2068.

4-Cyclopropylamino-*N*-(3,4-dimethoxyphenethyl)-1-(*p*-tolyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8j): The procedure for **8a** was applied to resin **11j** (75 mg, theoretically 0.055 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (30:1)) gave the desired product **8j** (14 mg, 55%). m.p. 81.3 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ=8.40 (s, 1H), 7.98 (m, 1H), 7.90 (d, *J*=8.3 Hz, 2H), 7.29 (d, *J*=8.3 Hz, 2H), 6.79 (t, *J*=8.2 Hz, 3H), 6.79 (br s, 1H), 3.86 (s, 3H), 3.81 (s, 3H), 3.73 (q, *J*=6.6 Hz, 2H), 2.87 (t, *J*= 6.7 Hz, 2H), 2.44 (s, 3H), 1.28 (m, 1H), 1.06 (m, 2H), 0.81 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=163.1, 155.1, 153.7, 149.0, 147.7, 136.8, 136.2, 136.2, 135.2, 131.5, 129.7, 121.8, 120.7, 112.0, 111.3, 101.3, 55.9, 41.0, 35.3, 29.7, 25.2, 21.1, 9.2 ppm; IR (ATR, neat): *v*=2921, 2852, 1734, 1670, 1587, 1560, 1510, 1457, 1418, 1375, 1342, 1259, 1235, 1191, 1155, 1139, 1084, 1026, 954, 908, 879, 854, 816, 777, 763, 686, 662 cm^{-1}; MS (ESI): *m/z*: 473 [*M*+H^+]; HRMS (EI): *m/z* calcd for $C_{26}H_{28}N_6O_3$: 472.2223 [M^+]; found: 472.2209.

4-Cyclopropylamino-*N*-(2-(thiophen-2-yl)ethyl)-1-(*p*-tolyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8k): The procedure for **8a** was applied to resin **11k** (99 mg, theoretically 0.13 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (30:1)) gave the desired product **8k** (12 mg, 31%). m.p. 145.1 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ=8.40 (s, 1H), 8.12 (br s, 1H), 7.93 (d, *J*=8.3 Hz, 2H), 7.31 (d, *J*=8.3 Hz, 2H), 7.18 (d, *J*=5.0 Hz, 1H), 6.95 (t, *J*=3.6 Hz, 1H), 6.90 (d, *J*=3.2 Hz, 1H), 6.53 (br s, 1H), 3.76 (q, *J*= 6.4 Hz, 2H), 3.16 (t, *J*=6.5 Hz, 2H), 2.44 (s, 3H), 1.28 (m, 1H), 1.06 (m, 2H), 0.82 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=163.1, 160.0, 155.0, 153.7, 141.4, 136.7, 136.3, 134.6, 129.7, 127.1, 125.5, 123.9, 121.9, 101.6, 41.0, 30.2, 21.1, 14.1, 9.2 ppm; IR (ATR, neat): *v*=3276, 2951, 2919, 2851, 1734, 1673, 1588, 1560, 1513, 1456, 1433, 1362, 1345, 1292, 1242, 1181, 1122, 1081, 1022, 972, 954, 870, 849, 816, 778, 691, 663 cm^{-1}; MS (ESI): *m/z*: 419 [*M*+H^+]; HRMS (EI): *m/z* calcd for $C_{22}H_{22}N_6OS$: 418.1576 [M^+]; found: 418.0734.

4-Cyclopropylamino-1-(4-fluorophenyl)-*N*-(2-(pyrrolidin-1-yl)ethyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8l): The procedure for **8a** was applied to resin **11l** (134 mg, theoretically 0.103 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (10:1)) gave the desired product **8l** (19 mg, 45%). m.p. 74.6 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ=9.13-8.93 (br s, 1H), 8.40 (s, 1H), 8.20 (m, 2H), 7.20 (m, 2H), 3.84 (m, 2H), 3.50 (m, 2H), 3.25 (m, 4H), 2.99 (br s, 1H), 2.04 (m, 4H), 1.25 (m, 1H), 1.06 (m, 2H), 0.84 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=164.4, 163.0, 161.2 (d, *J*= 243.9 Hz), 157.5, 154.4, 135.0, 134.5, 123.6 (d, *J*= 8.4 Hz), 115.9 (d, *J*= 21.7 Hz), 101.7, 54.8, 31.6, 25.2, 23.3, 14.1, 9.0 ppm; IR (ATR, neat): *v*=3259, 2921, 2850, 1734, 1671, 1586, 1509, 1457, 1438, 1416, 1362, 1348, 1295, 1196, 1173, 1123, 1021, 993, 975, 954, 835, 798, 777, 681, 669 cm^{-1}; MS (ESI): *m/z*: 413 [*M*+H^+]; HRMS (EI): *m/z* calcd for $C_{21}H_{24}FN_7O$: 409.2026 [M^+]; found: 409.2026

4-Cyclopropylamino-1-(4-fluorophenyl)-*N*-(2-(piperidin-1-yl)ethyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8m): The procedure for **8a** was applied to resin **11m** (135 mg, theoretically 0.103 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (15:1)) gave the desired product **8m** (22 mg, 50%). m.p. 148.4 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ=9.07 (br s, 1H), 8.42 (s, 1H), 8.21 (m, 2H), 7.24 (t, *J*=8.5 Hz, 2H), 3.90 (q, *J*=6.0 Hz, 2H), 3.52 (s, 2H), 3.28 (m, 2H), 3.16 (q, *J*=7.4 Hz, 2H), 2.99 (br s, 1H), 1.89 (m, 4H), 1.35 (t, *J*=7.4 Hz, 2H), 1.28 (m, 1H), 1.06 (q, *J*=6.3 Hz, 2H), 0.91 (t, *J*=6.6 Hz, 2H) ppm; ^{13}C NMR (125 MHz, , $CDCl_3$): δ=163.5, 161.1(d, *J*= 244.9 Hz), 157.5, 155.3, 153.9, 135.0, 134.5, 123.6 (d, *J*= 7.8 Hz), 115.9 (d, *J*= 22.6 Hz), 101.6, 56.9, 54.3, 36.4, 29.7, 25.7, 24.0, 8.9 ppm; IR (ATR, neat): *v*=3248, 3092, 2947, 2863, 1670, 1587, 1509, 1455, 1437, 1418, 1365, 1347, 1296, 1278, 1196, 1177, 1126, 1034, 1011, 976, 949, 907, 886, 835, 799, 779, 718, 690, 668 cm^{-1}; MS (ESI): *m/z*: 424 [*M*+H^+]; HRMS (EI): *m/z* calcd for $C_{22}H_{26}FN_7O$: 423.2183 [M^+]; found: 423.2182

1-(4-Cyanophenyl)-4-cyclopropylamino-*N*-(2-morpholinoethyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8n): The procedure for **8a** was applied to resin **11n** (90 mg, theoretically 0.068 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (20:1)) gave the desired product **8n** (14 mg, 48%). m.p. 326.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.54 (d, *J*= 8.1 Hz, 2H), 8.48 (s, 1H), 8.25 (br s, 1H), 7.82 (d, *J*=8.1 Hz, 2H), 6.68 (br s, 1H), 3.75 (t, *J*=4.5 Hz, 4H), 3.64 (q, *J*=5.9 Hz, 2H), 2.66 (t, *J*=5.5 Hz, 2H), 2.56 (t, *J*=4.5 Hz, 4H), 1.27 (m, 1H), 1.09 (m, 2H), 0.83 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=162.9, 159.7, 155.7, 142.4, 136.1, 133.2, 130.7, 121.2, 118.5, 109.6, 102.1, 67.1, 57.0, 53.8, 36.3, 25.3, 9.3 ppm; IR (ATR, neat): *v*=3389, 3277, 2918, 2850, 2226, 1668, 157, 1561, 1533, 1507, 152, 1431, 1409, 1397, 1358, 1341, 1295, 1269, 1229, 1144, 1116, 1078, 1026, 976, 839, 917, 88, 865, 843, 779, 735, 698 cm^{-1}; MS (ESI): *m/z*: 433 [M+H$^+$]; HRMS (EI): *m/z* calcd for $C_{22}H_{24}N_8O_2$: 432.2022 [M^+]; found: 432.2025.

1-(4-Cyanophenyl)-4-cyclopropylamino-*N*-(2-(1-methylpyrrolidin-2-yl)ethyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8o): The procedure for **8a** was applied to resin **11o** (90 mg, theoretically 0.068 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (15:1)) gave the desired product **8o** (16 mg, 53%). m.p. 113.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.54 (d, *J*=8.7 Hz, 2H), 8.47 (s, 1H), 7.81 (d, *J*=8.7 Hz, 2H), 7.04 (br s, 1H), 3.71 (m, 2H), 3.50 (t, *J*=4.8 Hz, 2H), 3.20 (m, 1H), 2.56 (br s, 1H), 2.44 (s, 3H), 2.03 (m, 2H), 1.81 (m, 4H), 1.26 (m, 1H), 1.09 (m, 2H), 0.87 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=162.9, 155.7, 142.3, 136.1, 133.3, 124.7, 121.3, 118.6, 109.6, 107.3, 102.6, 64.8, 57.0, 40.4, 37.2, 31.9, 29.7, 22.7, 14.1, 9.2 ppm; IR (ATR, neat): *v*=2951, 2926, 2780, 2223, 1724, 1670, 1618, 1585, 1509, 1448, 1431, 1408, 1345, 1272, 1178, 1115, 1077, 1022, 951, 917, 840, 814, 777, 729, 680, 662 cm^{-1}; MS (ESI): *m/z*: 431 [M+H$^+$]; HRMS (EI): *m/z* calcd for $C_{23}H_{26}N_8O$: 430.2230 [M^+]; found: 430.2227.

Resin 9l (R^1 = cyclopropyl): The procedure for **9a** was applied to AMEBA (1.80 g, theoretically 1.99 mmol) using cyclopropylamine (414 mg, 5.98 mmol) to give the desired resin **9l** (1.81 g). IR (ATR, neat): *v*=3022, 2918, 2846, 1609, 1586, 1502, 1491, 1450, 1419, 1369, 1283, 1263, 1194, 1155, 1128, 1028, 1017, 931, 906, 819, 756, 735, 969 cm^{-1}.

Resin 10p (Ar = C_6H_5, R^1 = cyclopropyl): The procedure for **10a** was applied to resin **9l** (160 mg, theoretically 0.169 mmol) using 1-phenyl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4a**, 87 mg, 0.34 mmol) to give the desired resin **10p** (176 mg). IR (ATR, neat): *v*=3023, 2918, 1709, 1653, 1584, 1492, 1450, 1420, 1287, 1195, 1157, 1111, 1028, 974, 754, 696 cm^{-1}.

Resin 10q (Ar = 4-MeO-C_6H_4, R^1 = cyclopropyl): The procedure for **10a** was applied to resin **9l** (150 mg, theoretically 0.159 mmol) using 1-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4b**, 91 mg, 0.32 mmol) to give the desired resin **10q** (164 mg). IR (ATR, neat): *v*=3022, 2919, 1706, 1656, 1584, 1507, 1491, 1448, 1288, 1248, 1114, 1028, 975, 828, 755, 696 cm^{-1}.

Resin 10r (Ar = 4-Me-C_6H_4, R^1 = cyclopropyl): The procedure for **10a** was applied to resin **9l** (150 mg, theoretically 0.159 mmol) using 1-(*p*-tolyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4c**, 86 mg, 0.32 mmol) to give the desired resin **10r** (152 mg). IR (ATR, neat): *v*=3024, 2917, 1701, 1651, 1584, 1507, 1491, 1449, 1194, 1157, 1113, 974, 817, 754, 696 cm^{-1}.

Resin 10s (Ar = 4-F-C_6H_4, R^1 = cyclopropyl): The procedure for **10a** was applied to resin **9l** (150 mg, theoretically 0.159 mmol) using 1-(4-fluorophenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4d**, 87 mg, 0.32 mmol) to give the desired resin **10s** (164 mg). IR (ATR, neat): *v*=3023, 2919, 1709, 1656, 1584, 1541, 1507, 1491, 1449, 1287, 1225, 1195, 1155, 1109, 975, 833, 752, 695 cm^{-1}.

Resin 10t (Ar = 4-NC-C_6H_4, R^1 = cyclopropyl): The procedure for **10a** was applied to resin **9l** (150 mg, theoretically 0.159 mmol) using 1-(4-cyanophenyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one-6-carboxylic acid (**4e**, 89 mg, 0.32 mmol) to give the desired resin **12s** (159 mg). IR (ATR, neat): *v*=3022, 2918, 2846, 2222, 1706, 1653, 1605, 1583, 1541, 1506, 1491, 1449, 1429, 1407, 1394, 1277, 1194, 1157, 1113, 1027, 973, 838, 753, 695 cm^{-1}.

Resin 11p (Ar = C_6H_5, R^1 = cyclopropyl, NR^2R^3 = piperonylamino): The procedure for **11a** was applied to resin **10p** (150 mg, theoretically 0.127 mmol) using piperonylamine (57 mg, 0.38 mmol) to give the desired resin **11p** (161 mg). IR (ATR, neat): *v*=3022, 2920, 1583, 1501, 1490, 1449, 1419, 1364, 1279, 1247, 1157, 1113, 977, 958, 917, 833, 812, 754, 696 cm^{-1}.

Resin 11q (Ar = C_6H_5, R^1 = cyclopropyl, NR^2R^3 = (pyridin-4-ylmethyl)amino): The procedure for **11a** was applied to resin **10p** (120 mg, theoretically 0.101 mmol) using 4-(aminomethyl)pyridine (55 mg, 0.30 mmol) to give the desired resin **11q** (122 mg). IR (ATR, neat): *v*=3022, 2921, 1654, 1582, 1560, 1502, 1491, 1450, 1418, 1363, 1344, 1260, 1194, 1157, 1113, 1027, 978, 953, 908, 830, 754, 696 cm^{-1}.

Resin 11r (Ar = 4-MeO-C_6H_4, R^1 = cyclopropyl, NR^2R^3 = (1-benzylpiperidin-4-yl)amino): The procedure for **11a** was applied to resin **10q** (155 mg, theoretically 0.128 mmol) using 4-amino-1-benzylpiperidine (73 mg, 0.38 mmol) to give the desired resin **11r** (166 mg). IR (ATR, neat): *v*=3023, 2922, 1651, 1605, 1582, 1560, 1509, 1491, 1450, 1364, 1297, 1246, 1156, 1114, 1027, 828, 755, 696 cm^{-1}.

Resin 11s (Ar = 4-MeO-C_6H_4, R^1 = cyclopropyl, NR^2R^3 = (2-(piperidin-1-yl)ethyl)amino): The procedure for **11a** was applied to resin **10q** (150mg, theoretically 0.124 mmol) using 1-(2-aminoethyl)piperidine (48 mg, 0.37 mmol) to give the desired resin **11s** (154 mg). IR (ATR, neat): *v*=3024, 2921, 1654, 1582, 1560, 1510, 1492, 1450, 1364, 1342, 1298, 1246, 1178, 1157, 1115, 1080, 1027, 977, 951, 829, 755, 696 cm^{-1}.

Resin 11t (Ar = 4-Me-C_6H_4, R^1 = cyclopropyl, NR^2R^3 = (2-morpholinoethyl)amino): The procedure for **11a** was applied to resin **10r** (130 mg, theoretically 0.109 mmol) using 4-(2-aminoethyl)morpholine (42 mg, 0.33 mmol) to give the desired resin **11t** (131 mg). IR (ATR, neat): *v*=3024, 2919, 1656, 1601, 1582, 1560, 1491, 1449, 1194, 1157, 1115, 817, 755, 696 cm^{-1}.

Resin 11u (Ar = 4-Me-C_6H_4, R^1 = cyclopropyl, NR^2R^3 = (2-(diethylamino)ethyl)(methyl)amino): The procedure for **11a** was applied to resin **10r** (130 mg, theoretically 0.109 mmol) using *N*,*N*-diethyl-*N*'-ethylethylenediamine (43 mg, 0.33 mmol) to give the desired resin **11u** (133 mg). IR (ATR, neat): *v*=3025, 2920, 1655, 1576, 1547, 1491, 1449, 1366, 1346, 1285, 1195, 1157, 1113, 1028, 979, 950, 817, 755, 696 cm^{-1}.

Resin 11v (Ar = 4-F-C_6H_4, R^1 = cyclopropyl, NR^2R^3 = morpholino): The procedure for **11a** was applied to resin **10s** (130 mg, theoretically 0.108 mmol) using morpholine (28 mg, 0.32 mmol) to give the desired resin **11v** (128 mg). IR (ATR, neat): *v*=3024, 2924, 1654, 1569, 1508, 1491, 1448, 1366, 1347, 1589, 1260, 1219, 1195, 1155, 1113, 1023, 974, 832, 755, 696 cm^{-1}.

Resin 11w (Ar = 4-F-C_6H_4, R^1 = cyclopropyl, NR^2R^3 = 4-(2-furoyl)piperazin-1-yl): The procedure for **11a** was applied to resin **10s** (140 mg, theoretically 0.117 mmol) using 1-(2-furoyl)piperazine (63 mg, 0.35 mmol) to give the desired resin **11w** (152 mg). IR (ATR, neat): *v*=3024, 2917, 1653, 1567, 1508, 1491, 1449, 1419, 1375, 1349, 1282, 1263, 1218, 1155, 1111, 1013, 974, 834, 750, 696 cm^{-1}.

Resin 11x (Ar = 4-NC-C_6H_4, R^1 = cyclopropyl, NR^2R^3 = 4-(pyrrolidin-1-yl)piperidin-1-yl): The procedure for **11a** was applied to resin **10t** (130 mg, theoretically 0.108 mmol) using 4-(1-pyrrolidinyl)piperidine (50 mg, 0.32 mmol) to give the desired resin **11x** (121 mg). IR (ATR, neat): *v*=3021, 2918, 2223, 1653, 1580, 1567, 1549, 1506, 1491, 1449, 1427, 1369, 1348, 1281, 1262, 1194, 1157, 1115, 1028, 970, 947, 838, 754, 735, 696 cm^{-1}.

Resin 11y (Ar = 4-NC-C_6H_4, R^1 = cyclopropyl, NR^2R^3 = 4-(3-methoxyphenyl)piperazin-1-yl): The procedure for **11a** was applied to resin **10t** (150 mg, theoretically 0.124 mmol) using 1-(3-methoxyphenyl)piperazine (72 mg, 0.37 mmol) to give the desired resin **11y** (155 mg). IR (ATR, neat): *v*=3024, 2919, 2227, 1654, 1579, 1561, 1507, 1491, 1448, 1415, 1345, 1282, 1258, 1196, 1157, 1114, 1029, 1015, 974, 945, 837, 755, 695 cm^{-1}.

***N*-Cyclopropyl-1-phenyl-4-piperonylamino-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8p):** The procedure for **8a** was applied to resin **11p** (108 mg, theoretically 0.0713 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (20:1)) gave the desired product **8p** (21 mg, 69%). m.p. 228.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.12 (m, 3H), 7.95 (br s, 1H), 7.49 (t, *J*=7.5 Hz, 2H), 7.33 (t, *J*=7.2 Hz, 1H), 6.83 (d, *J*=7.2 Hz, 2H), 6.75 (d, *J*=7.8 Hz, 1H), 6.50 (br s, 1H), 5.94 (s, 2H), 4.76 (d, *J*=5.5 Hz, 2H), 2.91 (m, 1H), 0.89 (q, *J*= 6.3 Hz, 2H), 0.65 (m, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ=164.9, 156.9, 156.6, 153.8, 147.8, 146.8, 139.2, 134.3, 133.3, 129.7, 126.9, 122.2, 121.5, 109.0, 108.6, 102.2, 101.4, 43.9, 23.4, 6.5 ppm; IR (ATR, neat): *v*=3369, 3258, 3078, 3023, 2902, 2868, 1674, 1612, 1592, 1561, 1515, 1502, 1489, 1458, 1443, 1420, 1377, 1350, 1293, 1246, 1212, 1196, 1185, 1138, 1102, 1061, 1035, 1013, 959, 927, 868, 852, 795, 777, 755, 683 cm^{-1}; MS (ESI): *m/z*: 429 [M+H^+]; HRMS (EI): *m/z* calcd for $C_{23}H_{20}N_6O_3$: 428.1597 [M^+]; found: 428.1596.

***N*-Cyclopropyl-1-phenyl-4-((pyridine-4-ylmethyl)amino)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8q):** The procedure for **8a** was applied to resin **11q** (105 mg, theoretically 0.0824 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (20:1)) gave the desired product **8q** (19 mg, 60%). m.p. 338.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.59 (d, *J*=5.6 Hz, 2H), 8.10 (m, 3H), 7.82 (br s, 1H), 7.51 (t, *J*=7.6 Hz, 2H), 7.34 (m, 3H), 6.58 (br s, 1H), 4.92 (d, *J*=6.0 Hz, 2H), 2.87 (m, 1H), 0.88 (m, 2H), 0.62 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=164.8, 156.8, 154.1, 150.1, 148.9, 148.7, 139.5, 134.3, 129.7, 127.0, 123.0, 121.5, 102.3, 43.0, 23.3, 6.5 ppm; IR (ATR, neat): *v*=3364, 3260, 3028, 2921, 1693, 1622, 1593, 1560, 1497, 1458, 1448, 1420, 1379, 1345, 1317, 1244, 1196, 1140, 1095, 1064, 1011, 994, 965, 940, 908, 875, 852, 811, 775, 696 cm^{-1}; MS (ESI): *m/z*: 386 [M+H^+]; HRMS (EI): *m/z* calcd for $C_{21}H_{19}N_7O$: 385.1651 [M^+]; found: 385.1650.

4-((1-Benzylpiperidin-4-yl)amino)-*N*-cyclopropyl-1-(4-methoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8r): The procedure for **8a** was applied to resin **11r** (145 mg, theoretically 0.105 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (15:1)) gave the desired product **8r** (37 mg, 71%). m.p. 245.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.09 (s, 1H), 7.99 (br s, 1H), 7.81 (d, *J*=8.7 Hz, 2H), 7.39 (m, 4H), 7.05 (d, *J*=8.7 Hz, 2H), 4.03 (br s, 1H), 3.88 (s, 3H), 3.41 (m, 2H), 3.13 (q, *J*= 6.9 Hz, 2H), 2.81 (m, 1H), 2.02 (m, 4H), 1.33 (t, *J*=7.3 Hz, 4H), 0.84 (m, 2H), 0.61 (m, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ=165.4, 158.1, 157.4, 156.2, 153.1, 139.1, 133.7, 132.4, 129.2, 128.6, 127.4, 123.2, 114.8, 101.8, 62.6, 55.9, 52.4, 47.9, 32.0, 23.3, 6.5 ppm; IR (ATR, neat): *v*=3387, 3267, 2923, 1675, 1616, 1565, 1508, 1454, 1438, 1366, 1339, 1301, 1246, 1172, 1146, 1114, 1080, 1058, 1034, 1022, 961, 940, 868, 830, 776, 740, 697, 668 cm^{-1}; MS (ESI): *m/z*: 498 [M+H^+]; HRMS (EI): *m/z* calcd for $C_{28}H_{31}N_7O_2$: 497.2539 [M^+]; found: 497.2539.

***N*-Cyclopropyl-1-(4-methoxyphenyl)-4-((2-(piperidin-1-yl)ethyl)amino)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8s):** The procedure for **8a** was applied to resin **11s** (130 mg, theoretically 0.0982 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (10:1)) gave the desired product **8s** (26 mg, 61%). m.p. 104.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=9.63 (br s, 1H), 8.40 (s, 1H), 7.93 (d, *J*=2.9 Hz, 1H), 7.86 (d, *J*=9.0 Hz, 2H), 7.02 (d, *J*=9.0 Hz, 2H), 4.05 (m, 2H), 3.87 (s, 3H), 3.39 (m, 2H), 2.89 (m, 1H), 1.92 (m, 4H), 1.71 (m, 2H), 1.26 (d, *J*=2.6 Hz, 2H), 0.88 (t, *J*=3.8 Hz, 4H), 0.67 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=164.7, 162.6, 158.4, 157.0, 154.4, 151.9, 133.8, 131.9, 123.6, 114.2, 102.4, 55.6, 53.2, 36.5, 31.6, 22.9, 14.1, 6.7 ppm; IR (ATR, neat): *v*=3266, 2953, 2923, 2852, 1733, 1670, 1618, 1561, 1512, 1457, 1441, 1363, 1348, 1300, 1246, 1197, 1171, 1123, 1084, 1026, 991, 968, 942, 828, 789, 776, 718, 664 cm^{-1}; MS (ESI): *m/z*: 436 [M+H^+]; HRMS (EI): *m/z* calcd for $C_{23}H_{29}N_7O_2$: 435.2383 [M^+]; found: 435.2381.

***N*-Cyclopropyl-4-((2-morpholinoethyl)amino)-1-(*p*-tolyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8t):** The procedure for **8a** was applied to resin **11t** (105 mg, theoretically 0.0801 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (20:1)) gave the desired product **8t** (16 mg, 49%). m.p. 98.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.14 (br s, 1H), 7.97 (m, 3H), 7.33 (d, *J*=8.2 Hz, 2H), 3.76 (t, *J*=4.4 Hz, 6H), 2.93 (m, 1H), 2.73 (t, *J*=6.0 Hz, 2H), 2.54 (t, *J*=4.4 Hz, 4H), 2.43 (s, 3H), 0.88 (m, 3H), 0.66 (m, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ=165.2, 158.9, 156.6, 136.7, 134.1, 130.1, 121.6, 118.9, 114.8, 102.4, 57.4, 46.1, 31.4, 23.5, 21.0, 14.5, 9.0 ppm; IR (ATR, neat): *v*=3269, 2954, 2921, 2851, 1671, 1618, 1561, 1515, 1456, 1431, 1364, 1349, 1313, 1245, 1198, 1173, 1123, 1085, 1032, 1020, 968, 942, 855, 820, 798, 776, 719, 668 cm^{-1}; MS (ESI): *m/z*: 422 [M+H^+]; HRMS (EI): *m/z* calcd for $C_{22}H_{27}N_7O_2$: 421.2226 [M^+]; found: 421.2229

***N*-Cyclopropyl-4-((2-(diethylamino)ethyl)(methyl)amino)-1-(*p*-tolyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8u):** The procedure for **8a** was applied to resin **11u** (110 mg, theoretically 0.0839 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (30:1)) gave the desired product **8u** (12 mg, 34%). m.p. 119.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.20 (s, 1H), 7.91 (br s, 1H), 7.86 (d, *J*=8.4 Hz, 2H), 7.35 (d, *J*=8.4 Hz, 2H), 4.27 (t, *J*=5.6 Hz, 2H), 3.61 (s, 3H), 3.54 (t, *J*=5.9 Hz, 2H), 3.34 (m, 4H), 2.88 (m, 1H), 2.45 (s, 3H), 1.36 (m, 6H), 0.89 (m, 2H), 0.66 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=164.5, 157.8, 153.9, 153.2, 137.4, 135.9, 134.4, 129.8, 122.4, 102.2, 50.2, 47.7, 42.2, 22.8, 21.1, 11.1, 8.5, 6.8 ppm; IR (ATR, neat): *v*=3390, 2990, 2921, 2850, 1733, 1671, 1590, 1513, 1453, 1434, 1420, 1389, 1360, 1291, 1236, 1196, 1172, 1123, 1078, 1009, 970, 943, 853, 822, 797, 775, 718, 676 cm^{-1}; MS (ESI): *m/z*: 422 [M+H^+]; HRMS (EI): *m/z* calcd for $C_{23}H_{31}N_7O$: 421.2590 [M^+]; found: 421.2588

***N*-Cyclopropyl-1-(4-fluorophenyl)-4-morpholino-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8v):** The procedure

for **8a** was applied to resin **11v** (110 mg, theoretically 0.0865 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (30:1)) gave the desired product **8v** (19 mg, 56%). m.p. 196.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.15 (s, 1H), 8.11 (m, 2H), 7.83 (br s, 1H), 7.23 (m, 2H), 4.07 (t, *J*=5.1 Hz, 4H), 3.91 (t, *J*=5.1 Hz, 4H), 2.92 (m, 1H), 0.89 (m, 2H), 0.66 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ=164.4, 161.3 (d, *J*= 244.8 Hz), 157.3, 154.7, 154.4, 134.8, 133.7, 123.9 (d, *J*= 8.2 Hz), 116.0 (d, *J*= 22.8 Hz), 101.6, 66.4, 45.7, 22.9, 6.9 ppm; IR (ATR, neat): *v*=3189, 2856, 1652, 1567, 1506, 1437, 1393, 1352, 1296, 1284, 1261, 1245, 1212, 1181, 1155, 1114, 1086, 1068, 1032, 1001, 966, 939, 878, 834, 809, 772, 737, 671 cm^{-1}; MS (ESI): *m/z*: 383 [*M*+H$^+$]; HRMS (EI): *m/z* calcd for $C_{19}H_{19}FN_6O_2$: 382.1554 [*M*$^+$]; found: 382.1557.

***N*-Cyclopropyl-1-(4-fluorophenyl)-4-(4-(2-furoyl)piperazin-1-yl)-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8w):** The procedure for **8a** was applied to resin **11w** (140 mg, theoretically 0.103 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (30:1)) gave the desired product **8w** (34 mg, 69%). m.p. 228.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.19 (s, 1H), 8.13 (dd, *J*=4.9, 9.1 Hz, 2H), 7.87 (br s, 1H), 7.57(s, 1H), 7.26 (m, 2H), 7.17 (d, *J*=3.3 Hz, 1H), 6.57 (q, *J*=1.7 Hz, 1H), 4.25 (m, 4H), 4.13 (m, 4H), 2.95 (m, 1H), 0.93 (m, 2H), 0.69 (m, 2H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ=164.4, 160.2 (d, *J*= 251.5 Hz), 156.4, 156.3, 155.7, 154.1, 146.9, 145.0, 135.2, 134.9, 123.4 (d, *J*= 8.4 Hz), 116.0, 115.9 (d, *J*= 22.7 Hz), 111.4, 101.0, 22.9, 6.0 (two carbon peaks missing) ppm; IR (ATR, neat): *v*=3402, 3119, 3096, 3003, 2847, 1684, 1631, 1559, 1510, 1479, 1435, 1391, 1371, 1340, 1327, 1281, 1258, 1230, 1208, 1183, 1142, 1112, 1090, 1049, 1027, 1183, 1142, 1112, 1090, 1049, 1027, 1005, 967, 944, 885, 851, 835, 807, 776, 750, 690, 671 cm^{-1}; MS (ESI): *m/z*: 476[*M*+H$^+$]; HRMS (EI): *m/z* calcd for $C_{24}H_{22}FN_7O_3$: 475.1768 [*M*$^+$]; found: 475.1768.

1-(4-Cyanophenyl)-*N*-cyclopropyl-4-(4-(pyrrolidin-1-yl)piperidin-1-yl)pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8x): The procedure for **8a** was applied to resin **11x** (100 mg, theoretically 0.0743 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (20:1)) gave the desired product **8x** (17 mg, 50%). m.p. 258.8 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ=8.75 (s, 1H), 8.59 (m, 1H), 8.57 (d, *J*=8.7 Hz, 2H), 8.07 (d, *J*=8.7 Hz, 2H), 2.84 (m, 1H), 2.58 (m, 4H), 2.03 (m, 2H), 1.72 (m, 4H), 1.54 (m, 2H), 1.24 (s, 2H), 1.18 (m, 2H), 0.86 (m, 1H), 0.75 (m, 2H), 0.67 (m, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ=165.0, 156.6, 156.5, 155.8, 142.5, 137.2, 134.1, 121.4, 119.1, 108.8, 101.8, 60.5, 51.3, 30.9, 23.5, 6.4 (two carbon peaks missing) ppm; IR (ATR, neat): *v*=3268, 2953, 2919, 2851, 2773, 2220, 1655, 1605, 1565, 159, 1457, 1434, 1392, 1351, 1276, 1238, 1204, 1188, 1167, 1131, 1083, 1048, 1016, 967, 964, 940, 875, 848, 800, 776, 721, 663 cm^{-1}; MS (ESI): *m/z*: 457 [*M*+H$^+$]; HRMS (EI): *m/z* calcd for $C_{25}H_{22}N_8O_3$: 456.2386 [*M*$^+$]; found: 456.2385.

1-(4-Cyanophenyl)-*N*-cyclopropyl-4-(4-(3-methoxyphenyl)piperazin-1-yl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-carboxamide (8y): The procedure for **8a** was applied to resin **11y** (130 mg, theoretically 0.0939 mmol). Silica gel column chromatography (a mixture of methylene chloride and methyl alcohol (20:1)) gave the desired product **8y** (25 mg, 49%). m.p. 253.3 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ=8.77 (s, 1H), 8.63 (d, *J*=4.2 Hz, 1H), 8.58 (d, *J*=8.8 Hz, 2H), 8.07 (d, *J*=8.8 Hz, 2H), 7.17 (t, *J*=8.2 Hz, 1H), 6.58 (q, *J*=2.0 Hz, 1H), 6.50 (t, *J*=2.1 Hz, 1H), 6.41 (q, *J*=2.0 Hz, 1H), 4.20 (m, 4H), 3.74 (s, 3H), 3.40 (m, 4H), 2.86 (m, 1H), 0.75 (m, 2H), 0.65 (m, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ=165.0, 160.8, 156.8, 156.3, 155.7, 152.2, 142.4, 136.9, 133.8, 130.1, 121.2, 118.9, 108.9, 108.3, 104.6, 102.0, 101.8, 55.1, 48.9, 23.3, 6.2 (one carbon peak missing) ppm; IR (ATR, neat): *v*=3270, 2991, 2835, 2646, 2484, 2221, 1672, 1654, 1605, 1565, 1509, 1495, 1456, 1434, 1392, 1355, 1318, 1295, 1277, 1243, 1200, 1168, 1127, 1092, 1055, 1023, 1002, 965, 940, 849, 830, 798, 776, 715, 681 cm^{-1}; MS (ESI): *m/z*: 495 [*M*+H$^+$]; HRMS (EI): *m/z* calcd for $C_{27}H_{26}N_8O_2$: 494.2179 [*M*$^+$]; found: 494.2178.

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Supplementary Material