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Regiospecific synthesis of 6-aryl-3-cyano-5-alkylamino/arylamino-1-*p*-tolyl-1*H*-pyrazolo[4,3-*d*]pyrimidin-7(6*H*)-ones via iminophosphorane-mediated annulation

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ABSTRACT

An efficient and straightforward approach to the synthesis of 6-aryl-3-cyano-5-alkylamino-1-*p*-tolyl-1*H*-pyrazolo[4,3-*d*]pyrimidin-7(6*H*)-ones **8** has been developed from the readily commercially available starting materials 4-methylaniline and malononitrile in five steps. The key to the pyrazolo[4, 3-*d*]pyrimidin-7(6*H*)-ones relies on an iminophosphorane-mediated annulation, followed by a nucleophilic addition with amines. The structures of the title compounds are clearly characterized by IR, ^{1}H NMR, MS, elemental analysis or X-ray diffraction crystallography.

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1. Introduction

Over the past decade, nitrogen-containing heterocyclic molecules have been considered as the privileged synthetic targets in the pharmaceutical and veterinary industries[1] because of the diverse biological properties and a wide variety of applications, e.g., anticancer, diuretic, anticonvulsant, *anti*-inflammatory and antihypertensive activities.[2] The nitrogen-containing heterocyclic molecules, particularly with fused heterocyclic, bis-heterocyclic, multi-heterocyclic structures, have demonstrated a high degree of binding affinity when they serve as ligands for various biological receptors.[3] The fused-pyrazolo pyrimidinone, a class of pyrazole derivatives, has been attracted considerable attention for medicinal chemistry in drug discovery area as nucleosides mimics, such as cGMP-PDE,[4,5] adenosine,[6] methionyl t-RNA synthetase,[7] DNA polyase,[8] release of histamine,[9] xanthine oxidase,[10] and regulative CDK2 of cell-division cycle.[11] Among the fused-pyrazolo pyrimidinones, the molecules bearing pyrazolo[4,3-*d*]pyrimidin-7-one structure have abirritative and hypnotic activities particularly when they contain a carbonitrile group as, for example, 3-carbonitrile-5-methyl-7-substituted pyrazolo[1,5-*a*]pyridine.[12a] Also, its appearance in the structure of zaleplon, which 3-carbonitrile is probably necessary to maintain the drug's effect.[12b]

Several known synthetic approaches to pyrazolo[4,3-*d*]pyrimidin-7-ones have been reported.[13,14] The most common and widely applicable route[13] was completed by the cyclization of 4-substituted amido-1*H*-pyrazole-3-carboxamide under basic conditions. The other approach involved in a S_N2 displacement of chloride in 5-amino-4,6-dichloropyrimidine with 4-chloroaniline, followed by acylation, cyclocondensation, hydrolysis, and N-alkylation to form the pyrazolo pyrimidinones.[15] However, the key intermediate 4-substituted amido-1*H*-pyrazole-3-carboxamide in these reported methods was synthesized with tedious synthetic route. In addition, 5-amino substituted pyrazolo[4,3-*d*]pyrimidin-7-ones are not easily accessible by currently existing routes.

Aza-Wittig-mediated annulation has been widely used for the synthesis of nitrogen-containing heterocyclic compounds[15,16], for example, the synthesis of quinzazolinones via an aza-Wittig reaction.[16e,f,m] However the synthesis of pyrazolo[4,3-*d*]pyrimidin-7-

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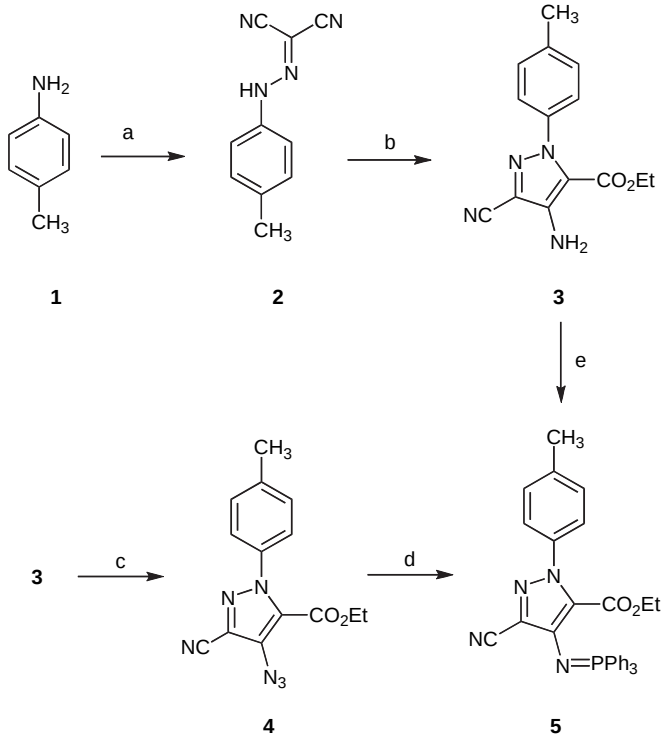
ones by means of tandem aza-Wittig reactions of iminophosphorane annulation with aryl isocyanates and amines has received less attention. In continuation with our ongoing heterocyclic synthesis and drug discovery project,[17] we have focused on the synthesis of quinzazolinones and other fused-heterocyclic pyrimidinone. Herein, we report an efficient approach to the synthesis of a new series of 6-aryl-3-cyano-5-alkylamino-1-*p*-tolyl-1*H*-pyrazolo[4,3-*d*]pyrimidin-7(6*H*)-ones **8** via iminophosphorane-mediated annulation with aromatic isocyanates, followed by nucleophilic addition with amines. Our convenient synthetic approach begins with an easy availability of starting material to synthesize functionalized fused-pyrazolo pyrimidinones. This method is potentially very useful in medicinal chemistry, as well as in synthetic and coordination chemistry.

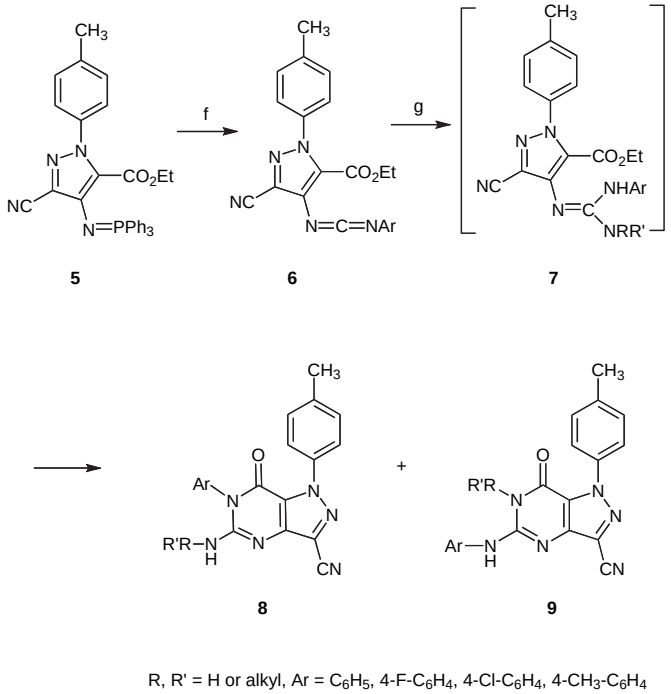
2. Results and discussion

Our strategy to 1*H*-pyrazolo[4,3-*d*]pyrimidin-7(6*H*)-ones commenced with the commercially available starting material *p*-toluidine (Scheme 1). The dicyanohydrazone **2** was synthesized by a one-pot protocol, which involved diazotization, followed by treatment with malononitrile in 99% yield. The hydrazone **2** was converted into 4-aminopyrazole **3** in 60% yield by an N-alkylation and in situ cyclization under basic conditions (K_2CO_3, DMF, 90 °C). Diazotization of 4-amino-1*H*-pyrazole-5-carboxylate **3** with HCl/$NaNO_2$ and subsequent azidation afforded the 4-azido-pyrazole, which was converted to iminophorane **5** with triphenylphosphine in a low yield (28% in two steps). To efficiently synthesize iminophorane **5**, an improved one-step procedure has been developed, which easily provided the important intermediate iminophorane **5** with a satisfactory yield (76%). Indeed, treatment of 4-amino-1*H*-pyrazole-5-carboxylate **3** with triphenylphosphine smoothly generated iminophosphorane **5** in presence of weakly basic conditions (Et_3N).

With iminophosphorane **5** in hand, we next turned our attention to the synthesis of final products 6-aryl-3-cyano-5-alkylamino-1-*p*-tolyl-1*H*-pyrazolo[4,3-*d*]pyrimidin-7(6*H*) -ones **8** (Scheme 2), which were obtained via aza-Wittig reaction and subsequent pyrimidinone formation in two steps. Iminophosphorane **5** was first treated with aromatic isocyanates to form carbodiimides **6** by the aza-Wittig reaction in good yields (76%). The reaction proceeded smoothly in mild conditions (0–5 °C) and was completed in 12 h. The carbodiimides **6** were then conveniently converted to 6-aryl-3-cyano-5-alkylamino-1-*p*-tolyl-1*H*-pyrazolo[4,3-*d*]pyrimidin-7(6*H*) -ones **8** (see Table 1) with aliphatic or aryl primary/secondary amines. Specifically, a nucleophilic addition of amines to the carbodiimide cumulenic system gave the highly reactive guanidine intermediates **7**, which in turn underwent intramolecular hetero-conjugate annulation to produce the 6-aryl-3-cyano-5-alkylamino-1-*p*-tolyl-1*H*-pyrazolo[4,3-*d*]pyrimidin-7(6*H*)-ones **8**. When primary amines were used, a small amount of potential regioisomers **9** (less than 5%) were observed as minor products and detected by LC/MS. Regardless of the presence or absence of EtONa/EtOH, the annulation could be accomplished smoothly to provide the title compounds **8** in good to excellent yields (70–97%, see Table 1). No significant differences in yields of producing the title compounds **8** were observed when a phenyl group at C-6 position was used for the final cyclization. Switching the phenyl group to an electronic withdrawing group (4-F-phenyl, 4-Cl-phenyl) or an electronic donating group (4-CH_3–phenyl) resulted in more than 92% yields to compounds **8** in several cases (**8j**, **8s**, **8u**, **8K**, **8L**). Either primary or sterically hindered secondary amines as nucleophiles in the annulation were not found to make significant difference for final yields of the synthesis of compounds **8**, whereas the reaction kinetics was significantly affected by the sterically hindered amines, such as cases **8h**, **8m**, **8o**, **8t**, **8D**, **8E**, **8I**, **8J**, **8N**.



Scheme 1. Synthesis of iminophorane **5**. Reagents and conditions: a. $NaNO_2$, MeOH, HCl/H_2O, 0 °C, then $NCCH_2CN$, NaOAc, H_2O (99%); b. $BrCH_2CO_2Et$, K_2CO_3, DMF, 90 °C, 6–7 h (60%); c. $NaNO_2$, TFA, 0 °C, then NaN_3 (70%); d. Ph_3P, CH_2Cl_2, rt, 6 h (40%); e. Ph_3P, C_2Cl_6, Et_3N, CH_3CN, rt, 5 h (76%).



Scheme 2. Synthesis of 6-aryl-3-cyano-5-alkylamino-1-*p*-tolyl-1*H*-pyrazolo[4, 3-*d*] pyrimidin-7(6*H*)-ones. Reagents and conditions: f. ArNCO, CH_2Cl_2, 0–5 °C, 12 h; g. RR′NH, CH_2Cl_2, rt, 6–12 h. When primary amine is used, **8** is the major product (73–96%), whereas when secondary amine is used, **8** is the sole product (70–97%).

Table 1
Preparation of 6-aryl-3-cyano-5-alkylamino/arylamino-1-*p*-tolyl-1*H*-pyrazolo[4,3-*d*]pyrimidin-7(6*H*)-ones **8**[a].

Entry	Aryl	R R′	Time (h)	Yield (%)[b]
8a	Ph	*n*-C_3H_7NH	6	86
8b	Ph	*n*-C_4H_9NH	6	75
8c	Ph	Cyclohexylamino	12	88
8d	Ph	*t*-C_4H_9NH	12	82
8e	Ph	(*R*)-α-Phenylethylamino	6	81
8f	Ph	PhNH	8	78
8g	Ph	$PhCH_2NH$	6	80
8h	Ph	*i*-C_3H_7NH	12	83
8i	4-F–Ph	*n*-C_3H_7NH	6	84
8j	4-F–Ph	*n*-C_3H_9NH	6	93
8k	4-F–Ph	Cyclohexylamino	6	87
8l	4-F–Ph	*t*-C_4H_9NH	12	88
8m	4-F–Ph	(*R*)-α-Phenylethylamino	12	79
8n	4-F–Ph	$PhCH_2NH$	6	86
8o	4-F–Ph	*i*-C_3H_7NH	12	85
8p	4-Cl–Ph	*n*-C_3H_7NH	6	78
8q	4-Cl–Ph	$PhCH_2NH$	8	73
8r	4-Cl–Ph	*n*-C_4H_9NH	6	86
8s	4-CH_3–Ph	$PhCH_2NH$	6	92
8t	4-CH_3–Ph	*i*-C_3H_7NH	12	77
8u	4-CH_3–Ph	*n*-C_3H_7NH	6	94
8v	4-CH_3–Ph	Cyclohexylamino	8	96
8A	4-CH_3–Ph	$(n\text{-}C_4H_9)_2N$	8	73
8B	Ph	$(CH_2)_5N$	8	80
8C	Ph	$(n\text{-}C_3H_7)_2N$	8	83
8D	Ph	$(i\text{-}C_3H_7)_2N$	12	78
8E	Ph	$(n\text{-}C_6H_{13})_2N$	12	70
8F	4-F–Ph	$(n\text{-}C_4H_9)_2N$	8	75
8G	4-F–Ph	$(CH_2)_5N$	8	85
8H	4-F–Ph	$(n\text{-}C_3H_7)_2N$	8	82
8I	4-F–Ph	$(i\text{-}C_3H_7)_2N$	12	79
8J	4-F–Ph	$(n\text{-}C_6H_{13})_2N$	12	76
8K	4-Cl–Ph	$(n\text{-}C_3H_7)_2N$	8	97
8L	4-Cl–Ph	$(n\text{-}C_4H_9)_2N$	8	95
8M	4-Cl–Ph	$(CH_2)_5N$	8	72
8N	4-CH_3–Ph	$(n\text{-}C_5H_{11})_2N$	12	82
8O	4-CH_3–Ph	$(CH_2)_5N$	8	81
8P	4-CH_3–Ph	$(n\text{-}C_4H_9)_2N$	8	79

[a] The reactions were carried out according to general experimental procedure.
[b] Isolated yields are based on iminophosphorane **5**.

As for the regioselectivity of annulation between the α- or β-ethoxylcarbonyl carbodiimines and amines seems to be controversial, 6-alkylamino substituted heterocycle was reported as the major or the only products,[18,19] whereas the 6-arylamino substituted heterocycle was produced as the sole product in the literature.[19] The regioselectivity in our approach was similar to that reported by Liu.[16e] Finally, the completely pure 6-aryl-3-cyano-5-alkylamino-1-*p*-tolyl-1*H*-pyrazolo[4,3-*d*]pyrimidin-7(6*H*) -ones **8** were easily obtained after recrystallization in EtOH and CH_2Cl_2.

The structures of the title compounds **8** were confirmed by spectral data: ^{1}H NMR, GC/MS, IR, and X-ray analysis. For example, the ^{1}H NMR spectra of the compound **8a** show the signal of NH at 4.20 ppm as a triplet and NCH_2 at 3.41 ppm as a quartet, which unambiguously demonstrates the existence of $NHCH_2CH_2CH_3$ group in the compound **8a**. The other signals at 7.62–7.21 (m, 9H, Ar–H), 2.37 (s, 3H, CH_3Ar), 1.51–1.64 (m, 2H, CH_2CH_3) and 0.86 (t, 3H, J=7.2 Hz, CH_2CH_3) ppm are also in agreement with its structure. The IR spectra of **8a** exhibit a strong stretching resonance peak at 1709 cm^{-1}, which indicates the presence of a C=O bond. The MS spectra of **8a** show M^+ at m/z 384 with 94% abundance. The ^{1}H NMR spectra of **8A** show the signals of NCH_2 at 3.03 ppm as a triplet, and the other signals appear at 7.56–7.23 (m, 9H, Ar–H), 2.38 (s, 3H, CH_3Ar), 1.23–1.12 (m, 8H, $2CH_2CH_2CH_3$) and 0.84 (t, 6H, J=7.2 Hz, $2CH_2CH_2CH_3$) ppm. The IR spectra of **8A** show the strong stretching resonance peak of C=O at 1707 cm^{-1}. It is also confirmed by the MS spectra of **8A** show M^+ at m/z 455 with 45% abundance. Furthermore, single-crystal X-ray analyses of products **8u** and **8H** allowed us to ascertain the structures (Figs 1 and 2).

3. Conclusion

In conclusion, a series of 6-aryl-3-cyano-5-alkylamino-1-*p*-tolyl-1*H*-pyrazolo [4,3-*d*] pyrimidin-7(6*H*)-ones **8** have been synthesized by a practical and efficient synthetic approach. The tandem aza-Wittig reaction of iminophosphorane and the subsequent intermolecular nucleophilic annulation with different amines have been utilized for the formation of pyrimidinone ring. This attractive synthetic route provides 6-aryl-3-cyano-5-alkylamino-1-*p*-tolyl-1*H*-pyrazolo [4,3-*d*] pyrimidin-7(6*H*)-ones **8** in good to excellent yields (70–97%) at final annulation reaction in presence of primary amines or sterically hindered secondary amines. The approach is also amenable to the synthesis of the other functionalized fused-heterocyclic compounds. Further application of this approach to the synthesis of other class of pyrazolo pyrimidinones and biological testing are currently ongoing and will be reported in due course.

4. Experimental section

4.1. General procedures

^{1}H NMR were recorded in $CDCl_3$ on a Varian Mercury 400 spectrometer and resonance are given in ppm (δ) relative to TMS. Mass spectra were obtained on a Finnigan trace MS spectrometer.

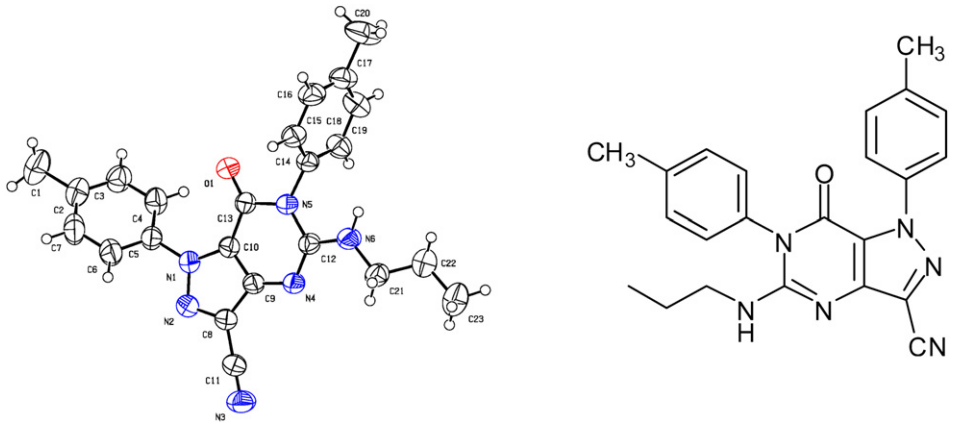


Figure 1. Crystal structure of **8u**.

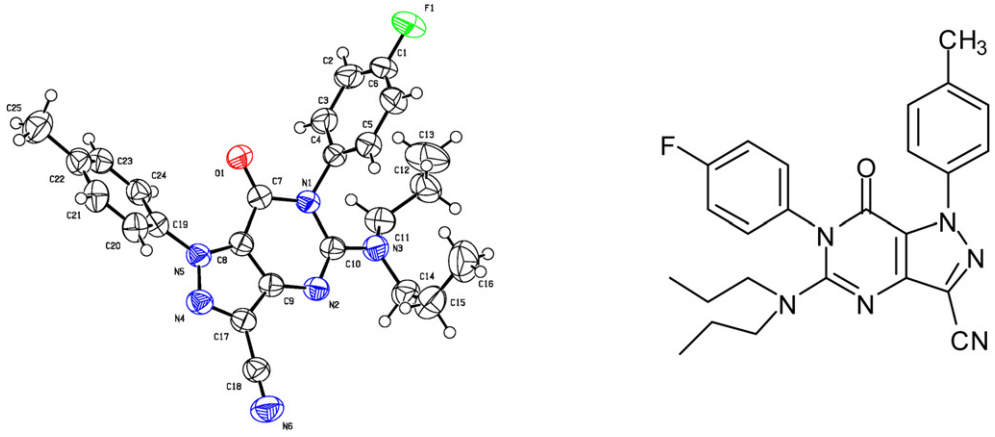


Figure 2. Crystal structure of **8h**.

Melting points were recorded on X-4 electrothermal melting point apparatus and were uncorrected. Elemental analyses were determined on a 2400 Perkin–Elmer elemental analysis instrument.

*4.1.1. Preparation of p-tolylcarbonohydrazonoyl dicyanide **2**.* Compound **2** was prepared according to the improved method described in the literature.[20] To a mixture of *p*-anisidine (10.72 g, 0.1 mol), MeOH (100 mL), water (50 mL), and concd HCl (60 mL), was added dropwise a solution of $NaNO_2$ (7.60 g, 0.11 mol) in water (20 mL) at 0 °C. The reaction mixture was stirred for 15 min. Then to the reaction mixture, a solution of NaOAc (12 g) in water (20 mL) was added dropwise followed by a solution of malononitrile (6.61 g, 0.1 mol), NaOAc (78 g), and water (130 mL), and the reaction mixture was stirred for additional 30 min. The reaction mixture was filtered, and the residual was washed with water and dried to afford the yellow solid, (18.23 g, 99 mmol, yield 99%), mp: 154–155 °C. IR (KBr): ν=3448 (NH), 2245 (CN), 1625, 1513, 1291 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=9.61 (s, 1H, NH), 7.29–7.19 (m, 4H, Ar–H), 2.37 (s, 3H, CH_3) ppm. ^{13}C NMR (MHz, $CDCl_3$): δ=21.4, 84.5, 112.2, 116.4, 129.7, 131.3, 140.4 ppm. MS: *m*/*z* (%)=184 (46, M^+). Anal. Calcd for $C_{10}H_8N_4$ (184.20): C, 65.21; H, 4.38; N, 30.42. Found: C, 63.31; H, 4.37; N, 30.40.

*4.1.2. Preparation of ethyl 4-amino-3-cyano-1-p-tolyl-1H-pyrazole-5-carboxylate **3**.* Compound **3** was prepared according to the improved method described in the literature.[19] To a stirring mixture of **2** (9.21 g, 0.05 mol), K_2CO_3 (6.91 g, 0.05 mol) in DMF (120 mL), was dropwise added bromoacetate (8.35 g, 0.05 mol) at room temperature. The reaction mixture heated to 90 °C and stirred for 6 h at this temperature. After cooling to room temperature, the reaction mixture was poured into ice water, and the resulting reside was collected, washed with water and dried to afford brick red solid **3** (8.1 g, 30 mmol, yield 60%), mp: 121–122 °C. IR (KBr): ν=3440 (NH), 2232 (CN), 1729 (C=O), 1623, 1513, 1291 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.29–7.25 (m, 4H, Ar–H), 4.75(s, 2H, NH_2), 4.23 (q, 2H, J=7.2 Hz, OCH_2CH_3), 2.42 (s, 3H, CH_3Ar), 1.17 (t, 2H, J=7.2 Hz, CH_2CH_3) ppm. ^{13}C NMR (MHz, $CDCl_3$): δ=14.2, 21.4, 60.6, 114.4, 117.7, 123.8, 125.1, 128.6, 129.6, 135.9, 136.8, 160.5 ppm. MS: *m*/*z* (%)=271 (11, $[M+1]^+$), 270 (100, M^+), 242 (19), 143(28), 117(88), 91 (50), 65(16). Anal. Calcd for $C_{14}H_{14}N_4O_2$ (270.29): C, 62.21; H, 5.22; N, 20.73. Found: C, 62.35; H, 5.21; N, 20.77.

*4.1.3. Synthesis of the iminophosphorane **5**.* 4-Aminopyrazole-carboxylate **3** (2.70 g, 0.01 mol), triphenylphosphine (7.87 g, 0.03 mol), and hexachloroethane(7.10 g, 0.03 mol) was dissolved in MeCN (50 mL). After stirred 15 min, triethylamine (6.07 g, 0.06 mol) was added dropwise to the reaction mixture and stirred for 5 h at room temperature. The reaction mixture was poured into an ice water (500 mL), extracted with CH_2Cl_2 (3×200 mL), dried under anhydrous $CaCl_2$, and concentrated to afford the crude residue, which was recrystallized with anhydrous ethanol to give white solid **5** (4.02 g, 7.6 mmol, yield 76%), mp: 116–117 °C IR (KBr): ν=3367 (NH), 2232 (CN), 1731 (C=O), 1624, 1557, 1514, 1449, 1411, 1291 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.81–7.15 (m, 19H, Ar–H), 3.91 (q, 2H, J=7.2 Hz, OCH_2CH_3), 2.38 (s, 3H, CH_3Ar), 0.99 (t, 3H, J=6.8 Hz, OCH_2CH_3) ppm. ^{13}C NMR (MHz, $CDCl_3$): δ=14.2, 21.4, 60.6, 109.1, 114.4, 125.1, 128.6, 128.8, 129.6, 131.2, 132.4, 132.6, 134.7, 135.8, 136.8, 160.5 ppm. MS: *m*/*z* (%), 531 (34, $[M+1]^+$), 530 (100, M^+), 457

(39), 288 (36), 183 (63), 91 (59), 77 (19), 65 (15). Anal. Calcd for $C_{32}H_{27}N_4O_2P$ (530.57): C, 72.44; H, 5.13; N, 10.56. Found: C, 72.27; H, 5.14; N, 10.50.

4.2. General procedure for synthesis of the carbodiimide 6

To a solution of iminophosphorane **5** (1.59 g, 3.0 mmol) in anhydrous THF (10 mL) was added rapidly aryl isocyanate (3.0 mmol) at room temperature. The reaction mixture was left unstirred for 6–12 h at 0–5 °C to generate carbodiimides **6**, which were used directly for next step without further purification.

4.3. General procedure for synthesis of the title compound 8

To the reaction mixture of **6** (3.0 mmol), was added a little excessive alkylamine or dialkylamine (3.1 mmol) at room temperature. The reaction mixture was allowed to stir for 6–12 h, condensed and the crude residue was recrystallized with EtOH and CH_2Cl_2 to give **8** in 70–97% yields.

*4.3.1. 3-Cyano-6-phenyl-5-propylamino-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8a**).* White crystals; mp: 177–178 °C. IR (KBr): ν=3367 (NH), 2236 (CN), 1709 (C=O), 1568, 1487, 1260 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.62–7.21 (m, 9H, Ar–H), 4.20 (s, 1H, HN), 3.41 (q, 2H, J=6.8 Hz, NCH_2), 2.37 (s, 3H, CH_3Ar), 1.51–1.64 (m, 2H, CH_2CH_3), 0.86 (t, 3H, J=7.2 Hz, CH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=11.5, 21.4, 24.6, 44.0, 112.9, 118.3, 121.0, 124.5, 128.7, 129.4, 130.7, 131.7, 134.1, 136.5, 139.3, 143.6, 148.8, 153.3 ppm. MS: m/z (%)=384 (94, M^+), 341 (100), 266 (7), 143 (13), 117 (22), 91 (54), 77 (46), 65 (15). Anal. Calcd for $C_{22}H_{20}N_6O$ (384.44): C, 68.73; H, 5.24; N, 21.86. Found: C, 68.80; H, 5.23; N, 21.85.

*4.3.2. 5-Butylamino-3-cyano-6-phenyl-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8b**).* White crystals; mp: 186–187 °C. IR (KBr): ν=3403 (NH), 2242 (CN), 1702 (C=O), 1579, 1488, 1242 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.62–7.21 (m, 9H, Ar–H), 4.15 (s, 1H, HN), 3.44 (q, 2H, J=6.8 Hz, NCH_2), 2.37 (s, 3H, CH_3Ar), 1.51–1.25 (m, 4H, $CH_2CH_2CH_3$), 0.903 (t, 3H, J=7.2 Hz, CH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=14.0, 20.5, 21.5, 30.1, 42.0, 112.5, 118.6, 121.5, 124.7, 128.7, 129.4, 130.8, 131.7, 136.4, 137.7, 139.6, 143.7, 148.5, 153.0 ppm. MS: m/z (%)=398 (84, M^+), 367 (4), 356 (53), 341 (100), 266 (10), 143 (18), 117.2 (23), 106 (23), 91 (65), 77 (37), 65 (15). Anal. Calcd for $C_{23}H_{22}N_6O$ (398.47): C, 69.33; H, 5.56; N, 21.09. Found: C, 69.34; H, 5.53; N 21.10.

*4.3.3. 3-Cyano-5-cyclohexylamino-6-phenyl-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8c**).* White crystals; mp: 227–229 °C. IR (KBr): ν=3398 (NH), 2234 (CN), 1712 (C=O), 1567, 1489, 1291 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.62–7.22 (m, 9H, Ar–H), 4.01 (s, 1H, HN), 2.35 (s, 3H, CH_3Ar), 1.95–1.03 (m, 11H, $(CH_2)_5CH$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.2, 24.8, 25.8, 32.9, 50.8, 112.7, 118.4, 121.7, 124.5, 128.9, 129.5, 130.9, 131.7, 136.5, 137.7, 139.7, 143.8, 148.5, 153.2 ppm. MS: m/z (%)=425 (82, $[M+1]^+$), 367 (9), 341 (100), 225 (6), 143 (10), 117 (16), 91 (29), 77 (29), 67 (10). Anal. Calcd for $C_{25}H_{24}N_6O$ (424.51): C, 70.72; H, 5.70; N, 19.81. Found: C, 70.76; H, 5.69; N, 19.83.

*4.3.4. 5-tert-Butylamino-3-cyano-6-phenyl-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8d**).* White crystals; mp: 219–220 °C. IR (KBr): ν=3426 (NH), 2237 (CN), 1709 (C=O), 1567, 1456, 1294 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.60–7.21 (m, 9H, Ar–H), 4.05 (s, 1H, HN), 2.37 (s, 3H, CH_3Ar), 1.39 (s, 9H, $(CH_3)_3C$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.3, 30.1, 53.6, 112.4, 118.8, 122.0, 124.7, 128.8, 129.2, 130.8, 131.8, 136.4, 137.5, 139.7, 143.6, 148.5, 153.1 ppm. MS: m/z (%)=398 (23, M^+), 377 (5), 342 (41), 341 (100), 225 (4), 143 (10), 117 (27), 91 (34), 77 (26), 65 (13), 57(16). Anal. Calcd for $C_{23}H_{22}N_6O$ (398.47): C, 69.33; H, 5.56; N, 21.09. Found: C, 69.30; H, 5.56; N, 21.08.

*4.3.5. (R)-3-Cyano-6-phenyl-5-(α-phenylethylamino)-1-p-tolyl-1H-pyrazolo[4,3-d] pyrimidin-7(6H)-one (**8e**).* White crystals; mp: 130–132 °C. IR (KBr): ν=3409 (NH), 2242 (CN), 1670 (C=O), 1571, 1531, 1489, 1297 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.63–7.21 (m, 14H, Ar–H), 5.36 (s, 1H, NCH), 4.42 (s, 1H, HN), 3.37 (s, 3H, CH_3Ar), 1.44 (d, 3H, J=6.4 Hz, $CHCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.3, 22.0, 51.4, 113.2, 118.4, 121.7, 124.5, 126.4, 127.1, 128.1, 128.7, 129.6, 130.5, 131.6, 136.4, 137.8, 139.9, 141.7, 143.5, 148.5, 153.0 ppm. MS: m/z (%)=446 (100, M^+), 342 (42), 341 (77), 120 (16), 105 (52), 103 (16), 77 (21). Anal. Calcd for $C_{27}H_{22}N_6O$ (446.19): C, 72.62; H, 4.97; N, 18.83. Found: C, 72.65; H, 4.96; N, 18.85.

*4.3.6. 3-Cyano-6-phenyl-5-phenylamino-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8f**).* White crystals; mp >250 °C (nobody give this number). IR (KBr): ν=3408 (NH), 2233 (CN), 1719 (C=O), 1601, 1547, 1290 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.57–7.00 (m, 14H, Ar–H), 6.06 (s, 1H, HN), 2.39 (s, 3H, CH_3Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.4, 113.5, 118.4, 121.1, 121.8, 122.3, 124.3, 128.7, 129.1, 129.6, 130.5, 131.5, 136.4, 137.6, 138.3, 139.6, 143.7, 148.8, 153.1 ppm. MS: m/z (%)=419 (100, $[M+1]^+$), 418 (56, M^+), 417 (56, $[M+1]^+$), 327 (8), 91 (5), 77 (8). Anal. Calcd for $C_{25}H_{18}N_6O$ (418.46): C, 71.76; H, 4.34; N, 20.08. Found: C, 71.80; H, 4.35; N, 20.09.

*4.3.7. 5-Benzylamino-3-cyano-6-phenyl-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8g**).* White crystals; mp >250 °C. IR (KBr): ν=3403 (NH), 2234 (CN), 1704 (C=O), 1567, 1534, 1460, 1294 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.61–7.22 (m, 14H, Ar–H), 4.65 (d, 2H, J=5.6 Hz, NCH_2), 4.55 (s, 1H, HN), 2.37 (s, 3H, CH_3Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.3, 45.5, 112.7, 118.4, 121.7, 124.5, 126.6, 127.0, 128.1, 128.9, 129.5, 130.8, 131.7, 136.4, 137.8, 138.3, 139.8, 143.7, 148.6, 153.0 ppm. MS: m/z (%)=433 (28, $[M+1]^+$), 432 (18, M^+), 431 (8, $[M-1]^+$), 182 (18), 167 (82), 91 (100), 77 (18). Anal. Calcd for $C_{26}H_{20}N_6O$ (432.48): C, 72.21; H, 4.66; N, 19.43. Found: C, 72.33; H, 4.65; N, 19.40.

*4.3.8. 3-Cyano-5-isopropylamino-6-phenyl-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8h**).* White crystals; mp: 178–179 °C. IR (KBr): ν=3418 (NH), 2234 (CN), 1710 (C=O), 1575, 1525, 1291 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.62–7.22 (m, 9H, Ar–H), 4.33 (s, 1H, HN), 3.92 (m, 1H, CCHC), 2.36 (s, 3H, CH_3Ar), 1.14 (d, 6H, J=6.8 Hz, $2(CH_3)_2C$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.2, 23.8, 42.9, 112.8, 118.7, 121.7, 124.5, 128.9, 129.5, 130.9, 131.7, 136.5, 137.7, 139.7, 143.8, 148.5, 153.2 ppm. MS: m/z (%)=384 (53, M^+), 369 (6), 359 (12), 341 (100), 266 (12), 117 (41), 91 (43), 77 (41). Anal. Calcd for $C_{22}H_{20}N_6O$ (384.44): C, 68.73; H, 5.24; N, 21.86. Found: C, 68.60; H, 5.23; N, 21.90.

*4.3.9. 3-Cyano-6-(4-fluorophenyl)-5-propylamino-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8i**).* White crystals; mp: 221–222 °C. IR (KBr): ν=3360 (NH), 2241 (CN), 1709 (C=O), 1571, 1435, 1294 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.55–7.22 (m, 8H, Ar–H), 4.19 (s, 1H, HN), 3.42 (q, 2H, J=7.2 Hz, NCH_2), 2.38 (s, 3H, CH_3Ar), 1.59–1.53 (m, 2H, CH_2CH_3), 0.87 (t, 3H, J=7.2 Hz, CH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=11.5, 21.3, 23.8, 42.5, 113.1, 115.5, 118.8, 121.8, 124.7, 129.8, 131.8, 136.4, 137.87, 139.8, 143.8, 148.9, 153.0, 163.2 ppm. MS: m/z (%)=404 (34, $[M+2]^+$), 402 (100, M^+), 373 (5), 361 (23), 359 (69), 344 (6), 117 (5), 91 (10), 89 (7). Anal. Calcd for $C_{22}H_{19}FN_6O$ (402.43): C; 65.66; H, 4.76; N, 20.88. Found: C, 65.68; H, 4.75; N, 20.82.

*4.3.10. 5-Butylamino-3-cyano-6-(4-fluorophenyl)-1-p-tolyl-1H-pyrazolo [4,3-d]pyrimidin-7(6H)-one (**8j**).* White crystals; mp

206.5–207.5 °C. IR (KBr): ν=3397 (NH), 2248 (CN), 1699 (C=O), 1602, 1579, 1513, 1290 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.56–7.23 (m, 8H, Ar–H), 4.11 (s, 1H, HN), 3.45 (q, 2H, J=7.2 Hz, NCH_2), 2.38 (s, 3H, CH_3Ar), 1.56–1.26 (m, 4H, CH_2CH_2C), 0.92 (t, 3H, J=7.2 Hz, CH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.9, 20.2, 21.5, 32.6, 42.2, 112.7, 115.4, 118.4, 121.7, 124.5, 130.5, 131.7, 136.3, 137.5, 139.8, 143.7, 148.5, 153.1, 162.9 ppm. MS: m/z (%)=418 (23, $[M+2]^+$), 416 (100, M^+), 387 (14), 374 (49), 360 (83), 344 (11), 225 (4), 250 (5), 195 (5), 117 (17) 109 (48), 95 (27), 91 (30), 75 (5), 65(14). Anal. Calcd for $C_{23}H_{21}FN_6O$ (416.46): C, 66.33; H, 5.08; N, 20.18. Found: C, 66.30; H, 5.09; N, 20.14.

*4.3.11. 3-Cyano-5-cyclohexylamino-6-(4-fluorophenyl)-1-p-tolyl-1H-pyrazolo [4,3-d] pyrimidin-7(6H)-one (**8k**).* White crystals; mp: 215.5–216 °C. IR (KBr): ν=3426 (NH), 2235 (CN), 1714 (C=O), 1601, 1567, 1489, 1254 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.56–7.23 (m, 8H, Ar–H), 3.98 (s, 1H, HN), 2.38 (s, 3H, CH_3Ar), 1.97–1.04 (m, 11H, $(CH_2)_5CH$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.5, 24.9, 25.9, 32.6, 50.0, 113.0, 115.7, 118.3, 121.6, 124.3, 130.5, 131.5, 136.2, 137.7, 139.7, 143.6, 148.4, 153.0, 163.0 ppm. MS: m/z (%)=444 (12, $[M+2]^+$), 442 (58, M^+), 385 (6), 361 (100), 359 (100), 344 (4), 225 (3), 117 (5), 95 (7), 91(9), 65 (5), 55 (9). Anal. Calcd for $C_{25}H_{23}FN_6O$ (442.50): C, 67.86; H, 5.24; N, 18.99. Found: C, 67.90; H, 5.24; N, 19.01.

*4.3.12. 5-tert-Butylamino-3-cyano-6-(4-fluorophenyl)-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8l**).* White crystals; mp: 211–212 °C. IR (KBr): ν=3431 (NH), 2238 (CN), 1709 (C=O), 1571, 1457, 1294 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.56–7.22 (m, 8H, Ar–H), 4.01 (s, 1H, HN), 2.37 (s, 3H, CH_3Ar), 1.40 (s, 9H, $(CH_3)_3C$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.3, 30.0, 53.6, 112.6, 115.4, 118.6, 121.8, 124.5, 130.8, 131.8, 136.2, 137.7, 139.8, 143.8, 148.5, 153.0, 163.0 ppm. MS: m/z (%)=418 (8, $[M+2]^+$), 416 (45, M^+), 401 (5), 362 (13), 360 (100), 359 (89), 250 (5), 225 (5) 117 (7) 95 (10), 91 (14), 89 (4) 65 (6), 57 (14). Anal. Calcd for $C_{23}H_{21}FN_6O$ (416.46): C, 66.33; H, 5.08; N, 20.18. Found: C, 66.32; H, 5.08; N, 20.21.

*4.3.13. (R)-3-Cyano-6-(4-fluorophenyl)-5-(α-phenylethylamino)-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8m**).* White crystals; mp 178–179 °C. IR (KBr): ν=3435 (NH), 2239 (CN), 1703 (C=O), 1601, 1571, 14,571, 1298 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.54–7.20 (m, 13H, Ar–H), 5.36 (s, 1H, NCH), 4.39 (s, 1H, HN), 2.37 (s, 3H, CH_3Ar), 1.47 (d, 3H, J=6.8 Hz, $CHCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.3, 22.0, 51.3, 112.7, 115.4, 118.4, 121.7, 126.5, 127.1, 128.6, 130.5, 131.7, 136.4, 137.5, 138.1, 139.7, 141.8, 143.7, 148.6, 153.2, 162.8 ppm. MS: m/z (%)=465 (73, $[M+1]^+$), 464 (58, M^+), 361 (19), 358 (16), 105 (100), 91 (29), 77 (23). Anal. Calcd for $C_{27}H_{21}FN_6O$ (464.50): C, 69.82; H, 4.56; N, 18.09. Found: C, 69.80; H, 4.55; N, 18.14.

*4.3.14. 5-Benzylamino-3-cyano-6-(4-fluorophenyl)-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8n**).* White crystals; mp: 247–249 °C. IR (KBr): ν=3405 (NH), 2237 (CN), 1705 (C=O), 1570, 1474, 1225 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.56–7.22 (m, 13H, Ar–H), 4.59 (d, 2H, J=5.6 Hz, NCH_2), 4.43 (s, 1H, HN), 2.39 (s, 3H, CH_3Ar) ppm. $CDCl_3$: δ=21.4, 45.3, 112.9, 115.5, 118.8, 121.8, 126.5, 127.3, 128.7, 130.6, 131.7, 136.5, 137.5, 138.2, 139.7, 141.8, 143.7, 148.6, 153.0, 162.9 ppm. MS: m/z (%)=451 (13, $[M+1]^+$), 450 (57, M^+), 449 (30, $[M-1]^+$), 185 (100), 184 (22), 91 (41). Anal. Calcd for $C_{26}H_{19}FN_6O$ (450.47): C, 69.32; H, 4.25; N, 18.66. Found: C, 69.30; H, 4.25; N, 18.65.

*4.3.15. 3-Cyano-6-(4-fluorophenyl)-5-isopropylamino-1-p-tolyl-1H-pyrazolo [4,3-d] pyrimidin-7(6H)-one (**8o**).* White crystals; mp: 202–203 °C. IR (KBr): ν=3378 (NH), 1708 (C=O), 1575, 1525, 12,890 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.55–7.23 (m, 8H, Ar–H), 4.32 (s, 1H, HN), 3.90 (m, 1H, CCHC), 2.38 (s, 3H, CH_3Ar), 1.16 (d, 6H, J=6.8 Hz, $2(CH_3)_2C$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.4, 23.6, 42.8, 112.7, 115.4, 118.4, 121.8, 124.5, 130.6, 131.7, 136.4, 137.6, 139.7, 143.8, 148.6, 153.0, 163.1 ppm. MS: m/z (%)=403 (36, $[M+1]^+$), 402 (100, M^+), 387 (11), 359 (93), 344 (12), 266 (15), 117 (15), 91 (40). Anal. Calcd for $C_{22}H_{19}FN_6O$ (402.43): C, 65.66; H, 4.76; N, 20.88. Found C, 65.60; H, 4.77; N, 20.82.

*4.3.16. 6-(4-Chlorophenyl)-3-cyano-5-propylamino-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8p**).* White crystals; mp: 207.5–208.5 °C. IR (KBr): ν=3369 (NH), 2240 (CN), 1708 (C=O), 1575, 1488, 1295 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.59–7.22 (m, 8H, Ar–H), 4.14 (s, 1H, HN), 3.42 (q, 2H, J=7.2 Hz, NCH_2), 2.38 (s, 3H, CH_3Ar), 1.59–1.53 (m, 2H, CH_2CH_3), 0.88 (t, 3H, J=7.6 Hz, CH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=11.3, 21.5, 23.4, 42.2, 112.9, 115.4, 118.3, 121.0, 124.6, 128.9, 130.5, 131.7, 133.3, 137.5, 139.8, 145.8, 150.9, 153.3 ppm. MS: m/z (%)=420 (11, $[M+2]^+$), 419 (21, $[M+1]^+$), 375 (99), 117 (69), 91(100). Anal. Calcd for $C_{22}H_{19}ClN_6O$ (418.89): C, 63.08; H, 4.57; N, 20.06. Found: C, 63.13; H, 4.56; N, 20.01.

*4.3.17. 5-Benzylamino-6-(4-chlorophenyl)-3-cyano-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8q**).* White crystals; mp 200–202 °C. IR (KBr): ν=3378 (NH), 2241 (CN), 1702 (C=O), 1571, 1512, 1254 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.56–7.22 (m, 13H, Ar–H), 4.64 (d, 2H, J=5.6 Hz, NCH_2), 4.53 (s, 1H, HN), 2.44 (s, 3H, CH_3Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.3, 46.2, 113.0, 118.8, 121.0, 124.6, 126.5, 127.0, 128.1, 128.9, 129.5, 130.5, 131.7, 133.3, 137.5, 138.10, 139.8, 145.8, 150.9, 153.3 ppm. MS: m/z (%)=468(20, $[M+2]^+$), 466 (83, $M]^+$), 216 (21), 201 (69), 165 (12), 106 (13), 91 (100). Anal. Calcd for $C_{26}H_{19}ClN_6O$ (466.93): C, 66.88; H, 4.10; N, 18.00. Found: C, 66.85; H, 4.09; N, 17.79.

*4.3.18. 5-Butylamino-6-(4-chlorophenyl)-3-cyano-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8r**).* White-White crystals; mp: 229–231 °C. IR (KBr): ν=3389 (NH), 2244 (CN), 1695 (C=O), 1578, 1489, 1295 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): 7.59–7.21 (m, 8H, Ar–H), 4.11 (s, 1H, HN), 3.45 (q, 2H, J=7.2 Hz, NCH_2), 2.38 (s, 3H, CH_3Ar), 1.57–1.27 (m, 4H, CH_2CH_2C), 0.92 (t, 3H, J=7.6 Hz, CH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=14.0, 20.4, 21.5, 30.1, 42.0, 112.9, 118.3, 121.0, 124.5, 128.9, 129.6, 130.3, 131.8, 133.4, 137.5, 139.7, 145.5, 150.9, 153.3 ppm. MS: m/z (%)=434 (57, $[M+2]^+$), 433 (100, $[M+1]^+$), 432 (87, $M]^+$), 378 (41), 375 (88), 91 (56). Anal. Calcd for $C_{23}H_{21}ClN_6O$ (432.91): C, 63.81; H, 4.89; N, 19.41. Found: C, 63.82; H, 4.89; N, 19.46.

*4.3.19. 5-Benzylamino-3-cyano-1, 6-di (p-tolyl)-1H-pyrazolo[4,3-d] pyrimidin-7(6H)-one (**8s**).* White crystals; mp: 178–180 °C. IR (KBr): ν=3429 (NH), 2236 (CN), 1711 (C=O), 1570, 1512, 1491, 1292 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.58–7.15 (m, 13H, Ar–H), 4.65 (s, 2H, NCH_2), 4.55 (s, 1H, HN), 2.42(s, 3H, CH_3Ar), 2.37 (s, 3H, CH_3Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.3, 21.4, 45.5, 112.6, 118.8, 121.5, 124.6, 126.5, 127.0, 128.0, 128.8, 129.5, 130.8, 131.7, 136.4, 137.6, 138.0, 139.7, 143.7, 148.6, 153.1 ppm. MS: m/z (%)=446 (100, M^+), 354 (10), 196 (38), 181 (91), 106 (21), 91 (82), 77 (8). Anal. Calcd for $C_{27}H_{22}N_6O$ (446.19): C, 72.63; H, 4.97; N, 18.82. Found: C, 72.58; H, 4.98; N, 18.77.

*4.3.20. 3-Cyano-5-isopropylamino-1, 6-di (p-tolyl)-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8t**).* White crystals; mp: 159–160 °C. IR (KBr): ν=3377 (NH), 2234 (CN), 1708 (C=O), 1563, 1511, 1488, 1292 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.58–7.12 (m, 8H, Ar–H), 4.32 (s, 1H, HN), 4.01 (m, 1H, CCHC), 2.45 (s, 3H, CH_3Ar), 2.37 (s, 3H, CH_3Ar), 1.14 (d, 6H, J=6.4 Hz, $2(CH_3)_2C$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.3, 21.4, 23.5, 42.8, 112.8, 118.9, 121.6, 124.8, 128.7, 129.5, 130.8, 131.7, 136.5, 137.9, 139.6, 143.9, 148.5, 153.1 ppm. MS: m/z (%)=400 (6, M^++2), 398 (45, M^+), 355 (77), 340 (6), 132 (48), 117 (26), 91 (100), 77 (10). Anal. Calcd for $C_{23}H_{22}N_6O$ (398.47): C, 69.33; H, 5.56; N, 21.09. Found: C, 69.23; H, 5.47; N, 21.02.

*4.3.21. 3-Cyano-5-propylamino-1, 6-di (p-tolyl)-1H-pyrazolo[4,3-d] pyrimidin-7(6H)-one (**8u**).* White-White crystals; mp: 164–165 °C.

IR (KBr): ν=3427 (NH), 2242 (CN), 1700 (C=O), 1580, 1490, 1297 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.58–7.13 (m, 8H, Ar–H), 4.25 (s, 1H, HN), 3.40 (q, 2H, J=6.8 Hz, NCH_2), 2.44 (s, 3H, CH_3Ar), 2.37 (s, 3H, CH_3Ar), 1.60–1.52 (m, 2H, CH_2C), 0.87 (t, 3H, J=7.2 Hz, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=11.3, 21.3, 21.5, 23.5, 42.3, 112.5, 118.6, 121.5, 124.7, 128.7, 129.5, 130.8, 131.6, 136.3, 137.8, 139.6, 143.7, 148.6, 153.2 ppm. MS: m/z (%)=398 (77, M^+), 355 (100), 314 (41), 117 (17), 91 (53). Anal. Calcd for $C_{23}H_{22}N_6O$ (398.47): C, 69.33; H, 5.56; N, 21.09. Found: C, 69.40; H, 5.56; N, 21.11.

*4.3.22. 3-Cyano-5-cyclohexylamino-1, 6-di (p-tolyl)-1H-pyrazolo [4,3-d]pyrimidin-7(6H)-one (**8v**).* White crystals; mp: 210–211 °C. IR (KBr): ν=3424 (NH), 2236 (CN), 1707 (C=O), 1567, 1489, 1291 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.58–7.12 (m, 8H, Ar–H), 4.08 (d, 1H, J=21.2, HN), 2.44 (s, 3H, CH_3Ar), 2.37 (s, 3H, CH_3Ar), 1.96–1.03 (m, 11H, $(CH_2)_5CH$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.3, 21.5, 24.8, 25.8, 33.0, 50.4, 112.7, 118.7, 121.6, 124.7, 128.8, 129.5, 130.8, 131.7, 136.4, 137.8, 139.6, 143.7, 148.4, 153.1 ppm. MS: m/z (%)=438 (77, M^+), 385 (6), 355 (100), 340 (6), 225 (7), 117 (18), 91 (31), 65 (7), 55 (7). Anal. Calcd for $C_{26}H_{26}N_6O$ (438.53): C, 71.21; H, 5.98; N, 19.16. Found: C, 71.34; H, 5.99; N, 19.20.

*4.3.23. 3-Cyano-5-dibutylamino-6-phenyl-1-p-tolyl-1H-pyrazolo [4,3-d]pyrimidin-7(6H)-one (**8A**).* Crystals; mp: 124–125 °C. IR (KBr): ν=2237 (CN), 1707 (C=O), 1593, 1490, 1288 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.56–7.23 (m, 9H, Ar–H), 3.03 (t, 4H, J=7.6 Hz, CH_2NCH_2), 2.38 (s, 3H, CH_3Ar), 1.23–1.12 (m, 8H, $2CH_2CH_2CH_3$), 0.84 (t, 6H, J=7.2 Hz, $2CH_2CH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=14.0, 20.5, 21.5, 30.1, 48.5, 112.8, 118.6, 121.5, 124.7, 128.7, 129.4, 130.8, 131.7, 136.4, 137.7, 139.6, 143.7, 148.5, 153.1 ppm. MS: m/z (%)=456 (9, $[M+2]^+$), 455 (45, $[M+1]^+$), 453 (87, $[M-1]^+$), 425 (29), 412 (36), 399 (33), 356 (85), 321 (42), 91(100). Anal. Calcd for $C_{27}H_{30}N_6O$ (454.57): C, 71.34; H, 6.65; N, 18.49. Found: C, 71.36; H, 6.64; N, 18.48.

*4.3.24. 3-Cyano-6-phenyl-5-(piperidin-1-yl)-1-p-tolyl-1H-pyrazolo [4,3-d]pyrimidin-7(6H)-one (**8B**).* White crystals; mp 211–212 °C. IR (KBr): ν=2237 (CN), 1709 (C=O), 1592, 1555, 1469, 1295 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.55–7.23 (m, 9H, Ar–H), 3.14 (t, 4H, J=5.6 Hz, CH_2NCH_2), 2.38 (s, 3H, CH_3Ar), 1.44–1.25 (m, 6H, $C(CH_2)_3C$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.3, 24.3, 25.7, 49.5, 112.5, 118.6, 121.5, 124.7, 128.7, 129.5, 130.8, 131.7, 136.5, 137.8, 139.6, 143.7, 148.5, 153.0 ppm. MS: m/z (%)=411 (40, M^+), 410 (56, $[M-1]^+$), 382 (18), 291(14), 160 (100), 91 (11), 77 (22). Anal. Calcd for $C_{24}H_{23}N_6O$ (411.49): C, 70.05; H, 5.63; N, 20.42. Found: C, 70.14; H, 5.64; N, 20.40.

*4.3.25. 3-Cyano-5-dipropylamino-6-phenyl-1-p-tolyl-1H-pyrazolo [4,3-d]pyrimidin-7(6H)-one (**8C**).* White crystals; mp: 105–106 °C. IR (KBr): ν=2237 (CN), 1705 (C=O), 1593, 1558, 1490, 1298 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.55–7.23 (m, 9H, Ar–H), 3.02 (t, 4H, J=5.6 Hz, CH_2NCH_2), 2.38 (s, 3H, CH_3Ar), 1.29–1.23 (m, 4H, $2CH_2CH_3$), 0.74 (t, 6H, J=7.6 Hz, $2CH_2CH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=11.7, 21.2, 21.5, 50.1, 112.8, 118.5, 121.6, 124.8, 128.7, 129.6, 130.9, 131.8, 136.5, 137.7, 139.6, 143.7, 148.6, 153.0 ppm. MS: m/z (%)=427 (70, $[M+1]^+$), 397 (44), 384 (100), 356 (24), 355 (47), 308 (30), 279 (77), 91 (84), 77 (71). Anal. Calcd for $C_{25}H_{26}N_6O$ (426.52): C, 70.40; H, 6.14; N, 19.70. Found: C, 70.35; H, 6.15; N, 19.68.

*4.3.26. 3-Cyano-5-diisopropylamino-6-phenyl-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8D**).* White crystals; mp: 134–135 °C. IR (KBr): ν=2238 (CN), 1705 (C=O), 1592, 1563, 1488, 1290 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.56–7.23 (m, 9H, Ar–H), 3.55 (m, 2H, 2CCHC), 2.37 (s, 3H, CH_3Ar), 0.74 (d, 12H, J=6.8 Hz, 2 $(CH_3)_2C$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.3, 21.6, 51.9, 112.5, 118.5, 121.5, 124.7, 128.7, 129.4, 130.6, 131.7, 136.6, 137.9, 139.6, 143.8, 148.7, 153.2 ppm. MS m/z (%)=427 (14, $[M+1]^+$), 383 (100), 370 (17), 326 (23), 307 (3), 116 (19), 91 (28), 77 (28). Anal. Calcd for $C_{25}H_{26}N_6O$ (426.52): C, 70.40; H, 6.14; N, 19.70. Found: C, 70.51; H, 6.14; N, 19.71.

*4.3.27. 3-Cyano-5-dihexylamino-6-phenyl-1-p-tolyl-1H-pyrazolo[4, 3-d]pyrimidin-7(6H)-one (**8E**).* White crystals; mp: 74–75 °C. IR (KBr): ν=2235 (CN), 1715 (C=O), 1593, 1558, 1467, 1290 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.55–7.23 (m, 9H, Ar–H), 3.03 (t, 4H, J=7.6 Hz, CH_2NCH_2), 2.38 (s, 3H, CH_3Ar), 1.29–1.23 (m, 16H, $2CH_2CH_2CH_2CH_2C$), 0.87 (t, 6H, J=7.2 Hz, $2CCCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.5, 25.2, 25.9, 30.4, 59.1, 112.8, 118.9, 121.6, 124.5, 128.6, 129.6, 130.7, 131.8, 136.5, 137.8, 139.6, 143.8, 148.5, 153.0 ppm. MS: m/z (%)=511 (48, $[M+1]^+$), 453 (24), 439 (30), 426 (100), 355 (47), 341 (49), 326 (27), 279 (23), 91 (47), 77(27). Anal. Calcd for $C_{31}H_{38}N_6O$ (510.68): C, 72.91; H, 7.50; N, 16.46. Found: C, 72.88; H, 7.51; N, 16.42.

*4.3.28. 3-Cyano-5-dibutylamino-6-(4-fluorophenyl)-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8F**).* White crystals; mp: 167.5–169 °C. IR (KBr): ν=2233 (CN), 1706 (C=O), 1561, 1467, 1291 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.54–7.17 (m, 8H, Ar–H), 3.04 (t, 4H, J=7.2 Hz, CH_2NCH_2), 2.38 (s, 3H, CH_3Ar), 1.25–1.16 (m, 8H, $2CH_2CH_2CH_3$), 0.86 (t, 6H, J=7.2 Hz, $2CH_2CH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.9, 20.1, 21.3, 30.2, 49.5, 112.5, 115.7, 118.6, 121.5, 124.7, 128.7, 130.8, 131.7, 136.4, 139.6, 143.7, 148.5, 153.0, 162.8 ppm. MS: m/z (%)=473 (29, $[M+1]^+$), 472 (73, M^+), 443 (26), 415 (100), 387 (35), 373 (95), 360 (26), 344 (28), 279 (32), 109 (31), 91 (25). Anal. Calcd for $C_{27}H_{29}FN_6O$ (472.57): C, 68.62; H, 6.19; N, 17.78. Found: C, 68.75; H, 6.19; N, 17.72.

*4.3.29. 3-Cyano-6-(4-fluorophenyl)-5-(piperidin-1-yl)-1-p-tolyl-1H-pyrazolo [4,3-d] pyrimidin-7(6H)-one (**8G**).* White crystals; mp: 218–219 °C. IR (KBr): ν=2236 (CN), 1705 (C=O), 1558, 1470, 1295 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.53–7.17 (m, 8H, Ar–H), 3.12 (t, 4H, J=5.6 Hz, CH_2NCH_2), 2.38 (s, 3H, CH_3Ar), 1.46–1.29 (m, 6H, $C(CH_2)_3C$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.4, 24.2, 25.9, 49.0, 113.0, 115.7, 118.3, 121.6, 124.3, 130.5, 131.5, 136.2, 137.7, 139.7, 143.6, 148.4, 153.0, 163.0 ppm. MS: m/z (%)=430 (20, $[M+2]^+$), 429 (100, $[M+1]^+$), 427 (65, $[M-1]^+$), 400 (56), 291 (21), 178 (52), 147 (5), 91 (8). Anal. Calcd for $C_{24}H_{21}FN_6O$ (429.48): C, 67.12; H, 5.16; N, 19.57. Found: C, 67.15; H, 5.16; N, 19.58.

*4.3.30. 3-Cyano-5-dipropylamino-6-(4-fluorophenyl)-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8H**).* White crystals; mp: 141–142 °C. IR (KBr): ν=2238 (CN), 1701 (C=O), 1602, 1555, 1463, 1292 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.54–7.17 (m, 8H, Ar–H), 3.02 (t, 4H, J=7.6 Hz, CH_2NCH_2), 2.39 (s, 3H, CH_3Ar), 1.31–1.29 (m, 4H, $2CH_2CH_3$), 0.77 (t, 6H, J=7.2 Hz, $2CH_2CH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=11.6, 21.1, 21.5, 50.0, 113.4, 115.8, 118.5, 121.7, 124.8, 130.5, 131.6, 136.2, 137.8, 139.8, 143.4, 148.7, 153.2, 163.0 ppm. MS: m/z (%)=446 (6, $[M+2]^+$), 445 (25, $[M+1]^+$), 444 (100, M^+), 416 (37), 401 (98), 373 (53), 344 (23), 308 (30), 279 (19), 91 (17). Anal. Calcd for $C_{25}H_{25}FN_6O$ (444.51): C, 67.55; H, 5.67; N, 18.91. Found: C, 67.50; H, 5.66; N, 18.87.

*4.3.31. 3-Cyano-5-diisopropylamino-6-(4-fluorophenyl)-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8I**).* White crystals; mp 140–141 °C. IR (KBr): ν=2236 (CN), 1707 (C=O), 1656, 1561, 1460, 1292 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.54–7.15 (m, 8H, Ar–H), 3.53 (m, 2H, 2CCHC), 2.38 (s, 3H, CH_3Ar), 1.13 (d, 12H, J=3.2 Hz, 2 $(CH_3)_2C$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.5, 21.9, 52.0, 113.2, 115.8, 118.4, 121.6, 124.5, 130.5, 131.6, 136.2, 137.5, 139.7, 143.6, 148.6, 153.0, 163.1 ppm. MS: m/z (%)=446 (3, $[M+2]^+$), 445 (13, $[M+1]^+$), 444 (8, M^+), 402 (100), 401 (38), 400 (54), 387 (20), 91 (5). Anal.

Calcd for $C_{25}H_{25}FN_6O$ (444.51): C, 67.55; H, 5.67; N, 18.91. Found: C, 67.51; H, 5.68; N, 18.89.

*4.3.32. 3-Cyano-5-dihexylamino-6-(4-fluorophenyl)-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8J**).* White crystals; mp: 75–76 °C. IR (KBr): ν=2237 (CN), 1708 (C=O), 1603, 1560, 1460, 1293 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.55–7.14 (m, 8H, Ar–H), 3.03 (t, 4H, J=7.6 Hz, CH_2NCH_2), 2.39 (s, 3H, CH_3Ar), 1.29–1.12 (m, 16H, $2CH_2CH_2CH_2CH_2C$), 0.88 (t, 6H, J=6.8 Hz, $2CCCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.3, 25.2, 25.8, 30.3, 59.8, 113.7, 115.9, 118.6, 121.7, 124.6, 130.6, 131.5, 136.3, 137.5, 139.8, 143.7, 148.5, 153.0, 163.0 ppm. MS: m/z (%)=528 (31, M^+), 472 (6), 471 (7), 444 (16), 388 (41), 374 (100), 372 (47), 279 (26), 109 (74), 91 (24). Anal. Calcd for $C_{31}H_{37}FN_6O$ (528.67): C, 70.43; H, 7.05; N, 15.90. Found: C, 70.40; H, 7.05; N, 15.88.

*4.3.33. 6-(4-Chlorophenyl)-3-cyano-5-dipropylamino-1-p-tolyl-1H-pyrazolo [4,3-d] pyrimidin-7(6H)-one (**8K**).* White crystals; mp 165.5–166.5 °C. IR (KBr): ν=2237 (CN), 1708 (C=O), 1558, 1493, 1298 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.54–7.20 (m, 8H, Ar–H), 3.02 (t, 4H, J=7.6 Hz, CH_2NCH_2), 2.39 (s, 3H, CH_3Ar), 1.33–1.31 (m, 4H, $2CH_2CH_3$), 0.77 (t, 6H, J=7.2 Hz, $2CH_2CH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=11.6, 21.0, 21.3, 50.0, 112.8, 118.2, 121.6, 124.6, 128.8, 129.5, 130.6, 131.8, 133.3, 137.6, 139.8, 145.8, 150.6, 153.2 ppm. MS: m/z (%)=463 (15, $[M+3]^+$), 462 (21, $[M+2]^+$), 461 (52, $[M+1]^+$), 459 (33), 417 (100), 389 (99), 377 (39), 309 (42), 279 (78), 91 (7). Anal. Calcd for $C_{25}H_{25}ClN_6O$ (460.97): C, 65.14; H, 5.47; N, 18.23. Found: C, 65.10; H, 5.48; N, 18.21.

*4.3.34. 6-(4-Chlorophenyl)-3-cyano-5-dibutylamino-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8L**).* White crystals; mp 180–181 °C. IR (KBr): ν=2233 (CN), 1708 (C=O), 1558, 1489, 1289 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.54–7.19 (m, 8H, Ar–H), 3.04 (t, 4H, J=7.6 Hz, CH_2NCH_2), 2.39 (s, 3H, CH_3Ar), 1.25–116 (m, 8H, $2CH_2CH_2C$), 0.86 (t, 6H, J=7.2 Hz, $2CH_2CH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=14.0, 20.2, 21.3, 30.4, 49.2, 112.9, 118.4, 121.0, 124.6, 128.9, 129.6, 130.5, 131.7, 133.3, 137.6, 139.6, 145.7, 150.8, 153.2 ppm. MS: m/z (%)=491 (37, $[M+3]^+$), 490 (10, $[M+2]^+$), 488 (100, M^+), 459 (21), 446 (13), 431 (62), 378 (40), 321 (19), 279 (9), 91 (14). Anal. Calcd for $C_{27}H_{29}ClN_6O$ (489.02): C, 66.32; H, 5.99; N, 17.19. Found: C, 66.45; H, 5.99; N, 17.21.

*4.3.35. 6-(4-Chlorophenyl)-3-cyano-5-(piperidin-1-yl)-1-p-tolyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8M**).* White crystals; mp: 212–213 °C. IR (KBr): ν=2236 (CN), 1709 (C=O), 1585, 1513, 1490, 1269 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.53–7.24 (m, 8H, Ar–H), 3.13 (t, 4H, J=5.6 Hz, CH_2NCH_2), 2.39 (s, 3H, CH_3Ar), 1.47–1.30 (m, 6H, $C(CH_2)_3C$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.5, 24.6, 25.8, 46.2, 112.7, 118.4, 121.2, 124.7, 128.8, 129.7, 130.6, 131.5, 133.4, 137.5, 139.8, 145.8, 150.7, 153.0 ppm. MS: m/z (%)=447 (25, $[M+3]^+$), 446 (30, $[M+2]^+$), 444 (100, M^+), 415 (29), 401 (8), 291 (5), 194 (25), 111 (23), 91 (62). Anal. Calcd for $C_{24}H_{21}ClN_6O$ (444.92): C, 64.84; H, 4.77; N, 18.92. Found: C, 65.20; H, 4.78; N, 18.89.

*4.3.36. 3-Cyano-5-dipentylamino-1, 6-di (p-tolyl)-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8N**).* White crystals; mp: 105–106 °C. IR (KBr): ν=2232 (CN), 1705 (C=O), 1562, 1513, 1278 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.56–7.11 (m, 8H, Ar–H), 3.02 (t, 4H, J=5.6 Hz, CH_2NCH_2), 2.38 (s, 6H, $2CH_3Ar$), 1.63–0.86 (m, 12H, $2CCH_2CH_2CH_2C$), 0.83 (t, 6H, J=7.2 Hz, $2CCCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=14.3, 21.3, 21.4, 22.0, 22.5, 30.1, 49.3, 112.7, 118.8, 121.5, 124.8, 128.6, 129.5, 130.8, 131.7, 136.3, 137.8, 139.6, 143.8, 148.6, 153.0 ppm. MS: m/z (%)=497 (15, $[M+1]^+$), 496 (52, M^+), 439 (85), 425 (100), 383 (30), 369 (68), 355 (53), 340 (17), 279 (11), 91 (28). Anal. Calcd for $C_{30}H_{36}N_6O$ (496.66): C, 72.55; H, 7.31; N, 16.92. Found: C, 72.47; H, 7.30; N, 16.98.

*4.3.37. 3-Cyano-5-(piperidin-1-yl)-1, 6-di (p-tolyl)-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (**8O**).* White crystals; mp: 223.5–224.5 °C. IR (KBr): ν=2236 (CN), 1706 (C=O), 1585, 1558, 1467, 1271 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.55–7.17 (m, 8H, Ar–H), 3.14 (t, 4H, J=5.6 Hz, CH_2NCH_2), 2.40 (s, 3H, CH_3Ar), 2.38 (s, 3H, CH_3Ar), 1.59–1.25 (m, 6H, $C(CH_2)_3C$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.3, 21.4, 24.3, 25.8, 46.5, 112.5, 118.7, 121.6, 124.7, 128.8, 129.5, 130.7, 131.6, 136.4, 137.8, 139.5, 143.7, 148.7, 153.0 ppm. MS: m/z (%)=425 (21, $[M+1]^+$), 424 (30, M^+), 395 (43), 381 (18), 319 (18), 291 (24), 174 (100), 91 (40). Anal. Calcd for $C_{25}H_{24}N_6O$ (424.5): C, 70.73; H, 5.70; N, 19.80. Found: C, 70.65; H, 5.73; N, 19.82.

*4.3.38. 5-Dibutylamino-3-cyano-1, 6-di (p-tolyl)-1H-pyrazolo[4,3-d] pyrimidin-7(6H)-one (**8P**).* White crystals; mp: 158–159 °C. IR (KBr): ν=2237 (CN), 1705 (C=O), 1588, 1558, 1486, 1288 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.56–7.11 (m, 8H, Ar–H), 3.05 (t, 4H, J=6.8 Hz, CH_2NCH_2), 2.40 (s, 3H, CH_3Ar), 2.38 (s, 3H, CH_3Ar), 1.21–1.12 (m, 8H, $2CH_2CH_2C$), 0.84 (t, 6H, J=7.2 Hz, $2CH_2CH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.9, 20.0, 21.3, 21.4, 30.5, 50.0, 112.8, 118.5, 121.6, 124.7, 128.5, 129.5, 130.9, 131.8, 136.6, 137.8, 139.8, 143.7, 148.5, 153.2 ppm. MS: m/z (%)=469 (21, $[M+1]^+$), 468 (60, M^+), 439 (16), 425 (37), 411 (100), 369 (67), 321 (24), 279 (19), 91(47). Anal. Calcd for $C_{28}H_{32}N_6O$ (468.60): C, 71.77; H, 6.88; N, 17.93. Found: C, 71.71; H, 6.88; N, 17.92.

4.4. X-ray crystal structure analysis for compound 8u

$C_{23}H_{22}N_6O$, M=398.47, colorless crystal, 0.30×0.20×0.20 mm, a=11.722(2) Å, b=9.411(2) Å, c=19.868(4) Å, β=92.873(3), V=2188.9(8) $Å^3$, ρcalcd=1.209 g cm^{-3}, μ=0.078 mm^{-1}, empirical absorption correction (0.9838≤T≤0.9597), Z=4, monoclinic, space group $P2(1)/c$, λ=0.71073 Å, T=293 K, ω and φ scans, 15,041 reflections collected (±h, ±k, ±l), 5768 independent (Rint=0.0199) and 3822 observed reflections [I>2σ(I)], 275 refined parameters, R=0.0463, $wR2$=0.1277, max. residual electron density 0.227 (−0.179) e $Å^{-3}$ and hydrogen atoms were calculated and refined as riding atoms.

4.5. X-ray crystal structure analysis for compound 8H

$C_{25}H_{25}FN_6O$, M=444.51, colorless crystal, 0.20×0.10×0.10 mm, a=7.929 (1) Å, b=11.708 (2) Å, c=12.962 (1) Å, α=78.524 (1), β= 82.170 (1), γ=85.592 (1), V=1166.8 (1) $Å^3$, ρcalcd=1.265 g cm^{-3}, μ=0.087 mm^{-1}, empirical absorption correction (0.9914≤T≤0.9829), Z=2, triclinic, space group $P\text{-}1$, λ=0.71073 Å, T=295 K, ω and φ scans, 7486 reflections collected (±h, ±k, ±l), 4509 independent (Rint=0.0456) and 3052 observed reflections [I>2σ(I)], 301 refined parameters, R=0.0567, $wR2$=0.1294, max. residual electron density 0.233 (−0.273) e $Å^{-3}$ and hydrogen atoms were calculated and refined as riding atoms.

4.6. Supplementary data

Supplementary data (see footnote on the first page of this article): CCDC-740004 and CCDC-740005 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge

Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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