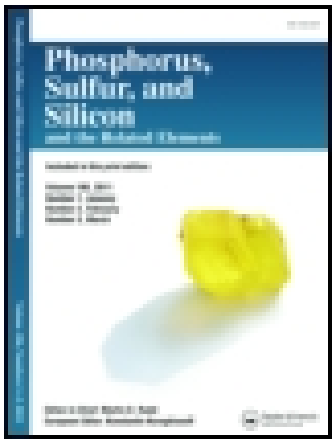

Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

VERSATILE SYNTHESIS AND FUNGICIDAL ACTIVITIES OF 6-AMINO-3- ALKYLTHIO-1,5-DIHYDRO-1-PHENYL-PYRAZOLO [3,4-D]PYRIMIDIN-4-ONE DERIVATIVES

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Published online: 16 Aug 2010.

To cite this article: Hong-Qing Wang , Zhao-Jie Liu & Ming-Wu Ding (2004) VERSATILE SYNTHESIS AND FUNGICIDAL ACTIVITIES OF 6-AMINO-3- ALKYLTHIO-1,5-DIHYDRO-1-PHENYL-PYRAZOLO [3,4-D]PYRIMIDIN-4-ONE DERIVATIVES, Phosphorus, Sulfur, and Silicon and the Related Elements, 179:10, 2039-2050, DOI: 10.1080/10426500490474897

To link to this article: http://dx.doi.org/10.1080/10426500490474897

Phosphorus, Sulfur, and Silicon, 179:2039–2050, 2004

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500490474897

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VERSATILE SYNTHESIS AND FUNGICIDAL ACTIVITIES OF 6-AMINO-3-ALKYLTHIO-1,5-DIHYDRO-1-PHENYL-PYRAZOLO [3,4-*d*]PYRIMIDIN-4-ONE DERIVATIVES

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(Received December 5, 2003; accepted March 16, 2004)

*A series of new 6-alkylamino-3-alkylthio-1-phenyl-1H-pyrazolo[3,4-*d*] pyrimidin-4(5H)-one derivatives* ***5*** *and* ***6*** *have been rapidly synthesized by a novel solution-phase regioselective synthetic method. Treatment of pyrazole o-aminoester* ***1*** *with dibromotriphenylphosphorane gave iminophosphorane* ***2****, which underwent a aza-Wittig reaction with phenyl ioscyanate to provide the carbodiimide* ***3****. The latter intermediate reacted with alkylamines and regioselectively provided the 1,5-dihydro-pyrazolo[3,4-*d*]pyrimidin-4-one derivatives* ***5*** *and* ***6****, some of which exhibited good fungicidal activity.*

Keywords: Aza-Wittig reaction; fungicidal activities; pyrazolo[3,4-*d*]pyrimidin-4-one; synthesis

INTRODUCTION

Pyrazolo[3,4-d]pyrimidine derivatives are of considerable chemical and pharmacological importance as purine analogs.[1,2] They exhibit excellent antibacterial, antiphlogistic,[3–5] and antiumor[6] activities, and they have been employed in the treatment of erectile dysfunction in male animals.[7–9] In previous reports, various synthetic procedures have been devised for the conversion of o-aminonitriles and o-aminoesters

We gratefully acknowledge the financial support of this work by the National Nature Science Foundation (No. 20101001).

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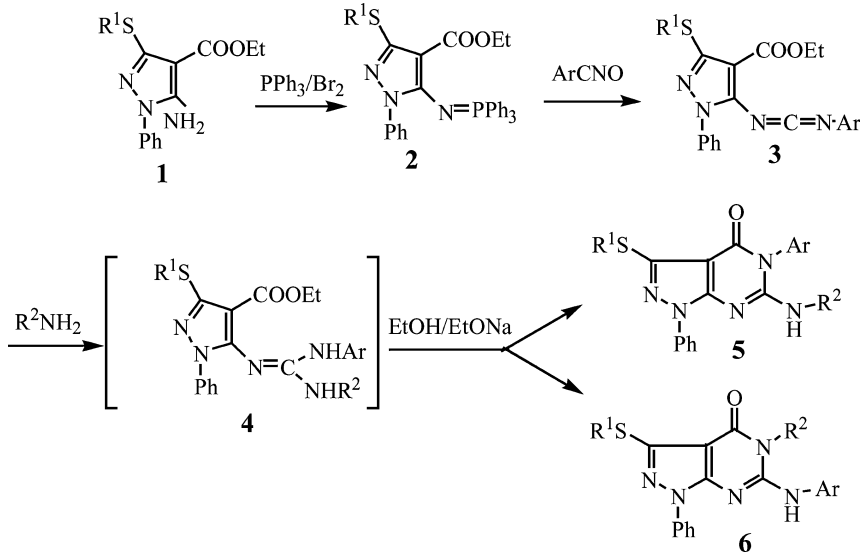
bearing pyrazole ring to pyrazolopyrimidinones derivatives, which involved inter alia (1) hydrolysis of aminonitriles, followed by reaction with aliphatic ester,[10,11] aromatic aldehydes,[12] and carboxylic acids;[12,13] (2) treatment of o-aminoesters with aryl isothiocycanates and subsequent reaction with hydrazine monohydrate;[14,15] or (3) generated pyrazolooxazine or o-ethoxymethyleneaminoesters which were reacted with amines.[16] Taylor[17] also reported the preparation of 6-phenylamino-1,5-dihydro-1-methyl-pyrazolo[3,4-*d*]pyrimidin-4-one by utilizing o-phosphoranylideneamino pyrazolyl ester to react with isocyanates and amines. As a part of an extension of our studies on tandem aza-Wittig reaction,[18–20] we developed a new versatile solution-phase regioselective annulation process to synthesize novel 6-amino-3-alkylthio-1-phenyl-1,5-dihydro-pyrazolo-[3,4-*d*]pyrimidin-4-one derivatives **5** and **6** (Scheme 1) and examined their fungicidal activities.



SCHEME 1

RESULTS AND DISCUSSION

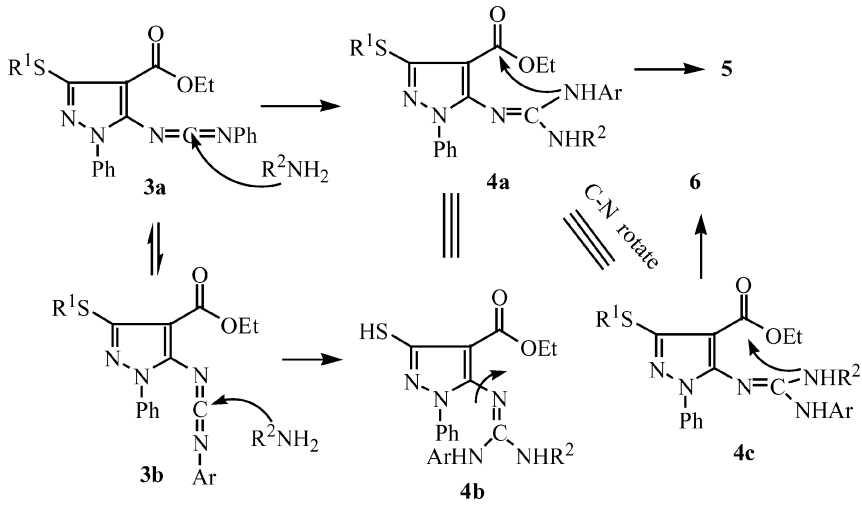
The iminophosphorance **2**, which was prepared from 5-aminopyrazole **1** in the presence of triphenylphosphine and bromine, reacted with phenyl isocyanate to give carbodiimide **3**, which was allowed to react with alkylamines at room temperature to give intermediate guanidines **4**. In

the presence of EtONa/EtOH, the reaction proceeded smoothly at room temperature to give **5** or **6** in good yields. Whenever R^2 was alkyl substituted with aliphatic group or aromatic group and small (R^2 = n-Pr) or bulky (R^2 = iso-Pr), the cyclization was achieved all in good yields with the same regioselective product **5** obtained separately from the reaction mixture by recrystallization or flash chromatography with a silica column. But when R^2 was hydrogen, **6** was the regioselective product. It was noteworthy that when Ar possessed a strong electron-drawing group, whenever R^2 was aliphatic or aromatic alkyl substituted, the cyclic product couldn't be obtained. Examples are **5k** and **5l**. The structures of 1,5-dihydro-1-phenyl-pyrazolo[3,4-*d*]pyrimidin-4-ones (**5** and **6**) were deduced from their ^{1}H NMR spectra data. For example, the ^{1}H NMR spectra data of **5b** showed the signals of NH at δ 4.89 as triplet, which were not the same as the proton of PhNH, the chemical shift of which is greater than δ 7.0.[17] Its methylene protons displayed a doublet also, which strongly suggested the existence of an $NHCH_{2-}$ group. Also, **6a** showed the signal of N-H at δ 9.70 as a broad absorption, which was the same in the literature.[15] It suggested the existence of PhNH group. It was found that various carbodiimides reacted with nucleophiles in need of excessive catalytic solid potassium carbonate in our previous research,[18–20] but we carried out the reactions of carbodiimide **3** with alkylamines in the presence of EtONa. However, in the absence of a base, the intermediate guanidine **4** did not cyclize completely and was recovered (see Table I).

TABLE I Preparation of 1,5-Dihydro-pyrazolo[3,4-*d*]pyrimidin-4-one Derivatives **5** and **6**

Compound	Ar	R^1	R^2	Conditions	Yield (%)*
5a	Ph	Me	p-FPhCH_2	r.t./3 h	83.7
5b	Ph	Me	3-pyridinemethyl	r.t./2 h	76.0
5c	Ph	Me	2-pyridinemethyl	r.t./2 h	96.0
5d	Ph	Me	2-(1-ethylpyrrolidine)methyl	r.t./3 h	74.6
5e	Ph	Me	2-thiophenemethyl	r.t./3 h	69.6
5f	Ph	Me	n-Pr	r.t./2 h	75.4
5g	Ph	PhCH_2	3-pyridinomethyl	r.t./5 h	66.2
5h	Ph	PhCH_2	2-pyridinomethyl	r.t./5 h	69.5
5i	Ph	PhCH_2	2-thiophenemethy	r.t./5 h	76.9
5j	Ph	PhCH_2	iso-Pr	r.t./2 h	92.8
5k	p-FPh	Me	3-pyridinemethyl	Reflux/6 h	0.0
5l	p-FPh	Me	n-Pr	Reflux/6 h	0.0
6a	Ph	Me	H	r.t./2 h	82.9
6b	Ph	PhCH_2	H	r.t./3 h	90.2

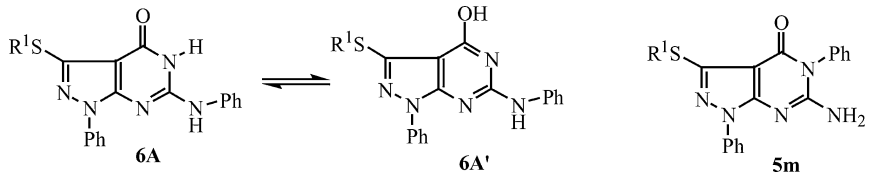
*Isolated yields based on iminophosphorance **2**.
r.t., Room temperature.



SCHEME 2

The formation of **5** or **6** (Scheme 2) can be rationalized in terms of geometry of the intermediate **4**, which might be Z-form suitable for arylamino group to cyclize, and conjugative effect of product **5** and **6**. It is estimated that the configurations of carbodiimide **3** are mainly coplanar due to the resonance effect. When the amines reacted with **3a**, *Z*-**4a** formed since the amines would attack **3a** mainly from the opposite direction of COOEt group due to the steric hindrance of COOEt group. When the amines reacted with **3b**, *Z*-**4b** formed since the amines would attack **3b** mainly from the opposite direction of phenyl group due to the steric hindrance of pyrazole ring and phenyl group. Actually, **4a** is equivalent to **4b** and **4c** through the C—N single-bond rotation. However, **4a** is suitable for arylamine group to cyclize, and **4c** is suitable for alkylamine group to cyclize. When R^2 is alkyl, the initially formed **4a** cyclizes to give **5** at first rather than mutating to afford **4c** because there is not a notable different steric hindrance to ester group between aryl group and alkyl, and the compounds **5** are more stable than the compounds **6** because of conjugative effect. However, when R^2 is hydrogen atom, the initially formed **4a** mutates into **4c**, followed by cyclization to give **6**, since **4c** is more stable than **4a** because of the steric hindrance and the cyclized compound from **4c** is more stable via its existence of two interconverting isomers. This is because the isomer **6A′** bearing a hydroxyl has a completely conjugated ring, but the **5m** does not (see Scheme 3). It demonstrates that **5k** and **5l** cannot also cyclize.

The structures of **5** and **6** have been fully characterized by ^{1}H NMR, IR, MS, and elementary analyses. In the IR spectral data of **5**, the



SCHEME 3

relatively strong stretching resonance absorption of N-H appears at 3352–3442 cm^{-1}, which is only one peak. The stretching resonance of C=O showed strong absorption at about 1684–1712 cm^{-1}. However, in the IR spectral data of **6**, there were two relatively strong stretching resonance absorption peaks at about 3432 cm^{-1} and 3110 cm^{-1}, and the absorption of C=O was very weak due to **6** interconverting (see Scheme 3). This demonstrated the identification of **6** also. The MS spectrum of all compounds prepared showed strong molecule ion peaks.

The structure of **5** was further confirmed by X-ray crystallographic analysis. The X-ray structural analysis of **5a** showed that it was 5-phenyl-6-(p-fluorobenzylamino)-substituted pyrazolo[3,4-*d*]-pyrimidin-4-one (see Figure 1). The single crystal of **5a** was orthorhombic, space group Pbca, unit cell dimensions A = 10.327(4) Å, B = 20.307(7) Å, C = 21.234(9) Å, $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 90^\circ$, V = 4453 (3) $Å^3$, Mc = 457.52,

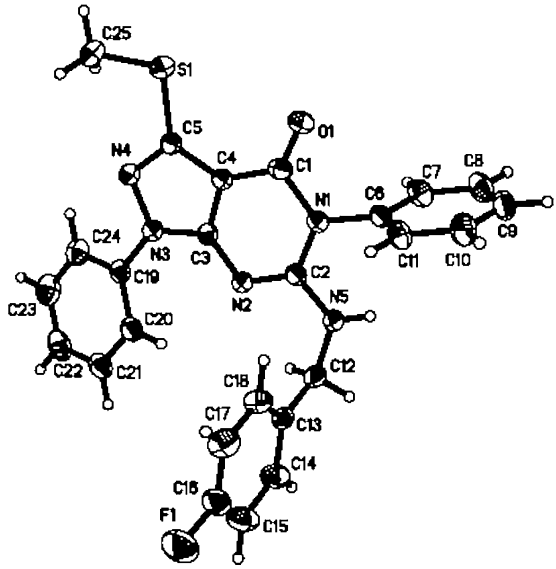


FIGURE 1 Crystal structure of **5a**.

TABLE II Selected Bond Lengths (Å) of **5a**

Bond	Dist.	Bond	Dist.
S(1)—C(5)	1.733(3)	S(1)—C(25)	1.786(3)
F(1)—C(16)	1.363(4)	N(1)—C(2)	1.383(3)
N(1)—C(1)	1.421(3)	N(1)—C(6)	1.443(3)
N(2)—C(2)	1.302(3)	N(2)—C(3)	1.348(3)
N(3)—C(3)	1.349(3)	N(3)—N(4)	1.388(3)
N(3)—C(19)	1.415(3)	N(4)—C(5)	1.314(3)
N(5)—C(2)	1.333(3)	N(5)—C(12)	1.440(3)
O(1)—C(1)	1.213(3)	C(1)—C(4)	1.409(4)
C(3)—C(4)	1.373(4)	C(4)—C(5)	1.409(4)
C(12)—C(13)	1.495(4)		

$Z = 8$, $Dc = 1.365$ g/cm^3, $\mu = 0.182$ mm^{-1}, F (000) = 1904, $R = 0.0600$, $Rw = 0.0932$. The selected bond distances and angles are listed in Tables II and III.

In this compound, the bond lengths of N (2)=C (2) and N (4)=C (5) are 1.302 (3) and 1.314 (3) Å, slightly shorter than the normal C=N bond distance (1.33 Å)[21] and close to 1.312 Å as reported by Chen.[22] The N (1)–C (3), N (1)–C (6), N (2)–C (3), N (3)–C (3), N (3)–C (19), N (5)–C (2), and C (3) = C (4) bond distances are 1.421(3), 1.383(3), 1.443(3), 1.348(3), 1.349(3), 1.415(3), 1.333(3), and 1.373(4) Å, respectively, between the classical single- and double-bond lengths. This is because the rough plane defined by S (1), C (1), C (2), C (3), C (4), C (5),

TABLE III Selected Bond Angles (°) of **5a**

Angle	(°)	Angle	(°)
C(5)—S(1)—C(25)	100.50(15)	C(2)—N(1)—C(1)	122.2(2)
C(2)—N(1)—C(6)	120.6(2)	C(1)—N(1)—C(6)	117.2(2)
C(2)—N(2)—C(3)	113.8(2)	C(3)—N(3)—N(4)	110.9(2)
C(3)—N(3)—C(19)	130.3(2)	N(4)—N(3)—C(19)	118.7(2)
C(5)—N(4)—N(3)	105.0(2)	C(2)—N(5)—C(12)	121.6(2)
O(1)—C(1)—C(4)	128.2(3)	O(1)—C(1)—N(1)	119.3(3)
C(4)—C(1)—N(1)	112.5(2)	N(2)—C(2)—N(5)	118.2(2)
N(2)—C(2)—N(1)	124.7(2)	N(5)—C(2)—N(1)	117.0(2)
N(2)—C(3)—N(3)	125.6(2)	N(2)—C(3)—C(4)	127.0(2)
N(3)—C(3)—C(4)	107.4(2)	C(3)—C(4)—C(1)	119.6(2)
C(3)—C(4)—C(5)	105.1(2)	C(1)—C(4)—C(5)	135.3(3)
N(4)—C(5)—C(4)	111.7(2)	N(4)—C(5)—S(1)	122.3(2)
C(4)—C(5)—S(1)	126.0(2)	C(7)—C(6)—N(1)	119.6(3)
C(11)—C(6)—N(1)	119.7(2)	N(5)—C(12)—C(13)	115.3(2)
C(14)—C(13)—C(12)	118.4(3)	C(18)—C(13)—C(12)	123.5(3)
C(17)—C(16)—F(1)	118.6(4)	C(15)—C(16)—F(1)	118.8(4)
C(20)—C(19)—N(3)	120.9(3)	C(24)—C(19)—N(3)	119.0(3)

TABLE IV The Fungicidal Activities of Compounds 5 (50 mg/l, Inhibitory Rate %)

Compound	**5a**	**5b**	**5c**	**5d**	**5e**	**5f**	**5g**	**5h**	**5i**	**5j**
Pellicularia sasakii	70.0	40.0	66.0	66.0	84.0	76.0	34.3	48.6	28.8	80.6
Cercospora beticola	66.7	61.1	44.4	61.1	72.2	61.1	18.8	56.2	28.1	15.6
Physalospora piricola	58.3	75.0	33.3	16.7	33.3	75.0	30.3	81.8	36.4	12.1

N (1), N (2), N (3), N (4), O (1), and N (5) atoms is coplanar within the average deviation of 0.0207 Å to form a fully delocalized system. The six-member ring of C (1), C (2), C (3), C (4), N (1), and N (2) formed a π_6^7 configuration in which the N (1) atom is sp^2 hydrobrid, which results in the formation of the trigonal configurations of the N (1) nitrogen. The sum of the C (2)-N (1)-C (1), C (2)-N (1)-C (6), and C (1)-N (1)-C (6) bond angle is 360°.

The preliminary fungicidal activities of some compounds **5** were measured in a concentration of 50 mg/l according to the reported method.[23] The results of biological assay are given in Table IV. The results showed that they exhibited good fungicidal activities, especially against *Pellicularia sasakii*. For example, **5e** showed 84.0% inhibitory rate of *Pellicularia sasakii* at the dosage of 50 mg/l.

EXPERIMENTAL

Melting points were determined with a WRS-1B Digital melting point apparatus and were uncorrected. EI-MS were measured on a Finnigen-Trace Mass 2000 Spectrometer, and LC-MS spectra were measured on API 2000. IR spectra were recorded on an Avatar 360 Spectrometer. ^{1}H NMR spectra were taken on a Varian XL-300 Spectrometer with TMS as the internal and with $CDCl_3$ or DMSO-d_6 as the solvents. Elementary analyses were recorded on a Vario EL III elementary analysis instrument. All of the solvents and materials were reagent grade and purified as required.

5-Aminopyrazole **1** was prepared according to the literature procedures,[24] $R^1 = Me$, yield, 92.6%, m.p. 102.2–103.6°C; $R^1 = PhCH_2$, yield, 85.6%, m.p. 85.7–86.5°C.

General Procedure for the Preparation of Iminophosphoranes 2[25]

For example, when R^1 is CH_3, a solution of triphenylphosphine (13.1 g, 50 mmol) in dichloromethane (120 ml) at 0°C was treated with bromine (8.0 g, 50 mmol). The resulting reaction mixture was stirred at 0°C for

30 min and then treated with triethylamine (10.1 g, 100 mmol) followed immediately by the addition of 5-aminopyrazole **1** (13.9 g, 50 mmol). After **1** was added, the cooling bath was removed, and the reaction mixture was allowed to stir at 25°C for 26 h. The reaction mixture was washed with water and then dried. After removing the solvent, the residues were recrystallized with benzene/*n*-hexane to give 22.63 g (26.85 g theoretical, 84.28%) of **2** as a pale yellow crystal, m.p. 192.1–193.8°C. ^{1}H NMR δ ($CDCl_3$, TMS, 300 MHz): 7.16–7.70 (m, 20H, Ph), 3.61 (q, 2H, J = 7.2Hz), 2.51 (s, 3H), 1.44 (t, 3H, J = 7.2Hz); R^1 is $PhCH_2$, yield, 80.2%, m.p. 162.0–163.2°C.

General Procedure for the Preparation of 6-Amino-3-alkylthio-1-phenyl-1,5-dihydro-pyrazolo [3,4-*d*]pyrimidin-4-one Derivatives 5 and 6

Phenyl isocyanate (0.36 g, 3 mmol) was added into a solution of iminophosphorane 2 (1.61 g, 3 mmol) in dry methylene dichloride (20 ml) under nitrogen at room temperature. After the reaction mixture was stirred for 1.5 h, alkylamine was added to the reaction solution, which was then stirred for 30 min. Then the solvent was removed under reduced pressure, and 25 ml of anhydrous ethanol and 1.5 ml 3 mol/l sodium ethoxide were added to the mixture. After stirring for 2–5 h at room temperature, the solution was condensed under reduced pressure. The mixture was cooled and filtered to afford a white solid. Recrystallization from dichloromethane/petroleum ether or via a silica gel column gave pure 6-alkylamino-3-alkylthio-1,5-diphenyl-1,5dihydro-pyrazolo[3,4-*d*]pyrimidin-4-one **5**, and recrystallization from acetone/ethanol to give pure 6-phenylamino-3-alkylthio-1-phenyl-1,5dihydro-pyrazolo-[3,4-*d*]pyrimidin-4-one **6**.

6-(*p*-Fluorobenzylamino)-3-methylthio-1,5-diphenyl-1,5-dihydro-pyrazolo[3,4-*d*]pyrimidin-4-one 5a

White crystals, m.p. 201.3–201.6°C, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.00 (d, 2H, J = 7.5 Hz, Ph or p-FC_6H_4), 7.56 (d, 2H, J = 7.2 Hz, Ph or p-FC_6H_4), 7.40 (t, 2H, J = 7.5 Hz, Ph or p-FC_6H_4), 7.19–7.30 (m, 6H, Ph or p-FC_6H_4), 6.98 (t, 2H, J = 8.4 Hz, Ph or p-FC_6H_4), 4.75 (s, 1H, NH), 4.52 (d, 2H, J = 4.5 Hz, CH_2), 2.65 (s, 3H, SCH_3); IR (KBr) υ (cm^{-1}): 3425 (N—H), 2919 (C—H), 1707 (C=O), 1597, 1553, 1503 (Ph); MS (70 eV, m/z) (relative intensity %): 458 (M+1, 39), 457 (M+, 79), 424 (22), 272 (42), 185 (89), 109 (100), 91 (19), 77 (73). Elemental Anal. Calcd. for $C_{25}H_{20}FN_5OS$: C, 65.63; H, 4.41; N, 15.31. Found: C, 65.58; H, 4.38; N, 15.31.

6-(3-Pyridinemethylamino)-3-methylthio-1,5-diphenyl-1,5-dihydropyrazolo[3,4-*d*] pyrimidin-4-one 5b

White crystals, m.p. 222.6–223.8°C, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.49 (d, 2H, $J = 4.2$ Hz, pyridine), 7.92 (d, 2H, $J = 7.8$ Hz, Ph), 7.22–7.60 (m, 10H, Ph and pyridine), 4.89 (t, 1H, $J = 5.4$ Hz, NH), 4.57 (d, 2H, $J = 5.4$ Hz, NCH_2), 2.64 (s, 3H, SCH_3); IR (KBr) υ (cm^{-1}): 3430 (N—H), 2924(C—H), 1698 (C=O), 1646, 1598, 1544 (Ph and pyridine); MS (70 eV, m/z) (relative intensity %): 441 (M+1,4), 440 (M+, 34), 333 (2), 107 (16), 92 (100), 77 (52), 65 (46). Elemental Anal. Calcd. for $C_{24}H_{20}N_6OS$: C, 65.44; H, 4.58; N, 19.08. Found: C, 65.56; H, 4.73; N, 19.29.

6-(2-Pyridinemethylamino)-3-methylthio-1,5-diphenyl-1,5-dihydro-pyrazolo[3,4-*d*]pyrimidin-4-one 5c

White crystals, m.p. 227.1–228.4°C, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.34 (d, 1H, $J = 2.4$ Hz, pyridine), 8.10 (d, 2H, $J = 6.9$ Hz, Ph), 7.13–7.62 (m, 10H, Ph and pyridine), 5.94 (s, 1H, NH), 4.65 (d, 2H, $J = 3.9$ Hz, CH_2), 2.66 (s, 3H, SCH_3); IR (KBr) υ (cm^{-1}): 3441 (N—H), 2919 (C—H), 1697 (C=O), 1598, 1548, 1539 (Ph and pyridine); MS (70 eV, m/z) (relative intensity %): 441 (M+1, 7), 440 (M+, 26), 349 (12), 168 (12), 93 (13), 92 (12), 77 (100). Elemental Anal. Calcd. for $C_{24}H_{20}N_6OS$: C, 65.44; H, 4.58; N, 19.08. Found: C, 65.33; H, 4.56; N, 18.87.

6-(2-(1-Ethylpyrrolidine)methylamino)-3-methylthio-1,5-diphenyl-1,5-dihydro-pyrazolo [3,4-*d*]pyrimidin-4-one 5d

White crystals, m.p. 161.2–162.5°C, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.17 (d, 2H, $J = 8.1$ Hz, Ph), 7.19–7.56 (m, 8H, Ph), 5.44 (d, 1H, $J = 6.0$ Hz, NH), 3.47–3.54 (m, 1H, $HNCH_2$), 3.20–3.26 (m, 1H, $HNCH_2$), 2.77–2.82 (m, 1H, CHN), 2.66 (s, 3H, SCH_3), 2.50–2.60 (m, 2H, NCH_2CH_3), 1.95–2.08 (m, 2H, CH_2), 1.57–1.62 (m, 2H, CH_2), 1.30–1.43 (m, 2H, CH_2), 0.81 (t, 3H, $J = 6.9$ Hz, CH_3); IR (KBr) υ (cm^{-1}): 3435 (N—H), 2967 (C—H), 1697 (C=O), 1598, 1568, 1554 (Ph); MS (70 eV, m/z) (relative intensity %): 461 (M+1, 5), 460 (M+, 24), 262 (20), 183 (20), 112 (23), 111 (80), 99 (50), 98 (100), 77 (54). Elemental Anal. Calcd. for $C_{25}H_{28}N_6OS$: C, 65.19; H, 6.13; N, 18.25. Found: C, 64.95; H, 6.01; N, 18.02.

6-(2-Thiophenemethylamino)-3-methylthio-1,5-diphenyl-1,5-dihydro-pyrazolo[3,4-*d*] pyrimidin-4-one 5e

White crystals, m.p. 161.6–162.8°C, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.12 (d, 2H, $J = 8.1$ Hz, Ph), 7.17–7.57 (m, 9H, Ph and thiophene), 6.90

(d, 2H, $J = 3.6$ Hz, thiophene), 4.73–4.76 (m, 3H, NH and CH_2), 2.66 (s, 3H, SCH_3); IR (KBr) υ (cm^{-1}): 3400 (N—H), 2924 (C—H), 1698 (C=O), 1593, 1548 (Ph); MS (70 eV, m/z) (relative intensity %): 446 (M+1, 47), 445 (M+, 76), 412 (28), 333 (26), 272 (28), 181 (40), 173 (95), 169 (39), 112 (40), 97 (100), 77 (82). Elemental Anal. Calcd. for $C_{25}H_{19}N_5OS2$: C, 62.00; H, 4.30; N, 15.7. Found: C, 61.91; H, 4.25; N, 15.42.

6-(*n*-Propanylamino)-3-methylthio-1,5-diphenyl-1,5-dihydro-pyrazolo[3,4-*d*]pyrimidin-4-one 5f

White crystals, m.p. 205.7–206.5°C, ^1H NMR ($CDCl_3$, 300 MHz) δ 7.20–8.18(10H, m, Ph); 4.342 (1H, s, NH); 3.36 (2H, q, NCH_2-, $J = 6.3$ Hz); 2.66 (3H, s, SCH_3); 1.54–1.61 (2H, m, $CH_2CH_2CH_3$); 0.87 (3H, t, CH_2CH_3, $J = 7.5$ Hz); IR (KBr) υ (cm^{-1}): 3433 (N—H), 1702 (C=O), 1649, 1598 (Ph); MS (70 eV, m/z) (relative intensity %): 391(M+, 94%), 358 (72), 169 (31), 119 (94), 91 (40), 77 (100); Elemental Anal. Calcd. for $C_{21}H_{21}N_5OS$: C, 64.43; H, 5.41; N, 17.89. Found: C, 64.56; H, 5.38; N, 17.96.

6-(3-Pyridinemethylamino)-3-benzylthio-1,5-diphenyl-1,5-dihydro-pyrazolo[3,4-d]pyrimidin-4-one 5g

White crystals, m.p. 200.0–203.0°C, ^1H NMR ($CDCl_3$, 300 MHz) δ 8.197 (s, 2H, pyridine), 7.91 (d, 2H, $J = 7.8$ Hz, Ph), 7.18–7.57 (m, 15H, Ph and pyridine), 4.82 (t, 1H, $J = 5.4$ Hz, NH), 4.55 (d, 2H, $J = 5.7$ Hz, 3-pyridino-CH_2N), 4.45 (s, 2H, $PhCH_2$); IR (KBr) υ (cm^{-1}): 3393 (N—H), 1712 (C=O), 1596, 1547 (Ph and pyridine); MS (70 eV, m/z) (relative intensity %): 517(M+1, 11), 516 (M+, 28), 483 (68), 426 (12), 3169 (11), 168 (23), 92 (80), 91 (100), 77 (47); Elemental Anal. Calcd. for $C_{30}H_{24}N_6OS$: C, 69.75; H, 4.68; N, 16.27. Found: C, 69.56; H, 4.61; N, 16.33.

6-(2-Pyridinemethylamino)-3-benzylthio-1,5-diphenyl-1,5-dihydro-pyrazolo[3,4-*d*]pyrimidin-4-one 5h

White crystals, m.p. 199.0–200.0°C, ^1H NMR ($CDCl_3$, 300 MHz) δ 8.34 (d, 1H, $J = 3.9$ Hz, pyridine), 8.08 (d, 2H, ph, $J = 7.5$ Hz), 7.11–7.63 (m, 16H, Ph and pyridine), 5.92 (s, 1H, CH_2NH), 4.64 (d, 2H, $J = 4.2$ Hz, 2-pyridino-CH_2N), 4.47 (s, 2H, $PhCH_2$); IR (KBr) υ (cm^{-1}): 3442 (N—H), 1684 (C=O), 1596, 1542 (Ph and pyridine); MS (70 eV, m/z) (relative intensity %): 517 (M+1, 23), 516 (M+, 32), 483 (42), 426 (19), 210 (24), 169 (24), 168 (28), 92 (100), 77 (40). Elemental Anal. Calcd. for $C_{30}H_{24}N_6OS$: C, 69.75; H, 4.68; N, 16.27. Found: C, 69.87; H, 4.61; N, 16.32.

6-(2-Thiophenemethylamino)-3-benzylthio-1,5-diphenyl-1,5-dihydro-pyrazolo[3,4-*d*] pyrimidin-4-one 5i

White crystals, m.p. 213.0–214.0°C, 1H NMR ($CDCl_3$, 300 MHz) δ 8.11 (d, 2H, $J = 7.8$ Hz, Ph), 7.16–7.57 (m, 14H, Ph and Thiophene), 6.90 (d, 2H, $J = 3.9$ Hz, Thiophene), 4.74 (s, 2H, 2-thiophene-CH_2N), 4.47 (s, 2H, $PhCH_2$); IR (KBr) υ (cm^{-1}): 3352 (N—H), 2936 (C—H), 1695 (C=O), 1593, 1539 (Ph); MS (70 eV, m/z) (relative intensity %): 522 (M+1, 19), 521 (M+, 51), 489 (32), 488(100), 392 (22), 319(5), 97(93), 91(92), 77(35). Elemental Anal. Calcd. for $C_{29}H_{23}N_5OS_2$: C, 66.77; H, 4.44; N, 13.43. Found: C, 66.81; H, 4.46; N, 13.53.

6-(*Iso*-propanylylamino)-3-benzylthio-1,5-diphenyl-1,5-dihydro-pyrazolo[3,4-*d*]pyrimidin-4-one 5j

White crystals, m.p. 169.1–171.7°C; ^{1}HNMR ($CDCl_3$, 300 MHz) δ: 8.15 (d, 2H, $J = 8.1$ Hz, Ph), 7.20–7.57 (m, 13H, Ph), 4.47 (s, 2H, $PhCH_2$), 4.16–4.22 (m, 1H, Me_2CH), 4.08 (d, 1H, $J = 6.6$ Hz, NH), 1.16 (d, 6H, $J = 6.6$ Hz, Me_2); IR (KBr) υ (cm^{-1}): 3429 (N—H), 1696 (C=O), 1596, 1541 (Ph); MS (70 eV, m/z) (relative intensity %): 469 (M+2, 17), 468 (M+1,50), 467 (M+, 83), 435 (59), 434 (100), 390 (26), 377 (25), 246 (33), 169 (22), 161 (19), 119 (84), 91 (97), 77 (84); Anal. Calcd. for $C_{27}H_{25}N_5OS$: C, 69.35; H, 5.39; N, 14.98. Found: C, 69.59; H, 5.45; N, 14.72.

3-Methylthio-6-phenylamino-1-phenyl-1,5-dihydro-pyrazolo[3,4-*d*]pyrimidin-4-one 6a

White crystals, m.p. 344.6–346.2°C, ^{1}H NMR (DMSO-d6, 300 MHz) δ 9.70 (br s, 1H, NH), 8.25 (d, 2H, $J = 8.0$ Hz, Ph), 7.88 (d, 2H, $J = 8.0$ Hz, Ph), 750 (t, 2H, $J = 8.0$ Hz, Ph), 7.29 (t, 2H, $J = 7.6$ Hz, Ph), 7.22 (t, 1H, $J = 7.6$ Hz, Ph), 6.91 (t, 1H, $J = 7.6$ Hz, Ph), 2.595 (s, 3H, SCH_3); IR(cm^{-1}): 3432, 3110 (N—H or O—H), 1685 (C=O, w), 1599, 1551, 1505 (Ph); LC-MS (m/z) (relative intensity %): 350 (M+1, 12), 349 (M, 32), 348 (M-1, 100), 109 (40), 108 (11). Elemental Anal. Calcd. for $C_{18}H_{15}N_5OS$: C, 61.87; H, 4.33; N, 20.04. Found: C, 61.99; H, 4.38; N, 19.92.

3-Benzylthio-6-phenylamino-1-phenyl-1,5-dihydro-pyrazolo[3,4-*d*]pyrimidin-4-one 6b

White crystals, m.p. 247.6–249.2°C, ^{1}H NMR (DMSO-d6, 300 MHz) δ 9.96 (br s, 1H, NH), 8.24 (d, 2H, $J = 7.6$ Hz , Ph), 7.88 (d, 2H, $J = 7.6$ Hz, Ph), 7.48–7.52 (m, 4H, Ph), 7.22–7.34 (m, 6H, Ph), 6.91 (t, 1H, $J = 7.6$ Hz, Ph), 4.54 (s, 2H, SCH_2Ph), IR(cm^{-1}): 3403, 3123 (N—H

or O—H), 1687 (C=O, w), 1597, 1560, 1506 (Ph); LC-MS (m/z) (relative intensity %): 426 (M+1, 15), 425 (M, 43), 424 (M-1, 100). Elemental Anal. Calcd. for $C_{24}H_{19}N_5OS$: C, 67.74; H, 4.50; N, 16.46. Found: C, 67.58; H, 4.56; N, 16.62.

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