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Carbon−Carbon Bond Cleavage Reaction: Synthesis of Multisubstituted Pyrazolo[1,5-*a*]pyrimidines

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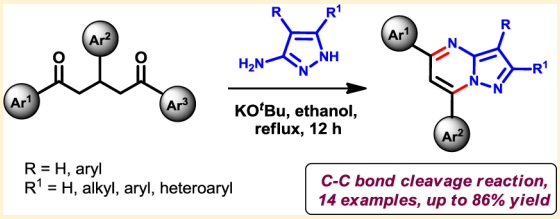
Supporting Information

ABSTRACT: A new carbon−carbon bond cleavage reaction was developed for the efficient synthesis of multisubstituted pyrazolo[1,5-*a*]pyrimidines. This base induced reaction of 1,3,5-trisubstituted pentane-1,5-diones and substituted pyrazoles afforded good yields of the pyrazolo[1,5-*a*]pyrimidines.



The cleavage of carbon−carbon bond is a significant issue in organic chemistry due to the inert nature of the C−C bond.[1] Although, the importance of this C−C bond cleavage had already resulted different methodologies for the cleavage of C−C,[2] C=C[3] and C≡C[4] bonds, the development of new routes for selective cleavage of C−C bond still remains as an important and challenging goal for the chemists and biologists.

The pyrazole fused heterocycle pyrazolo[1,5-*a*]pyrimidine is the key structural motif of several drugs and pesticides. For example, the hypnotic drugs zaleplon and indiplon, the anxiolytic drug ocinaplon, and the fungicide pyrazophos have this central motif of pyrazolo[1,5-*a*]pyrimidine (Figure 1). The

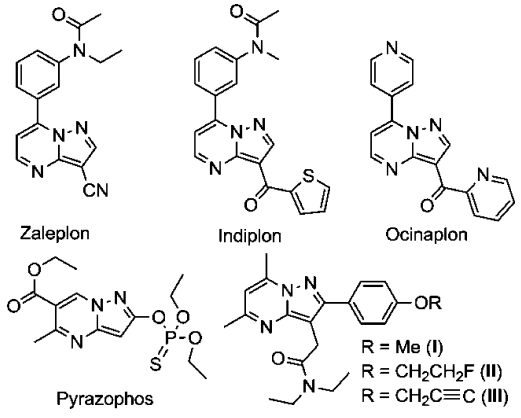


Figure 1. Examples of drugs/biologically active pyrazolo[1,5-*a*]-pyrimidines.

pyrazolo[1,5-*a*]pyrimidines **I**−**III** (Figure 1) are found to possess high affinity for translocator protein (TSPO), which is revealed as an attractive target in anticancer therapy.[5] The pyrazolo[1,5-*a*]pyrimidine derivatives are also known for their wide range of biological activities such as antimicrobial, antibacterial, antitrichomonal, antischistosomal, anticancer, antitumor, etc.[6] Some of the pyrazolo[1,5-*a*]pyrimidine derivatives are found to have potent and selective Pim-1 inhibitory activity, excellent activity against wild-type HIV-1 and CK2 Kinase inhibitory activity.[7] The importance of these pyrazolo[1,5-*a*]pyrimidines has led to the development of new methods for the synthesis of these molecules, typically by the condensation reaction of (i) aminopyrazole with 1,2-allenic ketones,[8] (ii) aminopyrazole with enaminonitriles or enaminones,[9] and (iii) aminopyrazole with 1, 3-dicarbonyl compounds or *α*,*β*-unsaturated carbonyl compounds.[10] Recently, we also reported the synthesis of pyrazolo[1,5-*a*]pyrimidines by the regioselective palladium catalyzed reaction of *β*-halovinyl aldehydes with 3-aminopyrazoles.[11c] In spite of the presence of methods for the synthesis of pyrazolo[1,5-*a*]pyrimidines, due to the tremendous biological profile of these heterocycles, new efficient methods which can accommodate a broad range of substituents on the heterocyclic scaffold are still highly desirable. In continuation of our work on search for novel methods for the syntheses of important heterocycles,[11] herein, we report an unprecedented reaction of 1,3,5-trisubstituted pentane-1,5-diones with substituted 3-amino pyrazoles in the presence of base, which proceeds via C−C bond cleavage for the easy construction of multisubstituted pyrazolo[1,5-*a*]-pyrimidines. Initially, we selected 1,5-diketone **1a** and 3-amino-1*H*-pyrazole (**2a**) as the model substrates for the synthesis of compound **3a** (Table 1). Refluxing a mixture of **1a** and **2a** in anhydrous ethanol in the presence of 2 equiv of NaOMe for 12 h furnished pyrazolo[1,5-*a*]pyrimidine **3a** in 57% yield (entry 1, Table 1). The product **3a** was identified from ^{1}H NMR, ^{13}C NMR and mass spectral data. To determine the ideal base and solvent for this base induced reaction, we studied this model reaction with some other bases and solvents as shown in Table 1. The bases such as KOMe, NaH and KOH led to lower yield of **3a** (entries 2 and 7−8). Gratifyingly, when we used NaO^{t}Bu and KO^{t}Bu as the bases (2 equiv) in the above reaction, the reaction afforded 78% and 84% yields of **3a**, respectively, in ethanol (entries 3−4). Further studies of KO^{t}Bu

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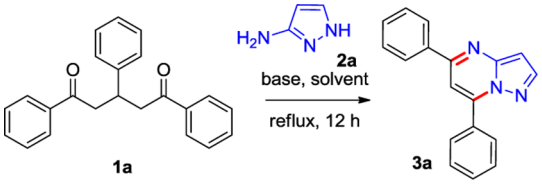
Table 1. Optimization of the Reaction Conditions for 3a

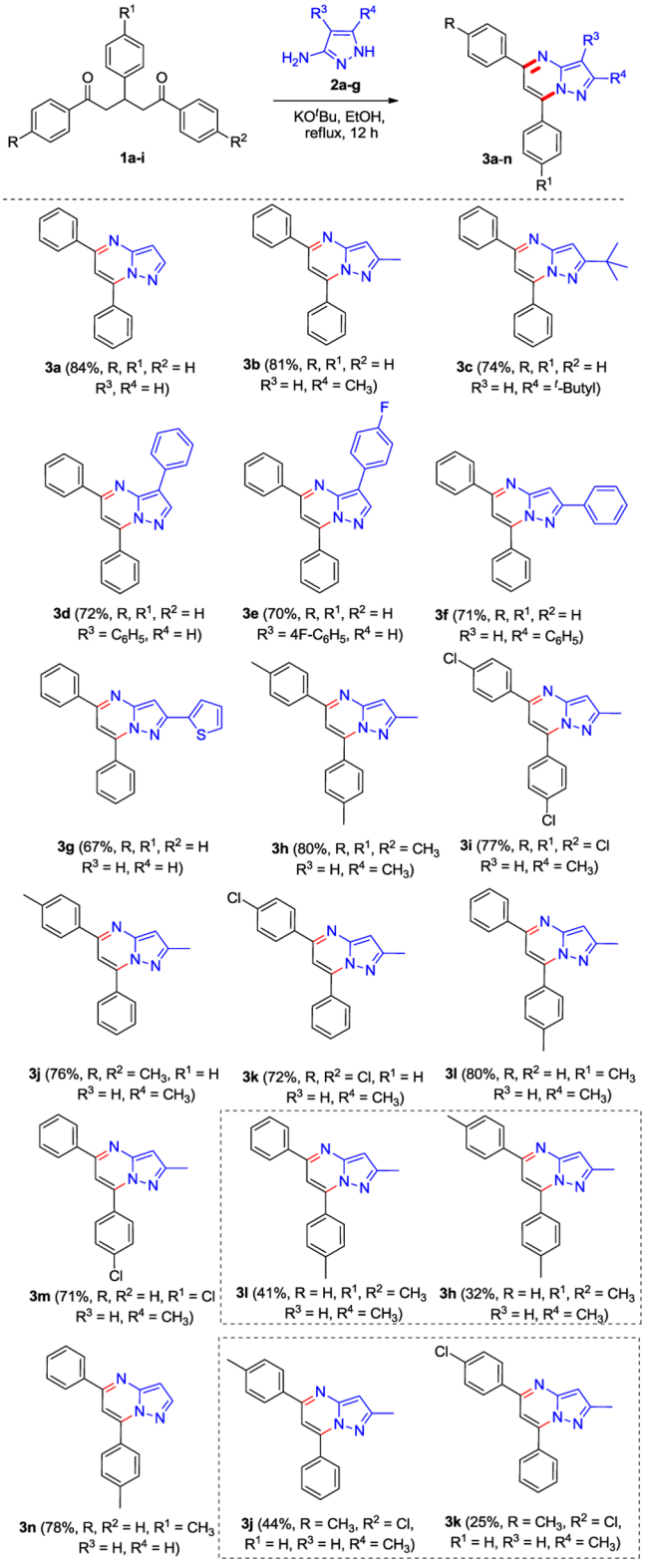


entry	base[a]	solvent	yield (%)[b]
1	NaOMe	EtOH	57
2	KOMe	EtOH	62
3	NaO^{t}Bu	EtOH	78
4	KO^{t}Bu	EtOH	84
5[c]	KO^{t}Bu	DMF	71
6[c]	KO^{t}Bu	DMSO	62
7	NaH	toluene	33
8	KOH	ethanol	24
9	-	ethanol	0

[a]Two equivalents of the base was used. [b]Yield of the isolated product. [c]Reaction was performed at 120 °C.

induced cyclization reaction in high boiling solvents DMF and DMSO could not improve the yield of the product **3a** (entries 5−6), and in the absence of the base, the reaction could not afford the product **3a** (entry 9). The reaction of **1a** and **2a** with 1 equiv of the base KO^{t}Bu, under the optimized reaction condition, provided less yield of **3a** (76%). With the optimized reaction conditions in hand (Table 1, entry 4), we then explored the substrate scope of the reaction with some representative 1,5-dicarbonyls (**1a−h**) and 3-amino-1*H*-pyrazoles (**2a−g**) which are shown in Table 2. The base induced cyclization reaction of 1,5-dicarbonyl **1a** with various 3-amino-1*H*-pyrazoles (**2a−g**) without substituents and with substituents such as methyl, *t*-butyl, phenyl and 4-fluorophenyl present in the pyrazole ring reacted smoothly to afford pyrazolo[1,5-*a*]pyrimidines **3a−f** in 70−84% yields under the optimized reaction conditions. Similarly, the reaction of **1a** and 5-(thiophen-2-yl)-3-amino-1*H*-pyrazole (**2g**) afforded pyrazolo-[1,5-*a*]pyrimidine **3g** in 67% yield. Next, the reaction of 5-methyl-3-amino-1*H*-pyrazole (**2b**) with various symmetrical and unsymmetrical 1,5-dicarbonyls with electron donating and electron-withdrawing groups present in the aromatic rings were studied to extend the substrate scope. Symmetrical 1,5-dicarbonyls with methyl and chloro groups present in the aromatic rings **1b−c** reacted efficiently with **2b** to give the corresponding substituted pyrazolo[1,5-*a*]pyrimidines **3h−i** in good yields (77−80%). Similarly, the cyclization reactions of **2b** with symmetrical 1,5-dicarbonyls such as 3-phenyl-1,5-di-*p*-tolylpentane-1,5-dione (**1d**), 3-phenyl-1,5-di-*p*-chlorophenyl-pentane-1,5-dione (**1e**), 1,5-diphenyl-3-(*p*-tolyl)pentane-1,5-dione (**1f**) and 3-(*p*-chlorophenyl)-1,5-diphenylpentane-1,5-dione (**1g**) proceeded very easily under the optimized condition to afford pyrazolo[1,5-*a*]pyrimidines **3j−m** in 71−80% yields. In addition, the reaction of **1f** with **2a** afforded 78% yield of pyrazolo[1,5-*a*]pyrimidine **3n**, whose single X-ray crystallography studies (Figure 2) confirmed the structure of compound **3**.[12] The reaction of unsymmetrical 1-phenyl-3,5-di-*p*-tolylpentane-1,5-dione (**1h**) with **2b** afforded a mixture of pyrazolo[1,5-*a*]pyrimidines **3l** (41%) and **3h** (32%) under the standard condition. Similarly, the condensation reaction of unsymmetrical 1-(4-chlorophenyl)-3-phenyl-5-(*p*-tolyl)-pentane-1,5-dione (**1i**) with **2b** afforded a mixture of

Table 2. Synthesis of Various Substituted Pyrazolo[1,5-*a*]pyrimidines[a]



[a]Reaction conditions: 1,5-dicarbonyl (1.0 mmol), 3-amino pyrazole (1.0 mmol) and KO^{t}Bu (2.0 mmol) in ethanol (3.0 mL) was heated at 120 °C for 12 h; isolated yields.

pyrazolo[1,5-*a*]pyrimidines **3j** (44%) and **3k** (25%) under the standard condition. This result indicated that phenyl ring substituted with electron withdrawing group eliminated

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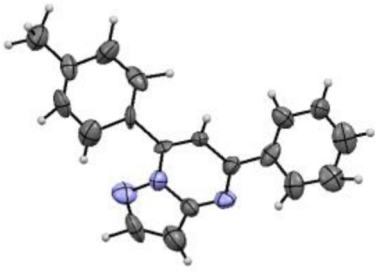
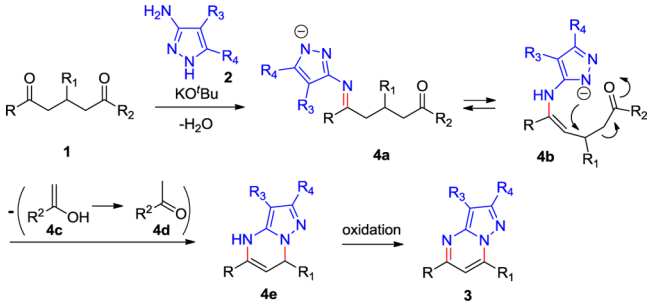


Figure 2. X-ray crystal structure of **3n**.

preferentially from the 1,5-dicarbonyl compound providing better yield of compound **3j**. The starting 1,5-dicarbonyl compounds were already used by different research groups for the construction of various important scaffolds[13a,b] and they were easily prepared by refluxing a mixture of acetophenone with chalcone following known procedure.[13c]

A probable mechanism for the formation of compound **3** is shown in Scheme 1. First, condensation of ketone **1** with 3-amino pyrazole **2**, followed by deprotonation of the formed imine derivative in the presence of base potassium *tert*-butoxide, generates the pyrazolide anion **4a**. Tautomerization of the imine **4a** to the enamine **4b**, followed by intramolecular nuclephilic attack of pyrazolide anion on the benzylic/allylic carbon (C3), affords intermediate **4e** by elimination of one molecule of acetophenone derivative **4d**. Finally, aerial oxidation of the resulting dihydropyrazolo[1,5-*a*]pyrimidine **4e** affords compound **3**.[14] To prove the mechanism, the GC–MS data of the crude reaction mixture of **1d** and **2b** was recorded (see Supporting Information), as well as, the side product of the reaction was isolated. The side product was found to be 4-methylacetophenone, which proved the proposed mechanism for the formation of **3** from intermediate **4b** (Scheme 1). The substrate **1d** on treatment with potassium *tert*-butoxide alone under standard condition did not provide the base promoted eliminated product 4-methylacetophenone which further suggested the reaction mechanism depicted in Scheme 1.

Scheme 1. Proposed Reaction Mechanism



In conclusion, we have developed a novel base induced reaction of 1,3,5-trisubstituted pentane-1,5-diones with substituted pyrazoles for the construction of poly substituted pyrazolo[1,5-*a*]pyrimidines via C–C/C–N bond cleavage reaction. The methodology has advantages such as wide substrate scope, easily available starting materials, high yields, and simple reaction procedure.

EXPERIMENTAL SECTION

General Information. Melting points were uncorrected. IR spectra were recorded using chloroform. NMR spectra were recorded on a 300 or 500 MHz spectrometer using tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded on GCMS instrument. All the commercially available regents were used as received. All experiments were monitored by thin layer chromatography (TLC). TLC was performed on precoated silica gel plates. Column chromatography was performed on silica gel (100–200 mesh).

General Procedure for the Synthesis of Pyrazolo[1,5-*a*]pyrimidines Derivatives 3a–n. A mixture of 1,5-diketone **1** (1.0 mmol), 3-amino-1*H*-pyrazole **2** (1.0 mmol), and KO^{t}Bu (2.0 mmol) in anhydrous ethanol was refluxed for 12 h. After completion of the reaction, the solvent was removed from the reaction mixture, water was added into it, and then it was extracted with ethyl acetate. The ethyl acetate layer was then washed with brine and water. Finally, it was dried over anhydrous Na_2SO_4, and the solvent was removed under vacuo. The crude product obtained was purified by column chromatography over silica gel (100–200 mesh) using EtOAc/hexane as the eluant.

5,7-Diphenylpyrazolo[1,5-a]pyrimidine (***3a***). Yellow solid (228 mg, 84%); mp: 88–90 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.81 (s, 1H), 7.34 (s, 1H), 7.51 (d, J = 6.5 Hz, 2H), 7.56–7.59 (m, 3H), 8.06 (d, J = 3.4 Hz, 2H), 8.11–8.17 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 97.2, 105.2, 127.3, 128.4, 128.7, 128.9, 129.3, 130.3, 130.9, 131.6, 137.5, 145.2, 146.9, 156.2; IR ($CHCl_3$, cm^{-1}): 760, 1028, 1222, 1377, 1491, 1549, 1607, 2924. MS (EI, m/z): 271 [M$^+$]. Anal. Calcd for $C_{18}H_{13}N_3$: C, 79.68; H, 4.83; N, 15.49. Found: C, 79.55; H, 4.99; N, 15.68.

2-Methyl-5,7-diphenylpyrazolo[1,5-a]pyrimidine (***3b***). Yellow solid (231 mg, 81%); mp: 115–117 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.53 (s, 3H), 6.57 (s, 1H), 7.48–7.50 (m, 6H), 7.55 (d, J = 4.2 Hz, 2H), 8.06–8.10 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.8, 96.4, 104.3, 127.1, 128.6, 128.8, 129.2, 130.0, 130.8, 131.6, 137.6, 146.1, 150.6, 155.4, 155.7; IR ($CHCl_3$, cm^{-1}): 771, 1017, 1218, 1373, 1490, 1554, 1608, 2924. MS (EI, m/z): 285 [M$^+$]. Anal. Calcd for $C_{19}H_{15}N_3$: C, 79.98; H, 5.30; N, 14.73. Found: C, 79.81; H, 5.59; N, 14.89.

2-tert-Butyl-5,7-diphenylpyrazolo[1,5-a]pyrimidine (***3c***). Gum (242 mg, 74%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.43 (s, 9H), 6.65 (s, 1H), 7.45–7.48 (m, 4H), 7.50–7.54 (m, 3H), 8.09 (d, J = 4.8 Hz, 2H), 8.20 (d, J = 5.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 30.4, 32.9, 93.0, 104.0, 127.1, 128.3, 128.8, 129.4, 129.9, 130.7, 131.6, 137.8, 145.9, 150.4, 155.4, 168.0; IR ($CHCl_3$, cm^{-1}): 762, 1017, 1239, 1490, 1551, 1606, 2960. MS (EI, m/z): 327 [M$^+$]. Anal. Calcd for $C_{22}H_{21}N_3$: C, 80.70; H, 6.46; N, 12.83. Found: C, 80.96; H, 6.61; N, 12.55.

3,5,7-Triphenylpyrazolo[1,5-a]pyrimidine (***3d***). Yellow solid (250 mg, 72%); mp: 175–177 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.40 (s, 1H), 7.50–7.56 (m, 7H), 7.60 (d, J = 6.6 Hz, 2H), 8.06 (d, J = 5.9 Hz, 2H), 8.21–8.25 (m, 4H), 8.49 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 105.1, 110.6, 126.0, 126.3, 127.3, 128.6, 128.8, 129.2, 130.3, 130.9, 132.3, 137.3, 142.9, 145.9, 146.9, 155.8; IR ($CHCl_3$, cm^{-1}): 691, 761, 1028, 1189, 1377, 1491, 1562, 1607, 2923. MS (EI, m/z): 347 [M$^+$]. Anal. Calcd for $C_{24}H_{17}N_3$: C, 82.97; H, 4.93; N, 12.10. Found: C, 82.68; H, 4.75; N, 12.39.

3-(4-Fluorophenyl)-5,7-diphenylpyrazolo[1,5-a]pyrimidine (***3e***). Yellow solid (256 mg, 70%); mp: 159–161 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.19 (d, J = 5.4 Hz, 2H), 7.41 (s, 1H), 7.55 (d, J = 8.4 Hz, 4H), 7.57 (s, 1H), 7.60 (d, J = 3.3 Hz, 1H), 8.07–8.24 (m, 6H), 8.44 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 105.1, 109.8, 115.4, 115.6, 127.2, 127.7, 127.8, 128.7, 128.9, 129.2, 130.4, 130.9, 131.3, 137.2, 142.6, 146.9, 155.9; IR ($CHCl_3$, cm^{-1}): 750, 835, 1227, 1492, 1565, 1613, 2924. MS (EI, m/z): 365 [M$^+$]. Anal. Calcd for $C_{24}H_{16}FN_3$: C, 78.89; H, 4.41; N, 11.50. Found: C, 78.90; H, 4.62; N, 11.71.

2,5,7-Triphenylpyrazolo[1,5-a]pyrimidine (***3f***). Yellow solid (246 mg, 71%); mp 161–162 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.10 (s, 1H), 7.36 (s, 1H), 7.45–7.61 (m, 8H), 8.02 (d, J = 3.1 Hz, 1H) 8.14–8.22 (m, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 93.7, 104.9, 126.5,

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127.2, 128.2, 128.5, 128.6, 128.8, 129.4, 130.2, 130.9, 131.4, 137.5, 146.3, 150.9, 156.0, 156.2; IR ($CHCl_3$, cm^{-1}): 759, 845, 1027, 1233, 1490, 1552, 1607, 2926. MS (EI, *m*/*z*): 347 [M^+]. Anal. Calcd for $C_{24}H_{17}N_3$: C, 82.97; H, 4.93; N, 12.10. Found: C, 82.78; H, 4.81; N, 12.34.

5,7-Diphenyl-2-(thiophen-2-yl)pyrazolo[1,5-a]pyrimidine (**3g**). Yellow solid (237 mg, 67%); mp: 182−184 °C. ^1H NMR ($CDCl_3$, 500 MHz) δ 6.96 (s, 1H), 7.09−7.58 (m, 10H), 8.12 (d, J = 5.4 Hz, 2H), 8.18 (d, J = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 93.5, 105.0, 125.7, 126.2, 127.2, 127.6, 128.5, 128.8, 129.4, 130.2, 130.9, 137.4, 146.2, 150.9, 151.5, 156.2; IR ($CHCl_3$, cm^{-1}): 762, 1017, 1218, 1490, 1565, 1606, 2923. MS (EI, *m*/*z*): 353 [M^+]. Anal. Calcd for $C_{22}H_{15}N_3S$: C, 74.76; H, 4.28; N, 11.89. Found: C, 74.59; H, 4.55; N, 11.67.

2-Methyl-5,7-di-p-tolylpyrazolo[1,5-a]pyrimidine (**3h**). Gum (251 mg, 81%); ^1H NMR ($CDCl_3$, 500 MHz) δ 2.42 (s, 3H), 2.46 (s, 3H), 2.52 (s, 3H), 6.54 (s, 1H), 7.21 (s, 1H), 7.31 (d, J = 4.8 Hz, 2H), 7.37 (d, J = 4.5 Hz, 2H), 7.86 (d, J = 4.9 Hz, 2H), 7.97−7.99 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.8, 21.5, 96.1, 103.8, 127.0, 129.3, 129.5, 134.6, 140.3, 141.2, 155.2, 155.7; IR ($CHCl_3$, cm^{-1}): 762, 826, 1176, 1478, 1610, 2937. MS (EI, *m*/*z*): 313 [M^+]. Anal. Calcd for $C_{21}H_{19}N_3$: C, 80.48; H, 6.11; N, 13.41. Found: C, 80.16; H, 6.32; N, 13.66.

5,7-Bis(4-chlorophenyl)-2-methylpyrazolo[1,5-a]pyrimidine (**3i**). Yellow solid (272 mg, 77%); 172−175 °C. ^1H NMR ($CDCl_3$, 500 MHz) δ 2.54 (s, 3H), 6.59 (s, 1H), 7.19 (s, 1H), 7.49 (d, J = 4.8 Hz, 4H), 7.56 (d, J = 5.1 Hz, 4H), 8.06 (d, J = 5.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 29.6, 96.7, 103.7, 128.4, 129.0, 129.8, 135.8, 136.4, 137.1, 145.0, 150.4, 154.3, 155.7; IR ($CHCl_3$, cm^{-1}): 774, 817, 1013, 1090, 1486, 1593, 1607, 2924. MS (EI, *m*/*z*): 353 [M^+]. Anal. Calcd for $C_{19}H_{13}Cl_2N_3$: C, 64.42; H, 3.70; N, 11.86. Found: C, 64.79; H, 3.84; N, 11.62.

2-Methyl-7-phenyl-5-p-tolylpyrazolo[1,5-a]pyrimidine (**3j**). Brown gum (227 mg, 76%); ^1H NMR ($CDCl_3$, 500 MHz) δ 2.43 (s, 3H), 2.53 (s, 3H), 6.55 (s, 1H), 7.22 (s, 1H), 7.31 (d, J = 7.8 Hz, 2H), 7.55−7.58 (m, 2H), 8.01 (d, J = 4.2 Hz, 2H), 8.06−8.09 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.8, 21.3, 96.2, 104.2, 127.0, 128.6, 129.2, 129.5, 130.8, 131.6, 134.7, 140.4, 146.1, 150.5, 155.3, 155.7; IR ($CHCl_3$, cm^{-1}): 765, 817, 1180, 1492, 1606, 2924. MS (EI, *m*/*z*): 299 [M^+]. Anal. Calcd for $C_{20}H_{17}N_3$: C, 80.24; H, 5.72; N, 14.04. Found: C, 80.02; H, 5.84; N, 13.98.

5-(4-Chlorophenyl)-2-methyl-7-phenylpyrazolo[1,5-a]pyrimidine (**3k**). Brown solid (230 mg, 72%); mp: 132−134 °C. ^1H NMR ($CDCl_3$, 500 MHz) δ 2.54 (s, 3H), 6.57 (s, 1H), 7.20 (s, 1H), 7.49 (s, 1H), 7.56−7.58 (m, 3H), 8.05−8.08 (m, 5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.9, 96.6, 104.0, 128.5, 128.7, 129.1, 129.3, 131.0, 131.5, 136.4, 146.4, 154.5, 155.7; IR ($CHCl_3$, cm^{-1}): 764, 827, 1013, 1488, 1556, 1594, 2924. MS (EI, *m*/*z*): 319 [M^+]. Anal. Calcd for $C_{19}H_{14}ClN_3$: C, 71.36; H, 4.41; N, 13.14. Found: C, 71.59; H, 4.65; N, 13.01.

2-Methyl-5-phenyl-7-p-tolylpyrazolo[1,5-a]pyrimidine (**3l**). Brown solid (239 mg, 80%); mp: 109−111 °C. ^1H NMR ($CDCl_3$, 500 MHz) δ 2.46 (s, 3H), 2.53 (s, 3H), 6.58 (s, 1H), 7.21 (s, 1H), 7.24 (s, 2H), 7.49−7.52 (m, 3H), 7.99−8.11 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.9, 21.6, 96.2, 96.4, 103.9, 104.1, 127.3, 128.9, 129.2, 129.4, 129.6, 130.1, 141.3, 146.4, 155.3, 155.8; IR ($CHCl_3$, cm^{-1}): 772, 1019, 1463, 1596, 1661, 2922. MS (EI, *m*/*z*): 299 [M^+]. Anal. Calcd for $C_{20}H_{17}N_3$: C, 80.24; H, 5.72; N, 14.04. Found: C, 80.46; H, 5.44; N, 14.27.

7-(4-Chlorophenyl)-2-methyl-5-phenylpyrazolo[1,5-a]pyrimidine (**3m**). Gum (227 mg, 71%); ^1H NMR ($CDCl_3$, 500 MHz) δ 2.54 (s, 3H), 6.58 (s, 1H), 7.51 (s, 2H), 7.56−7.59 (m, 3H), 8.08−8.12 (m, 5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.9, 96.5, 104.5, 127.3, 128.7, 128.9, 129.3, 130.1, 130.9, 139.0, 143.9, 154.8, 155.0; IR ($CHCl_3$, cm^{-1}): 763, 1028, 1217, 1373, 1490, 1554, 1607, 2923. MS (EI, *m*/*z*): 319 [M^+]. Anal. Calcd for $C_{19}H_{14}ClN_3$: C, 71.36; H, 4.41; N, 13.14. Found: C, 71.12; H, 4.69; N, 13.35.

5-Phenyl-7-p-tolylpyrazolo[1,5-a]pyrimidine (**3n**). White solid (222 mg, 78%); mp: 110−112 °C. ^1H NMR ($CDCl_3$, 300 MHz) δ 2.47 (S, 3H), 6.79 (s, 1H), 7.33 (s, 1H), 7.35−7.55 (m, 4H), 7.96 (d, J = 3.4 Hz, 2H), 8.11−8.16 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 97.1, 104.9, 127.3, 128.6, 128.9, 129.2, 129.4, 130.3, 137.6, 141.4, 145.1, 146.9, 156.2, 161.3; IR ($CHCl_3$, cm^{-1}): 2924, 1610, 1550, 1369, 1220, 1028, 761. MS (EI, *m*/*z*): 285 [M]$^+$. Anal. Calcd for $C_{19}H_{15}N_3$: C, 79.98; H, 5.30; N, 14.73. Found: C, 79.65; H, 4.91 N, 14.55.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^1H NMR and ^{13}C NMR spectra for **3a**−**n** and X-ray crystallographic data (CIF file) for **3n**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00933.

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Notes

The authors declare no competing financial interest.

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