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A SIMPLIFIED GREEN CHEMISTRY APPROACH TO SYNTHESIS OF AZOLO[1,5-*a*]PYRIMIDINE INCORPORATED THIOPHENE MOIETY

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Abstract – A highly efficient and environmentally friendly protocol has been developed for a facile synthesis of novel azolo[1,5-*a*]pyrimidines incorporated thiophene moiety under microwave irradiation. The advantages of short reaction time, high efficiency, no separation of in situ generated intermediate, using cheap, non-corrosive sodium persulfate as the oxidant, together with a very simple work-up procedure, make this one-pot and solvent-free protocol a green and powerful alternative to traditional methods for the synthesis of these kinds of compounds.

Many efforts of synthetic chemists are directed to work out new high-effective synthetic protocols for heterocycles production. Due to its importance of heterocycles in medicinal chemistry, pharmaceutical chemistry, and drug discovery.^{1,2} Among these heterocycles azolo[1,5-*a*]pyrimidine scaffold, in which it has been contributing more and more in biological, pharmacological fields and so on.³⁻⁵

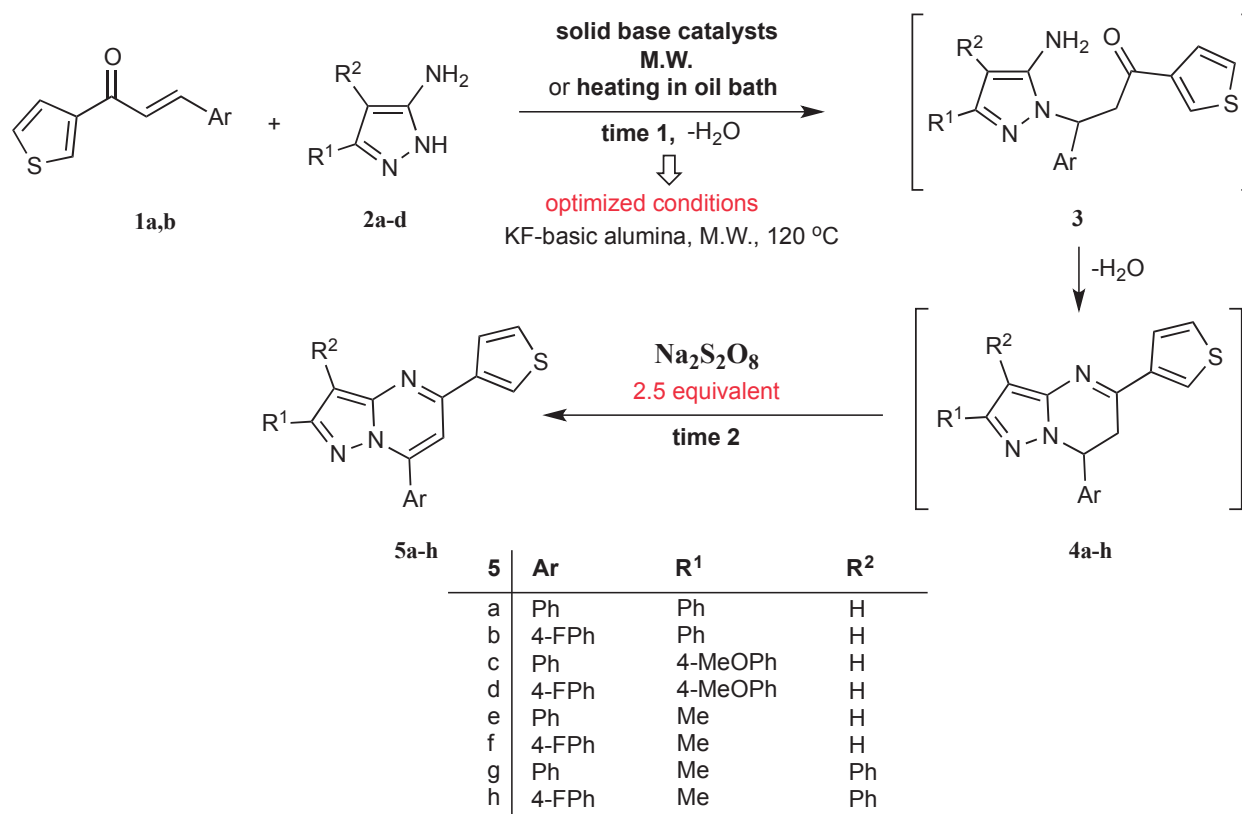
Also, thiophene moiety is present in a large number of bioactive molecules having diverse biological activities such as anti-inflammatory,⁶ anticonvulsant,⁷ antibacterial,⁸ and antitumor⁹ activities. Moreover, thiophene moiety is a well-known isostere for benzene in which the replacement of benzene ring of the antidepressant drug led to a prolongation of half-life.¹⁰

Due to the scarcity in nature of azolo[1,5-*a*]pyrimidines heterocyclic ring system, various methods have been developed for the synthesis of azolo[1,5-*a*]pyrimidines, the most commonly used strategies is cyclocondensations of α -aminoazoles with α,β -unsaturated carbonyls.¹¹⁻¹⁷ However, there are still drawbacks such as rigorous or hazardous conditions, intractable side reactions; use of hazardous organic solvent, caustic and corrosive materials, non-economic materials, long reaction time, tedious procedures and one of the challenging objects for the comprehensive study is the partially hydrogenated heterocyclic

compounds formed. These dehydro products consider one of the problems sometimes preventing efficient pharmacological applications.¹⁸ Thereby, development of strategy allowing tuning oxidation of heterocycles formed is the actual goal.

One of the best alternatives is to carry out this kind of reactions under solvent-free conditions, utilizing microwave irradiations. Considering the requirement of green chemistry, we have also successfully applied the microwave irradiation technique in some organic transformation in recent year.¹⁹⁻²² Herein, we want to report a one-pot and solvent-free synthesis of various azolo[1,5-*a*]pyrimidines from chalcones and aminoazole.

A wide variety of catalysts were scanned for the reaction of chalcone **1a** with 5-amino-3-phenylpyrazole (1 equivalent, **2a**) (Scheme 1) as a model reaction under microwave irradiation in the presence of sodium persulfate as the oxidant.



Scheme 1. Synthesis of pyrazolo[1,5-*a*]pyrimidine

Although we do this model reaction as one-pot protocol but it consist mainly from two steps: step one: formation of intermediate **4** (dehydro form) and step two: formation of desired product **5** (oxidation step) as represented in Scheme 1. Therefore we will optimize first the reaction condition of step one to select the best catalyst. Thus, some solid base catalysts, namely, basic alumina, KF/basic alumina, and potassium carbonate were selected. This group of catalysts has the advantage over the other bases due to having a low impact on the environment, for instance, and to be easily recycled. To find the specific effect

of microwave on this reaction, the above-mentioned reaction was carried out under the same conditions in the absence of microwave irradiation (Table 1).

Table 1. Synthesis of pyrazolo[1,5-*a*]pyrimidine derivative **5a** using different solid base catalysts under both microwave irradiation or conventional heating (oil bath)

Entry	Solid base catalyst	Microwave irradiation			Conventional heating		
		Time 1 (min)	Time 2 (min)	Yield%	Time 1 (h)	Time 2 (h)	Yield%
1	None	180	-	-	18	-	-
2	K ₂ CO ₃	90	40	74%	14	5	53%
3	basic alumina	80	25	83%	10	4	64%
4	KF/basic alumina	50	20	88%	8	4	71%

It is clear from results cited in Table 1, that under the condition of microwave irradiation at 120 °C, the addition-cyclization of **2a** with chalcone **1a** to form intermediate 6,7-dihydropyrazolo[1,5-*a*]pyrimidine **4** can be almost completely accomplished within 50 min (time 1, till no starting materials detected by TLC). Then we add the oxidant (Na₂S₂O₈) to convert the *in situ* generated, 7-dihydropyrazolo[1,5-*a*]pyrimidine **4** into pyrazolo[1,5-*a*]pyrimidine derivative **5** within 20 min (time 2, till no intermediate **4** detected by TLC).

Noteworthy, the yield of reaction depend mainly on the formation of intermediate **4** due to the presence of the solid basic catalyst. It was found that the best yield is 88% of the desired product **5a** was reached using KF/basic alumina under microwave irradiations. The conventional heating method in an oil bath at 120 °C needed to obtain 71% yield of the product. The obtained results revealed that reactions required a longer time to attain considerable yields under conventional heating methods and the yield is lower than the obtained using microwave protocol. From these results, it is evident that microwave irradiation showed the beneficial effect on the above-mentioned reaction in which it is possible to decrease the reaction time significantly from several hours to minutes with higher yields. Potassium carbonate and basic alumina were employed also as basic catalysts, but lower yield 74% and 83% respectively were obtained under microwave irradiation after longer working time than a case of KF/basic alumina, also the same trend under conventional conditions (Experimental). The slight difference in catalytic activity between basic alumina and KF/basic alumina mainly may be due to the local basicity effect. We also performed the reactions without a catalyst under both microwave and conventional methods and no reaction products were observed (intermediate **4** not formed) even after 180 min and 18 h under microwave and conventional heating, respectively.

It was found that the amount of oxidant used is crucial, therefore we will optimize the conditions of step two, to select the appropriate oxidant amounts necessary to perform the reaction under microwave irradiation, different amounts of oxidant (mol/mol) ratios were tested. Table 2 represents the effect of oxidant amount on the yield of compound **5**. From the results cited in Table 2, it is clear that 2.5 equivalents of oxidant furnishes the respective product in an excellent yield (Table 2, entry 5), unless this specific amount used, a mixture product of **4a** and **5a** has been obtained in case lower than the mentioned ratio and the same yield of desired product **5a** was produced for 3.00 equivalents of oxidant. The influence of the temperature of reaction on the reaction yield and kinetic also investigated to find the best reaction conditions.

Table 2. Optimization of reaction condition for synthesis of pyrazolo[1,5-*a*]pyrimidine derivative **5a**

Entry	Oxidant Amount (Na ₂ S ₂ O ₈) mol/mol ratio	Temperature °C	Time ^{**, **} min	Yield% ^{***}	
				4a	5a
1	0.5	120	60	83	trace
2	1.00	120	60	79	trace
3	1.5	120	60	35	56
4	2.00	120	60	trace	79
5	2.5	120	20	-	88
6	3.00	120	20	-	88
7	2.5	140	20	-	88
8	2.5	160	60	56	32
9	2.5	180	60	62	trace

*Under microwave irradiation, **Time 2 for the reaction, ***Yield from ¹H NMR.

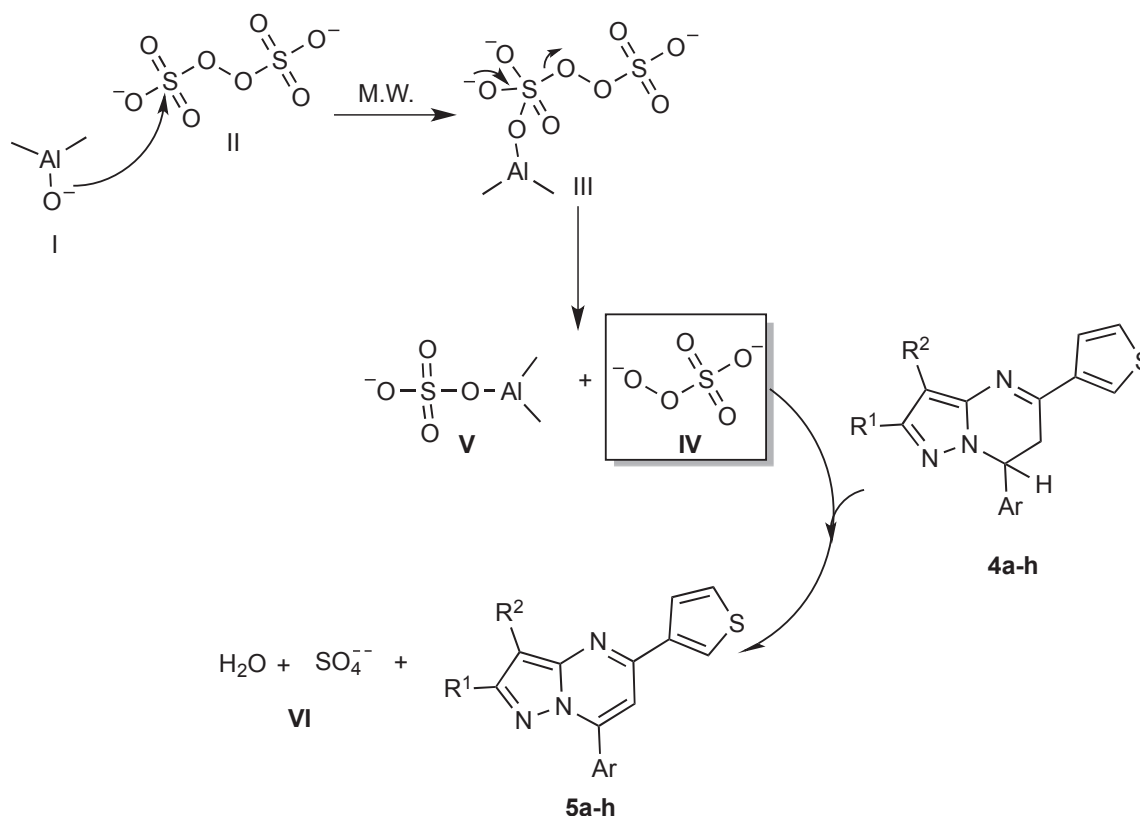
From the obtained data for the model reaction under microwave irradiation it was found that, at a higher temperature than 120 °C (140 °C, 160 °C, and 180 °C), the first addition-cyclization step became significantly rapid, in which chalcone **1a** was consumed within 25 min then, when Na₂S₂O₈ was added and irradiation was kept for one hour, both the conversion of intermediate **4a** to **5a** and the yield of pyrazolo[1,5-*a*]pyrimidine derivative **5a** decreased to a certain extent. The reason may be that Na₂S₂O₈ would decompose when heated at these temperatures, making the desired usage amount of the oxidant insufficient.

The isolated product **5a** gave satisfactory elemental analysis and spectroscopic data (IR, ¹H NMR, ¹³C NMR, MS) consistent with their assigned structures. Their IR spectra of the products showed absence of carbonyl absorption, NH and NH₂ bands and the mass spectra of the isolated product **5a** showed, a peak

corresponding to the molecular ion at 353, also its ^1H NMR spectrum shows two singlet signals at δ 6.89 and 8.09 due to pyrazole-3-CH and pyrimidine-6-CH respectively, and doublet signals at 7.23 due to thiophene protons in addition to three multiplets due to aromatic and thiophene protons (Experimental).

The formation of pyrazolo[1,5-*a*]pyrimidine derivative **5a** from the reaction of chalcone **1a** with 5-aminopyrazole derivative **2a** seems more likely based on spectral data and its similarity to the well-established behavior of chalcones towards aminopyrazole,²³⁻²⁵ which is assumed to proceed *via* an initial addition of ring nitrogen (imino group) across the activated bond system (intermediate **3**, Scheme 1), followed by elimination of molecule of water from the non-isolable intermediate **3** to give intermediate **4a** which upon treatment with sodium persulfate yield pyrazolo[1,5-*a*]pyrimidine derivative **5a** as depicted in Scheme 1 in almost quantitative yield.

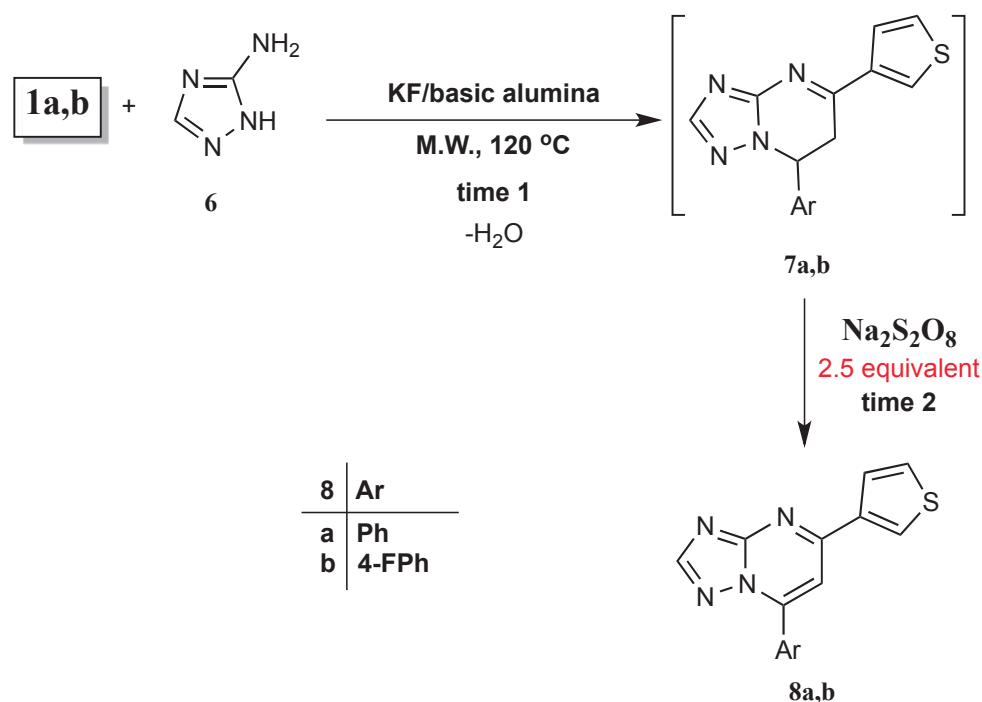
The direct oxidation behavior (dehydrogenation) of intermediate **4a** to product **5a** push us to suggest a possible mechanism for the above reaction depicted in Scheme 1. We suggest that the sodium persulfate is activated by action of microwave irradiation²⁶ in which, a nucleophilic attack of basic alumina (**I**) occurs at the sulfur atom of persulfate (**II**),²⁷ followed by a heterolytic cleavage of the peroxydisulfate anion (**III**). The deprotonation of the dihydropyrazolopyrimidiness **4a-h** by this reactive anion species (**IV**) and the following expulsion sulfate anion^{27,28} and water result in the formation of the pyrazolopyrimidine derivatives **5a-h**.



Scheme 2. Suggested mechanism for the oxidation reaction utilizing $\text{Na}_2\text{S}_2\text{O}_8$

Inspired by the above-optimized results, we then employed the best conditions under microwave irradiation to access a wide variety of pyrazolo[1,5-*a*]pyrimidine derivatives from various chalcones **1a,b** as represented in Scheme 1 in a one-pot pathway. The reactions proceeded cleanly without intermediate workup and left no, or only traces of byproducts (Experimental).

The structure of pyrazolo[1,5-*a*]pyrimidine derivatives **5b-h** was assigned on the basis of their elemental analyses and spectral data, for example, the ¹H NMR spectrum of compound **5c** revealed three singlet signal at δ 3.76, 6.98 and 8.06 due to methyl proton, pyrazole-3-CH and pyrimidine-6-CH respectively in addition to three multiplets signals due to aromatic protons and thiophene protons (Experimental); the mass spectrum of the same compound revealed a peak corresponding to its molecular ion at *m/z* 383. We extended our study to find out the reactivity of 3-amino-1,2,4-triazole (**6**) towards chalcone derivatives **1a,b** under the optimized reaction (Scheme 3).



Scheme 3. Reaction of chalcone **1a,b** with 3-amino-1,2,4-triazole (**6**)

The structures of compounds **8a,b** were assigned based on their elemental analyses and spectral data. The ¹H NMR spectrum of compound **8a** reveals three singlet signals at δ 7.98, 8.03 and 9.03 due to thiophene, pyrimidine CH-6, and triazole-CH-2 protons respectively in addition to a multiplet at δ 7.05-7.71 due to aromatic and thiophene protons. The IR spectrum of the same compound reveals the absence of absorption band due to carbonyl function.

The formation of 1,2,4-triazolo[1,5-*a*]pyrimidine derivatives **8a,b** seems to follow the sequence outlined in Scheme 2, which shows that the reaction starts via an initial addition of ring nitrogen across the

activated bond system, then elimination of a molecule of water from the non-isolable intermediate **7**, which undergo oxidation via Na₂S₂O₈ under microwave irradiation to produce **8a,b** as end products. The time of reaction and yields represented in the experimental part.

In conclusions, an efficient green protocol for the synthesis of expected biologically active azolo[1,5-*a*]pyrimidine derivatives incorporating thiophene moiety using KF/basic alumina catalyst and sequential addition of Na₂S₂O₈ as the an oxidant, under microwave irradiation has been established. A significantly higher yield and shorter reaction time were observed when the KF/basic alumina rather than the other catalyst used. The amount of oxidant added and the temperature used was found affect the yield of reaction product significantly. This protocol avoids using a hazardous organic solvent such DMF and caustic, corrosive materials and provides an easy way to get azolo[1,5-*a*]pyrimidine derivatives from other heterocyclic chalcones, such as furan, pyrrole, and pyridine-including substrates.

EXPERIMENTAL

All organic solvents were purchased from commercial sources and used as received unless otherwise stated. All other chemicals were purchased from Merck, Aldrich or Acros and used without further purification. Thin-layer chromatography (TLC) was performed on pre-coated Merck 60 GF254 silica gel plates using a fluorescent indicator, and detection was carried out using UV light at 254 and 360 nm. Melting points were measured on a Stuart melting point apparatus and were uncorrected. IR spectra were recorded on Nicolet iS10 FT-IR spectrometer with Smart iTR, which is an ultra-high-performance, versatile attenuated total reflectance (ATR) sampling accessory. The NMR spectra were recorded on a Bruker Avance III 400 (9.4 T, 400.13 MHz for ¹H, 100.62 MHz for ¹³C, 376.25 MHz for ¹⁹F and 40.56 MHz for ¹⁵N) spectrometer with a 5-mm BBFO probe, at 298 K. Chemical shifts (δ in ppm) are given relative to the internal solvent: DMSO-*d*₆ 2.50 for ¹H and 39.50 for ¹³C. Mass spectra were recorded on a Thermo ISQ single quadrupole gas chromatography-mass spectrometer. Elemental analyses were conducted on a EuroVector instrument C, H, N, S analyzer EA3000 Series.

Microwave experiments were conducted on a CEM Discover & Explorer SP microwave apparatus (300 W), utilizing 35 mL capped glass reaction vessels with automated power control based on temperature feedback.

Starting Materials. *E*-3-aryl-1-(thiophen-3-yl)prop-2-en-1-one **1a,b**,²⁹ 5-amino-1*H*-pyrazole derivatives **2a-d**³⁰⁻³² and KF/basic alumina³³ were prepared according to the reported literature.

Synthesis of azolo[1,5-*a*]pyrimidine derivatives **5a-h**, and **8a,b**

Microwave irradiation method. KF/basic alumina (0.5g) was added to chalcone derivative **1a,b** (10 mmol) and the appropriate 5-aminopyrazole derivative **2a-d** (10 mmol) and/or 3-amino-1,2,4-triazole (**6**) in a mortar, and the mixture was grounded thoroughly with a pestle at room temperature. The total

mixture was placed in a glass process vial and it was irradiated by microwaves with the power of 300 W to reach a reaction temperature of 120 °C under auto generated pressure. The vial was exposed to microwaves for a required time to complete the reaction [for designated time, Time 1(T1)]. Then the vial was opened and Na₂S₂O₈ (25 mmol) were added into the resulted mixtures, then the mixtures were homogenized before covering the tube *via* spatula to mix all ingredients, and the sealed vial was continued to irradiate by microwave for designated time, Time 2 (T2). The progress of the reaction was monitored by TLC eluent; petroleum ether: CHCl₃. Upon completion of the reaction, the products were extracted by dissolution in EtOH. The catalyst was removed by filtration and washed with hot ethanol and the solvent was evaporated under reduced pressure to obtain the solid product. The obtained solid product was purified by crystallization using EtOH/DMF solvent mixture to afford the pure azolo[1,5-*a*]pyrimidine derivatives **5a-h** and **8a,b** in excellent yield. (**5a**: T1 50 min, T2 20 min, 88%; **5b**: T1 50 min, T2 20 min, 90%; **5c**: T1 60 min, T2 30 min, 85%; **5d**: T1 60 min, T2 30 min, 88%; **5e**: T1 45 min, T2 30 min, 82%; **5f**: T1 45 min, T2 30 min, 87%; **5g**: T1 40 min, T2 20 min, 90%; **5h**: T1 40 min, T2 20 min, 92%; **8a**: T1 60 min, T2 40 min, 84%; **8b**: T1 60 min, T2 40 min, 88 %).

Compound **5a** was obtained by using various heterogeneous catalysts (basic alumina and K₂CO₃) under microwave irradiation (**5a**: basic alumina T1 80 min, T2 25 min, 83%; K₂CO₃ T1 90 min, T2 40 min, 74%).

Conventional electrical heating method. The reactions were performed on the same scale as described above. The reactants **1a**, **2a** and solid basic catalyst were put in a reflux system (round bottom flask connected with glass condenser). The reaction mixture was heated at 120 °C on a thermostatic oil-bath for required time [Time 1 (T1, till consuming the starting materials) and Time 2 (T2, after addition of oxidant)] to complete the reaction as monitored by TLC. After the completion of the reaction, the reaction mixture was cooled to room temperature and the products were obtained and purified as described in the previous method (**5a**: basic alumina T1 10 h, T2 4 h, 64%; K₂CO₃ T1 14 h, T2 5 h, 53%; KF-basic alumina T1 8 h, T2 4 h, 71%).

The Physical and spectral data of the compounds **5a-h** and **8a-b** are listed below:

2,7-Diphenyl-5-(thiophen-3-yl)pyrazolo[1,5-*a*]pyrimidine (5a): Yellow solid, mp 219-221 °C; IR (KBr) ν/cm^{-1} : 1601 (C=N); ¹H NMR (DMSO-*d*₆): δ 6.89 (s, 1H, pyrazole-3-CH), 7.14 (m, 2H, ArH), 7.23 (d, 1H, thiophene-H), 7.29-7.52 (m, 4H, ArH and thiophene-H), 7.58-7.63 (m, 3H, ArH), 7.89-8.05 (m, 3H, ArH and thiophene-H), 8.09 (s, 1H, pyrimidine-6-CH), ¹³C NMR (DMSO-*d*₆): δ 103.11, 106.32, 123.71, 125.03, 125.14, 127.00, 127.19, 128.88, 128.91, 129.09, 129.13, 131.00, 138.43, 142.10, 143.35, 149.81, 159.89; MS: *m/z* 353 (M⁺); Anal. Calcd for C₂₂H₁₅N₃S (353.44): C, 74.76; H, 4.28; N, 11.89; S, 9.07. Found: C, 75.01; H, 4.22; N, 11.78; S, 8.99%.

7-(4-Fluorophenyl)-2-phenyl-5-(thiophen-3-yl)pyrazolo[1,5-*a*]pyrimidine (5b): Beige solid, mp 210-211 °C; IR (KBr) ν/cm^{-1} : 1598 (C=N); ^1H NMR (DMSO-*d*₆): δ 6.86 (s, 1H, pyrazole-3-CH), 7.24-7.36 (m, 3H, thiophene-H and ArH), 7.51-7.79 (m, 4H, ArH and thiophene-H), 7.89-8.01 (m, 2H, ArH), 8.05 (s, 1H, pyrimidine-6-CH), 8.06-8.23 (m, 3H, ArH and thiophene-H), ^{13}C NMR (DMSO-*d*₆): δ 102.99, 106.21, 113.91, 122.84, 126.13, 127.00, 127.12, 128.62, 128.73, 129.29, 130.00, 132.05, 138.32, 143.12, 149.00, 152.10, 159.22, 160.71; MS: m/z 371 (M^+); Anal. Calcd for $\text{C}_{22}\text{H}_{14}\text{FN}_3\text{S}$ (371.43): C, 71.14; H, 3.80; N, 11.31; S, 8.63. Found: C, 71.37; H, 3.73; N, 11.22; S, 8.56%.

2-(4-Methoxyphenyl)-7-phenyl-5-(thiophen-3-yl)pyrazolo[1,5-*a*]pyrimidine (5c): Yellow solid, mp 229-231 °C; IR (KBr) ν/cm^{-1} : 1598 (C=N); ^1H NMR (DMSO-*d*₆): δ 3.76 (s, 3H, OCH₃), 6.98 (s, 1H, pyrazole-3-CH), 7.01-7.39 (m, 5H, ArH and thiophene-H), 7.49-7.72 (m, 2H, ArH and thiophene-H), 7.89-8.05 (m, 5H, ArH and thiophene-H), 8.06 (s, 1H, pyrimidine-6-CH), ^{13}C NMR (DMSO-*d*₆): δ 52.12, 103.12, 106.39, 112.84, 122.15, 124.31, 126.05, 128.31, 128.34, 128.96, 129.01, 129.75, 137.93, 139.21, 144.01, 145.21, 151.17, 159.43, 161.03; MS: m/z 383 (M^+); Anal. Calcd for $\text{C}_{23}\text{H}_{17}\text{N}_3\text{OS}$ (383.47): C, 72.04; H, 4.47; N, 10.96; S, 8.36. Found: C, 72.30; H, 4.42; N, 10.85; S, 8.26%.

7-(4-Fluorophenyl)-2-(4-methoxyphenyl)-5-(thiophen-3-yl)pyrazolo[1,5-*a*]pyrimidine (5d): Yellow solid, mp 252-254 °C; IR (KBr) ν/cm^{-1} : 1602(C=N); ^1H NMR (DMSO-*d*₆): δ 3.77 (s, 3H, OCH₃), 6.92 (s, 1H, pyrazole-3-CH), 7.10 (d, 2H, ArH, $J = 8$ Hz), 7.24-7.41 (m, 3H, ArH and thiophene-H), 7.54 (d, 2H, ArH, $J = 8$ Hz), 7.71-7.92 (m, 4H, ArH and thiophene-H), 8.01 (s, 1H, pyrimidine-6-CH), ^{13}C NMR (DMSO-*d*₆): δ 53.03, 103.57, 106.19, 112.73, 114.29, 122.85, 124.01, 128.73, 128.77, 128.91, 129.79, 138.01, 143.12, 145.00, 151.13, 158.12, 160.94; MS: m/z 401 (M^+); Anal. Calcd for $\text{C}_{23}\text{H}_{16}\text{FN}_3\text{OS}$ (401.46): C, 68.81; H, 4.02; N, 10.47; S, 7.99. Found: C, 69.05; H, 3.96; N, 10.39; S, 7.89%.

2-Methyl-7-phenyl-5-(thiophen-3-yl)pyrazolo[1,5-*a*]pyrimidine (5e): Yellow solid, mp 198-200 °C; IR (KBr) ν/cm^{-1} : 1607 (C=N); ^1H NMR (DMSO-*d*₆): δ 2.35 (s, 3H, CH₃), 6.81 (s, 1H, pyrazole-3-CH), 7.02 (d, 2H, ArH, $J = 8$ Hz), 7.29-7.46 (m, 2H, ArH and thiophene-H), 7.59 (d, 2H, ArH, $J = 8$ Hz), 7.69-7.89 (m, 2H, thiophene-H), 7.77 (s, 1H, pyrimidine-6-CH), ^{13}C NMR (DMSO-*d*₆): δ 12.85, 85.16, 106.73, 123.94, 125.03, 126.55, 128.19, 128.45, 128.67, 138.00, 141.74, 143.39, 146.94, 149.54, 158.02; MS: m/z 291 (M^+); Anal. Calcd for $\text{C}_{17}\text{H}_{13}\text{N}_3\text{S}$ (291.37): C, 70.08; H, 4.50; N, 14.42; S, 11.00. Found: C, 70.34; H, 4.41; N, 14.31; S, 10.92%.

7-(4-Fluorophenyl)-2-methyl-5-(thiophen-3-yl)pyrazolo[1,5-*a*]pyrimidine (5f): Buff solid, mp 212-214 °C; IR (KBr) ν/cm^{-1} : 1599 (C=N); ^1H NMR (DMSO-*d*₆): δ 2.28 (s, 3H, CH₃), 6.65 (s, 1H, pyrazole-3-CH), 7.22-7.49 (m, 3H, ArH and thiophene-H), 7.69-8.01 (m, 4H, ArH and thiophene-H), 7.81 (s, 1H, pyrimidine-6-CH), ^{13}C NMR (DMSO-*d*₆): δ 12.95, 82.31, 106.40, 112.54, 122.91, 128.32, 128.37, 129.67, 137.01, 139.83, 143.00, 149.11, 161.74; MS: m/z 309 (M^+); Anal. Calcd for $\text{C}_{17}\text{H}_{12}\text{FN}_3\text{S}$ (309.36): C, 66.00; H, 3.91; N, 13.58; S, 10.36. Found: C, 66.23; H, 3.85; N, 13.49; S, 10.28%.

2-Methyl-3,7-diphenyl-5-(thiophen-3-yl)pyrazolo[1,5-*a*]pyrimidine (5g): Yellow solid, mp 271-273 °C; IR (KBr) ν/cm^{-1} : 1609 (C=N); ^1H NMR (DMSO-*d*₆): δ 2.24 (s, 3H, CH₃), 7.02 (d, 2H, ArH, *J* = 8 Hz), 7.24-7.89 (m, 10H, ArH and thiophene-H), 7.92 (s, 1H, thiophene-H), 7.96 (s, 1H, pyrimidine-6-CH), ^{13}C NMR (DMSO-*d*₆): δ 14.10, 106.27, 122.59, 124.33, 126.03, 126.12, 128.94, 128.97, 128.98, 129.06, 129.14, 131.76, 133.05, 136.21, 139.80, 141.03, 143.00, 160.58; MS: *m/z* 367 (M⁺); Anal. Calcd for C₂₃H₁₇N₃S (367.47): C, 75.18; H, 4.66; N, 11.44; S, 8.73. Found: C, 75.43; H, 4.61; N, 11.32; S, 8.65%.

7-(4-Fluorophenyl)-2-methyl-3-phenyl-5-(thiophen-3-yl)pyrazolo[1,5-*a*]pyrimidine (5h): Yellow solid, mp 243-245 °C; IR (KBr) ν/cm^{-1} : 1605 (C=N); ^1H NMR (DMSO-*d*₆): δ 2.18 (s, 3H, CH₃), 7.12-7.79 (m, 9H, ArH and thiophene-H), 7.99 (d, 2H, ArH, *J* = 8 Hz), 7.91 (s, 1H, thiophene-H), 8.01 (s, 1H, pyrimidine-6-CH), ^{13}C NMR (DMSO-*d*₆): δ 14.13, 106.11, 112.25, 122.06, 124.47, 125.91, 127.93, 127.96, 129.62, 129.80, 131.01, 133.43, 135.16, 139.08, 143.10, 160.12, 161.57; MS: *m/z* 385 (M⁺); Anal. Calcd for C₂₃H₁₆FN₃S (385.46): C, 71.67; H, 4.18; N, 10.90; S, 8.32. Found: C, 71.91; H, 4.12; N, 10.81; S, 8.23%.

7-Phenyl-5-(thiophen-3-yl)-[1,2,4]triazolo[1,5-*a*]pyrimidine (8a): White solid, mp 174-176 °C; IR (KBr) ν/cm^{-1} : 1596 (C=N); ^1H NMR (DMSO-*d*₆): δ 7.05-7.71 (m, 7H, ArH and thiophene-H), 7.98 (s, 1H, thiophene-H), 8.03 (s, 1H, pyrimidine-6-CH), 9.03 (s, 1H, triazole-CH), ^{13}C NMR (DMSO-*d*₆): δ 106.03, 122.62, 126.35, 127.92, 127.95, 128.63, 131.00, 139.91, 143.56, 150.86, 154.37, 158.67; MS: *m/z* 278 (M⁺); Anal. Calcd for C₁₅H₁₀N₄S (278.33): C, 64.73; H, 3.62; N, 20.13; S, 11.52. Found: C, 64.95; H, 3.58; N, 20.02; S, 11.45%.

7-(4-Fluorophenyl)-5-(thiophen-3-yl)-[1,2,4]triazolo[1,5-*a*]pyrimidine (8b): White solid, mp 158-160 °C; IR (KBr) ν/cm^{-1} : 1599 (C=N); ^1H NMR (DMSO-*d*₆): δ 7.18-7.28 (m, 3H, ArH and thiophene-H), 7.84 (m, 1H, thiophene-H), 7.98 (s, 1H, thiophene-H), 7.99 (s, 1H, pyrimidine-6-CH), 8.96 (s, 1H, triazole-CH), ^{13}C NMR (DMSO-*d*₆): δ 105.93, 112.27, 122.79, 127.93, 127.98, 129.43, 139.04, 143.24, 150.09, 155.37, 160.16, 161.14; MS: *m/z* 296 (M⁺); Anal. Calcd for C₁₅H₉FN₄S (296.32): C, 60.80; H, 3.06; N, 18.91; S, 10.82. Found: C, 61.01; H, 2.99; N, 18.83; S, 10.76%.

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