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A MICROWAVE ASSISTED SYNTHESIS OF HIGHLY SUBSTITUTED 7-METHYL-5*H*-THIAZOLO[3,2-*a*]PYRIMIDINE-6-CARBOXYLATE DERIVATIVES VIA ONE-POT REACTION OF AMINOTHIAZOLE, ALDEHYDE AND ETHYL ACETOACETATE

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Abstract – The synthesis of highly substituted 7-methyl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate derivatives by one-pot reaction of aminothiazole, aldehyde and ethyl acetoacetate under microwave irradiation have been accomplished without any catalyst. This approach provides a simple, rapid, and green method for the synthesis of 7-methyl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate derivatives.

Since Strecker in 1850 reported the first multicomponent reactions for the synthesis of amino acids,[1] multicomponent reactions (MCRs) as a powerful tool have been widely utilized in organic synthesis, combinatorial and medicinal chemistry due to their simplicity and flexibility, good yield, high variability and selectivity, superior atom economy, energy savings, and reduced waste. In the past decades, these types of reactions were used to produce a number of interesting heterocyclic scaffolds, and are useful in the construction of diverse chemical libraries of 'drug-like' molecules.[2,3]

Thiazolopyrimidine derivatives are an important kind of heterocyclic compound and have been paid particular attention and widely recognized as biologically useful systems because of their being important structural components of purine bases. Accordingly, thiazolopyrimidine derivatives exhibited a wide range of biological activities, acting as calcium channel antagonists and CXCR2 receptor antagonist,[4,5] anti-tumor, anti-metastatic and anti-inflammatory agents.[6,7] As a consequence, some methods have been

contributed for the synthesis of thiazolo[3,2-*a*]pyrimidine derivatives.[8,9] Among the existed methodologies, the preparation of most thiazolo[3,2-*a*]pyrimidine derivatives was completed by the dihydropyrimidinones (DHPMs)[10] as precursors. Recently, the reactions of DHPMs with α-bromophenylacetaldehyde,[8e] enolizable ketones,[9a] α-bromoketones,[8c,9b] methyl chloroacetate[8a] etc. have been reported. However, in spite of their potential utility in the synthesis of this type of compounds, the precursors DHPMs have to be prepared in advance, during the synthetic procedure of which usually involves harsh reaction conditions, such as expensive or highly metal catalyst, organic solvent, long reaction time and unsatisfactory yield. Herein, the development of a direct, efficient and green alternative approach to functionalized thiazolo[3,2-*a*]pyrimidine derivatives is current interest to organic chemistry.

Generally, to our knowledge, all of the studies have been proved that the reaction of aldehyde, primary amines (either aryl or alkyl amine) and acetoacetate could give the products of *N*-substituted 1,4-dihydropyridines (1,4-DHP).[11] Surprisingly, when the 2-aminothiazole takes the place of other *N*-alkyl or *N*-aryl primary amine to engage in the Hantzsch reaction with the aldehyde and acetoacetate, the target product was not *N*-thiazolo-1,4-dihydropyridines, but thiazolo[3,2-*a*]pyrimidine derivative. Further experiments have shown that a new synthetic protocol for the thiazolo[3,2-*a*]pyrimidine derivatives has been formed through the reaction of 2-aminothiazole, aldehyde and ethyl acetoacetate. Herein, we describe the efficient protocol avoiding the use of DHPMs and microwave combination for a environment-friendly, rapid, and convenient synthesis of thiazolo[3,2-*a*]pyrimidine derivatives in excellent yield through a one-pot three component condensation reaction of 2-aminothiazole, aldehyde and ethyl acetoacetate. To the best of our knowledge, there is few studies related to the multicomponent reactions (MCRs) in one-pot for the synthesis of thiazolo[3,2-*a*]pyrimidine derivatives.

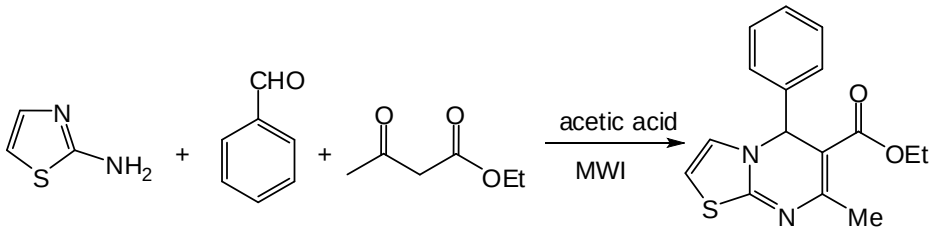
The studies were initiated to carry out the reaction of a one-pot three component condensation reaction of 2-aminothiazole, benzaldehyde, and ethyl acetoacetate in acetic acid, in which the aim product of *N*-thiazolo-1,4-dihydropyridine dicarboxylate should be afforded according to the literature. After work up, a yellow solid was isolated in about 30% yield and characterized. Amazingly, the result showed that the solid was not *N*-thiazolo-1,4-dihydropyridine dicarboxylate, but ethyl 7-methyl-5-phenyl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate and there is no unit of 1,4-dihydropyridine in the molecule. This interesting result encouraged us to further optimize the reaction conditions and to achieve a highly efficient protocol for the synthesis of 5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate derivatives.

The initial three components of 2-aminothiazole, benzaldehyde, and ethyl acetoacetate were stirred in the refluxing acetic acid for the 48 h to obtain the ethyl 7-methyl-5-phenyl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate in about 30% yield. In order to elevate the efficiency and reduce the reaction time, we carried out the same reaction under the microwave heating. The result came out as we had hoped and the microwave reaction provided a faster reaction time and a higher yield compared with the conventional

methods. Furthermore, the pure product was easily obtained through the simple recrystallization with ethyl acetate along with the improvement in yield. Under microwave assistant, the optimization of reaction conditions for the three components of 2-aminothiazole, benzaldehyde, and ethyl acetoacetate as model reaction were studied and the results are shown summarized in Table 1. Varying microwave powers (100–450 W) and the reaction temperatures were investigated during the experiments. The results were found that, if the microwave power exceeded 400 W and the temperature achieve 100 °C (Table 1, entry 6), the color of reaction system became dark quickly and there was a decrease in the yield (60%), which could be attributed that the higher temperature led to decomposition of the component. To our delight, when the microwave power was 350 W and the temperature was decreased to 80 °C, the desired product was got in 89% (entry 3). Finally, it was found that at 80 °C irradiation with microwave for 30 min gave the quantitative amounts of ethyl 7-methyl-5-phenyl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate as a light yellow solid in acetic acid.

Given that chemists have paid much attention to the solvent-free reaction, we tried to carry out the model reaction in solvent-free condition. But the results were very disappointing. When there are no solvents in the reaction system, the reaction mixture became highly viscous, then churned and formed a hard lump even if the intensity of microwave radiation decreased (Table 1, entries 7–9). Although the model reaction could be in progress and afford the aim product in the presence of ethanol, [Bmin]Br, [Bmin]HSO_4, and H_2O, the yields were fallen to below 50% (Table 1, entries 10–13). So acetic acid is an effective solvent in this one-pot reaction.

Table 1. The effect of different conditions on the model reaction



1 2 3 4

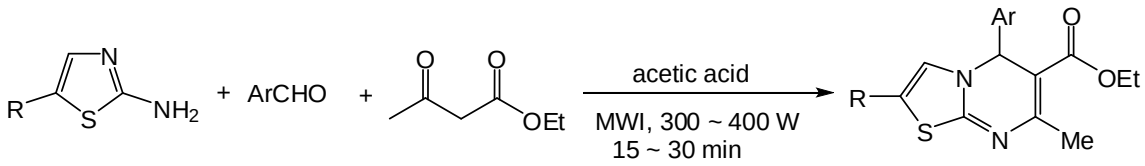
Entry	Solvent	Temp (°C)	Time (min)	Power (Watt)	Aminothiazole (equiv)	Aldehyde (equiv)	Ethyl acetoacetate (equiv)	Yield[a] (%)
1	AcOH	80	10	350	1.0	1.0	1.5	65
2	AcOH	80	20	350	1.0	1.0	1.5	80
3	AcOH	80	30	350	1.0	1.0	1.5	89
4	AcOH	80	30	350	1.0	1.0	1.0	45

5	AcOH	80	30	350	1.0	1.0	2.0	90
6	AcOH	100	30	450	1.0	1.0	1.5	60
7	–	40	30	200	1.0	1.0	1.5	nr[b]
8	–	70	30	350	1.0	1.0	1.5	trace
9	–	100	30	350	1.0	1.0	1.5	trace
10	EtOH	reflux	30	350	1.0	1.0	1.5	30
11	[Bmin]Br	80	30	350	1.0	1.0	1.5	37
12	[Bmin]HSO_4	80	30	350	1.0	1.0	1.5	48
13	H_2O	80	30	350	1.0	1.0	1.5	nr

a Isolated yields.
b No reaction.

Under the optimized set of microwave reaction conditions the role of aromatic aldehydes with various substituent groups on the benzene ring was examined in this one-pot reaction (Table 2). The results have shown that, all aromatic aldehydes with electron-donating or electron-withdrawing at different positions gave the corresponding products **4** in reasonable good to excellent yields within 30 min. Moreover, 4-nitrobenzaldehyde expressed more efficiently in comparison to those bearing electron-donating groups and gave better yield and shorter reaction time (Table 2, entries 4 and 10). Next, we replaced the 2-aminothiazole with 2-aminobenzo[*d*]thiazole. The similar results were observed and the corresponding 5*H*-benzo[*d*]thiazolo[3,2-*a*]pyrimidine-6-carboxylate derivatives were obtained in excellent yield (85–93%).

Table 2. Synthesized 5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate derivative by a one-pot three-component condensation reaction [a]



1 2 3 4

Entry	R	Ar	Product	Time (min)	Yield[b] (%)
1	H	C_6H_5	4a	30	89
2	H	4-ClC_6H_5	4b	20	85
3	H	4-$MeOC_6H_5$	4c	30	83
4	H	4-$O_2NC_6H_5$	4d	10	95

5	H	3-MeO-4-HOC_6H_4	4e	30	85
6	H	2-C_4H_3O	4f	20	88
7	benzo[*d*]	C_6H_5	4g	30	88
8	benzo[*d*]	4-ClC_6H_5	4h	20	85
9	benzo[*d*]	4-$MeOC_6H_5$	4i	30	86
10	benzo[*d*]	4-$O_2NC_6H_5$	4j	10	93
11	benzo[*d*]	3-MeO-4-HOC_6H_4	4k	30	87
12	benzo[*d*]	2-C_4H_3O	4l	20	90

a The reaction were performed useing aminothiazole (1.0 mmol), aldehyde (1.0 mmol) and ethyl acetoacetate (1.5 mmol) in acetic acid (5 mL) under microwave irradiation.
b Isolated yield based on aldehyde.

Each compound was isolated by easy recrystallization method by the solvent of ethyl acetate. The products were characterized by the IR, ^{1}H NMR, ^{13}C NMR and elementary analysis, further confirmed by single-crystal X-ray diffraction determination of compound **4g** (Figure 1). The crystal structure of compound **4g** had been deposited at the Cambridge Crystallographic Data Center (CCDC). Any request to the CCDC for this material should quote the full literature citation and the reference number 956188.

In conclusion, we have described an efficient, clean, and direct procedure to generate the 5*H*-benzo[*d*]thiazolo[3,2-*a*]pyrimidine-6-carboxylate derivative via a microwave assisted multicomponent reaction of 2-aminothiazole or 2-aminobenzo[*d*]thiazole, aromatic aldehydes, and ethyl acetoacectate in acetic acid without any catalyst. The advantages of this protocol are catalyst-free reaction conditions, easy work-up, easy of product isolation and high yield. We believe that this method is a useful condensation reaction for synthesis of 5*H*-benzo[*d*]thiazolo[3,2-*a*]pyrimidine-6-carboxylate derivative.

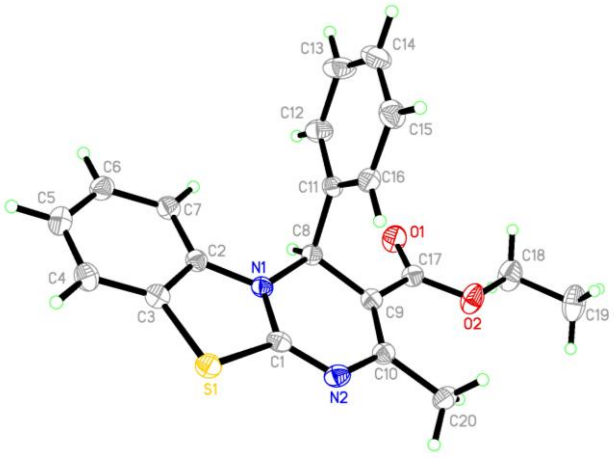


Figure 1. ORTEP view of compound **4g**. Displacement ellipsoids are drawn at the 55% probability level.

EXPERIMENTAL

All melting points were estimated using a X4 melting apparatus apparatus in open capillaries and are uncorrected. IR spectra were determined as KBr disks with a Perkin-Elmer Spectrum one FT-IR. The ^{1}H NMR spectra were recorded using a Bruker AV400MHz spectrometer using $CDCl_3$ as solvent and TMS as an internal standard. The ^{13}C NMR spectra were determined using TMS as an internal reference with a Bruker AV400MHz spectrometer operating at 100 MHz. Elemental analyses were performed on a Perkin-Elmer 240 microanalyser. Purity of compounds was checked by TLC. TLC was carried out on a Merck Kieselgel GF254. Column chromatography was performed using Merck Kieselgel 60 (0.075-0.15 mm). All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

Starting Materials. All other chemicals used in this study were commercially available.

Typical Procedure for the Preparation of Products 4a-4l. A mixture of thiazol-2-amine or benzo[*d*]thiazol-2-amine (1 mmol), appropriate aldehyde (1 mmol), ethyl acetoacetate (1.5 mmol) and 5 mL acetic acid was placed in a pressurized microwave vial with snap on cap. The reaction mixture was subjected to microwave irradiation for appropriate time at 350 W at 80 °C. After the completion of the reaction (as indicated by TLC), the reaction mixture was cooled to room temperature and added to the ice water. The result precipitate was collected and recrystallized with EtOAc to give pure product for analysis.

Ethyl 7-methyl-5-phenyl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate (4a): light yellow solid, 89%, mp 240.4–240.8 °C. IR (KBr): υ 3098, 2983, 1691, 1540, 1290 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40 (m, 3H, ArH), 7.32 (m, 2H, ArH), 7.17 (d, J = 4.0 Hz, 1H, ArH), 7.01 (d, J = 4.0 Hz, 1H, ArH), 6.38 (s, 1H, CH), 4.08–4.19 (m, 2H, CH_2), 2.67 (s, 3H, CH_3), 1.19 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.9, 158.3, 135.3, 129.1, 127.5, 110.2, 100.5, 61.5, 58.7, 23.3, 14.7. Anal. Calcd for $C_{16}H_{16}N_2O_2S$: C, 63.98; H, 5.37; N, 9.33%. Found: C, 63.87; H, 5.31; N, 9.56%.

Ethyl 5-(4-chlorophenyl)-7-methyl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate (4b): light yellow solid, 85%, mp 138.6–139.6 °C. IR (KBr): υ 3068, 2982, 1693, 1575, 1320 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.28 (d, J = 8.0 Hz, 2H, ArH), 7.26 (d, J = 8.0 Hz, 2H, ArH), 6.52 (d, J = 4.8 Hz, 1H, ArH), 6.29 (d, J = 4.8 Hz, 1H, ArH), 6.16 (s, 1H, CH), 4.04–4.10 (m, 2H, CH_2), 2.44 (s, 3H, CH_3), 1.18 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.2, 165.7, 134.8, 129.1, 128.3, 126.4, 99.5, 60.1,

59.8, 23.4, 14.3. Anal. Calcd. for $C_{16}H_{15}ClN_2O_2S$: C, 57.40; H, 4.52; N, 8.37%. Found: C, 57.58; H, 4.40; N, 8.26%.

Ethyl 5-(4-methoxyphenyl)-7-methyl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate (4c): light yellow solid, 83%, mp 135.0–135.6 °C. IR (KBr): υ 3114, 2981, 1683, 1573, 1317 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.27 (d, J = 8.4 Hz, 2H, ArH), 6.83 (d, J = 8.4 Hz, 2H, ArH), 6.55 (d, J = 4.8 Hz, 1H, ArH), 6.25 (d, J = 4.8 Hz, 1H, ArH), 6.13 (s, 1H, CH), 4.04–4.09 (m, 2H, CH_2), 3.77 (s, 3H, OCH_3), 2.44 (s, 3H, CH_3), 1.17 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.5, 159.7, 135.6, 128.2, 126.7, 114.1, 99.9, 60.1, 59.7, 55.2, 23.0, 14.3. Anal. Calcd for $C_{17}H_{18}N_2O_3S$: C, 61.80; H, 5.49; N, 8.48%. Found: C, 61.95; H, 5.37; N, 8.47%.

Ethyl 7-methyl-5-(4-nitrophenyl)-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate (4d): light yellow solid, 95%, mp 137.2–138.3 °C. IR (KBr): υ 3073, 2971, 2927, 1653, 1522, 1451, 1202 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.18 (d, J = 8.8 Hz, 2H, ArH), 7.54 (d, J = 8.8 Hz, 2H, ArH), 6.57 (d, J = 4.8 Hz, 1H, ArH), 6.38 (d, J = 4.8 Hz, 1H, ArH), 6.32 (s, 1H, CH), 4.05–4.13 (m, 2H, CH_2), 2.44 (s, 3H, CH_3), 1.19 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.2, 149.1, 147.8, 127.7, 126.1, 124.1, 123.7, 122.7, 111.7, 102.5, 60.7, 57.3, 24.8, 14.3. Anal. Calcd for $C_{16}H_{15}N_3O_4S$: C, 55.64; H, 4.38; N, 12.17%. Found: C, 55.52; H, 4.41; N, 12.32%.

Ethyl 5-(4-hydroxy-3-methoxyphenyl)-7-methyl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate (4e): light yellow solid, 85%, mp 142.3–143.9 °C. IR (KBr): υ 3434, 2971, 1694, 1490, 1277, 1200, 1080 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 6.83–6.88 (m, 3H, ArH), 6.57 (d, J = 4.8 Hz, 1H, ArH), 6.26 (d, J = 4.8 Hz, 1H, ArH), 6.10 (s, 1H, CH), 5.95 (b, 1H, OH), 4.03–4.13 (m, 2H, CH_2), 3.84 (s, 3H, OCH_3), 2.45 (s, 3H, CH_3), 1.18 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.3, 164.2, 136.4, 128.6, 126.3, 120.9, 101.7, 60.3, 58.9, 56.8, 23.3, 14.3. Anal. Calcd for $C_{17}H_{18}N_2O_4S$: C, 58.94; H, 5.24; N, 8.09%. Found: C, 60.04; H, 5.11; N, 7.95%.

Ethyl 5-(furan-2-yl)-7-methyl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate (4f): light yellow solid, 88%, mp 148.4–149.1 °C. IR (KBr): υ 3045, 2974, 2920, 1637, 1480, 1202, 1079 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.33 (b, 1H, ArH), 6.82 (d, J = 4.4 Hz, 1H, ArH), 6.35 (d, J = 4.8 Hz, 1H, ArH), 6.28 (b, 2H, ArH + CH), 6.22 (d, J = 4.8 Hz, 1H, ArH), 4.10–4.14 (m, 2H, CH_2), 2.45 (s, 3H, CH_3), 1.19 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.5, 163.5, 154.2, 152.7, 143.1, 133.6, 123.0, 110.6, 106.5, 97.8, 61.5, 60.9, 20.7,14.2; Anal. Calcd for $C_{14}H_{14}N_2O_3S$: C, 57.92; H, 4.86; N, 9.65%. Found: C, 57.88; H, 4.77; N, 9.89%.

Ethyl 7-methyl-5-phenyl-5*H*-benzo[*d*]thiazolo[3,2-*a*]pyrimidine-6-carboxylate (4g): light yellow solid, 88%, mp 184.2–185.1 °C. IR (KBr): υ 3069, 2957, 1572, 1519, 1247, 1100 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.47 (t, 3H, J = 8.0 Hz, ArH), 7.18–7.27 (m, 4H, ArH), 7.12 (t, J = 8.0 Hz, 3H, ArH), 6.41 (s, 1H, CH), 4.12–4.21 (m, 2H, CH_2), 2.46 (s, 3H, CH_3), 1.28 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.4, 162.8, 158.7, 136.2, 132.9, 127.7, 126.4, 124.0, 123.9, 122.2, 113.9, 111.9, 103.4, 60.09, 57.32, 55.2, 23.3, 14.3. Anal. Calcd for $C_{20}H_{18}N_2O_2S$: C, 68.55; H, 5.18; N, 7.99%. Found: C, 68.69; H, 5.07; N, 7.71%.

Ethyl 5-(4-chlorophenyl)-7-methyl-5*H*-benzo[*d*]thiazolo[3,2-*a*]pyrimidine-6-carboxylate (4h): light yellow solid, 85%, mp 181.1–182.3 °C. IR (KBr): υ 3112, 2971, 1696, 1504, 1240, 1090 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.42 (d, J = 8.0 Hz, 1H, ArH), 7.33 (d, J = 8.0 Hz, 2H, ArH), 7.18 (t, J = 8.0 Hz, 3H, ArH), 7.11 (t, J = 8.0 Hz, 1H, ArH), 7.02 (t, J = 8.0 Hz, 1H, ArH), 6.35 (s, 1H, CH), 4.08–4.18 (m, 2H, CH_2), 2.41 (s, 3H, CH_3), 1.25 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.3, 163.2, 139.6, 137.7, 134.3, 128.9, 128.5, 126.8, 124.3, 123.9, 122.4, 111.7, 102.8, 60.3, 57.2, 23.4, 14.4. Anal. Calcd for $C_{20}H_{17}ClN_2O_2S$: C, 62.41; H, 4.45; N, 7.28%. Found: C, 62.20; H, 4.62; N, 7.15%.

Ethyl 5-(4-methoxyphenyl)-7-methyl-5*H*-benzo[*d*]thiazolo[3,2-*a*]pyrimidine-6-carboxylate (4i): light yellow solid, 86%, mp 184.2–185.0 °C. IR (KBr): υ 2956, 1695, 1511, 1243, 1175 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.44 (d, J = 8.0 Hz, 1H, ArH), 7.35 (d, J = 8.0 Hz, 2H, ArH), 7.23 (d, J = 8.0 Hz, 1H, ArH), 7.13 (t, J = 8.0 Hz, 2H, ArH), 6.77 (d, J = 8.0 Hz, 2H, ArH), 6.35 (s, 1H, CH), 4.11–4.21 (m, 2H, CH_2), 3.77 (s, 3H, OCH_3), 2.45 (s, 3H, CH_3), 1.27 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.2, 163.4, 159.7, 147.9, 145.2, 137.9, 129.2, 128.0, 127.6, 127.2, 126.6, 124.1, 123.6, 122.7, 102.4, 60.7 57.3, 23.2, 14.3. Anal. Calcd for $C_{21}H_{20}N_2O_3S$: C, 66.29; H, 5.30; N, 7.36%. Found: C, 66.11; H, 5.46; N, 7.19%.

Ethyl 5-(4-nitrophenyl)-7-methyl-5*H*-benzo[*d*]thiazolo[3,2-*a*]pyrimidine-6-carboxylate (4j): light yellow solid, 93%, mp 181.5–182.1 °C. IR (KBr): υ 3024, 2951, 1702, 1520, 1242, 1078 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.13 (d, J = 8.0 Hz, 2H, ArH), 7.61 (d, J = 8.0 Hz, 2H, ArH), 7.49 (d, J = 8.0 Hz, 1H, ArH), 7.26 (t, J = 8.0 Hz, 1H, ArH), 7.18 (t, J = 8.0 Hz, 1H, ArH), 7.03 (d, J = 8.0 Hz, 1H, ArH), 6.53 (s, 1H, CH), 4.17–4.21 (m, 2H, CH_2), 2.45 (s, 3H, CH_3), 1.30 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.2, 163.4, 158.1, 147.8, 145.2, 138.3, 129.7, 126.5, 125.7, 123.1, 122.0, 119.6, 118.5, 115.2, 63.6, 61.7, 2.0, 14.6. Anal. Calcd for $C_{20}H_{17}N_3O_4S$: C, 60.75; H, 4.33; N, 10.63%. Found: C, 60.82; H, 4.18; N, 10.46%.

Ethyl 5-(4-hydroxy-3-methoxyphenyl)-7-methyl-5*H*-benzo[*d*]thiazolo[3,2-*a*]pyrimidine-6-carboxylate (4k): light yellow solid, 87%, mp 189.0–191.2 °C. IR (KBr): υ 3434, 2920, 1701, 1497, 1274, 1125, 1068 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.46 (d, J = 8.0 Hz, 1H, ArH), 7.27 (s, 1H, ArH), 7.15 (t, J = 8.0 Hz, 2H, ArH), 6.92 (d, J = 8.0 Hz, 1H, ArH), 6.91 (d, J = 8.0 Hz, 1H, ArH), 6.77 (d, J = 8.0 Hz, 1H, ArH), 6.35 (s, 1H, CH), 4.13–4.22 (m, 2H, CH_2), 3.81 (s, 3H, OCH_3), 2.46 (s, 3H, CH_3), 1.29 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.6, 163.1, 146.9, 145.9, 138.0, 133.3, 126.4, 124.0, 123.9, 122.1, 120.4, 114.1, 109.4, 103.4, 60.1, 57.6, 55.9, 23.4, 14.4. Anal. Calcd for $C_{21}H_{20}N_2O_4S$: C, 63.62; H, 5.08; N, 7.07%. Found: C, 63.80; H, 5.24; N, 7.25%.

Ethyl 5-(furan-2-yl)-7-methyl-5*H*-benzo[*d*]thiazolo[3,2-*a*]pyrimidine-6-carboxylate (4l): light yellow solid, 90%, mp 182.2–183.0 °C. IR (KBr): υ 3052, 2971, 2918, 1646, 1509, 1455, 1239, 1011 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.48 (d, J = 8.0 Hz, 1H, ArH), 7.37 (d, J = 15.0 Hz, 1H, ArH), 7.35 (t, J = 15.0 Hz, 1H, ArH), 7.25 (d, J = 8.0 Hz, 1H, ArH), 7.20 (t, J = 8.0 Hz, 1H, ArH), 6.52 (s, 1H, CH), 6.29 (d, J = 3.0 Hz, 1H, ArH), 6.24 (d, J = 3.0 Hz, 1H, ArH), 4.13–4.24 (m, 2H, CH_2), 2.50 (s, 3H, CH_3), 1.26 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.5, 163.1, 154.0, 152.6, 142.1, 139.4, 130.2, 126.4, 122.3, 122.0, 117.5, 113.8, 110.6, 106.7, 61.2, 60.5, 23.0, 14.4. Anal. Calcd for $C_{18}H_{16}N_2O_3S$: C, 63.51; H, 4.74; N, 8.23%. Found: C, 63.36; H, 4.81; N, 8.40%.

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