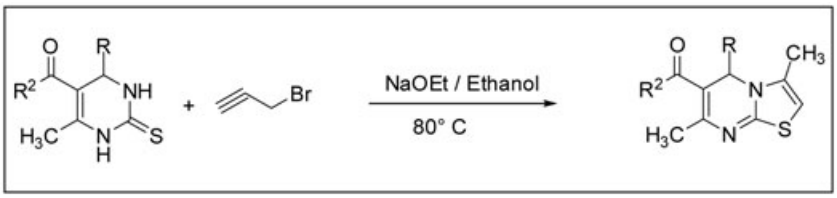
Seerat Fatima, Anindra Sharma, Rahul Sharma, and Rama P. Tripathi*

Medicinal and Process Chemistry Division, Central Drug Research Institute (CSIR), Lucknow 226001, Uttar Pradesh, India

This article is a CDRI communication (No. 8007).

*E-mail: rpt.cdri@gmail.com

Received October 18, 2010
DOI 10.1002/jhet.831
View this article online at wileyonlinelibrary.com.



One-pot economical and efficient synthesis of multifunctional *5H*-thiazolo[3,2-a]pyrimidines by the reaction of 4-aryl dihydrothiopyrimidines with propargyl bromide in the presence of inorganic base has been reported in very short time.

J. Heterocyclic Chem., **49**, 600 (2012).

INTRODUCTION

The discovery of Biginelli reaction and its subsequent modifications have led to access a variety of dihydropyrimidines of great synthetic and chemotherapeutic significance [1–5]. The dihydropyrimidinones and thiodihydropyrimidinones in particular have been used as the key substrates to develop several synthetic molecules as drugs or potent leads in medicinal chemistry. Among various derivatives of thiodihydropyrimidines, the thiazolo[3,2-*a*]pyrimidine derivatives are of great significance because of their wide range of biological activities such as calcium channel blocking activity [6], antimalarial and antitubercular activity [7], acetylcholine esterase inhibitory activity [8], glutamate receptor antagonistic activity [9], 5-HT2a receptor antagonistic activity [10], antiH5N1 activity [11], anticancer activity [12], kinase inhbitory activity [13] and so on.

Typically they have been synthesized by the condensation of an aminothiazole with a malonate derivative followed by intramolecular cycloacylation [14–16]. The protocols for the synthesis of these molecules, reported so far, suffer the drawbacks of heating at high temperatures, prolonged reaction times and low yields. Very recently a two-step high-yield process involving the condensation of 2-aminothiazole and diethylmalonate followed by intramolecular cyclization with Eaton's reagent (a mixture of 7.7 wt % phosphorus pentoxide solution in methanesulfonic acid) at low temperature has been disclosed [17]. Reactions of 1,4-dihydropyrimidine-thiones with haloketones have also been reported to give various thiazolo[3,2-*a*]pyrimidine derivatives [15,18,19]. These synthetic methodologies too are plagued with drawbacks, as 2-aminothizole preparation via Hantzsch synthesis involves thioureas and α-haloketones or aldehydes. The preparation and isolation of α-haloketones or haloaldehydes required for synthesis in the laboratory is hazardous in nature and sometimes they are commercially unavailable also. Therefore, developments of new, simple, and practically efficient synthesis of these molecules are highly desirable.

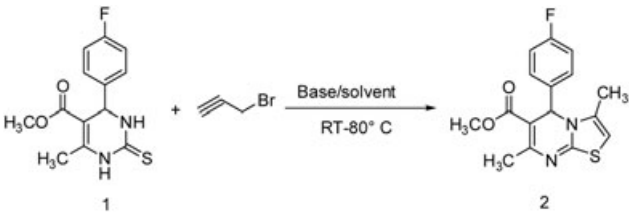
Recently such a highly efficient synthesis of thiazolo [3,2-a]-pyrimidinones has been reported [20] by reacting alkynyl bromides with thiopyrimidinones under microwave irradiation at 130°C using K_2CO_3 as a base. The scope of their study was limited to only-alkyl substituted thiopyrimidinones, and the scope of this reaction with thiopyrimdines was not fully investigated. The scope of study was also limited to microwave at higher temperature. Encouraged by this report and to fulfill our quest to develop new chemotherapeutic agents from dihydropyrimidines [21,22], we were interested to synthesize library of thiazolo[3,2-a]pyrimidines using safer and better yielding routes. Because propargyl bromide has been considered to be equivalent to α-bromoacetones [23], and it is commercially available in plenty; we have carried out reaction of thiodihydropyrimidines with propargyl bromide in presence of base to get the desired thizolo[3,2-a]-pyrimidines with ester and ketone groups. Our method of synthesis is quite simple, rapid, ecofriendly, economical, and high yielding.

RESULT AND DISCUSSION

To optimize the reaction condition initially we have carried out reaction of 5-carbmethoxy-6-methyl-4-(4-fluorophenyl) dihydropyrimidine-2-thione with propargyl bromide in the

© 2012 HeteroCorporation

Scheme 1. Reaction of **1** with propargyl bromide in different bases and solvents at different temperature.



presence of various catalysts at different temperatures in a wide variety of solvents (Scheme 1), and the results are shown in Table 1.

As shown in Table 1, with organic bases such as Et_3N, DBU, and DABCO, reaction did not proceed, even after prolonged heating (entries 11, 12, and 14 Table 1). Reaction preceded by the use of inorganic bases carbonates (K_2CO_3, Na_2CO_3 in protic and aprotic solvents, entries 1, 2, 3, 4, 17, 18, 20 Table 1). However, $CsCO_3$ proved to be an unsuccessful catalyst (entry13) with only 5% yield. The reaction with K_2CO_3 was successful even in aprotic solvent acetonitrile. However, by using NaOMe, or NaOEt in their respective alcohol solvents, compounds were obtained in good yields. Reaction was completed in about 8 h in the presence of NaOMe in methanol (entry 9) at ambient temperature, whereas on heating at 80°C, it was completed in only 30 min (entry 8). With ethylene glycol, reaction was sluggish, and the product formation was <5% (TLC) as most of the starting material was recovered. With $NaHCO_3$ as base and acetone as solvent, the yield of the reaction was only 10% (entry19). KOH as catalyst gave the reaction product in comparatively lower yields (entries 6 and 7) when compared with carbonates and alkoxides. Thus, NaOMe as base and MeOH as solvent or NaOEt as base and EtOH as solvent and heating the reaction mixture at 80°C was found to be the most optimum reaction condition.

Out of the two possibilities of *7H*-thiazolo[3,2-a]-and *5H*-[3,2-a]-pyrimidines **A** and **B** (Fig. 1), the product obtained in the above reaction was found to be methyl 5-(4-fluorophenyl)-3,7-dimethyl-*5H*-thiazolo[3,2-a]pyrimidine-6-carboxylate (**2**). The structure was elucidated on the basis of spectroscopic data and analysis. In the ^{1}H-NMR spectrum of compound **2**, the methyl proton of the thiazole ring appeared as singlet at δ 2.07, whereas the other methyl proton of the pyrimidine ring appeared as singlet at δ 2.36 ppm. The methyl proton of the ester group appeared as singlet at δ 3.71 ppm. The CH proton of the dihydropyrimidine ring appeared as singlet at δ 6.14 whereas that of the thiazole ring appeared at δ 5.96 ppm. The aromatic protons were observed at their usual chemical shift values. The detailed NOESY and HSQC spectra of compound **2** revealed the position of different susbtitutents in the molecule. As evident from the NOESY spectrum, the thizolyl methyl protons show interaction with H-2 and H-5 protons and no interaction with 7-methyl protons (Fig. 2). The regioselectivity in the above reaction of thiodihydropyrimdines with propargyl bromide may be explained in terms of difference in the electron density at N3 and N1 position. The higher basicity of the N3 results in preferential nucleophilic attack at the thiopropargylic moiety to give the N3-regioslective product. Such observations were earlier reported in the reaction of dihydropyrimdines in literature [18,24,25] by different workers.

Table 1

Optimization of reaction conditions for the formation of **2**.

Entry	Catalyst (base)	Solvent	Temperature (°C)	Time	Yield (%)
1	K_2CO_3	Acetone	RT	10 h	70
2	K_2CO_3	Acetone	80°C	8 h	80
3	K_2CO_3	Methanol	80°C	10 h	20
4	K_2CO_3	Ethylene glycol	80°C	8 h	<5
5	KOH	Methanol	RT	8 h	50
6	KOH	Methanol	80°C	40 min	85
7	KOH	Water	80°C	40 min	40
8	NaOMe	Methanol	80°C	30 min	94
9	NaOMe	Methanol	RT	8 h	90
10	NaOEt	Ethanol	80°C	2 h	50
11	Et_3N	Ethanol	RT	8 h	0
12	DBU	Acetone	RT	8 h	0
13	Cs_2CO_3	Acetone	RT	12 h	5
14	DABCO	Acetone	RT	8 h	0
15	NaOMe	THF	80°C	40 min	85
16	NaOMe	ArCN	80°C	45 min	88
17	K_2CO_3	ArCN	80°C	8 h	75
18	Na_2CO_3	Acetone	80°C	8 h	10
19	$NaHCO_3$	Acetone	80°C	8 h	10
20	K_2CO_3	THF	80°C	8 h	70

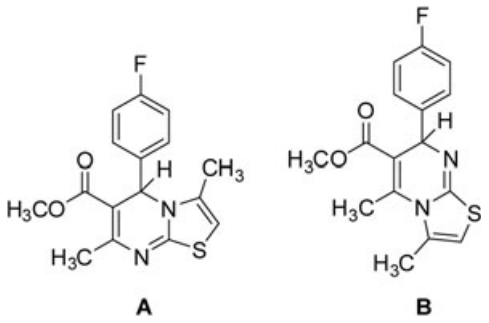


Figure 1. The chemical structure of two possible regioisomer.

Having established the standard reaction condition to access thizolopyrimidine, we have investigated the scope of this reaction with different substrates. Thus, a wide variety of thiodihydropyrimidines with carbmethoxy, carbethoxy, and acetyl groups at C-3 and substituted phenyl ring at C-4 were reacted with propargyl bromide to get the desired 5*H*-thiazolo[3,2-a] pyrimidines (Scheme 2), and the results are shown in Table 2.

As shown in Table 2, the reaction was successful with a wide range of thiodihydropyrimidines having acetyl, carbethoxy, and carbmethoxy susbtitutents at C-5. Further, substitution in the 4-phenyl ring either with electron-donating or electron-withdrawing substituents does not alter the course of reaction as the yields are comparable. Thus, it is equally applicable in all kinds of 5-(carbmethoxy/carbethoxy/acetyl)-4-phenyl-1,4-dihydropyrimidines. Structures of these compounds were established on the basis of their spectroscopic data and microanalyses.

Formation of the above thiazolo[3,2-a]-pyrimidines could be rationalized via a mechanism similar to that proposed by Botta and coworkers [20] (Fig. 3). The *S*-propargylation of the thiodihydromidine **I** results in the intermediate compound **II**. The latter may undergo cylization adopting either of the two pathways, (i) path A consists in *exo*-dig cyclization via nucleophilic attack of imine on to the triple bond to give an intermediate **III**, which isomerizes to the desired thiazolo [3,2-a]-pyrimidine (**IV**) or (ii) path B in isomerization consists of triple bond to allene intermediate **V** followed by attack of imine nitrogen on to the central carbon atom leading to

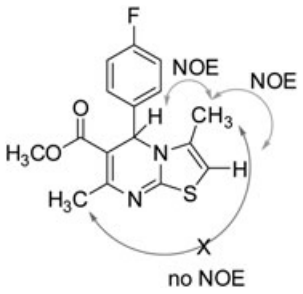
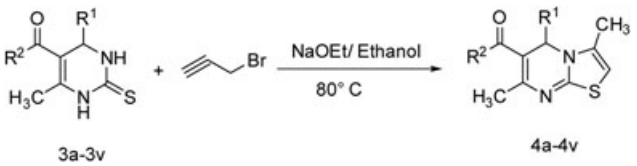


Figure 2. Possible NOE interactions.

Scheme 2. Synthesis of multifunctional 5*H*-thiazolo[3,2-a]-pyrimidines.



intermediate **III**, which again isomerises to the product **IV**. Botta and coworkers have hypothesized Path A for the reaction as only mild base K_2CO_3 was used for the reaction where the formation of allene is not feasible easily. However, we have carried out reactions in the presence of both mild and strong base. Under K_2CO_3-catalyzed reaction, the yields were comparatively low, but we observed allene formation by NMR studies of one of the reaction mixture.

In summary, we have developed a simple, economical, and high yield process for the preparation of multifunctional *5H*-thiazolo[3,2-a]pyrimidines by the reaction of 4-aryl thiopyrimidines with propargyl bromide in presence of inorganic base. These compounds are of great synthetic and chemotherapeutic importance. Application of these compounds in designing of new biologically important molecules is underway.

EXPERIMENTAL

Commercially available reagent grade chemicals were used as received. TLC was carried out with E. Merck Kieselgel 60 F_{254}, Spots were visualized under UV light, I_2 vapors and by spraying with a 20% aq. $KMnO_4$. Column chromatography was performed on silica gel (60–120 mesh, E. Merck). IR spectra were recorded as thin films or in KBr solution with a Perkin–Elmer Spectrum RX-1 (4000–450 cm^{-1}) spectrophotometer. The ^{1}H-NMR (200 and 300 MHz) and ^{13}C-NMR (50 MHz) spectra were recorded on a Brucker DRX-300 in $CDCl_3$. Chemical shift values are reported in ppm relative to TMS as internal reference, unless otherwise stated; s (singlet), d (doublet), t (triplet); J in Hz. FAB mass spectra were performed using a mass Spectrometer Jeol SX-102 and ESI mass spectra with Quattro II (Micromass). Elemental analyses were performed on a Perkin–Elmer 2400 II elemental analyzer.

General procedure for the synthesis of multifunctional 5*H*-thiazolo[3,2-a]-pyrimidines. To a stirred solution of 4-pheyl-2-thio-dihydropyrimidines (1.0 equiv), propargyl bromide (1.1 equiv), and in ethanol/ methanol appropriate base was added and stirring continued at 80°C till the disappearance of the starting thiodihydropyridmine (TLC). The reaction mixture was cooled and neutralized by 4% aq. HCl solution and concentrated in vacuum to evaporate the solvent. Then, the reaction mixture was extracted by ethyl acetate/water. The organic layer was dried over sodium sulphate (Na_2SO_4) and concentrated under reduced pressure. The product was purified by either by crystallization with appropriate solvent or by column chromatography on a short column of silica gel (60–120 mesh) using hexane: ethylacetate as eluant to give the desired thiazolo[3,2-*a*]pyrimidine derivatives.

Table 2

Synthesis of multifunctional 5*H*-thiazolo[3,2-a]-pyrimidines from different thiodihdropyrimidines with propargyl bromide.

Entry	R_1	R_2	Product	Time	Isolated yield (%)
1	Phenyl	OCH_2CH_3	**4a**	30	92
2	4-Methoxy phenyl	OCH_2CH_3	**4b**	25	91
3	4-Bromo phenyl	OCH_2CH_3	**4c**	30	93
4	4-Chloro phenyl	OCH_2CH_3	**4d**	25	93
5	3-Chloro phenyl	OCH_2CH_3	**4e**	25	92
6	4-Fluoro phenyl	OCH_2CH_3	**4f**	30	88
7	3-Nitrophenyl	OCH_2CH_3	**4g**	35	90
8	2-Naphthyl	CH_3	**4h**	9h	85
9	Phenyl	CH_3	**4i**	8h	86
10	4-Fluoro phenyl	CH_3	**4j**	8h	82
11	3,4-Dimethoxy phenyl	CH_3	**4k**	9h	84
12	Phenyl	OCH_3	**4l**	30	94
13	4-Methoxy phenyl	OCH_3	**4m**	25	90
14	1-Naphthyl	OCH_3	**4n**	30	93
15	2-Naphthyl	OCH_3	**40**	35	94
16	2-Chloro phenyl	OCH_3	**4p**	30	93
17	3-Chloro phenyl	OCH_3	**4q**	30	92
18	4-Chloro phenyl	OCH_3	**4r**	35	90
19	3,4-Dimethoxy phenyl	OCH_3	**4s**	30	94
20	3-Methoxy-4-hydroxy phenyl	OCH_3	**4t**	35	89
21	2,3,4-Trimethoxy phenyl	OCH_3	**4u**	30	90
22	4-Benzloxy phenyl	OCH_3	**4v**	30	92

[a]To a stirred solution of thiodihydropyrimidines (1.0 equiv), propargyl bromide (1.1 equiv) in ethanol, NaOEt (1.1 eq) was added and stirring continued at 80°C till the disappearance of the starting.
[b]To a stirred solution of thiodihydropyrimidines (1.0 equiv), propargyl bromide (1.1 equiv) in acetone K_2CO_3 (1.5 eq) was added and stirring continued at 80°C till the disappearance of the starting.
[c]To a stirred solution of thiodihydropyrimidines (1.0 equiv), propargyl bromide (1.1 equiv) in methanol, NaOMe (1.1 eq) was added and stirring continued at 80°C till the disappearance of the starting.

Methyl 5-(4-fluorophenyl)-3,7-dimethyl-5*H*-thiazolo[3,2-a] pyrimidine-6-carboxylate (2). This compound was obtained as yellow solid, yield 92%; mp 138–140°C; R_f = 0.5 (6:4 hexane/ethylacetate); IR (KBr): 3432, 3121, 3036, 2945, 1694, 1600, 1474, 1360, 1215, 1080, 971, 829 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$ + CCl_4): δ = 7.32–7.26 (m, 2H, ArH), 7.02–6.93 (m, 2H, ArH), 6.14 (s, 1H, CH), 5.96 (s, 1H, CH), 3.71 (s, 3H, OCH_3), 2.36 (s, 3H, CH_3), 2.07 (s, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$ + CCl_4,): δ = 166.9, 166.5, 156.1, 139.1, 139.0, 135.0, 128.1, 128.0, 115.8, 115.4, 100.3, 99.9, 57.0, 50.8, 23.9, 13.9; ms (ESI^+): *m/z*: 319 $[M+H]^+$. *Anal.* Calcd. for $C_{16}H_{15}FO_2N_2S$ (318.37): C, 60.36; H, 4.75; N, 8.80. Found: C, 60.33; H, 4.76; N, 8.78.

Ethyl 3,7-dimethyl-5-phenyl-5*H*-thiazolo[3,2-a]pyrimidine-6-carboxylate (4a). This compound was obtained as yellow

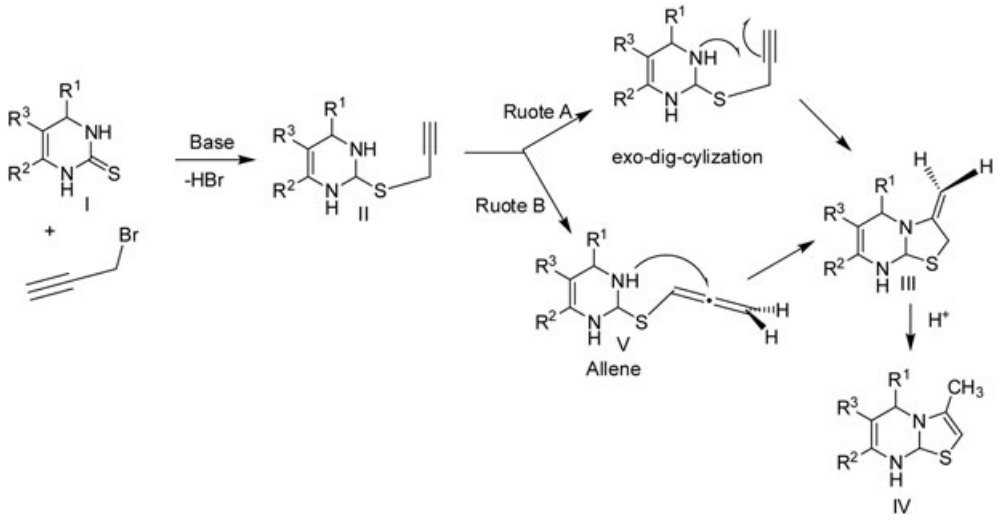


Figure 3. Reaction mechanism proposed.

solid, yield 92%, mp 110–111°C, R_f = 0.5 (6:4 hexane/ethylacetate); ir (KBr): 3355, 2932, 2365, 1665, 1590, 1481, 1219, 1084, 765 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 7.30–7.26 (m, 5H, ArH), 6.16 (s, 1H, CH), 5.92 (s, 1H, CH), 4.19 (q, *J* = 7.20 Hz, 2H, OCH_2), 2.37 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 1.32 (t, *J* = 7.05 Hz, 3H, CH_3); ^{13}C nmr (50 MHz, $CDCl_3$ + CCl_4,): δ = 166.7, 166.5, 155.9, 143.1, 135.2, 128.7, 128.1, 126.4, 100.1, 100.0, 59.6, 57.7, 23.9, 14.4, 14.0; ms (ESI^+): *m/z*: 315 $[M+H]^+$. *Anal*. Calcd. for $C_{17}H_{18}N_2O_2S$ (314.40): C, 64.94; H, 5.77; N, 8.91. Found: C, 64.90; H, 5.73; N, 8.90.

Ethyl 5-(4-methoxyphenyl)-3,7-dimethyl-5*H*-thiazolo[3,2-a] pyrimidine-6-carboxylate (4b). It was obtained as yellow solid, yield 91%, mp 112–113°C; R_f = 0.4 (6:4 hexane/ethylacetate); IR (KBr): 3430, 3019, 1658, 1481, 1217, 762 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$ + CCl_4): δ = 7.30–7.20 (m, 2H, ArH), 6.82–6.76 (m, 2H, ArH), 6.08 (s, 1H, CH), 5.92 (d, *J* = 1.2 Hz, 1H, CH), 4.19 (q, *J* = 7.0 Hz, 2H, OCH_2), 3.77 (s, 3H, OCH_3), 2.36 (s, 3H, CH_3), 2.08 (d, *J* = 1.1 Hz, 3H, CH_3), 1.32 (t, *J* = 7.12 Hz, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 166.6, 166.3, 159.3, 155.5, 135.6, 135.2, 127.7, 113.9, 100.4, 99.8, 59.5, 57.2, 55.0, 23.8, 14.4, 14.0; ms (ESI^+): *m/z*: 345 $[M+H]^+$. *Anal*. Calcd. for $C_{18}H_{20}N_2O_3S$ (344.43): C, 62.77; H, 5.85; N, 8.13. Found: C, 62.74; H, 5.87; N, 8.12.

Ethyl 5-(4-bromophenyl)-3,7-dimethyl-5*H*-thiazolo[3,2-a] pyrimidine-6-carboxylate (4c). It was obtained as yellow solid, yield 93%, mp 115–116°C; R_f = 0.5 (6:4 hexane/ethylacetate); IR (KBr): 3397, 3016, 1810, 1663, 1480, 1218, 1028, 762 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$+CCl_4): δ = 7.44–7.41(m, 2H, ArH), 7.28–7.21 (m, 2H, ArH), 6.14 (s, 1H, CH), 5.97 (s, 1H, CH), 4.19 (q, *J* = 7.53 Hz, 2H, OCH_2), 2.38 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 1.31 (t, *J* = 7.11 Hz, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 166.5, 166.4, 156.1, 142.0, 134.9, 131.8, 128.1, 122.2, 100.2, 99.7, 59.7, 57.2, 23.9, 14.4, 13.9; MS (ESI^+): *m/z*: 394 $[M+H]^+$. *Anal*. Calcd. for $C_{17}H_{17}Br\ N_2O_2S$ (393.30): C, 51.92; H, 4.36; N, 7.12. Found: C, 51.91; H, 4.38; N, 7.10.

Ethyl 5-(4-chlorophenyl)-3,7-dimethyl-5*H*-thiazolo[3,2-a] pyrimidine-6-carboxylate (4d). It was obtained as **y**ellow solid, yield 93%, mp 117–118°C; R_f = 0.5 (6:4 hexane/ethylacetate); IR (KBr): 3776, 3423, 3019, 2928, 2363, 1662, 1590, 1481, 1217, 1084, 766, 670 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$+CCl_4): δ = 7.25–7.22 (m, 4H, ArH), 6.09 (s, 1H, CH), 5.91 (d, *J* = 1.22 Hz, 1H, CH), 4.16 (q, *J* = 7.10 Hz, 2H, OCH_2), 2.32 (s, 3H, CH_3), 2.02 (d, *J* = 1.2 Hz, 3H, CH_3), 1.29 (t, *J* = 7.12 Hz, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 166.6, 166.5, 156.0, 141.5, 135.0, 134.1, 128.9, 127.8, 100.3, 99.8, 59.8, 57.1, 23.9, 14.4, 14.0; MS (ESI^+): *m/z*: 349 $[M+H]^+$. *Anal*. Calcd. for $C_{17}H_{17}ClO_2N_2S$ (348.85): Calcd. C, 58.53; H, 4.91; N, 8.03 Found: C, 58.50; H, 5.92; N, 8.00.

Ethyl 5-(3-chlorophenyl)-3,7-dimethyl-5*H*-thiazolo[3,2-a] pyrimidine-6-carboxylate (4e). It was obtained as yellow viscous liquid yield 92%; R_f = 0.5 (6:4 hexane/ethylacetate); IR (Neat): 3571, 2928, 2387, 1688, 1479, 1218, 1082, 767 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$+CCl_4): δ = 7.32–7.20 (m, 4H, ArH), 6.17 (s, 1H, CH), 6.00 (d, *J* = 1.2 Hz, 1H, CH), 4.24 (q, *J* = 7.14 Hz, 2H, OCH_2), 2.39 (s, 3H, CH_3), 2.10 (d, *J* = 1.2 Hz, 3H, CH_3), 1.37 (t, *J* = 7.12 Hz, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 166.4, 156.3, 144.8, 134.9, 134.5, 130.1, 128.4, 126.5, 124.5, 100.4, 99.5, 59.8, 57.2, 23.9, 14.4, 14.0; ms (ESI^+): *m/z*: 349 $[M+H]^+$. *Anal*. Calcd. for $C_{17}H_{17}ClO_2N_2S$ (348.85): C, 58.53; H, 4.91; N, 8.03. Found: C, 58.51; H, 4.92; N, 8.00.

Ethyl 5-(4-fluorophenyl)-3,7-dimethyl-5*H*-thiazolo[3,2-a] pyrimidine-6-carboxylate (4f). It was obtained as yellow solid, yield 88%, mp 100–101°C; R_f = 0.5 (6:4 hexane/ethylacetate); ir (KBr): 3520, 3398, 3019, 2928, 2358, 1661, 1481, 1218, 795, 669 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$+CCl_4): δ = 7.34–7.27 (m, 2H, ArH), 7.03–6.93 (m, 2H, ArH), 6.14 (s, 1H, CH), 5.95 (d, *J* = 1.2 Hz, 1H, CH), 4.21 (q, *J* = 7.0 Hz, 2H, OCH_2), 2.37 (s, 3H, CH_3), 2.07 (d, *J* = 1.2 Hz, 3H, CH_3), 1.33 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 166.5, 166.3, 155.8, 139.1, 139.0, 135.0, 128.2, 128.1, 115.8, 115.4, 100.2, 100.1, 59.7, 57.0, 23.9, 14.4, 13.9; ms (ESI^+): *m/z*: 333 $[M+H]^+$. *Anal*. Calcd. for $C_{17}H_{17}FN_2\ O_2S$ (332.39): C, 61.43; H, 5.16; N, 8.43. Found: C, 61.40; H, 5.18; N, 8.42.

Ethyl 3,7-dimethyl-5-(3-nitrophenyl)-5*H*-thiazolo[3,2-a] pyrimidine-6-carboxylate (4g). It was obtained as yellow solid, yield 90%, mp 151–152°C; R_f = 0.4 (6:4 hexane/ethylacetate); IR (KBr): 3406, 2357, 1665, 1478, 1218, 1083, 770 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$+CCl_4): δ = 8.15–8.11 (m, 2H, ArH), 7.66–7.62 (m, 1H, ArH), 7.52–7.45 (m, 1H, ArH), 6.28 (s, 1H, CH), 6.01 (d, *J* = 1.1 Hz, 1H, CH), 4.20 (q, *J* = 6.9 Hz, 2H, OCH_2), 2.36 (s, 3H, CH_3), 2.07 (d, *J* = 1.1 Hz, 3H, CH_3), 1.34 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 166.6, 166.3, 156.9, 148.2, 144.8, 134.6, 132.4, 130.0, 123.1, 121.2, 100.9, 99.1, 60.0, 57.1, 23.9, 14.4, 14.0; ms (ESI^+): *m/z*: 360 $[M+H]^+$. *Anal*. Calcd. for $C_{17}H_{17}O_4N_3S$ (359.40): C, 56.81; H, 4.77; N, 11.69. Found: C, 56.80; H, 4.79; N, 11.67.

1-(3,7-dimethyl-5-(naphthalen-2-yl)-5*H*-thiazolo[3,2-a] pyrimidin-6-yl)ethanone (4h). It was obtained as yellow viscous liquid, yield 85%; R_f = 0.5 (6:4 hexane/ethylacetate); IR (Neat): 3749, 3021, 2398, 1705, 1217, 763, 670 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$+CCl_4): δ = 7.79–7.70 (m, 4H, ArH), 7.50–7.30 (m, 3H, ArH), 6.59 (s, 1H, CH), 6.04 (s, 1H, CH), 2.43 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 2.15 (s, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 193.8, 166.8, 155.8, 140.0, 136.1, 133.1, 133.0, 128.8, 128.3, 127.5, 126.1, 125.0, 124.5, 111.8, 100.8, 56.9, 31.6, 25.4, 14.0; ms (ESI^+): *m/z*: 335 $[M+H]^+$. *Anal.* Calcd. for $C_{20}H_{18}N_2OS$ (334.43): C, 71.83; H, 5.42; N, 8.38. Found: C, 71.80; H, 5.44; N, 8.36.

1-(3,7-dimethyl-5-phenyl-5*H*-thiazolo[3,2-a]pyrimidin-6-yl) ethanone (4i). It was obtained as yellow viscous liquid, yield 86%; R_f = 0.5 (6:4 hexane/ethylacetate); IR (Neat): 3419, 3020, 2366, 1728, 1468, 1219, 769 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$+CCl_4): δ = 7.27–7.23 (m, 5H, ArH), 6.40 (s, 1H, CH), 6.00 (s, 1H, CH), 2.38 (s, 6H, 2 X CH_3), 2.10 (s, 3H, CH_3); ms (ESI^+): *m/z*: 285 $[M+H]^+$. *Anal*. Calcd. for $C_{16}H_{16}N_2OS$ (284.38): C, 67.58; H, 5.67; N, 9.85. Found: C, 67.55; H, 5.66; N, 9.81.

1-(5-(4-Fluorophenyl)-3,7-dimethyl-5*H*-thiazolo[3,2-a] pyrimidin-6-yl)ethanone (4j). It was obtained as **y**ellow solid, yield 82%, mp 135–136°C; R_f = 0.4 (6:4 hexane/ethylacetate); IR (KBr): 3427, 3019, 2368, 1604, 1467, 1219, 768 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$+CCl_4): δ = 7.28–7.23 (m, 2H, ArH), 6.96–6.90 (m, 2H, ArH), 6.36 (s, 1H, CH), 6.01 (s, 1H, CH), 2.37 (s, 6H, 2 X CH_3), 2.08 (s, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 193.7, 166.6, 155.8, 138.7, 138.6, 135.8, 128.1, 128.0, 115.6, 115.3, 111.9, 100.8, 56.0, 31.5, 25.3, 13.8; ms(ESI^+): *m/z*: 303 $[M+H]^+$. *Anal.* Calcd for $C_{16}H_{15}FN_2OS$ (302.37): C, 63.56; H, 5.00; N, 9.26. Found: C, 63.55; H, 5.05; N, 9.23.

1-(5-(3,4-dimethoxyphenyl)-3,7-dimethyl-5*H*-thiazolo[3,2-a] pyrimidin-6-yl)ethanone (4k). It was obtained as **y**ellow solid, yield 84%, mp 129–130°C; R_f = 0.4 (6:4 hexane/ethylacetate); ir (KBr): 3463, 3019, 2364, 1599, 1465, 1218, 765 cm^{-1}. ^{1}H-NMR

(200 MHz, $CDCl_3$+CCl_4): δ = 6.87 (s, 1H, ArH), 6.70 (s, 2H, ArH), 6.31 (s, 1H, CH), 5.98 (s, 1H, CH), 3.81 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 2.36 (s, 6H, 2 X CH_3), 2.09 (s, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 194.0, 166.6, 155.6, 149.0, 148.6, 136.1, 135.6, 128.1, 128.0, 118.2, 115.6, 115.3, 112.0, 111.0, 109.7, 100.8, 100.5, 56.3, 55.8, 55.7, 31.6, 25.3, 13.9; ms (ESI^+): *m/z*: 345 $[M+H]^+$. *Anal*. Calcd. for $C_{18}H_{20}N_2O_3S$ (344.43): C, 62.77; H, 5.85; N, 8.13. Found: C, 62.75; H, 5.87; N, 8.10.

Methyl 3,7-dimethyl-5-phenyl-5*H*-thiazolo[3,2-a]pyrimidine-6-carboxylate (4l). It was obtained as yellow solid, yield 94%, mp 120–121°C; R_f = 0.5 (6:4 hexane/ethylacetate); IR (KBr): 3567, 2914, 2337, 1673, 1492, 1220, 1089, 976, 697 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$+CCl_4): δ = 7.32–7.26 (m, 5H, ArH), 6.16 (s, 1H, CH), 5.94 (d, *J* = 0.9 Hz, 1H, CH), 3.71 (s, 3H, OCH_3), 2.37 (s, 3H, CH_3), 2.07 (s, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 167.0, 166.6, 156.1, 143.1, 135.2, 128.7, 128.1, 126.3, 100.0, 99.8, 57.7, 50.8, 23.9, 14.0; ms (ESI^+): *m/z*: 301 $[M+H]^+$. *Anal*. Calcd. for $C_{16}H_{16}O_2N_2S$ (300.38): C, 63.98; H, 5.37; N, 9.33. Found: C, 63.95; H, 5.30; N, 9.31.

Methyl 5-(4-methoxyphenyl)-3,7-dimethyl-5*H*-thiazolo[3,2-a] pyrimidine-6-carboxylate (4m). It was obtained as yellow solid, yield 90%, mp 126–127°C; R_f = 0.4 (6:4 hexane/ethylacetate); IR (KBr): 3417, 2930, 1626, 1480, 1218, 1088, 765, 699 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$+CCl_4): δ = 7.28–7.19 (m, 2H, ArH), 6.79–6.76 (m, 2H, ArH), 6.06 (s, 1H, CH), 5.90 (s, 1H, CH), 3.75 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 2.34 (s, 3H, CH_3), 2.05 (s, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 167.0, 166.3, 159.4, 155.5, 135.5, 135.2, 127.6, 114.0, 100.3, 100.0, 57.2, 55.0, 50.7, 23.7, 13.9; MS (ESI^+): *m/z*: 331 $[M+H]^+$. Elemental Anal. Calcd for $C_{17}H_{18}O_3N_2S$: C, 61.80; H, 5.49; N, 8.48. Found: C, 61.75; H, 5.46; N, 8.42.

Methyl 3,7-dimethyl-5-(naphthalen-1-yl)-5*H*-thiazolo[3,2-a] pyrimidine-6-carboxylate (4n). It was obtained as yellow solid, yield 93%, mp 164–165°C; R_f = 0.4 (6:4 hexane/ethylacetate); IR (KBr): 3392, 3020, 2930, 2370, 1662, 1481, 1217, 765, 670 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$+CCl_4): δ = 8.48 (d, *J* = 8.52 Hz, 1H, ArH), 7.84–7.75 (m, 3H, ArH), 7.63–7.39 (m, 3H, ArH), 6.98 (s, 1H, CH), 5.80 (d, *J* = 1.2 Hz, 1H, CH), 3.51 (s, 3H, OCH_3), 2.43 (s, 3H, CH_3), 1.88 (d, *J* = 1.2 Hz, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 166.9, 166.6, 155.5, 140.9, 135.7, 133.3, 129.2, 129.1, 128.7, 127.2, 126.4, 126.1, 125.5, 123.4, 100.8, 99.7, 53.5, 50.5, 23.8, 14.6; MS (ESI^+): *m/z*: 351 $[M+H]^+$. *Anal.* Calcd for $C_{20}H_{18}N_2O_2S$ (350.43): C, 68.55; H, 5.18; N, 7.99. Found: C, 68.52; H, 5.19; N, 7.94.

Methyl 3,7-dimethyl-5-(naphthalen-2-yl)-5*H*-thiazolo[3,2-a] pyrimidine-6-carboxylate (4o). It was obtained as yellow solid, yield 94%, mp 124–125°C; R_f = 0.4 (6:4 hexane/ethylacetate); IR (KBr): 3380, 3021, 2364, 2173, 1659, 1216, 766, 671 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$+CCl_4): δ = 7.83–7.72 (m, 4H, ArH), 7.51–7.30 (m, 3H, ArH), 6.33 (s, 1H, CH), 5.92 (s, 1H, CH), 3.71 (s, 3H, OCH_3), 2.40 (s, 3H, CH_3), 2.08 (s, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 167.0, 166.6, 156.1, 140.3, 135.3, 133.1, 128.9, 128.3, 127.5, 126.2, 125.0, 124.4, 100.1, 99.8, 58.0, 50.8, 23.9, 14.0; ms (ESI^+): *m/z*: 351 $[M+H]^+$. *Ana*l. Calcd for $C_{20}H_{18}N_2O_2S$ (350.43): C, 68.55; H, 5.18; N, 7.99. Found: C, 68.50; H, 5.15; N, 7.93.

Methyl 5-(2-chlorophenyl)-3,7-dimethyl-5*H*-thiazolo[3,2-a] pyrimidine-6-carboxylate (4p). It was obtained as yellow solid, yield 93%, mp 118–120°C; R_f = 0.5 (6:4 hexane/ethylacetate); IR (KBr): 3370, 2950, 2366, 1480, 1218, 1090, 769, 670 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$+CCl_4): δ = 7.69–7.64 (m, 1H, ArH), 7.35–7.21 (m, 3H, ArH), 6.58 (s, 1H, CH), 5.90 (s, 1H, CH), 3.67 (s, 3H, OCH_3), 2.43 (s, 3H, CH_3), 2.17 (s, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ =166.6, 166.4, 156.4, 141.7, 135.7, 130.5, 130.3, 129.5, 128.2, 99.8, 99.7, 54.6, 50.6, 23.5, 14.5; ms (ESI^+): *m/z*: 335 $[M+H]^+$. *Anal*. Calcd for $C_{16}H_{15}ClN_2O_2S$ (334.82): C, 57.40; H, 4.52; N, 8.37. Found: C, 57.38; H, 4.53; N, 8.35.

Methyl 5-(3-chlorophenyl)-3,7-dimethyl-5*H*-thiazolo[3,2-a] pyrimidine-6-carboxylate (4q). It was obtained as yellow viscous liquid, yield 92%; R_f = 0.5 (6:4 hexane/ethylacetate); ir (Neat): 3378, 3022, 2366, 2264, 1880, 1662, 1590, 1478, 1217, 763, 671 cm^{-1}; ^{1}H nmr (200MHz, $CDCl_3$+CCl_4): δ = 7.30-7.22 (m, 4H, ArH), 6.18 (s, 1H, CH), 6.01 (d, J = 1.2 Hz, 1H, CH), 3.75 (s, 3H, OCH_3), 2.39 (s, 3H, CH_3), 2.11(d, J = 1.2 Hz, 3H, CH_3); ^{13}C nmr (50MHz, $CDCl_3$+CCl_4,): δ = 166.9, 166.5, 144.8, 134.9, 134.7, 130.1, 128.4, 126.4, 124.4, 100.5, 57.2, 50.9, 23.8, 14.0; ms (ESI^+): *m/z*: 335 $[M+H]^+$. *Anal*. Calcd for $C_{16}H_{15}ClN_2O_2S$ (334.82): C, 57.40; H, 4.52; N, 8.37. Found: C, 57.37; H, 4.50; N, 8.33.

Methyl 5-(4-chlorophenyl)-3,7-dimethyl-5*H*-thiazolo[3,2-a] pyrimidine-6-carboxylate (4r). It was obtained as yellow viscous liquid, yield 90%; R_f = 0.5 (6:4 hexane/ethylacetate); IR (Neat): 3468, 3366, 3021, 2364, 1579, 1477, 1217, 767, 670 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$+CCl_4): δ = 7.37–7.28 (m, 4H, ArH), 6.16 (s, 1H, CH), 5.98 (d, *J* = 1.2 Hz, 1H, CH), 3.73 (s, 3H, OCH_3), 2.37 (s, 3H, CH_3), 2.09(d, *J* = 1.2 Hz, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 167.0, 166.5, 156.1, 141.5, 135.0, 134.1, 128.9, 127.7, 100.4, 99.6, 57.1, 50.9, 23.9, 13.8; ms (ESI^+): *m/z*: 335 $[M+H]^+$. *Anal*. Calcd for $C_{16}H_{15}ClN_2O_2S$ (334.82): C, 57.40; H, 4.52; N, 8.37. Found: C, 57.38; H, 4.51; N, 8.36.

Methyl 5-(3,4-dimethoxyphenyl)-3,7-dimethyl-5*H*-thiazolo [3,2-a]pyrimidine-6-carboxylate (4s). It was obtained as yellow solid, yield 94%, mp 167–168°C; R_f = 0.4 (6:4 hexane/ethylacetate); IR (KBr): 3572, 3020, 2396, 1685, 1516, 1217, 767, 670 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$+CCl_4): δ = 6.87–6.72 (m, 3H, ArH), 6.10 (s, 1H, CH), 5.94 (d, *J* = 1.2 Hz, 1H, CH), 3.85 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 2.36 (s, 3H, CH_3), 2.09(d, *J* = 1.0 Hz, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 167.1, 166.5, 155.8, 149.2, 148.9, 135.8, 135.3, 118.4, 111.0, 109.4, 100.1, 99.9, 57.4, 55.7, 50.8, 23.9, 14.0; ms (ESI^+): *m/z*: 361 $[M+H]^+$. *Anal*. Calcd. for $C_{18}H_{20}N_2O_4S$ (360.43): C, 59.98; H, 5.59; N, 7.77. Found: C, 59.95; H, 5.60; N, 7.74.

Methyl 5-(4-hydroxy-3-methoxyphenyl)-3,7-dimethyl-5*H*-thiazolo[3,2-a]pyrimidine-6-carboxylate (4t). It was obtained as yellow viscous liquid, yield 89%; R_f = 0.4 (6:4 hexane/ethylacetate); ir (Neat): 3427, 3021, 2363, 1660, 1593, 1217, 766, 671 cm^{-1}; ^{1}H nmr (200MHz, $CDCl_3$+CCl_4): δ = 6.96-6.78 (m, 3H, ArH), 6.12 (s, 1H, CH), 5.97 (s, 1H, CH), 4.73 (d, *J* = 2.30 Hz, 1H, OH), 3.84 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 2.37 (s, 3H, CH_3), 2.03(s, 3H, CH_3); ^{13}C nmr (50MHz, $CDCl_3$+CCl_4,): δ = 167.1, 166.5, 155.8, 149.8, 146.8, 137.0, 135.3, 118.2, 114.0, 109.8, 100.1, 100.0, 57.3, 55.7, 50.8, 23.8, 14.0; ms (ESI^+): *m/z*: 347 $[M+H]^+$. *Anal.* Calcd. for $C_{17}H_{18}O_4N_2S$ (346.40): C, 58.94; H, 5.24; N, 8.09. Found: C, 58.90; H, 5.26; N, 8.05.

Methyl 3,7-dimethyl-5-(2,3,4-trimethoxyphenyl)-5*H*-thiazolo[3,2-a] pyrimidine-6-carboxylate (4u). It was obtained as yellow viscous liquid, yield 90%; R_f = 0.4 (6:4 hexane/ethylacetate); IR (Neat): 3367, 3022, 2364, 2077, 1660, 1592, 1327, 1213, 762, 671 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$+CCl_4): δ = 7.30 (s, 1H, ArH), 6.51 (s, 2H, ArH), 6.13 (s, 1H, CH), 5.99 (d, *J* = 1.2 Hz, 1H, CH), 3.83

(s, 12H, 3 X OCH_3), 3.76 (s, 3H, OCH_3), 2.38 (s, 3H, CH_3), 2.12 (s, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 167.2, 166.6, 153.9, 138.4, 135.4, 128.8, 103.0, 100.1, 99.9, 60.6, 57.6, 56.0, 50.9, 23.8, 14.0; ms (ESI^+): *m/z*: 391 $[M+H]^+$. *Anal*. Calcd. for $C_{19}H_{22}O_5N_2S$ (390.45): C, 58.45; H, 5.68; N, 7.17. Found: C, 58.42; H, 5.66; N, 7.16.

Methyl 5-(4-(benzyloxy)phenyl)-3,7-dimethyl-5*H*-thiazolo[3,2-a] pyrimidine-6-carboxylate (4v). It was obtained as yellow solid, yield 92%, mp 198–199°C; R_f = 0.4 (6:4 hexane/ethylacetate); IR (KBr): 3512, 2398, 2367, 1700, 1484, 1213, 1079, 1012, 748, 546 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$+CCl_4): δ = 7.44–7.26 (m, 7H, ArH), 6.95–6.89 (m, 2H, ArH), 6.13 (s, 1H, CH), 5.96 (d, *J* = 1.3 Hz, 1H, CH), 5.04 (s, 2H, OCH_2), 3.72 (s, 3H, OCH_3), 2.41 (s, 3H, CH_3), 2.09(d, *J* = 1.2 Hz, 3H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$+CCl_4,): δ = 167.3, 166.7, 158.7, 156.0, 136.8, 135.9, 135.4, 128.6, 128.0, 127.7, 127.5, 114.9, 100.2, 100.1, 70.0, 57.2, 50.9, 23.9, 14.0; ms (ESI^+): *m/z*: 407 $[M+H]^+$. *Anal*. Calcd. for $C_{23}H_{22}O_3N_2S$ (406.50): C, 67.96; H, 5.46; N, 6.89. Found: C, 67.95; H, 5.43; N, 6.85.

Acknowledgments. The authors thank CSIR and DRDO, New Delhi for financial assistance. Seerat and Anindra are thankful to CSIR New Delhi for their SRF and Rahul is thankful to DRDO New Delhi for PA. The authors also thank SAIF staff for providing the spectral data and microanalysis.

REFERENCES AND NOTES

[1] Biginelli, P. Gazz Chim Ital 1893, 23, 360.

[2] Kappe, C. O. Tetrahedron 1993, 49, 6937.

[3] Kappe, C. O. Acc Chem Res 2000, 33, 879.

[4] Kappe, C. O.; Kumar, D.; Varma, R. S. Synthesis 1999, 1799 and references cited therein.

[5] Simon, C.; Constantieux, T.; Rodriguez, J. Eur J Org Chem 2004, 4957 and references cited therein.

[6] Kappe, C. O. QSAR Comb Sci 2003, 22, 630.

[7] Geist, J. G.; Lauw, S.; Illarionova, V.; Illarionov, B.; Fischer, M.; Grawert, T.; Rohdich, F.; Eisenreich, W.; Kaiser, J.; Groll, M.; Scheurer, C.; Wittlin, S.; Alonso-Gómez, J. L.; Schweizer, W. B.; Bacher, A. Chem Med Chem 2010, 5, 1092.

[8] Liu, S.; Yang, L.; Jin, Z.; Huang, E.; Wan, D. C. C.; Lin, H.; Hua, C. ARKIVOC 2009, x, 333.

[9] Wichmann, J.; Adam, G.; Kolczewski, S.; Mutel, V.; Woltering, T. Bioorg Med Chem Lett 1999, 9, 1573.

[10] Awadallah, F. M. Sci Pharm 2008, 76, 415.

[11] Rashad, A. E.; Shamroukh, A. H.; Abdel-Megeid, R. E.; Kandeil, A. M.; Mostafa, A.; Elshesheny, R.; Ali, M. A.; Banert, K. Eur J Med Chem 2010, 11, 5251.

[12] Shridhar, D. R.; Jogibhukta, M.; Krishnan, V. S. H. Indian J Chem B 1986, 25, 345.

[13] Munchhof, M. J.; Beebe, J. S.; Casavant, J. M.; Cooper, B. A.; Doty, J. L.; Higdon, R. C.; Hillerman, S. M.; Soderstrom, C. I.; Knauth, E. A.; Marx, M. A.; Rossi, A. M. K.; Sobolov, S. B.; Sun, J. Bioorg Med Chem Lett 2004, 14, 21.

[14] Balkan, A.; Uma, S.; Ertan, M.; Wiegrebe, W. Pharmazie 1992, 47, 687.

[15] Wichmann, J.; Adam, G.; Kolczewski, S.; Mutel, V.; Woltering, T. Bioorg Med Chem Lett 1999, 9, 1573.

[16] Shridhar, D. R.; Jogibhukta, M.; Joshi, P. P.; Rao, C.; Seshagiri, J. A. Y. Indian J Chem B 1984, 23, 492.

[17] Ahmad, N. M.; Jones, K. Tetrahedron lett 2010, 51, 3263.

[18] Quan, Z.; Zhang, Z.; Wang, J.; Wang, X.; Liu, Y.; Ji, P.-Y. Heteroatom Chem 2008, 19, 149.

[19] Al-Rashood, K. A.; Abdel-Aziz, H. A. Molecules 2010, 15, 3775.

[20] Castagnolo, D.; Pagano, M.; Bernardini, M.; Botta, M. Synlett 2009, 13, 2093.

[21] Singh, B. K.; Mishra, M.; Saxena, N.; Yadav, G. P.; Maulik, P. R.; Sahoo, M. K.; Gaur, R. L.; Murthy, P. K.; Tripathi, R. P. Eur J Med Chem 2008, 43, 2717.

[22] Katiyar, D.; Tiwari, V. K.; Tripathi, R. P.; Srivastava, A.; Chaturvedi, V.; Srivastava, R.; Srivastava, B. S. Bioorg Med Chem 2003, 11, 4369.

[23] Mahalingam, S. M.; Aidhen, I. S. J Org Chem 2006, 71, 349.

[24] Wang, X.; Quan, Z.; Wang, J. K.; Zhang, Z.; Wang, M. Bioorg Med Chem Lett 2006, 16, 4592.

[25] Dallinger, D.; Gorobets, N. Y.; Kappe, C. O. Org Lett 2003, 5, 1205.