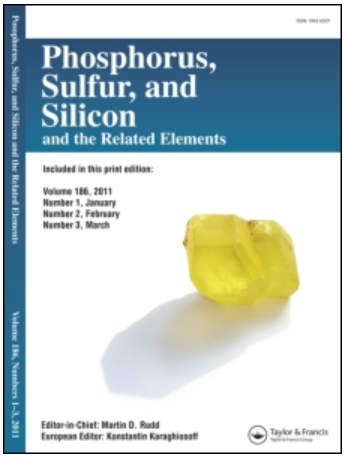

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Catalyst-Free, Rapid Synthesis of Fused Bicyclic Thiazolo-Pyrimidine and Pyrimido-Thiazine Derivatives by a Microwave-Assisted Method

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Catalyst-Free, Rapid Synthesis of Fused Bicyclic Thiazolo-Pyrimidine and Pyrimido-Thiazine Derivatives by a Microwave-Assisted Method

Vijay R. Virsodia,[1] Nikhil R. Vekariya,[1] Atul T. Manvar,[2] Rupesh C. Khunt,[2] Bhavin R. Marvania,[2] Bharat S. Savalia,[2] and Anamik K. Shah[2]
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The present investigation deals with the rapid microwave-assisted synthesis of compounds containing fused bicyclic systems. Dihydropyrimidines obtained via a microwave-assisted Biginelli reaction were treated with dibromo alkanes under microwave conditions to yield thiazolo-pyrimidine and pyrimido-thiazine systems. The usefulness of this method lies in carrying out the reaction without a catalyst and solvent in a shorter time. The reaction was successfully extended to develop fused systems from benzimidazole-2-thiol.

Keywords Fused bicyclic systems; MAOS; pyrimido-thiazine; thiazolo-pyrimidine; without catalyst

INTRODUCTION

The synthesis of dihydropyrimidine derivatives by the Biginelli reaction is not only important because these structural classes are known to exhibit very interesting pharmacological profiles,[1–7] but because various fused bicyclic systems can also be developed from this precursor.[8] Various modified building blocks, e.g. β-ketoesters, ureas/thioureas, and aldehydes, are used to synthesize molecules with targeted substitutions on a basic skeleton. A large number of catalysts[9–14] are reported to catalyze the reaction efficiently and to provide higher yields. Different methods of synthesis, e.g., microwave-assisted synthesis,[15–17] solid

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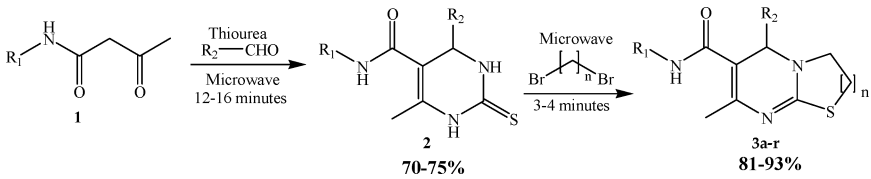
phase synthesis,[18] and use of ionic liquids,[19] have also been investigated. This reaction may be utilized to its maximum by developing a rapid method of synthesis of various bicyclic fused systems from this precursor to produce a library of compounds. C. Oliver Kappe has been involved with the high speed scaffold decoration of this heterocyclic core, exploring the diversity on at least six points around the scaffold.[20] During the last few years, we have intensively studied the effects of different modifications to the 1,4-dihydropyridine structural class on their therapeutic activity.[21–26] Very interesting results were obtained for 1,4-dihydropyridine derivatives with a phenyl carbamoyl side chain, which inspired us to apply the same modification to aza analogues of 1,4-dihydropyridine, i.e., dihydropyrimidine, and to develop various bicyclic systems with a phenyl carbamoyl moiety. Recently, we reported[26] the synthesis of dihydropyrimidine derivatives bearing a phenyl carbamoyl side chain, their anti-tubercular activity, and 3D-QSAR study. In continuation of our work, this current article reports a rapid microwave-assisted synthesis of fused bicyclic systems with aphenyl carbamoyl side chain without the use of a catalyst.

RESULTS AND DISCUSSION

In the conventional method, substituted acetoacetanilide, thiourea, and aromatic aldehydes were reacted in methanol, and dihydropyrimidines were obtained in 40–45% yield after a long reaction time (12–15 h). Earlier the Biginelli reaction was reported under microwave irradiation, but we wished to optimize the reaction conditions for the current reaction where substituted acetoacetanilides are used as new building blocks. To check the effect of microwave power, the reactions were carried out at 200 W and 400 W at 120°C. The reaction was found to complete in shorter time at 400 W than at 200 W. At higher temperature (400 W, 140°C), slightly less or equivalent yields were obtained after same reaction time. Dihydropyrimidines, thus synthesized, were used as a precursor to develop fused bicyclic systems.

To develop fused bicyclic systems, dihydropyrimidines were reacted with dibromo alkanes. In the conventional method, the reaction was carried out in methanol and dimethylformamide using potassium carbonate as a base. By employing methanol as a solvent media, 30–40% yields were obtained after 5 h of refluxing; while in dimethylformamide, the reaction proceeded faster and 50–55% yields were obtained after 2–2.5 h of refluxing. In order to get higher yields and shorten reaction time, the reaction was subjected to microwave irradiation procedure (Scheme 1). Surprisingly, the reaction was found to proceed without a



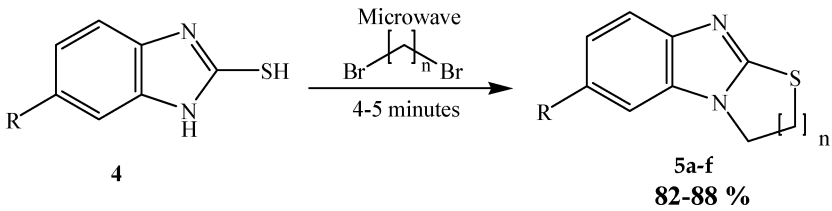
SCHEME 1 Catalyst-free microwave-assisted synthesis of thiazolo-pyrimidine and pyrimido-thiazine derivatives.

catalyst, leading to the formation of final compounds in good yield (81–93%). Dihydropyrimidine and dibromo ethane were taken in the ratio of 1:1.5 and irradiated using microwaves. Higher ratios of dihydropyrimidine and dibromo ethane did not provide any advantage in terms of yield and reaction time. Similarly, pyrimido-thiazine–fused systems were also synthesized efficiently by this method using dibromo propane. The compounds were characterized by spectral analysis. To expand the use of these optimized reaction conditions, benzimidazole-2-thiol was reacted with dibromo alkanes to develop bicyclic fused systems, and target compounds were synthesized with the advantages of high yield (80–85%) and shorter reaction time (4–5 min) (Scheme 2). The conventional method requires the use of potassium carbonate as a base and solvent media, while under microwave the reactions could proceed without a catalyst and solvent.

EXPERIMENTAL

Materials and Methods

All the chemicals and solvents were purchased from Spectrochem (Mumbai, India) and used without further purification. ^{1}H NMR spectra were recorded on a Bruker Avance II 400MHz spectrometer in DMSO d_6. Chemical shifts (δ) are given in ppm relative to TMS, coupling constants (J) in Hz. IR spectra were recorded on a Shimadzu



SCHEME 2 Catalyst-free microwave-assisted synthesis of thiazolo-pyrimidine and pyrimido-thiazine derivatives.

FTIR-8400 using KBr optics. Mass spectra were recorded on Shimadzu GC-MS, QP2010 by EI method. A microwave synthesizer (Questron Technologies Corporation, Canada) QPro-M model monomode open-vessel was used for the synthesis. Elemental analysis of the compounds was carried out on Elementar Vario EL III Carlo Erba 1108 model.

General Method of Synthesis of N-(substituted phenyl)-7-methyl-5-(4-substituted phenyl)-2,3-Dihydro-5H-[1,3]thiazolo-[3,2-α]pyrimidine-6-carboxamide (3a–r)

N-(substituted phenyl)-4-(substituted phenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxo-pyrimidine-5-carboxamide (0.01 mol) and a dibromoalkane (0.015 mol) were taken into the reaction vessel. The reaction mixture was subjected to microwave irradiation and was monitored with thin layer chromatography. After completion of the reaction, as indicated by TLC (ethyl acetate:hexane [3:2]), methanol was added to the reaction mixture. The crude product obtained was filtered and subjected to silica gel column chromatography (60–100 mesh) to elute the pure product. A similar procedure was adopted for the synthesis of the compounds listed in Table I.

General Method of Synthesis of 2,3-Dihydro[1,3]thiazolo-[3,2-a]benzimidazole (5a–f)

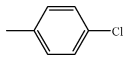
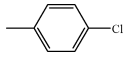
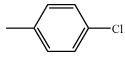
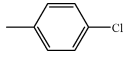
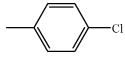
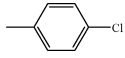
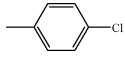
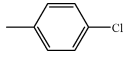
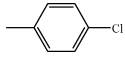
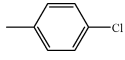
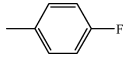
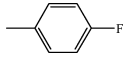
Benzimidazole-2-thiol (0.01 mol) and dibromoalkane (0.015 mol) were taken into the reaction vessel and subjected to microwave irradiation. The reaction was monitored with thin layer chromatography. After completion of the reaction, as indicated by TLC (chloroform:methanol [4:1]), acetone was added to the reaction mixture. Acetone was stripped off at reduced pressure to leave the crude product. Finally it was purified by silica gel column chromatography (60–100 mesh) using chloroform and methanol as eluents. This process was adopted to synthesize compounds listed in Table II.

SPECTRAL DATA

N-(4-chlorophenyl)-3,5-dihydro-7-methyl-5-phenyl-2H-thiazolo-[3,2-α]pyrimidine-6-carboxamide (3a, $C_{20}H_{18}ClN_3OS$)

White solid, mp 153–154°C; IR (cm^{-1}): 3256 (N—H), 3089 (Ar-H), 2914 (—CH_3), 2818 (—CH_2), 1673 (C=O), 1614 (C=C), 1126 (C—O); ^{1}H NMR (DMSO-d_6) $\delta = 2.23$ (3H, s), 3.11 (1H, m), 3.22 (1H, m), 3.42 (1H, m), 3.61 (1H, m), 5.48 (1H, s), 7.16–7.40 (9H, m), 8.16(1H, brs); ^{13}C NMR (DMS-d_6) $\delta = 183.9$, 165.2, 152.9, 138.5, 134.4, 129.8, 129.1, 128.9, 128.5, 127.5, 126.1, 123.4, 63.8, 49.8, 24.5, 20.8; Mass (M/z): 384 (M^+). Anal.

TABLE I Effect of Microwave Power on Synthesis of Thiazolo-Pyrimidine and Pyrimido-Thiazine Derivatives (3a–r)

			MW(200 W) at 140°C		MW (400 W) at 140°C		MW(400 W) at 160°C	
Entry	R_1	R_2	Time (min)	Yield (%)	Time (min)	Yield (%)	Time (min)	Yield (%)
3a		Ph	5	82	3	87	3	85
3b		3,4-di-OCH_3-Ph	6	85	4	86	4	85
3c		3-NO_2-Ph	5	76	4	89	4	89
3d		4-OH-Ph	5	80	3	85	3	83
3e		4-OCH_3-Ph	5	83	3	84	3	84
3f		2-Cl-Ph	6	78	3	84	3	85
#3g		3-NO_2-Ph	6	76	4	89	4	88
#3h		4-Cl-Ph	6	80	3	93	3	90
#3i		2-OCH_3-Ph	6	77	4	81	4	83
#3j		Ph	5	84	3	89	5	88
3k		2-OH-Ph	5	87	3	91	3	92
3l		4-$N(CH_3)_2$-Ph	6	84	4	85	4	85
3m		2-Cl-Ph	6	87	4	93	4	93
3n		4-NO_2-Ph	6	82	4	84	4	84
3o		4-OCH_3-Ph	5	88	3	92	3	92
3p		4-$N(CH_3)_2$-Ph	5	86	3	90	3	90
3q		2-Cl-Ph	5	85	3	88	3	89
3r		2-OH-Ph	5	87	3	89	3	89

$n = 2$.

TABLE II Effect of Microwave Power on Synthesis of ThiazoloBbenzimidaole and Thiazino-Benzimidazole Derivatives (5a–f)

		MW (200 W) at 140°C		MW (400 W) at 140°C		MW (400 W) at 160°C	
Entry	R	Time (min)	Yield (%)	Time (min)	Yield (%)	Time (min)	Yield (%)
5a	H	7	82	4	88	4	88
#5b	H	7	86	4	86	4	85
5c	—OCH_3	6	80	4	85	4	84
#5d	—OCH_3	6	82	5	83	5	83
5e	—CH_3	7	78	5	82	5	84
#5f	—CH_3	6	81	4	84	3	85

$n = 2$.

Calc.: C, 62.57; H, 4.73; Cl, 9.24; N, 10.95; O, 4.17; S, 8.35%; Anal. Observed: C, 62.62; H, 4.77, N, 10.91.

N-(4-chlorophenyl)-3,5-dihydro-7-methyl-5-(3-nitrophenyl)-2H-thiazolo[3,2-*a*]pyrimidine-6-carboxamide (3c, $C_{20}H_{17}ClN_4O_3S$)

White solid, mp 214–214°C; IR (cm^{-1}): 3174 (—NH, str), 3021 (—CH=CH), 2926 (Ar-CH,asym), 2845 (Ar-CH,sym), 1675 (—C=O), 1532 (—C—C skeletal vibration), 1270 (C—S, str), 1175 (C—H IPD), 1083 (C—O—C), 781 (C—H, OPD); ^{1}H NMR (DMSO-d_6) $\delta = 2.17$ (3H, s), 3.20 (2H, m), 3.39 (1H , m), 3.68 (1H, m), 5.71 (1H, s), 7.19 (2H, m, J = 2.84, 2.92 Hz), 7.42 (2H, m, J = 2.00, 2.96 Hz), 7.53 (1H, t, J = 7.92, 7.88 Hz), 7.72 (1H, d, J = 7.64 Hz), 8.15 (1H, m), 8.24 (1H, t, $J = 1.84$ Hz), 8.14 (1H, brs); ^{13}C NMR (DMSO-d_6) δ ppm = 183.8, 163.9, 153.5, 148.9, 138.6, 134.7, 134.0, 130.0, 129.5, 129.7, 125.9, 123.8, 123.1, 120.5, 62.8, 49.8, 25.1, 21.5; Mass (M/z): 429 (M^+). Anal. Calc.: C, 56.01; H, 4.00; Cl, 8.27; N, 13.06; O, 11.19; S, 7.48%; Anal. Observed: C, 56.05; H, 4,05; N, 13.01%.

N-(4-chlorophenyl)-3,5-dihydro-5-(4-methoxyphenyl)-7-methyl-2H-thiazolo[3,2-*a*]pyrimidine-6-carboxamide (3e, $C_{21}H_{20}ClN_3O_2S$)

Yellow solid, mp 160–162°C; IR (cm^{-1}): 3273 (N—H), 3051 (Ar-H), 2924 (—CH_3), 2868 (—CH_2), 1662 (C=O), 1639 (C=C), 1107 (C—O); ^{1}H NMR (DMSO-d_6) $\delta = 2.25$ (3H, s), 2.93 (1H, m), 3.01 (1H, m), 3.23 (1H, m),

3.41 (1H, m), 3.46 (3H, s), 5.39 (1H, s), 7.23 (2H, m), 7.37 (2H, m), 7.53 (1H, t, J = 7.96), 7.76 (1H, d, J = 7.76 Hz), 8.13 (1H, dd, $J = 8.12$, 2.16 Hz), 8.17 (1H, brs), 8.22 (1H, t, $J = 2.11$ Hz); ^{13}C NMR (DMSO-d_6) $\delta = 183.7$, 163.7, 159.5, 153.2, 134.8, 130.8, 129.0, 129.5, 129.9, 125.8, 123.2, 114.5, 63.8, 56.8, 49.8, 24.8, 21.1; Mass (M/z): 414 (M^+). Anal. Calc.: C, 60.94; H, 4.87; Cl, 8.57; N, 10.15; O, 7.73; S, 7.75%; Anal. Observed: C, 60.99; H, 4.92; N, 10.11%.

5-(2-Chlorophenyl)-N-(4-chlorophenyl)-3,5-dihydro-7-methyl-2H-thiazolo[3,2-*a*]pyrimidine-6-carboxamide (3f, $C_{20}H_{17}C_{12}N_3OS$)

White solid, mp 177–178°C; IR (cm^{-1}): 3284 (N—H), 3012 (Ar-H), 2926 (—CH_3), 2878 (—CH_2), 1674 (C=O), 1637 (C=C), 1112 (C—O); ^{1}H NMR (DMSO-d_6) $\delta = 2.21$ (3H, s), 3.14 (1H, m), 3.25 (1H, m), 3.44 (1H, m), 3.61 (1H, m), 7.20–7.34 (8H, m), 8.12 (1H, brs); ^{13}C NMR (DMSO-d_6) $\delta = 183.8$, 163.4, 153.8, 137.8, 134.2, 133.5, 129.8, 129.5, 129.0, 128.9, 127.2, 126.9, 125.7, 123.2, 54.8, 49.9, 24.4, 21.4; Mass (M/z): 418 (M^+); Anal. Calc.: C, 57.42; H, 4.10; Cl, 16.95; N, 10.04; O, 3.82; S, 7.66%; Anal. Observed: C, 57.48; H, 4.15, N, 10.0%.

N-(4-chlorophenyl)-2,3,4,6-tetrahydro-8-methyl-6-(3-nitrophenyl)Pyrimido[2,1-*b*][1,3]thiazine-7-carboxamide (3g, $C_{21}H_{19}ClN_4O_3S$)

Yellow solid, 214–217°C; IR (cm^{-1}): 3216 (—NH, str), 3015 (—CH=CH), 2968 (Ar-CH, asym), 2842 (Ar-CH, sym), 1677 (—C=O), 1570 (—C—C skeletal vibration), 1290 (C—S, str), 1182 (C—H IPD), 1075 (C—O—C), 771 (C—H, OPD); ^{1}H NMR (DMSO-d_6) $\delta = 2.25$ (3H, s), 2.19 (1H, m), 2.25 (1H, m), 2.93 (1H, m), 3.02 (1H, m), 3.2 (1H, m), 3.42 (1H, m), 5.39 (1H, s), 7.23 (2H, tt, $J = 2.92$, 1.96 Hz), 7.37 (2H, m), 7.53 (1H, t, $J = 7.88$, 7.96 Hz), 7.76 (1H, t, $J = 1.32$, 6.44 Hz), 8.15 (1H, qt-qt, $J = 1.86$ Hz), 8.15(brs, 1H), 8.20 (1H, t, $J = 1.92$ Hz); ^{13}C NMR (DMSO-d_6) $\delta = 157.9$, 163.5, 153.1, 148.6, 139.4, 134.8, 134.2, 130.5, 129.8, 129.5, 125.5, 123.7, 123.2, 119.5, 62.8, 39.7, 25.8, 22.1, 21.4; Mass (M/z): 443 (M^+); Anal. Calc.: C, 58.34; H, 4.43; Cl, 16.40; N, 9.72; O, 3.70; S, 7.42%; Anal. Observed: C, 58.38; H, 4.47; N, 9.76%.

N,6-bis(4-chlorophenyl)-2,3,4,6-tetrahydro-8-methylpyrimido-[2,1-*b*][1,3]thiazine-7-carboxamide (3h, $C_{21}H_{19}C_{12}N_3OS$)

White solid, mp 210–212°C; IR (cm^{-1}): 3284 (—NH, str), 3012 (—CH=CH), 2924 (Ar-CH, asym), 2868 (Ar-CH, sym), 1674 (—C=O),

1516 (—C—C skeletal vibration), 1263 (C—S, str), 1190 (C—H IPD), 1089 (C—O—C), 813 (C—H, OPD); ^{1}H NMR (DMSO-d_6) $\delta = 2.15$ (1H, m), 2.23 (1H, m), 2.23 (1H, m), 2.90 (1H, m), 2.98 (1H, m), 3.21 (1H, m), 3.33 (1H, m), 5.21 (1H, s), 7.07 (1H, s), 7.21–7.24 (2H, tt, $J = 2.04$, 2.88 Hz), 7.29–7.37 (5H, m), 8.16 (brs, 1H); ^{13}C NMR (DMSO-d_6) $\delta = 163.5$, 157.9, 153.8, 136.2, 134.5, 132.9, 130.2, 129.8, 129.2, 128.4, 125.5, 123.1, 63.9, 39.5, 25.2, 22.4, 21.5; Mass (M/z): 432 (M^+); Anal. Calc.: C, 58.34; H, 4.43; Cl, 16.40; N, 9.72; O, 3.70; S, 7.42%; Anal. Observed: C, 58.35; H, 4.46; N, 9.76%.

N-(4-chlorophenyl)-2,3,4,6-tetrahydro-6-(2-methoxyphenyl)-8-methyl pyrimido[2,1-*b*] [1,3]thiazine-7-carboxamide (3i, $C_{22}H_{22}ClN_3O_2S$)

White solid 222–224°C; IR (cm^{-1}): 3256 (—NH, str), 3018 (—CH=CH), 2965 (Ar-CH, asym), 2829 (Ar-CH, sym), 1668 (—C=O), 1570 (—C—C skeletal vibration), 1253 (C—S, str),1168 (C—H IPD),1072 (C—O—C), 786 (C—H, OPD); ^{1}H NMR (DMSO-d_6) $\delta = 2.10$ (3H, m), 2.23 (1H, m), 2.29 (1H, s), 2.82–2.95 (2H, m), 3.20 (1H, m), 3.43 (1H, m), 3.47 (3H, s), 5.80 (1H, s), 7.66 (1H, dd, $J = 1.72$, 7.68 Hz), 7.26–7.37 (5H, m), 7.20 (2H, tt, $J = 2.92$ Hz), 8.14 (1H, brs); ^{13}C NMR (DMSO-d_6) $\delta = 163.5$, 158.2, 157.5, 153.2, 134.5, 130.4, 129.5, 129.1, 128.5, 125.6, 123.4, 121.5, 116.8, 114.2, 56.4, 53.9, 39.6, 25.3, 22.3, 21.5; Mass (M/z): 428 (M^+); Anal. Calc.: C, 61.74; H, 5.18; Cl, 8.28; N, 9.82; O, 7.48; S, 7.49%; Anal. Observed: C, 61.77; H, 5.21; N, 9.79%.

5-(2-chlorophenyl)-N-(4-fluorophenyl)-3,5-dihydro-7-methyl-2H-thiazolo[3,2-*a*] pyrimidine-6-carboxamide (3m, $C_{20}H_{17}ClFN_3OS$)

White solid, mp 196–197°C; IR (cm^{-1}): 3214 (—NH, str), 3010 (—CH=CH), 2915 (Ar-CH, asym), 2852 (Ar-CH, sym), 1662 (—C=O), 1546 (—C—C skeletal vibration), 1274 (C—S, str), 1168 (C—H IPD), 1075 (C—O—C), 768 (C—H, OPD); ^{1}H NMR (DMSO-d_6) $\delta = 2.17$ (3H, s), 3.11 (1H, m), 3.25 (1H, m), 3.35 (1H, m), 3.74 (1H, m), 6.11 (1H, s), 6.92 (2H, tt, $J = 3.32$, 2.04 Hz), 7.25 (1H, tt, $J = 1.64$, 2.04 Hz), 7.33 (2H, qt-qt, $J = 1.04$, 3.04 Hz), 7.46 (2H, m, $J = 2.04$, 3.24, 4.92 Hz), 7.60 (1H, t, $J = 7.00$ Hz), 8.16 (1H, brs); ^{13}C NMR (DMSO-d_6) $\delta = 183.8$, 163.5, 159.2, 153.2, 137.8, 133.6, 131.8, 129.7, 128.9, 128.7, 126.9, 125.5, 123.4, 115.9, 54.7, 49.8, 24.8, 21.2; Mass (M/z): 402 (M^+); Anal. Calc.: C, 59.77; H, 4.26; Cl, 8.82; F, 4.73; N, 10.46; O, 3.98; S, 7.98%; Anal. Observed: C, 59.80; H, 4.29; N, 10.44%.

3,5-Dihydro-5-(4-methoxyphenyl)-7-methyl-N-(naphthalen-1-yl)-2H-thiazolo [3,2-*a*] pyrimidine-6-carboxamide (3o, $C_{25}H_{23}N_3O_2S$)

White solid, mp 234-236°C; IR (cm^{-1}): 3186 (–NH, str), 3025 (–CH=CH), 2916 (Ar-CH, asym), 2834 (Ar-CH, sym), 1670 (–C=O), 1526 (–C–C skeletal vibration), 1276 (C–S, str), 1191 (C–H IPD), 1069 (C–O–C), 768 (C–H, OPD); ^{1}H NMR (DMSO-d_6) $\delta = 2.31$ (3H, s), 3.10 (1H, m), 3.20(1H, m), 3.44 (1H, m), 3.56 (1H, m), 3.82 (1H, s), 5.44 (1H, s), 7.77 (2H, $J = 9.2$Hz), 7.38 (1H, d, $J = 8.2$ Hz), 6.91–7.29 (4H, m, $J = 8.76$, 7.02 Hz), 7.34–7.43 (4H, m), 8.17 (brs, 1H); ^{13}C NMR (DMSO-d_6) $\delta = 183.8$, 163.5, 159.5, 153.2, 141.0, 134.5, 130.5, 129.2, 128.9, 126.8, 126.0, 125.5, 125.1, 124.8, 121.2, 119.2, 114.6, 109.4, 63.5, 56.2, 49.5, 24.5, 21.4; Mass (M/z): 429 (M^+); Anal. Calc.: C, 69.91; H, 5.40; N, 9.78; O, 7.45; S, 7.47%; Anal. Observed: C, 69.95; H, 5.43; N, 9.75%.

5-(2-Chlorophenyl)-3,5-dihydro-7-methyl-N-(naphthalen-1-yl)-2H-thiazolo [3,2-*a*] pyrimidine-6-carboxamide (3q, $C_{24}H_{20}ClN_3OS$)

Yellow solid, mp 162–163°C; IR (cm^{-1}): 3277 (N–H), 3032 (Ar-H), 2947 ($-CH_3$), 2877 ($-CH_2$), 1681 (C=O), 1620 (C=C), 1116 (C–O); ^{1}H NMR (DMSO-d_6) $\delta = 2.36$ (3H, s), 3.09 (1H, m), 3.22 (1H, m), 3.40 (1H, m), 3.72 (1H, m), 6.13 (1H, s), 7.16 (1H, s), 7.37 (2H, m), 7.40 (4H, m), 7.64 (2H, dd, J = 8.2, 2.1 Hz), 7.73 (1H, d, J = 7.48 Hz), 7.80 (1H, d, J = 8.2 Hz), 8.19(1H, brs); ^{13}C NMR (DMSO-d_6) $\delta = 183.9$, 163.5, 153.0, 140.9, 137.9, 134.5, 133.5, 129.8, 129.0, 128.7, 128.2, 126.9, 126.6, 126.2, 125.5, 125.0, 124.7, 121.4, 119.2, 109.9, 54.8, 49.8, 24.8, 21.4; Mass (M/z): 434 (M^+) Anal. Calc.: C, 66.43; H, 4.65; Cl, 8.17; N, 9.68; O, 3.69; S, 7.39%; Anal. Observed: C, 66.45; H, 4.67; N, 9.66%.

6-Methoxy-2,3-dihydro[1,3]thiazolo[3,2-*a*]benzimidazole (5c, $C_{10}H_{10}N_2OS$)

White solid, 190–191°C; IR (cm^{-1}): 3055 (Ar-H), 2969, 2947, 2850 (alkane), 1604, 1583, 1531, 1494 (C=C), 1348 (C–N), 748 (OOP); ^{1}H NMR (DMSO-d_6) $\delta = 3.18$ (2H, m), 3.83 (3H, s), 4.10 (2H, m), 6.79 (1H, dd, $J = 2.37$, 8.73 Hz), 7.06 (1H, d, $J = 8.72$ Hz), 7.11 (1H, d, $J = 2.36$ Hz); ^{13}C NMR (DMSO-d_6) $\delta = 156.4$, 152.9, 135.6, 131.8, 116.4, 110.5, 101.4, 57.8, 56.6, 36.3; Mass (M/z): 202 (M^+) Anal. Calc.: C, 58.23; H, 4.89; N, 13.58; O, 7.76; S, 15.55%; Anal. Observed: C, 58.25; H, 4.92; N, 13.55%.

7-Methoxy-3,4-dihydro-2H-[1,3]thiazino[3,2-*a*]benzimidazole (5d, $C_{11}H_{12}N_2OS$)

White solid, mp 205—207°C; IR (cm^{-1}): 3060 (Ar-H), 2944, 2908, 2859, 2811 (alkane), 1589, 1547, 1486, 1453 (C=C), 1330 (C—N), 711 (OOP); ^{1}H NMR (DMSO-d_6) $\delta = 2.45$ (2H, m), 3.20 (2H, m), 3.84 (3H, s), 4.14 (2H, m), 6.82 (1H, dd, $J = 2.26$, 8.67 Hz), 7.09 (1H, d, $J = 8.68$ Hz), 7.12 (1H, d, $J = 2.32$ Hz); ^{13}C NMR (DMSO) δ ppm = 156.9, 152.9, 135.8, 131.5, 116.9, 110.0, 101.6, 60.2, 50.7, 25.2, 23.7; Mass (M/z): 220 (M^+) Anal. Calc.: C, 59.97; H, 5.49; N, 12.72; O, 7.26; S, 14.56%; Anal. Observed: C, 59.99; H, 5.52; N, 12.69%.

CONCLUSION

A bicyclic fused system can be synthesized efficiently under microwave irradiation with advantages of high yield and shorter reaction time. The use of a catalyst or solvent can be eliminated, which enhances the current method, and we anticipate that it may be used further to develop a library of differently substituted compounds containing fused bicyclic systems.

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