An Efficient Synthesis of New Dispiropyrrolidine Derivatives *via* Three-Component 1,3-Dipolar Cycloaddition Reaction

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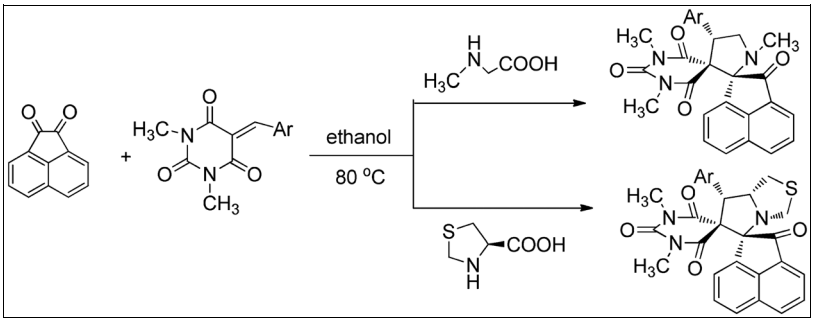

A series of new dispiropyrrolidine derivatives were synthesized *via* the three-component 1,3-dipolar cycloaddition reaction of azomethine ylides generated *in situ* by the decarboxylative condensation of acenaphthenequinone and sarcosine or L-thioproline with 5-benzylidene-1,3-dimethylpyrimidine-2,4,6-trione. The structures of the products were identified by IR, ^{1}H-NMR, and HRMS spectra.

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INTRODUCTION

Multi-component reactions (MCRs), in which multiple reactions are combined into the synthetic operation have been used extensively to form carbon–carbon bonds in the synthetic chemistry [1]. Such reactions offer a wide range of possibilities for the efficient construction of highly complex molecules in a single procedural step, thus avoiding the complicated purification operations and allowing savings of both solvents and reagents. In the past decade, there have been tremendous development in three- and four-component reactions; and great efforts will continue to be made for developing more efficient MCRs [2].

1,3-Dipolar cycloaddition reactions are efficient methods for the construction of heterocyclic units [3]. One of the most important classes for 1,3-dipolar cycloaddition involves azomethine ylide. The azomethine ylides were easily formed and readily trapped by dipolarophiles. Such reaction can take place either inter- or intramolecularly [4], and the corresponding pyrrolidine derivatives were achieved. Particularly, 1,3-dipolar cycloaddition of azomethine ylide for synthesizing compounds with the spiro moiety are usually accompanied by highly regio- and stereo-selectivity.

Barbituric acid has widely been used in the manufacturing of plastics [5], textiles [6], polymers [7], and pharmaceuticals [8]. Barbiturates (derivatives of barbituric acid) like pentobarbital and phenobarbital were long used as anxiolytics and hypnotics. Spirobarbiturates are a class of compounds with interesting pharmacological and physiological activity [9]. Pyrrolidines are important heterocycles which have glucosidase inhibitory activity, potent antiviral, antibacterial, antidiabetic, and anticancer activities [10].

We have reported the region- and stereo-selective synthesis of novel dispiropyrrolidine bisoxindole derivatives *via* MCRs recently [11]. To expand our research program which aims to synthesize new spiro compounds and nitrogen heterocycles with biological activities, herein, we report the efficient synthesis of novel dispiropyrrolidine derivatives by the 1,3-dipolar cycloaddition reaction of non-stabilized azomethine ylides generated *in situ* by the decarboxylative condensation of acenaphthenequinone and sarcosine or L-thioproline with 5-benzylidene-1,3-dimethylpyrimidine-2,4,6-trione using ethanol under reflux condition in excellent yields.

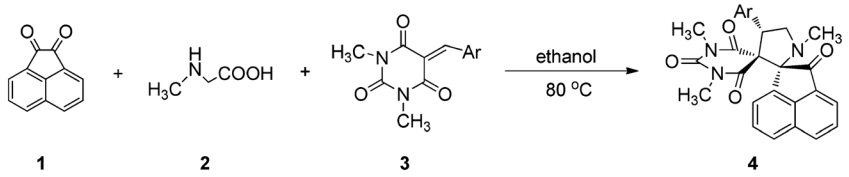
RESULTS AND DISCUSSION

When the mixture of acenaphthenequinone **1**, sarcosine **2**, and 5-benzylidene-1,3-dimethylpyrimidine-2,4,6-trione **3** were stirred for 1–2.5 h at 80°C in ethanol solution, the desired products **4** were obtained in good yields (Scheme 1), and the results are summarized in Table 1.

As expected, when the sarcosine **2** was replaced by L-thioproline **5**, another series of new dispiropyrrolidine derivatives **6** were obtained under the same reaction conditions (Scheme 2). The results are summarized in Table 2.

As shown in Tables 1 and 2, this protocol could be applied not only to the aromatic rings with electron-withdrawing groups (such as halide and nitro groups) but also to aromatic ring with electron-donating groups (such as alkyl and alkoxy

Scheme 1



1 **2** **3** **4**

Table 1

The synthetic results of new dispiropyrrolidine derivatives **4** via three-component reaction.

Entry	Ar	Product	Time (h)	Isolated yield (%)
1	4-BrC_6H_4	**4a**	1	83
2	4-$CH_3C_6H_4$	**4b**	1	70
3	4-$NO_2C_6H_4$	**4c**	1	90
4	4-ClC_6H_4	**4d**	1	86
5	C_6H_5	**4e**	1	82
6	3,4-$Cl_2C_6H_3$	**4f**	1.5	80
7	Thiophen-2-yl	**4g**	2	82
8	4-$CH_3OC_6H_4$	**4h**	2.5	83

groups). Therefore, we concluded that the electronic nature of the substituents of aromatic ring in compounds **3** has no significant effect on this reaction.

The structures of the products were identified by IR, ^{1}H-NMR, and high resolution mass spectra (HRMS). The structure of compound **4f** was confirmed by X-ray analysis. The crystal structure of **4f** is represented in Figure 1.

Although the detailed mechanism of the above reaction has not been clarified yet, the formation of **6** can be explained by the possible mechanism presented in Scheme 3. The reaction proceeds through the generation of azomethine ylide (dipole **7**) *via* the condensation of acenaphthenequinone **1** with thiazolidine-4-carboxylic acid **5** and decarboxylation [12]. The dipolarophiles **3** regioselectively react with azomethine ylides (dipole **7**) in ethanol to give the desired products dispiro compounds **6** (Scheme 3, path A). The regioselectivity in the product formation can be explained by considering the secondary orbital interaction (SOI) [13] of the orbital of the carbonyl group of dipolarosphile **3** with those of the ylide **7** as shown in Scheme 3. Accordingly, the observed regioisomer **6** *via* path A is more favorable because of the SOI which is not possible in path **B**.

In conclusion, we have successfully developed the 1,3-dipolar cycloaddition of azomethine ylides, and a series of novel dispiro cycloadducts were obtained. This method has the advantages of convenient operation, mild reaction conditions, short reaction time, and high efficiency.

EXPERIMENTAL

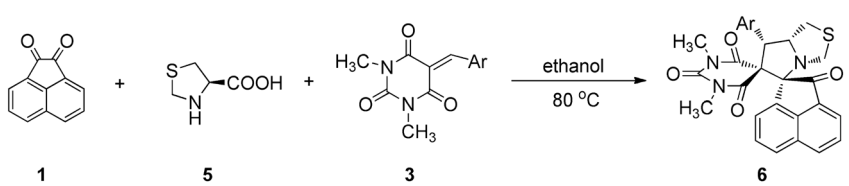
Commercial solvents and reagents were used as received. Melting points are uncorrected. IR spectra were recorded on Nicolet 6700 spectrometer in KBr with absorptions in cm^{-1}. ^{1}H-NMR and ^{13}C-NMR were determined on Varian Invoa-400 MHz or Invoa-300 MHz spectrometer in DMSO-d_6 solution. *J* values are in Hz. Chemical shifts are expressed in ppm downfield from internal standard tetramethylsilane (TMS). HRMS analyses were carried out using Bruker micrOTOF-Q instrument or time-of-flight mass spectrometry (TOF-MS) instrument. The starting compounds **3** were prepared according to the previously reported procedures [14].

General procedure for the synthesis of dispiropyrrolidine derivatives 4 and 6. A dry 50 mL flask was charged with acenaphthenequinone **1** (0.5 mmol), sarcosine **2** or L-thioproline **5** (0.5 mmol), 5-benzylidene-1,3-dimethylpyrimidine-2,4,6-trione **3** (0.5 mmol), and ethanol (10 mL). The reaction mixture was stirred at reflux temperature for 1.5–2.5 h. After completion of the reaction, the solvent was removed under vacuum. The solid was recrystallizated from ethanol, and then dried at 80°C for 4 h under vacuum to give the pure products **4** or **6**.

Compound 4a. Yellow solid; m.p.: 172–174°C; IR (potassium bromide): 2944, 1748, 1717, 1681, 1599, 1491, 1413, 1371, 831, 780 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.14 (s, 3H, CH_3), 2.17 (s, 3H, CH_3), 2.90 (s, 3H, CH_3), 3.80 (t, *J* = 8.0 Hz, 1H, CH-H), 4.02–4.05 (m, 1H, CH-H), 5.13 (t, *J* = 8.0 Hz, 1H, CH), 7.13–7.15 (m, 2H, ArH), 7.28–7.29 (m, 1H, ArH), 7.41–7.43 (m, 2H, ArH), 7.72 (s, 1H, ArH), 7.82–7.84 (m, 1H, ArH), 7.88 (s, 1H, ArH), 8.05–8.07 (m, 1H, ArH), 8.31 (d, *J* = 7.2 Hz, 1H, ArH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 27.80, 28.69, 28.72, 35.78, 43.32, 57.18, 67.90, 84.56, 120.35, 122.04, 122.14, 127.39, 128.96, 129.47, 130.19, 130.47, 130.92, 131.70, 132.97, 133.13, 137.67, 142.05, 149.92, 164.77, 167.07, 203.16. HRMS calculated for $C_{27}H_{22}BrN_3O_4Na$: [M+Na] 554.0686, found 554.0679.

Compound 4b. Yellow solid; m.p.: 180–182°C; IR (potassium bromide): 3048, 2932, 1730, 1686, 1515, 1439, 1370, 783, 752

Scheme 2



1 **5** **3** **6**

Table 2

The synthetic results of new dispiropyrrolidine derivatives **6** via three-component reaction.

Entry	Ar	Product	Time (h)	Isolated yield (%)
1	4-BrC_6H_4	**6a**	1	83
2	4-$NO_2C_6H_4$	**6b**	1	90
3	4-ClC_6H_4	**6c**	1	82
4	C_6H_5	**6d**	1	96
5	2-$NO_2C_6H_4$	**6e**	1	95
6	3,4-$Cl_2C_6H_3$	**6f**	1.5	84
7	4-$CH_3OC_6H_4$	**6g**	2	87

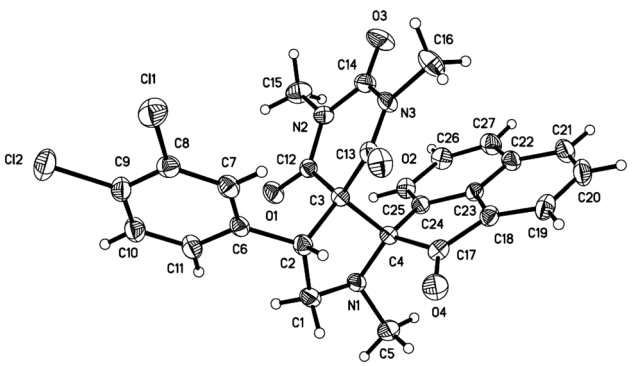


Figure 1. The X-ray structure of **4f.**

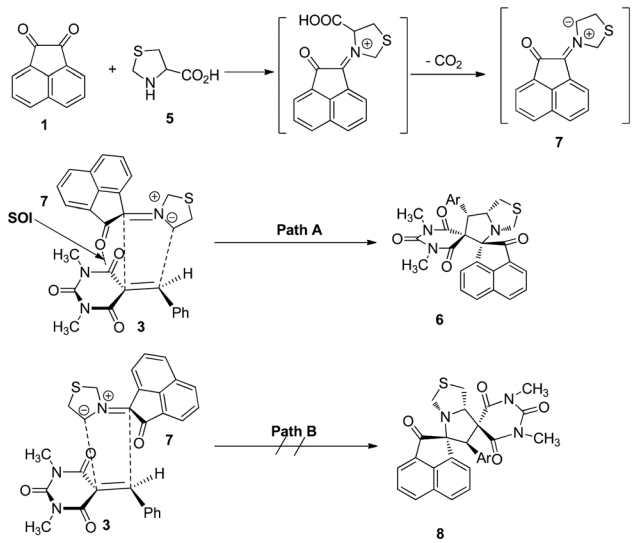
cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.17 (s, 6H, 2×CH_3), 2.21 (s, 3H, CH_3), 2.89 (s, 3H, CH_3), 3.77 (t, *J* = 9.2 Hz, 1H, CH-H), 4.04 (t, *J* = 8.0 Hz, 1H, CH-H), 5.13 (t, *J* = 9.2 Hz, 1H, CH), 7.03 (s, 4H, ArH), 7.28–7.29 (m, 1H, ArH), 7.71 (t, *J* = 7.6 Hz, 1H, ArH), 7.80–7.83 (m, 1H, ArH), 7.87–7.88 (m, 1H, ArH), 8.04 (d, *J* = 8.0 Hz, 1H, ArH), 8.29 (d, *J* = 7.6 Hz, 1H, ArH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 19.91, 27.36, 27.41, 34.48, 42.64, 56.11, 66.85, 83.12, 120.72, 126.01, 127.12, 127.68, 127.90, 128.22, 129.11, 129.23, 131.53, 132.08, 133.74, 134.96, 140.69, 148.64, 163.48, 165.96, 201.88. HRMS calculated for $C_{28}H_{25}N_3O_4Na$: [M+Na] 490.1737, found 490.1739.

Compound 4c. Yellow solid; m.p.: 196–198°C; IR (potassium bromide): 2951, 1720, 1683, 1601, 1518, 1447, 1350, 783 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.15–2.19 (m, 6H, 2×CH_3), 2.91 (s, 3H, CH_3), 3.92 (s, 1H, CH-H), 4.08 (s, 1H, CH-H), 5.26 (s, 1H, CH), 7.29 (s, 1H, ArH), 7.45 (s, 2H, ArH), 7.74 (s, 1H, ArH), 7.84 (s, 1H, ArH), 7.90 (s, 1H, ArH), 8.08 (s, 3H, ArH), 8.33 (s, 1H, ArH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 26.47, 27.46, 34.50, 42.25, 55.87, 66.54, 83.30, 120.66, 120.99, 122.57, 126.23, 127.69, 127.87, 128.26, 128.51, 128.79, 129.20, 131.68, 131.82, 140.88, 145.41, 162.04, 163.57, 165.71, 201.89. HRMS calculated for $C_{27}H_{22}N_4O_6Na$: [M+Na] 521.1432, found 521.1448.

Compound 4d. Yellow solid; m.p.: 174–176°C; IR (potassium bromide): 3058, 2945, 1747, 1717, 1680, 1599, 1443, 1372, 832, 780, 751 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.14–2.17 (m, 6H, 2×CH_3), 2.90 (s, 3H, CH_3), 3.80 (t, *J* = 8.8 Hz, 1H, CH-H), 4.03 (t, *J* = 8.0 Hz, 1H, CH-H), 5.15 (t, *J* = 9.2 Hz, 1H, CH), 7.19–7.21 (m, 2H, ArH), 7.28–7.29 (m, 2H, ArH), 7.72 (t, *J* = 7.2 Hz, 1H, ArH), 7.80–7.84 (m, 1H, ArH), 7.88–7.93 (m, 1H, ArH), 8.05–8.08 (m, 1H, ArH), 8.31 (d, *J* = 7.6 Hz, 1H, ArH), 8.43 (d, *J* = 8.4 Hz, 1H, ArH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 27.41, 34.49, 42.03, 55.95, 66.72, 83.28, 120.85, 126.12, 127.51, 127.68, 128.20, 128.95, 129.29, 130.58, 131.69, 131.90, 135.94, 148.65, 163.51, 165.82, 201.89. HRMS calculated for $C_{27}H_{23}ClN_3O_4$: [M+H] 488.1372, found 488.1399.

Compound 4e. Yellow solid; m.p.: 168–170°C; IR (potassium bromide): 3063, 2920, 1748, 1723, 1685, 1442, 1371, 833, 783, 751 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.19 (s, 6H, 2×CH_3), 2.91 (s, 3H, CH_3), 3.83 (t, *J* = 8.0 Hz, 1H, CH-H), 4.08 (t, *J* = 8.0 Hz, 1H, CH-H), 5.18 (t, *J* = 8.0 Hz, 1H, CH), 7.16 (s, 3H, ArH), 7.25 (s, 2H, ArH), 7.30 (d, *J* = 8.0 Hz, 1H, ArH), 7.72 (s, 1H, ArH), 7.82–7.88 (m, 2H, ArH), 8.04–8.06 (m, 1H, ArH), 8.29–8.31 (m, 1H, ArH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 33.40, 33.45, 40.51, 48.79, 62.13, 72.64, 89.12, 126.78, 126.80, 131.85, 132.07, 133.12, 133.68, 133.70,

Scheme 3 Proposed reaction mechanism for the formation of compound **6.**



134.19, 135.06, 135.22, 137.60, 138.01, 143.03, 146.74, 154.67, 169.55, 171.95, 207.93. HRMS calculated for $C_{27}H_{23}N_3O_4Na$: [M+Na] 476.1581, found 476.1582.

Compound 4f. Yellow solid; m.p.: 192–194°C; IR (potassium bromide): 2965, 1721, 1684, 1640, 1372, 783, 750 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.12 (s, 3H, CH_3), 2.17 (s, 3H, CH_3), 2.89 (s, 3H, CH_3), 3.79 (t, J = 8.0 Hz, 1H, CH-H), 4.05 (t, J = 8.0 Hz, 1H, CH-H), 5.15 (t, J = 7.6 Hz, 1H, CH), 7.17–7.19 (m, 1H, ArH), 7.28–7.30 (m, 1H, ArH), 7.46–7.51 (m, 2H, ArH), 7.71–7.75 (m, 1H, ArH), 7.83–7.90 (m, 2H, ArH), 8.07 (d, J = 8.0 Hz, 1H, ArH), 8.32 (d, J = 7.2 Hz, 1H, ArH); ^{13}C-NMR (75 MHz, DMSO-d_6) δ:28.66, 35.73, 42.82, 56.93, 56.95, 68.00, 84.70, 120.77, 122.08, 122.15, 127.42, 128.89, 129.44, 129.99, 130.07, 130.42, 130.70, 131.09, 131.22, 131.39, 133.01, 139.12, 142.07, 149.89, 164.73, 166.92, 203.09. HRMS calculated for $C_{27}H_{21}Cl_2N_3O_4Na$: [M +Na] 509.1313, found 509.1338.

Compound 4g. Yellow solid; m.p.: 136–138°C; IR (potassium bromide): 3059, 2950, 1748, 1721, 1681, 1561, 1441, 1372, 847, 751 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.16 (s, 6H, 2×CH_3), 2.92 (s, 3H, CH_3), 3.74 (s, 1H, CH-H), 4.06 (s, 1H, CH-H), 5.36 (s, 1H, CH), 6.92 (s, 2H, ArH), 7.30–7.35 (m, 2H, ArH), 7.73–7.88 (m, 3H, ArH), 8.06 (s, 1H, ArH), 8.31 (s, 1H, ArH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 27.61, 28.89, 35.23, 42.89, 55.92, 66.37, 84.20, 120.35, 121.64, 124.96, 125.89, 126.53, 126.90, 127.45, 127.92, 128.12, 128.90, 131.72, 133.69, 141.32, 143.20, 158.79, 163.65, 166.87, 201.92. HRMS calculated for $C_{25}H_{21}N_3O_4SNa$: [M+Na] 482.1145, found 482.1157.

Compound 4h. Yellow solid; m.p.: 162–164°C; IR (potassium bromide): 3043, 2926, 1724, 1681, 1628, 1512, 1417, 1365, 782, 752 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.17 (s, 6H, 2×CH_3), 2.89 (s, 3H, CH_3), 3.69–3.74 (m, 4H, CH_3 and CH-H), 4.05 (s, 1H, CH-H), 5.12 (s, 1H, CH), 6.81 (s, 2H, ArH), 7.13 (s, 2H, ArH), 7.31 (s, 1H, ArH), 7.72 (s, 1H, ArH), 7.83–7.88 (m, 2H, ArH), 8.05 (s, 1H, ArH), 8.30 (s, 1H, ArH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 27.36, 34.47, 42.59, 54.32, 56.14, 67.10, 83.12, 113.00, 120.70, 125.98, 127.68, 128.15, 128.21, 128.66, 129.15, 129.23, 131.50, 132.15, 140.64, 148.61, 157.31, 163.47, 165.94, 201.87. HRMS calculated for $C_{28}H_{25}N_3O_5$: (M^+) 483.1789, found 483.1791.

Compound 6a. Yellow solid; m.p.: 188–190°C; IR (potassium bromide): 2902, 1750, 1723, 1680, 1490, 1444, 1366, 833, 783 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.10 (s, 3H, CH_3), 2.88 (s, 3H, CH_3), 3.45 (s, 3H, CH_2 and CH), 3.80 (s, 1H, CH), 4.77 (s, 1H, CH-H), 4.87 (s, 1H, CH-H), 7.27 (s, 2H, ArH), 7.44 (s, 3H, ArH), 7.74 (s, 1H, ArH), 7.85 (s, 1H, ArH), 7.93 (s, 1H, ArH), 8.08 (s, 1H, ArH), 8.34 (s, 1H, ArH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 33.43, 42.24, 52.87, 55.63, 77.99, 87.74, 125.65, 126.57, 127.22, 132.32, 133.76, 134.22, 134.82, 135.15, 136.07, 136.57, 138.04, 138.36, 140.72, 146.23, 154.34, 169.64, 170.97, 208.30. HRMS calculated for $C_{28}H_{22}BrN_3O_4SNa$: (M+Na) 598.0407, found 598.0405.

Compound 6b. Yellow solid; m.p.: 189–191°C; IR (potassium bromide): 3028, 2933, 1727, 1687, 1597, 1515, 1439, 1366, 1347, 785, 745 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.10 (s, 3H, CH_3), 2.88 (s, 3H, CH_3), 3.42–3.50 (m, 3H, CH_2 and CH), 3.82 (s, 1H, CH), 4.90 (s, 2H, CH_2), 7.42 (s, 1H, ArH), 7.57 (s, 2H, ArH), 7.75 (s, 1H, ArH), 7.85 (s, 1H, ArH), 7.94 (s, 1H, ArH), 8.10 (s, 3H, ArH), 8.36 (s, 1H, ArH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 33.48, 42.34, 53.01, 55.69, 77.95, 87.79, 126.69, 127.32, 128.65, 132.42, 133.76, 134.25, 134.72, 134.99, 136.19, 138.15, 146.35, 149.50, 151.70, 154.37, 169.69, 170.95, 208.28. HRMS calculated for $C_{28}H_{22}N_4O_6SNa$: (M+Na) 565.1152, found 565.1139.

Compound 6c. Yellow solid; m.p.: 182–184°C; IR (potassium bromide): 3041, 2902, 1751, 1724, 1682, 1492, 1444, 1367, 783 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.12 (s, 3H, CH_3), 2.89 (s, 3H, CH_3), 3.44 (s, 3H, CH_2 and CH), 3.81 (s, 1H, CH), 4.81 (s, 1H, CH-H), 4.90 (s, 1H, CH-H), 7.32 (s, 4H, ArH), 7.43 (s, 1H, ArH), 7.75 (s, 1H, ArH), 7.85 (s, 1H, ArH), 7.93 (s, 1H, ArH), 8.07 (s, 1H, ArH), 8.34 (s, 1H, ArH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 28.72, 28.75, 37.51, 48.09, 50.90, 73.07, 73.36, 83.02, 121.87, 122.49, 127.61, 128.95, 129.52, 130.11, 130.42, 130.98, 132.40, 133.32, 133.67, 135.58, 141.51, 149.63, 164.91, 166.25, 203.58. HRMS calculated for $C_{28}H_{22}ClN_3O_4SNa$: (M+Na) 554.0912, found 554.0913.

Compound 6d. Yellow solid; m.p.: 178–180°C; IR (potassium bromide): 3053, 2909, 1748, 1722, 1686, 1442, 1368, 835, 785 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.13 (s, 3H, CH_3), 2.89 (s, 3H, CH_3), 3.44 (d, J = 7.6 Hz, 3H, CH_2 and CH), 3.80 (dd, J_1 = 3.6 Hz, J_2 = 7.6 Hz, 1H, CH), 4.79–4.82 (m, 1H, CH-H), 4.85–4.89 (m, 1H, CH-H), 7.27–7.28 (m, 4H, ArH), 7.41–7.43 (m, 1H, ArH), 7.72–7.76 (m, 1H, ArH), 7.83–7.87 (m, 1H, ArH), 7.93–7.94 (m, 1H, ArH), 8.07–8.09 (m, 1H, ArH), 8.33–8.35 (m, 1H, ArH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 31.63, 37.89, 51.49, 53.70, 56.69, 73.03, 73.32, 84.10, 121.94, 127.19, 127.58, 128.84, 129.14, 129.52, 129.96, 131.19, 131.71, 132.97, 133.61, 136.34, 141.60, 144.99, 150.28, 165.07, 166.40, 166.92, 207.22. HRMS calculated for $C_{28}H_{23}N_3O_4SNa$: (M+Na) 520.1301, found 520.1287.

Compound 6e. Yellow solid; m.p.: 168–170°C; IR (potassium bromide): 3051, 2930, 1724, 1687, 1628, 1534, 1443, 1368, 785 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 1.75 (s, 3H, CH_3), 2.90 (s, 3H, CH_3), 3.14–3.19 (m, 2H, CH_2), 3.45–3.47 (m, 1H, CH), 3.85–3.86 (m, 1H, CH), 5.09 (s, 1H, CH-H), 5.22 (m, 1H, CH-H), 7.51 (s, 1H, ArH), 7.70–7.87 (m, 5H, ArH), 8.05–8.10 (m, 2H, ArH), 8.35–8.38 (m, 2H, ArH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 33.69, 41.78, 51.75, 53.90, 56.29, 77.52, 88.21, 126.32, 127.65, 128.72, 129.13, 129.88, 130.91, 131.71, 132.89, 133.24, 133.90, 137.12, 142.10, 147.68, 151.23, 155.90, 162.44, 169.21, 169.92, 207.88. HRMS calculated for $C_{28}H_{23}N_4O_6S$: (M+H) 543.1333, found 543.1350.

Compound 6f. Yellow solid; m.p.: 174–176°C; IR (potassium bromide): 2930, 1725, 1686, 1594, 1441, 1367, 785 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 1.79 (s, 3H, CH_3), 2.89 (s, 3H, CH_3), 3.14 (s, 3H, CH_2 and CH), 3.78 (s, 1H, CH), 4.44 (s, 1H, CH-H), 5.12 (s, 1H, CH-H), 7.51 (s, 2H, ArH), 7.78 (s, 5H, ArH), 8.08 (m, 1H, ArH), 8.31 (s, 1H, ArH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 33.10, 41.93, 55.25, 58.72, 77.64, 88.89, 126.64, 127.27, 131.98, 132.17, 133.76, 134.71, 135.26, 135.38, 135.87, 136.24, 137.66, 138.33, 141.66, 146.34, 155.00, 169.97, 171.61, 206.81. HRMS calculated for $C_{28}H_{21}Cl_2N_3O_4$ SNa: (M+Na) 554.0686, found 554.0679.

Compound 6g. Yellow solid; m.p.: 178–180°C; IR (potassium bromide): 3043, 2934, 1729, 1687, 1515, 1438, 1372, 1251, 781 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.09 (s, 3H, CH_3), 2.84 (s, 3H, CH_3), 3.29 (s, 3H, CH_2 and CH), 3.65 (s, 3H, CH_3), 3.74 (s, 1H, CH), 4.72–4.85 (m, 2H, CH_2), 6.80 (s, 2H, ArH), 7.19 (s, 2H, ArH), 7.40 (s, 1H, ArH), 7.71–8.04 (m, 4H, ArH), 8.30 (s, 1H, ArH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 30.62, 39.36, 50.40, 52.80, 57.53, 75.17, 75.61, 84.82, 116.33, 123.71, 124.27, 129.41, 129.89, 129.92, 130.97, 131.39, 132.28, 135.10, 135.79, 135.81, 143.30, 151.49, 160.80, 168.84, 168.26, 205.56. HRMS calculated for $C_{29}H_{25}N_3O_5S$: (M^+) 527.1509, found 527.1617.

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REFERENCES AND NOTES

[1] (a) Bienayme, H.; Hulme, C.; Oddon, G.; Schmitt, P. Chem—Eur J 2000, 6, 3321; (b) Tietze, L. F.; Modi, A. Med Res Rev 2000, 20, 304; (c) Dömling, A.; Ugi, I. Angew Chem Int Ed 2000, 39, 3168; (d) Zhu, J. Eur J Org Chem 2003, 1133; (e) Orru, R. V. A.; de Greef, M. Synthesis 2003, 1471; (f) Nair, V.; Rajesh, C.; Vinod, A. U.; Bindu, S.; Sreekanth, A. R.; Mathen, J. S.; Balagopal, L. Acc Chem Res 2003, 36, 899; (g) Ramon, D. J.; Yus, M. Angew Chem Int Ed 2005, 44, 1602.

[2] (a) Nair, V.; Vinod, A. U.; Rajesh, C. J Org Chem 2001, 66, 4427; (b) List, B.; Castello, C. Synlett 2001, 1687; (c) Shestopalov, A. M.; Emeliyanova, Y. M.; Shestiopolov, A. A.; Rodinovskaya, L. A.; Niazimbetova, Z. I.; Evans, D. H. Org Lett 2002, 4, 423; (d) Bertozzi, F.; Gustafsson, M.; Olsson, R. Org Lett 2002, 4, 3147; (e) Bora, U.; Saikia, A.; oruah, R. C. Org Lett 2003, 5, 435; (f) Dallinger, D.; Gorobets, N. Y.; Kappe, C. O. Org Lett 2003, 5, 1205.

[3] (a) Padwa, A. 1,3-Dipolar Cycloaddition Chemistry; Wiley: New York, 1984; (b) Grigg, R.,Sridharan, V.,Curran, D. P. Advances in Cycloaddition; Jai Press: London, 1993.

[4] Coldham, L.; Hufton, R. Chem Rev 2005, 105, 2765.

[5] Thetford, D.; Chorlton, A. P.; Hardman, J. Dyes Pigm 2003, 59, 185.

[6] Bartzatt, R. J Pharm Biomed Anal 2002, 29, 909.

[7] (a) Andreu, R.; Garin, J.; Orduna, J.; Alcala, R.; Villacumpa, B. Org Lett 2003, 5, 3143; (b) McClenaghan, N. D.; Absalon, C.; Bassani, D. M. J Am Chem Soc 2003, 125, 13004.

[8] (a) Meusel, M.; Ambrozak, A.; Hecker, T. K.; Gutschow, M. J Org Chem 2003, 68, 4684; (b) Brunner, H.; Ittner, K. P.; Lunz, D.; Schmatloch, S.; Schmidt, T.; Zabel, M. Eur J Org Chem 2003, 5, 855; (c) Neumann, D. M.; Jursic, B. S.; Martin, K. L. Tetrahedron Lett 2002, 43, 1603; (d) Jursic, B. S.; Neumann, D. M. Tetrahedron Lett 2001, 42, 8435; (e) Jursic, B. S.; Neumann, D. M. Tetrahedron Lett 2001, 42, 4103; (f) Jursic, B. S. Tetrahedron Lett 2000, 41, 5325.

[9] (a) Mokrosz, J. L. Pharmazie 1985, 40, 359; (b) Prankerd, R. J.; McKeown, R. H. Int J Pharm 1992, 83, 39; (c) Galati, E. M.; Monforte, M. T.; Miceli, N.; Raneri, E. Farmaco 2001, 56, 459; (d) Singh, P.; Paul, K. J Heterocycl Chem 2006, 43, 607; (e) Lomlin, L.; Einsiedel, J.; Heinemann, F. W.; Meyer, K.; Gmeiner, P. J Org Chem 2008, 73, 3608.

[10] (a) Augustine, T.; Kanakam, C. C.; Vithiya, S. M.; Ramkumar, V. Tetrahedron Lett 2009, 50, 5906; (b) Karthikeyan, K.; Kumar, R. S.; Muralidharan, D.; Perumal, P. T. Tetrahedron Lett 2009, 50, 7175.

[11] (a) Liu, H.; Dou, G. L.; Shi, D. Q. J Comb Chem 2010, 12, 294; (b) Liu, H.; Dou, G. L.; Shi, D. Q. J Comb Chem 2010, 12, 633; (c) Liu, H.; Zou, Y.; Hu, Y.; Shi, D. Q. J Heterocyclic Chem 2011, 48, 877.

[12] (a) Grigg, R.; Surendrakumar, S.; Thianpatanagul, S.; Vipond, D. J Chem Soc Perkin Trans 1 1988, 2693; (b) Grigg, R.; Idle, J.; McMeekin, P.; Vipond, D. J Chem Soc Perkin Trans 1 1988, 2703; (c) Tsuge, O.; Kanemasa, S. Adv Heterocycl Chem 1989, 45, 231.

[13] (a) Pardasani, R. T.; Pardasani, P.; Chaturvedi, V.; Yadav, S. K.; Saxena, A.; Sharma, I. Heteroat Chem 2003, 14, 36; (b) Lakshmi, N. V.; Thirumuragan, P.; Perumal, P. T. Tetrahedron Lett 2010, 51, 1064.

[14] (a) Jursic, B. S.; Neumann, D. M. Tetrahedron Lett 2001, 42, 4103; (b) Krasnow, K. A.; Kartsev, V. G.; Gorodovoi, A. S.; Khrustalev, V. N. Chem Nat Compd 2002, 38, 450.