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A facile strategy for the annulation of 2-phenylsulfonyl methylene thiazolidin-4-one via multicomponent reactions

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ABSTRACT

An efficient synthesis of 5-amino-7-aryl-3-oxo-8-(phenylsulfonyl)-thiazolo[3,2-a]pyridine-6-carbonitriles was conducted utilizing multicomponent condensation reaction of malononitrile, aromatic aldehydes and 2-phenylsulfonylmethylenethiazolidin-4-one in one pot. Depending on the equivalence of the aldehyde, two different products were obtained from moderate to excellent yields. Thirteen novel structures were characterized by physical and spectroscopic methods (m.p., Rf, IR, NMR and mass analysis).

1. Introduction

The chemistry of 2-alkylidenethiazolidin-4-one compounds has been extensively studied over the years. These compounds can be used for the synthesis of diverse functionalized molecules, depending on the substituent of the alkylidene part [1], and scaffolds prepared using these compounds have shown to exhibit various biological properties [2]. However, the synthetic applications of 2-phenylsulfonylmethylenethiazolidin-4-one are rare in the literature comparing to those of 2-alkylidenethiazolidin-4-ones [3]. This has encouraged us to investigate this substituent in multicomponent reactions, since phenylsulfonyl substituent increases biological activity in some heterocyclic compounds [4].

Multicomponent reactions (MCRs) play a significant role to synthesize complex molecules [5] by reacting at least three reagents in one pot. Mild reaction conditions and easy purification steps attracted attention to these kinds of reactions, and placed them into one of the green chemistry routes [6]. Recently, we have reported the multicomponent reactions of 2-nitromethylenethiazolidine with various active methylene, containing nitriles and a broad range of aldehydes [7]. In continuation of our interest in heterocyclic enamine chemistry [8], we now report multicomponent reactions of 2-phenylsulfonylmethylenethiazolidin-4-one with various aromatic aldehydes and malonitrile. We found that two different products could be obtained depending on the equivalence of the aldehyde.

2. Results and discussion

2-Phenylsulfonylmethylenethiazolidin-4-one was prepared according to a literature procedure [3a], and identified by means of m.p., IR, ^{1}H and ^{13}C NMR. After reviewing related alkylidenethiazolidin-4-ones and alkylidenepyrrolidine ester and nitrile geometries in previous publications [9], we have decided to draw the double bond geometry of the starting compound **1** *Z* isomer rather than *E* isomer. Multicomponent reactions of 2-phenylsulfonylmethylene thiazolidin-4-one with malonitrile and aromatic aldehydes were performed in anhydrous acetonitrile at reflux temperature, and monitored by thin layer chromatography (TLC). After 1 h, no 2-phenylsulfonylmethylene thiazolidin-4-one remained on the TLC plate, which is

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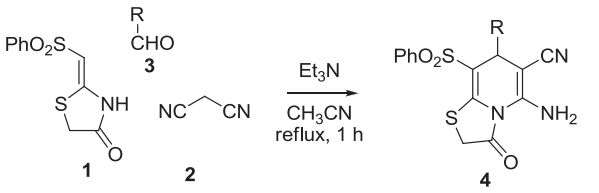
Table 1
Reactions of 2-phenylsulfonylmethylenethiazolin-4-one with malononitrile and aldehydes.



Compound	R	Yield/%
4a	C_6H_5	73
4b	4-NCC_6H_4	84
4c	4-ClC_6H_4	74
4d	2,6-$DiClC_6H_3$	86
4e	2,4-$DiClC_6H_3$	68
4f	4-$O_2NC_6H_4$	71

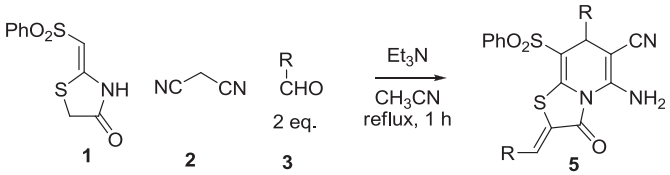
indicative of the completion of reaction. The reactions proceeded rapidly and afforded the corresponding thiazolopyridin-4-ones **4a–f** and benzylidene thiazolopyridin-4-ones **5a–g** in high yields. The results shown in Tables 1 and 2 clearly indicate the scope and generality of the reaction with respect to aldehydes and malononitrile. The reactions worked efficiently with a variety of aldehydes including both electron-releasing and hetero-aromatic groups. Additionally, aforementioned reactions were also performed in water as a solvent and without use of solvent via solid state reaction. In both cases desired products were not obtained.

The reactions (Tables 1 and 2) proceed through the Knoevenagel condensation of the aldehyde with malononitrile, and then the addition of benzylidenemalononitrile **6** to enamine **1** followed by secondary amine attacks to one of nitrile on benzylidenemalononitrile **6** ends with ring cyclization. In our previous work, when 2-alkylidenethiazolin reacted with 2-phenylsulfonylacetonitrile and aldehyde, a mixture of enamine **4**, and imine **8** tautomers was obtained [7]. In the present work, we obtained compound **4** as a sole product (Scheme 1).

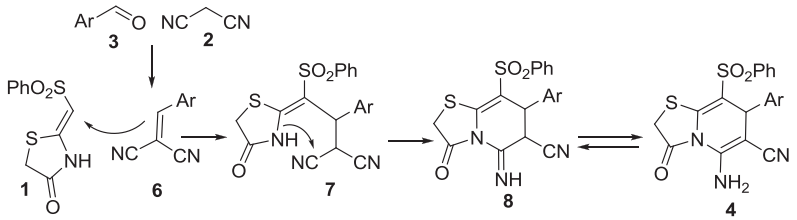
When two equivalents of aldehyde were used, benzylidene substituted 5-amino-7-aryl-3-oxo-8-(phenylsulfonyl)-thiazolo[3,2-a]pyridine-6-carbonitriles were observed in moderate to high yields as shown in Table 2. It was also found that there was no direct effect of the stoichiometric amount of Et_3N as a base to the MCR yield of 2-phenylsulfonylmethylene thiazolidin-4-one with malononitrile and aldehyde.

In infrared spectra of compounds **4a–f** and **5a–g**, sulfone groups showed two strong bands due to asymmetric stretching at ca. 1307–1329 cm^{-1} and symmetric stretching at ca. 1144–1154 cm^{-1}. Bands at ca. 3312–3439 cm^{-1} are ascribed to NH_2 groups. Stretching vibrations of carbonyl groups appeared at ca. 1658–1743 cm^{-1} and distinct cyano peaks were observed at ca. 2189–2201 cm^{-1}. The ^1H and ^{13}C NMR spectra of compounds **4a–f** and **5a–g** were recorded in d_6-DMSO and gave good results, although the peak due to adventitious water in the d_6-DMSO obscured the one of OCH_3 resonance in compound **5f** in one case, the resulting proton, carbon NMR spectra as well as HRMS confirmed the expected structure **5f**. The signals due to the NH_2 protons

Table 2
Reactions of 2-phenylsulfonylmethylenethiazolin-4-one **1** with malononitrile **2** and two equivalence of aldehydes **3**.



Compound	R	Yield/%
5a	4-ClC_6H_4	68
5b	4-FC_6H_4	62
5c	4-NCC_6H_4	64
5d	3-BrC_6H_4	73
5e	2,4-$DiMeOC_6H_3$	69
5f	4-HO-3,5-$DiMeOC_6H_2$	81
5g	3-Thienyl	80



Scheme 1. Possible reaction mechanism for the formation of compounds **4**.

appeared at ca. δ 7.08–7.55 ppm, but in some cases (compounds **4c**, **5g**, **5b**) NH_2 proton resonances overlapped with aromatic protons and they were not easily detectable. The chemical shifts of **4a–f** *CH*Ar protons showed remarkable differences (δ 5.02–5.92 ppm) compared with *CH*Ar protons **5a–f** (δ 4.49–4.70 ppm) due to the substitution of the benzylidene groups on the thiazoline fused to pyridine ring. Carbonyl carbons of compounds **5a–g** showed more deshielded peaks than that of the compounds **4a–f** due to electron-withdrawing effects of the benzylidene group next to carbonyl group in compounds **5a–g**. In mass spectra of compounds **5e** and **5f**, loss of M-Ar peaks 25 and 15% were obtained, respectively.

3. Conclusion

In summary, we have achieved the synthesis of thirteen novel phenylsulfonyl substitute thiazolopyridin-4-ones *via* multicomponent reactions and identified these compounds by means of spectroscopic methods.

4. Experimental

4.1. General

Infrared spectra were recorded on a SHIMADZU FTIR-8400S instrument (KBr disc). Mass spectra were recorded on a Fisons VG Platform II spectrometer and on a Micromass Q-TOF Micro spectrometer. NMR spectra were recorded on a Bruker DPX 400 spectrometer operating at 400 MHz for ^1H and at 100 MHz for ^{13}C at 25 °C. All chemical shifts are reported in ppm downfield from TMS. Coupling constants (*J*) are reported in Hz. Melting points were determined on a MELTEMP apparatus and uncorrected. TLC was performed using pre-coated plates with fluorescent indicator (Merck 5735). The stain solutions of permanganate and PMBA were used for visualization of the TLC spots.

4.2. 2-Phenylsulfonylmethylenethiazolidin-4-one (1)

Phenylsulfonylacetonitrile (20 mmol, 3.624 g) and mercaptoacetic acid (20 mmol, 1.842 g) were mixed in pyridine (15 mL) in a round-bottomed flask and refluxed at 115 °C for overnight. After cooling, pyridine was removed by evaporation, and the residue was applied for column chromatography (EtOAc/Hexane: 1/3).

Obtained as yellow solid (3.2 g, 63%), m.p. 120–122 °C. υ_{max}, cm^{-1} (KBr) 3101 (NH_2), 1735 (CO), 1589 (C = C), 1301 (SO_2), 1138 (SO_2). δ_H (400 MHz, DMSO-d_6) 10.1 (br s, 1H, NH), 7.89 (d, 2H, *J* = 7.1 Hz, aromatic CH), 7.64 (t, 1H, *J* = 7.4 Hz, aromatic CH), 7.57 (t, 2H, *J* = 7.4, 7.1 Hz, aromatic CH), 5.36 (s, 1H, CH = C), 3.80 (s, 2H, CH_2S). δ_C (100 MHz; DMSO-d_6) 171.6, 152.2, 142.2, 133.3, 129.4, 126.6, 96.1, 77.3, 77.0, 76.8, 31.2.

4.3. General reaction procedure for preparation of thiazolo[3,2-a]pyridin-4-ones

Aromatic aldehyde (1 mmol, 1.0 equiv for compounds **4a–f**, 2 mmol, 2.0 equiv for compounds **5a–g**), 2-phenylsulfonylmethylenethiazolidine (1 mmol, 1 equiv, 255 mg) and malononitrile (1 mmol, 1.0 equiv, 66 mg) were mixed in MeCN (10 mL) in a round-bottomed flask, and the reaction mixture was stirred and heated. Triethylamine (50 mg, 0.5 mmol) was added and the reaction mixture was heated under reflux for 1 h (Tables 1 and 2). After cooling, the solvent was removed under reduced pressure, and the residue recrystallised from hexane/ethyl acetate mixtures to give the pure products with data given below.

4.4. 5-Amino-3-oxo-7-phenyl-8-(phenylsulfonyl)-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6-carbonitrile (4a)

Obtained as yellow solid (300 mg, 73%), m.p. 229–230 °C. υ_{max}, cm^{-1} (KBr) 3416 (NH_2), 2189 (CN), 1701 (CO), 1647 (C = C), 1307 (SO_2), 1153 (SO_2). HRMS: requires for $C_{20}H_{15}N_3O_3S_2$ [M^+] 409.0555, found M^+, 409.0558. δ_H (400 MHz, DMSO-d_6) 7.79–7.70 (m, 3H, aromatic CH of SO_2Ph), 7.61 (t, *J* = 7.7 Hz, 2H, aromatic CH of SO_2Ph), 7.38 (t, *J* = 7.4 Hz, 2H, aromatic CH), 7.30 (t, *J* = 7.3 Hz, 2H, aromatic CH), 7.20 (d, *J* = 7.0 Hz, 1H, aromatic CH), 7.16 (s, 2H, NH_2), 5.16 (s, 2H, SCH_2), 5.02 (s, 1H, C*H*Ph). δ_C (100 MHz; DMSO-d_6) 160.7, 154.2, 152.2, 144.5, 138.1, 134.7, 129.7, 129.2, 128.5, 127.9, 127.4, 120.1, 112.8, 58.4, 55.9, 38.6.

4.5. 5-amino-7-(4-cyanophenyl)-3-oxo-8-(phenylsulfonyl)-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6-carbonitrile (4b)

Obtained as brown solid (365 mg, 84%), mp. 197–199 °C. υ_{max}, cm^{-1} (KBr) 3331 (NH_2), 2228 (CN of Ar), 2199 (CN), 1743 (CO), 1649 (C = C), 1327 (SO_2), 1144 (SO_2). HRMS: Found M^+ 435.0585 $C_{21}H_{15}N_4O_3S_2$ [M^+] requires 435.0586. δ_H (400 MHz, DMSO-d_6) 7.87 (d, J = 8.2 Hz, 2H, aromatic CH), 7.78–7.70 (m, 3H, aromatic CH of $PhSO_2$), 7.61 (app. t, *J* = 7.9 Hz, 2H, aromatic CH), 7.41 (d, *J* = 8.2 Hz, 1H, aromatic CH), 7.30 (2H, br s, NH_2), 5.18 (2H, app. s, CH_2S), 5.17 (1H, app. s, C*H*Ar). δ_C (100 MHz; DMSO-d_6) 160.9, 154.8, 152.4, 149.7, 138.0, 134.8, 133.2, 129.7, 128.6, 128.5, 122.2, 118.8, 111.4, 110.8, 58.9, 54.9, 38.5.

4.6. 5-Amino-7-(4-chlorophenyl)-3-oxo-8-(phenylsulfonyl)-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6-carbonitrile (4c)

Obtained as pale yellow solid (330 mg, 74%), mp. 244–246 °C. υ_{max}, cm^{-1} (KBr) 3374 (NH_2), 2201 (CN), 1720 (CO), 1647 (C = C), 1329 (SO_2), 1146 (SO_2). HRMS: Found M^+, 443.0163. $C_{20}H_{14}N_3O_3S_2{}^{35}Cl$ [M^+] requires 443.0165. δ_H (400 MHz, DMSO-d_6) 7.79–7.70 (3H, m, aromatic CH of SO_2Ph), 7.61 (2H, t, *J* = 7.8 Hz, aromatic CH of SO_2Ph), 7.45 (2H, d, *J* = 8.4 Hz, aromatic CH), 7.25–7.19 (4H, m, aromatic CH obscured with NH_2), 5.17 (2H, s, CH_2S), 5.06 (1H, s, C*H*Ar). δ_C (100 MHz; DMSO-d_6) 160.3, 154.1, 151.9, 143.0, 137.8, 134.3, 132.1, 129.3, 129.0, 128.8, 128.1, 119.6, 111.9, 58.1, 55.3, 37.6.

4.7. 5-Amino-7-(2,6-dichlorophenyl)-3-oxo-8-(phenylsulfonyl)-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6-carbonitrile (4d)

Obtained as yellow solid (410 mg, 86%), mp. 277–278 °C. υ_{max}, cm^{-1} (KBr) 3422 (NH_2), 2189 (CN), 1728 (CO),

1647 (C = C), 1307 (SO_2), 1154 (SO_2). HRMS: Found M^+, 476.9758. $C_{20}H_{13}N_3O_3S_2{}^{35}Cl_2[M^+]$ requires 476.9775. δ_H (400 MHz, DMSO-d_6) 7.75–7.69 (3H, m, aromatic CH of SO_2*Ph*), 7.60 (2H, d, *J* = 7.7 Hz, aromatic CH of SO_2*Ph*), 7.57 (1H, dd, *J* = 8.0, 1.3 Hz, aromatic CH), 7.48 (1H, d, *J* = 6.9 Hz, aromatic CH), 7.40 (1H, t, *J* = 8.0 Hz, aromatic CH), 7.29 (2H, brs, NH_2), 5.92 (1H, s, C*H*Ar), 5.20 (2H, q, *J* = 14.5 Hz, CH_2S). δ_C (100 MHz; DMSO-d_6) 161.6, 153.9, 153.6, 137.9, 135.7, 135.6, 134.7, 134.4, 131.5, 130.9, 129.6, 129.2, 128.6, 119.5, 108.7, 58.4, 52.4 and 35.3.

4.8. 5-amino-7-(2,4-dichlorophenyl)-3-oxo-8-(phenylsulfonyl)-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6-carbonitrile (4e)

Obtained as yellow solid (325 mg, 68%), mp. 251–252 °C. υ_{max}, cm^{-1} (KBr) 3439 (NH_2), 2189 (CN), 1722 (CO), 1657 (C = C), 1319 (SO_2), 1152 (SO_2). HRMS: Found M^+, 476.9764. $C_{20}H_{13}N_3O_3S_2{}^{35}Cl_2$ [M^+] requires 476.9775. δ_H (400 MHz, DMSO-d_6) 7.74–7.69 (3H, m, aromatic CH of SO_2*Ph*), 7.68 (1H, d, *J* = 2.0 Hz, aromatic CH), 7.59 (2H, t, *J* = 7.8 Hz, aromatic CH of SO_2*Ph*), 7.50 (1H, dd, *J* = 8.3, 2.0 Hz, aromatic CH), 7.37 (1H, s, aromatic CH), 7.34 (2H, br s, NH_2), 5.40 (1H, s, C*H*Ar), 5.18 (2H, d, *J* = 2.6 Hz, CH_2S). δ_C (100 MHz; DMSO-d_6) 161.5, 154.4, 152.7, 139.4, 138.1, 134.6, 133.6, 133.1, 131.8, 129.9, 129.7, 128.7, 128.5, 119.8, 110.5, 58.3, 53.5 and 36.3.

4.9. 5-Amino-7-(4-nitrophenyl)-3-oxo-8-(phenylsulfonyl)-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6-carbonitrile (4f)

Obtained as pale yellow solid (322 mg, 71%), mp. 255–256 °C. υ_{max}, cm^{-1} (KBr) 3312 (NH_2), 2201 (CN), 1654 (CO), 1647 (C = C), 1327 (SO_2), 1144 (SO_2). HRMS: Found M^+, 454.0406. $C_{20}H_{14}N_4O_5S_2$ [M^+] requires 454.0406. δ_H (400 MHz, DMSO-d_6) 8.26 (2H, d, *J* = 7.9 Hz, aromatic CH), 7.77 – 7.70 (3H, m, aromatic CH of SO_2*Ph*), 7.62 (2H, t, *J* = 7.5 Hz, aromatic CH of SO_2*Ph*), 7.51 (2H, d, *J* = 7.9 Hz, aromatic CH), 7.33 (2H, br s, NH_2), 5.26 (1H, s, C*H*Ar), 5.19 (2H, s, CH_2S). δ_C (100 MHz; DMSO-d_6) 160.9, 154.9, 152.5, 151.6, 147.3, 138.1, 134.7, 129.7, 129.0, 128.5, 124.6, 119.9, 111.3, 58.4, 54.9, 38.3.

4.10. 5-Amino-2-(4-chlorobenzylidene)-7-(4-chlorophenyl)-3-oxo-8-(phenylsulfonyl)-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6-carbonitrile (5a)

Obtained as yellow solid (384 mg, 68%), mp. 293–294 °C. υ_{max}, cm^{-1} (KBr) 3373 (NH_2), 2199 (CN), 1721 (CO), 1653 (C = C), 1325 (SO_2), 1148 (SO_2). (Found: $(M–H)^+$, 566.0176. $C_{27}H_{18}N_3O_3S_2{}^{35}Cl_2$ requires M, 566.0167). δ_H (400 MHz, DMSO-d_6) 7.79–7.75 (m, 3H, aromatic CH of SO_2*Ph*), 7.72 (d, *J* = 8.1 Hz, 2H, aromatic CH of SO_2*Ph*), 7.65–7.56 (m, 3H, C*H* = C and aromatic CH), 7.52 (br s, 2H, NH_2), 7.47–7.40 (m, 2H, aromatic CH), 7.28–7.21 (m, 2H, aromatic CH), 7.18–7.12 (m, 2H, aromatic CH), 4.54 (s, 1H, C*H*Ar). δ_C (100 MHz; DMSO-d_6) 166.1, 148.2, 142.1, 141.5, 140.7, 135.5, 134.2, 132.6, 132.5, 132.3, 130.5, 130.3, 130.1, 129.6, 128.6, 127.3, 122.1, 119.0, 113.3, 65.9, 41.2. *m/z* (TOF ES^+) 566 (M–H + , 100) and 331 (15).

4.11. 5-Amino-2-(4-fluorobenzylidene)-7-(4-fluorophenyl)-3-oxo-8-(phenyl sulfonyl)-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6-carbonitrile (5b)

Obtained as pale yellow solid (425 mg, 80%), mp. 278–279 °C. υ_{max}, cm^{-1} (KBr) 3412 (NH_2), 2203 (CN), 1707 (CO), 1649 (C = C), 1327 (SO_2), 1144 (SO_2). (Found: $(M–H)^+$, 534.0751. $C_{27}H_{18}N_3O_3S_2F_2$ requires M, 534.0758). δ_H (400 MHz, DMSO-d_6) 7.95–7.72 (m, 3H, aromatic CH of SO_2Ph and CH = C), 7.72–7.58 (m, 3H, aromatic CH of SO_2Ph), 7.58 – 7.51 (m, 4H, aromatic CH of ArF and NH_2), 7.49–7.42 (m, 2H, aromatic CH of ArF), 7.35–7.16 (m, 2H, aromatic CH of ArF), 7.01–6.80 (m, 2H), 4.57 (d, 1H). δ_C (100 MHz; DMSO-d_6) 166.2, 164.5, 163.0, 162.0, 160.6, 148.2, 142.1 140.9, 138.7, 134.2, 133.19, 130.6, 129.6, 127.3, 120.9, 119.1, 117.3, 115.6, 113.5, 66.2, 41.1. *m/z* (TOF ES^+) 534 ($M–H^+$, 100).

4.12. 5-Amino-2-(4-cyanobenzylidene)-7-(4-cyanophenyl)-3-oxo-8-(phenyl sulfonyl)-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6-carbonitrile (5c)

Obtained as yellow solid (339 mg, 62%), mp. 292–294 °C. υ_{max}, cm^{-1} (KBr) 3421 (NH_2), 2245 (CN), 2230 (CN), 2195 (CN of pyridine), 1701 (CO), 1643 (C = C), 1327 (SO_2), 1146 (SO_2). (Found: $(M–H)^+$, 548.0850. $C_{29}H_{18}N_5O_3S_2$ requires M, 548.0851). δ_H (400 MHz, DMSO-d_6) 8.08 (d, *J* = 7.7 Hz, 2H, aromatic CH), 7.91 (d, *J* = 7.6 Hz, 2H, aromatic CHof SO_2*Ph*), 7.84 (s, 1H, C*H* = C), 7.68–7.62 (m, 3H, aromatic CH of SO_2*Ph*), 7.59 (d, *J* = 7.7 Hz, 2H, aromatic CH), 7.55 (brs, 2H, NH_2), 7.45 (app d, *J* = 5.5 Hz, 4H), 4.65 (s, 1H, C*H*Ar). δ_C (100 MHz; DMSO-d_6) 165.9, 148.4, 147.8, 142.5, 140.4, 138.1, 134.5, 133.7, 132.7, 131.1, 129.7, 129.6, 129.4, 127.4, 125.1, 119.1, 118.9, 118.8, 113.0, 112.4, 110.6, 65.2, 41.6. *m/z* (TOF ES^+) 548 (M – H^+, 100) and 405 (20).

4.13. 5-Amino-2-(3-bromobenzylidene)-7-(3-bromophenyl)-3-oxo-8-(phenyl sulfonyl)-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6-carbonitrile (5d)

Obtained as yellow solid (480 mg, 73%), mp. 275–276 °C. υ_{max}, cm^{-1} (KBr) 3404 (NH_2), 2201 (CN), 1697 (CO), 1653 (C = C), 1329 (SO_2), 1147 (SO_2). (Found: $(M–H)^+$, 653.9155. $C_{27}H_{18}N_3O_3S_2{}^{79}Br_2$ requires M, 653.9156). δ_H (400 MHz, DMSO-d_6) 7.97 (s, 1H, aromatic CH), 7.77 (s, 1H, C*H* = C), 7.73 (d, *J* = 7.8 Hz, 2H, aromatic CH), 7.67–7.56 (m, 4H, aromatic CH of SO_2Ph and aromatic CH of *Ar*Br), 7.53 (brs, 2H, NH_2), 7.47–7.40 (m, 2H, aromatic CH of SO_2Ph), 7.38 (s, 1H, aromatic CH), 7.30 (d, *J* = 7.7 Hz, 1H, aromatic CH), 7.24 (d, 1H, *J* = 7.7 Hz, aromatic CH), 7.12 (t, *J* = 7.7 Hz, 1H, aromatic CH), 4.57 (s, 1H, C*H*Ar). δ_C (100 MHz; DMSO-d_6) 166.0, 148.2, 144.8, 142.3, 140.6, 136.2, 134.4, 133.8, 133.4, 132.1, 131.4, 130.9, 130.8, 129.8, 129.6, 128.5, 127.9, 127.2, 123.3, 123.1, 122.4, 119.1, 113.0, 65.8, 41.5. *m/z* (TOF ES^+) 655 (M – H^+, 100) and 653 (52).

4.14. 5-Amino-2-(2,4-dimethoxybenzylidene)-7-(2,4-dimethoxyphenyl)-3-oxo-8-(phenylsulfonyl)-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6-carbonitrile (5e)

Obtained as yellow solid (395 mg, 64%), mp. 248–249 °C. υ_{max}, cm^{-1} (KBr) 3309 (NH_2), 2187 (CN), 1707 (CO),

1643 (C = C), 1325 (SO_2), 1144 (SO_2). (Found: $(M–H)^+$, 618.1362. $C_{31}H_{28}N_3O_7S_2$ requires M, 618.1369). δ_H (400 MHz, DMSO-d_6) 7.93 (s, 1H, C*H* = C), 7.57–7.53 (m, 3H, aromatic CH of SO_2*Ph*), 7.47 (app d, *J* = 7.6 Hz, 2H, aromatic CH of SO_2*Ph*), 7.37 (m, 1H, aromatic CH), 7.36 (br s, 2H, NH_2), 6.95 (d, *J* = 8.4 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.74 (d, *J* = 1.9 Hz, 1H), 6.32 (d, *J* = 7.2 Hz, 1H), 6.14 (s, 1H, aromatic CH), 4.63 (s, 1H, C*H*Ar), 3.95 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 3.45 (s, 3H, OCH_3). δ_C (100 MHz; DMSO-d_6) 166.3, 163.8, 160.6, 160.3, 158.3, 153.8, 148.9, 141.9, 141.0, 133.8, 131.2, 131.0, 129.3, 126.9, 126.8, 121.2, 119.4, 116.7, 115.1, 112.6, 107.2, 105.5, 99.2, 98.9, 64.9, 56.5, 56.2, 55.9, 55.7. *m/z* (TOF ES^+) 618 ($M–H^+$, 100), 480 ($M–Ar^+$, 15) and 336 (35).

4.15. 5-Amino-2-(4-hydroxy-3,5-dimethoxybenzylidene)-7-(4-hydroxy-3,5-dimethoxy phenyl)-3-oxo-8-(phenylsulfonyl)-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6-carbonitrile (5f)

Obtained as yellow solid (450 mg, 69%), mp. 220 decomp. υ_{max}, cm^{-1} (KBr) 3412 (NH_2), 2203 (CN), 1701 (CO), 1649 (C = C), 1327 (SO_2), 1144 (SO_2). (Found: $(M–H)^+$, 653.9155. $C_{27}H_{18}N_3O_3S_2{}^{79}Br_2$ requires M, 653.9156). δ_H (400 MHz, DMSO-d_6) 8.42 (s, 1H, OH), 8.24 (s, 1H, OH), 7.77 (app. d, *J* = 7.5 Hz, 2H, aromatic CH of SO_2Ph), 7.64–7.57 (m, 2H, C*H* = C and aromatic CH of SO_2Ph), 7.51–7.45 (m, 1H, aromatic CH of SO_2Ph), 7.37 (t, *J* = 7.1 Hz, 1H, aromatic CH of SO_2Ph), 7.08 (br s, 2H, NH_2), 6.48 (s, 1H, aromatic CH), 6.29 (s, 1H, aromatic CH), 5.16 (s, 1H, aromatic CH), 4.93 (s, 1H, aromatic CH), 4.49 (s, 1H, C*H*Ar), 3.88 (s, 3H, CH_3O), 3.73 (s, 3H, CH_3O), 3.59 (s, 2H, CH_3O), 3.36 (s, 3H, obscured by water in DMSO, CH_3O). δ_C (100 MHz; DMSO-d_6) 160.8, 153.9, 151.9, 148.7, 148.6, 148.2, 141.2, 138.4, 135.8, 134.7, 133.8, 129.7, 129.2, 128.5, 127.2, 124.1, 120.3, 117.2, 113.6, 108.9, 106.8, 105.0, 66.6, 58.5, 56.6, 56.6, 56.5, 56.0, 42.1, 38.8. *m/z* (TOF ES^+) 650 ($M–H^+$, 100), 496 ($M-Ar^+$, 25).

4.16. 5-Amino-3-oxo-8-(phenylsulfonyl)-7-(thiophen-3-yl)-2-(thiophen-3-ylmethylene)-3,7-dihydro-2H-thiazolo[3,2-a]pyridine-6-carbonitrile (5g)

Obtained as pale yellow solid (410 mg, 81%), mp. 265–266 °C. υ_{max}, cm^{-1} (KBr) 3408 (NH_2), 2205 (CN), 1701 (CO), 1647 (C = C), 1325 (SO_2), 1144 (SO_2). (Found: $(M–H)^+$, 510.0062. $C_{23}H_{16}N_3O_3S_4$ requires M, 510.0075). δ_H (400 MHz, DMSO-d_6) 8.16 (s, 1H, aromatic CH of thienyl), 7.90 – 7.76 (m, 2H, aromatic CH of thienyl), 7.68–7.56 (m, 3H, aromatic CH of SO_2Ph), 7.52 (s, 1H, CH = C), 7.50 – 7.36 (m, 4H, NH_2 and aromatic CH of SO_2Ph), 7.31 (s, 1H, aromatic CH of thienyl), 7.19 (s, 1H, aromatic CH of thienyl), 6.92–6.82 (m, 1H, aromatic CH of thienyl), 4.70 (s, 1H, C*H*Ar). δ_C (100 MHz; DMSO-d_6) 166.2, 148.5, 143.1, 141.6, 140.8, 135.8, 134.1, 131.9, 129.5, 129.1, 128.6, 127.8, 127.4, 126.9, 125.8, 123.4, 119.7, 119.3, 113.3, 65.7, 36.8. *m/z* (TOF ES^+) 510 ($M–H^+$, 100), 336 (25) and 280 (45).

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.crci.2012.11.002.

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