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Solvent-free one-pot reactions for annulating a pyrimidine ring on thiazoles under microwave irradiation

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Abstract—One-pot reactions of glycine, acetic anhydride and thiazole Schiff bases (**2a**–**f**) diastereoselectively and expeditiously annulate a pyrimidine ring on the thiazole nucleus to yield 6,7-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-ones (**4a**–**f**) under microwave irradiation and solvent-free conditions.

Thiazole and pyrimidine nuclei are the active core of various bioactive molecules. In general, heterocycles encompassing a pyrimidine unit have found applications in a wide spectrum of biological and therapeutic areas.[1–6] Thus, the heterocyclic system resulting from the annulation of a pyrimidine ring on the biologically versatile thiazole nucleus is an attractive scaffold to be utilized for exploiting chemical diversity.

The application of microwave (MW) irradiation as a non-conventional energy source for activation of reactions has now become a very popular and useful technology in organic chemistry.[7,8] The combination of microwave irradiation and solvent-free reaction conditions leads to enhanced reaction rates, higher yields of pure products, easier work-up and, sometimes, to selective conversions with several advantages of the eco-friendly approach in the framework of green chemistry.[7,8] Consequently, this protocol should be welcome in these environmentally conscious days.

Considering the above reports and our continued interest in devising new solvent-free cyclisation methods,[9–11] We report herein microwave-enhanced one-pot ring forming reactions for highly diastereoselective annulation of a pyrimidine ring on thiazoles to give thiazolo-pyrimidines **4** under catalyst and solvent-free conditions (Scheme 1). This is among a few examples available on the application of microwave methodology to stereoselective synthesis and ring forming reactions.[8,12]

1. Results and discussion

The envisaged annulation method in its entirety involves intermittent irradiation of an intimate mixture of glycine, acetic anhydride and thiazole Schiff base **2** for 1 min in an unmodified domestic microwave oven followed by thorough mixing for 2 min outside the oven to ensure minimum loss of acetic anhydride by evaporation. This intermittent irradiation-mixing cycle was repeated for the total irradiation time (Table 1) to furnish thiazolo-pyrimidines **4** which were deacetylated with dilute sulphuric acid to their 6-amino analogues **5** (Table 1).

For comparison purposes, the temperature of the bulk reaction mixture was also measured immediately after MW irradiations and it was found to be <70°C. That the effect of microwaves may not be purely thermal[8,13] is supported by the fact that the reaction could not be completed to even 40% in 12 h at the same bulk temperature (70°C) employing conventional heating in an oil bath (Table 1). This observation may be rationalised in view of the formation of a dipolar transition state (TS) from an uncharged ground state GS in these reactions (Scheme 2), and the greater stabilisation of the more polar TS by dipole–dipole interactions with the electric field of microwaves as compared to the less polar GS, which may reduce the activation energy ($\Delta G^{\neq}$) resulting in the rate enhancement.[8,13]

The formation of **4** is best explained by the conjugate addition of oxazolone **1**, generated in situ, to thiazole Schiff bases **2** to furnish adducts **3** which undergo intramolecular nucleophilic attack of the nitrogen atom of the thiazole ring (*N*-3) at the carbonyl carbon (*C*-5) of the oxazolone nucleus to yield **4** (Scheme 2). This conclusion is based on the observation that the representative intermediate compounds **3a**, **3c** and **3f** could be isolated in 42–49% yield and that

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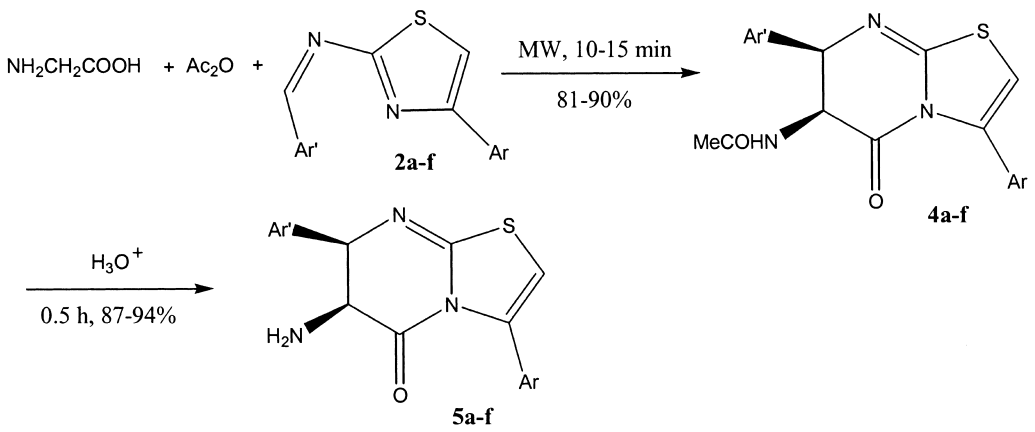


2-5	Ar	Ar'	2-5	Ar	Ar'
a	Ph	Ph	**d**	4-MeC_6H_4	Ph
b	Ph	4-$MeOC_6H_4$	**e**	4-MeC_6H_4	4-$MeOC_6H_4$
c	Ph	4-ClC_6H_4	**f**	4-MeC_6H_4	4-ClC_6H_4

Scheme 1.

these could be converted into the corresponding annulated products **4a**, **4c** and **4f** in quantitative yield (see Section 3).

The formation of adducts **3** and their annulation to **4** were highly diastereoselective in favour of *cis* (*syn*) isomers. The diastereomer ratios of crude products were checked by ^{1}H NMR, prior to purification, to ensure accurate and true diastereomeric ratios are reported. The diastereomeric ratio in case of MW method was found to be >96:<4 and that in conventional heating was >58:<42 as determined by ^{1}H NMR spectroscopy. The high diastereoselectivity (>96%) in favour of *cis* (*syn*) isomers under MW irradiation may be explained by considering that MW radiation favours the reactions occurring via more polar TS,[8] and that the TS leading to the formation of *cis* (*syn*) isomers is more polar than that leading to the *trans* (*anti*) isomers because, in general, *cis* (*syn*) isomers are more polar than the *trans* (*anti*).

Table 1. Compounds **4** and **5** prepared

Product	Time, MW in min (Oil bath in h)	Yield[a] (%) MW (Oil bath)	Mp (°C)[b]
4a	13 (12)	85 (37)	165–167
4b	12 (12)	88 (39)	177–179
4c	10 (12)	90 (40)	188–191
4d	15 (12)	81 (35)	171–172
4e	13 (12)	85 (37)	185–187
4f	12 (12)	88 (39)	196–199
5a	(0.5)	(88)	148–149
5b	(0.5)	(90)	155–156
5c	(0.5)	(94)	167–169
5d	(0.5)	(87)	151–152
5e	(0.5)	(89)	169–171
5f	(0.5)	(92)	179–181

[a] Yields of isolated and purified product.
[b] All compounds compared favourably with their samples obtained by an alternative method.

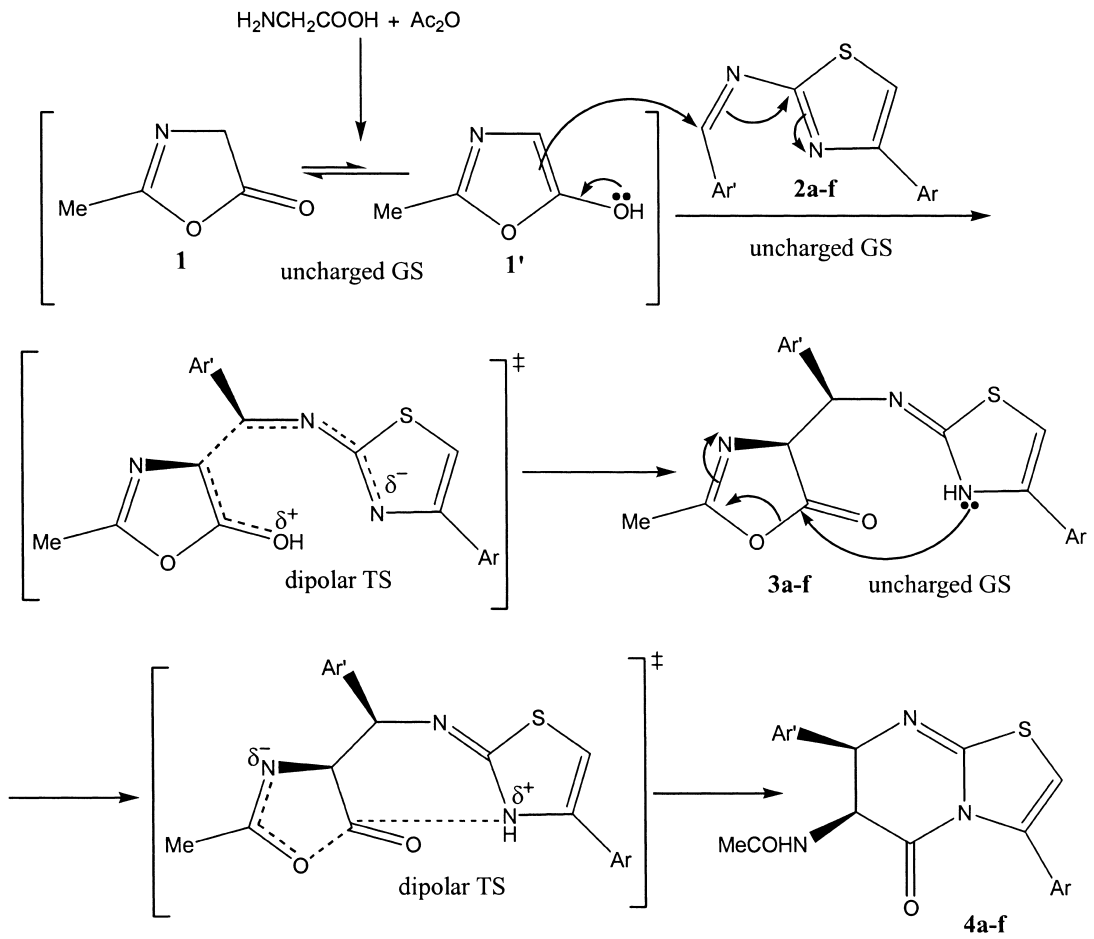
2. Conclusion

In summary, we have devised one-pot expeditious ring forming reactions for highly diastereoselective annulation of widely and readily available thiazole Schiff bases with acetic anhydride and an α-amino acid employing microwaves under catalyst- and solvent-free conditions to yield thiazolo-pyrimidines. This is a general, eco-friendly and straight-forward method for the library synthesis of thiazolo-pyrimidines, which may find application in the search for therapeutic and agrochemical lead compounds of this type.

3. Experimental

3.1. General

An unmodified domestic microwave oven (Kenstar, Model MWO 9808, operating at 2450 MHz) was used at an output of 560 W for all the experiments. Melting points were determined by open glass capillary method and are uncorrected. IR spectra in KBr were recorded on a Perkin–Elmer 993 IR spectrophotometer. ^{1}H NMR spectra were recorded on a Bruker WM-40 C (400 MHz) FT spectrometer in DMSO-d_6 using TMS as internal reference. ^{13}C NMR spectra were recorded on the same instrument at 100 MHz using the same solvent and internal reference. Mass spectra were recorded on a JEOL D-300 mass spectrometer. Elemental analyses were carried out in a Coleman automatic carbon, hydrogen and nitrogen analyser.



Scheme 2.

All chemicals used were reagent grade. Silica gel-G was used for TLC.

3.2. 6-Acetamido-6,7-dihydro-5*H*-thiazolo[3,2-*a*] pyrimidin-5-ones 4. General procedure

Thoroughly mixed glycine (10.0 mmol), thiazole Schiff base **2** (10.0 mmol) and acetic anhydride (10 mL) were taken in a 100 mL conical flask and subjected to MW irradiation for 1 min. The reaction mixture was then thoroughly mixed outside the MW oven for 2 min and again irradiated for another 1 min. This intermittent irradiation-mixing cycle was repeated for the total irradiation time (Table 1). After completion of the reaction as indicated by TLC (hexane/AcOEt, 8:2, v/v), water (30 mL) was added to the reaction mixture and stirred well. The yellowish precipitate thus obtained was washed with water to give the crude product, which was recrystallised from ethanol to afford a diastereomeric mixture (>96:<4; in the crude products the ratio was >95:<5 as determined by ^{1}H NMR spectroscopy). The products on second recrystallisation from ethanol furnished an analytical sample of a single diastereomer **4** (Table 1). On the basis of ^{1}H NMR spectra and literature precedent,[4,14–18] *cis* stereochemistry was assigned to **4**, as the coupling constant ($J_{6,7}$=4 Hz) for **4** was lower than that for the very minor (<4%) diastereomer (*trans*), $J_{6,7}$=9 Hz.

3.2.1. Compound 4a. IR (KBr) $\nu_{C=O}$: 1638, 1685 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS) δ: 2.10 (s, 3H, COMe), 6.60 (d, 1H, J=4 Hz, H-7), 6.73 (dd, 1H, J=4, 8 Hz, H-6), 7.66–7.83 (m, 11H$_{arom}$), 8.47 (br s, 1H, NH, exchanges with D_2O). ^{13}C NMR (DMSO-d_6/TMS) δ: 21.2 (Me), 61.4, 64.7 (6-C, 7-C), 118.5 (2-C), 127.1, 127.7, 128.6, 129.8, 131.0, 132.2, 132.9, 133.8 (2×Ph), 150.1 (3-C), 159.7 (SC=N), 170.8, 172.0 (2×C=O). Mass (m/z): 363 (M$^+$). Analysis found: C, 66.31; H, 4.53; N, 11.36%. Calcd for $C_{20}H_{17}N_3O_2S$: C, 66.10; H, 4.71; N, 11.56%.

3.2.2. Compound 4b. IR (KBr) $\nu_{C=O}$: 1640, 1688 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS) δ: 2.12 (s, 3H, COMe), 3.73 (s, 3H, OMe), 6.62 (d, 1H, J=4 Hz, 7-H), 6.74 (dd, 1H, J=4, 8 Hz, 6-H), 7.10–7.98 (m, 10H$_{arom}$), 8.62 (br s, 1H, NH, exchanges with D_2O). ^{13}C NMR (DMSO-d_6/TMS) δ: 21.3 (CO*Me*), 54.2 (OMe), 61.6, 64.9 (6-C, 7-C), 118.6 (2-C), 127.3, 128.5, 129.4, 130.2, 131.0, 132.4, 133.5, 134.4 (Ph, 4-MeOC_6H_4), 150.2 (3-C), 159.9 (SC=N), 170.9, 172.2 (2×C=O). Mass (m/z): 393 (M$^+$). Analysis found: C, 64.31; H, 4.63; N, 10.46%. Calcd for $C_{21}H_{19}N_3O_3S$: C, 64.10; H, 4.87; N, 10.68%.

3.2.3. Compound 4c. IR (KBr) $\nu_{C=O}$: 1643, 1690 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS) δ: 2.13 (s, 3H, COMe), 6.64 (d, 1H, J=4 Hz, 7-H), 6.77 (dd, 1H, J=4, 8 Hz, 6-H), 7.10–7.82 (m, 10H$_{arom}$), 8.64 (br s, 1H, NH, exchanges with D_2O). ^{13}C

NMR (DMSO-d_6/TMS) δ: 21.4 (Me), 61.8, 65.0 (6-C, 7-C), 118.8 (2-C), 127.2, 128.6, 129.6, 130.4, 131.1, 132.5, 133.6, 134.7 (Ph, 4-ClC_6H_4), 150.3 (3-C), 160.1 (SC=N), 171.0, 172.3 (2×C=O). Mass (*m/z*): 397 (M^+). Analysis found: C, 60.20; H, 3.92; N, 10.38%. Calcd for $C_{20}H_{16}ClN_3O_2S$: C, 60.37; H, 4.05; N, 10.56%.

3.2.4. Compound 4d. IR (KBr) $\nu_{C=O}$: 1635, 1682 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 2.10 (s, 3H, COMe), 2.26 (s, 3H, Ar-*Me*), 6.61 (d, 1H, *J*=4 Hz, 7-H), 6.75 (dd, 1H, *J*=4, 8 Hz, 6-H), 7.08–7.98 (m, $10H_{arom}$), 8.62 (br s, 1H, NH, exchanges with D_2O). ^{13}C NMR (DMSO-d_6/TMS) δ: 20.1, 21.0 (2×Me), 61.5, 64.5 (6-C, 7-C), 118.3 (2-C), 126.8, 127.5, 128.4, 129.6, 130.8, 132.0, 132.6, 133.5 (Ph, 4-MeC_6H_4), 149.9 (3-C), 159.5 (SC=N), 170.6, 171.9 (2×C=O). Mass (*m/z*): 377 (M^+). Analysis found: C, 66.52; H, 4.86; N, 11.28%. Calcd for $C_{21}H_{19}N_3O_2S$: C, 66.82; H, 5.07; N, 11.13%.

3.2.5. Compound 4e. IR (KBr) $\nu_{C=O}$: 1638, 1685 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 2.11 (s, 3H, COMe), 2.28 (s, 3H, Ar-*Me*), 3.76 (s, 3H, OMe), 6.64 (d, 1H, *J*=4 Hz, 7-H), 6.78 (dd, 1H, *J*=4, 8 Hz, 6-H), 7.11–7.98 (m, $9H_{arom}$), 8.61 (br s, 1H, NH, exchanges with D_2O). ^{13}C NMR (DMSO-d_6/TMS) δ: 20.2, 21.3 (CO*Me*, Ar-*Me*), 54.1 (OMe), 61.5, 64.8 (6-C, 7-C), 118.4 (2-C), 126.9, 127.7, 128.6, 129.6, 130.9, 132.2, 132.8, 133.6 (4-MeC_6H_4, 4-MeOC_6H_4), 150.1 (3-C), 159.6 (SC=N), 170.8, 172.2 (2×C=O). Mass (*m/z*): 407 (M^+). Analysis found: C, 64.62; H, 4.96; N, 11.28%. Calcd for $C_{22}H_{21}N_3O_3S$: C, 64.85; H, 5.19; N, 11.39%.

3.2.6. Compound 4f. IR (KBr) $\nu_{C=O}$: 1636, 1688 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 2.12 (s, 3H, COMe), 2.27 (s, 3H, Ar-*Me*), 6.63 (d, 1H, *J*=4 Hz, 7-H), 6.78 (dd, 1H, *J*=4, 8 Hz, 6-H), 7.13–8.00 (m, $9H_{arom}$), 8.65 (br s, 1H, NH, exchanges with D_2O). ^{13}C NMR (DMSO-d_6/TMS) δ: 20.3, 21.4 (2×Me), 61.6, 64.9 (6-C, 7-C), 118.5 (2-C), 126.9, 127.8, 128.8, 129.7, 131.0, 132.1, 132.9, 133.8 (4-MeC_6H_4, 4-ClC_6H_4), 150.2 (3-C), 160.0 (SC=N), 170.9, 172.2 (2×C=O). Mass (*m/z*): 411 (M^+). Analysis found: C, 60.98; H, 4.21; N, 10.00%. Calcd for $C_{21}H_{18}ClN_3O_2S$: C, 61.23; H, 4.40; N, 10.20%.

3.2.7. Compound 5a. IR (KBr) $\nu_{C=O}$: 1682 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 4.22 (s, 2H, NH_2, exchanges with D_2O), 6.59 (d, 1H, *J*=4 Hz, 7-H), 6.71 (dd, 1H, *J*=4, 8 Hz, 6-H), 7.63–7.89 (m, $11H_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 61.2, 64.5 (6-C, 7-C), 118.4 (2-C), 127.2, 127.8, 128.7, 129.8, 131.1, 132.1, 132.9, 133.7 (2×Ph), 150.0 (3-C), 159.7 (SC=N), 171.8 (C=O). Mass (*m/z*): 321. Analysis found: C, 67.00; H, 4.52; N, 12.91%. Calcd for $C_{18}H_{15}N_3OS$: C, 67.27; H, 4.70; N, 13.07%.

3.2.8. Compound 5b. IR (KBr) $\nu_{C=O}$: 1686 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 4.24 (s, 2H, NH_2, exchanges with D_2O), 3.75 (s, 3H, OMe), 6.62 (d, 1H, *J*=4 Hz, 7-H), 6.72 (dd, 1H, *J*=4, 8 Hz, 6-H), 7.11–7.96 (m, $10H_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 54.1 (OMe), 61.4, 64.8 (6-C, 7-C), 118.5 (2-C), 127.2, 128.5, 129.5, 130.3, 131.1, 132.4, 133.6, 134.5 (Ph, MeOC_6H_4), 150.1 (3-C), 159.8 (SC=N), 171.9 (C=O). Mass (*m/z*): 351. Analysis found: C, 64.63; H, 4.72; N, 12.16%. Calcd for $C_{19}H_{17}N_3O_2S$: C, 64.94; H, 4.88; N, 11.96%.

3.2.9. Compound 5c. IR (KBr) $\nu_{C=O}$: 1690 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 4.25 (s, 2H, NH_2, exchanges with D_2O), 6.60 (d, 1H, *J*=4 Hz, 7-H), 6.70 (dd, 1H, *J*=4, 8 Hz, 6-H), 7.13–7.8.00 (m, $10H_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 61.6, 64.9 (6-C, 7-C), 118.7 (2-C), 127.2, 128.7, 129.8, 130.6, 131.3, 132.5, 133.6, 134.6 (Ph, 4-ClC_6H_4), 150.2 (3-C), 160.0 (SC=N), 172.0 (C=O). Mass (*m/z*): 355. Analysis found: C, 60.53; H, 3.79; N, 12.00%. Calcd for $C_{18}H_{14}ClN_3OS$: C, 60.76; H, 3.97; N, 11.81%.

3.2.10. Compound 5d. IR (KBr) $\nu_{C=O}$: 1680 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 2.25 (s, 3H, Me) 4.23 (s, 2H, NH_2, exchanges with D_2O), 6.58 (d, 1H, *J*=4 Hz, 7-H), 6.70 (dd, 1H, *J*=4, 8 Hz, 6-H), 7.10–7.94 (m, $10H_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 20.1 (Me), 61.2, 64.4 (6-C, 7-C), 118.2 (2-C), 126.7, 127.6, 128.5, 129.6, 130.7, 132.1, 132.7, 133.4 (Ph, 4-MeC_6H_4), 149.8 (3-C), 159.5 (SC=N), 171.7 (C=O). Mass (*m/z*): 335. Analysis found: C, 68.23; H, 4.98; N, 12.32%. Calcd for $C_{19}H_{17}N_3OS$: C, 68.03; H, 5.11; N, 12.53%.

3.2.11. Compound 5e. IR (KBr) $\nu_{C=O}$: 1683 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 2.26 (s, 3H, Ar-*Me*) 4.25 (s, 2H, NH_2, exchanges with D_2O), 3.75 (s, 3H, OMe), 6.63 (d, 1H, *J*=4 Hz, 7-H), 6.77 (dd, 1H, *J*=4, 8 Hz, 6-H), 7.11–7.96 (m, $9H_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 20.1 (Ar-*Me*), 54.2 (OMe), 61.4, 64.7 (6-C, 7-C), 118.3 (2-C), 126.8, 127.8, 128.5, 129.6, 130.8, 132.1, 132.8, 133.5 (4-MeC_6H_4, 4-MeOC_6H_4), 150.0 (3-C), 159.6 (SC=N), 171.8 (C=O). Mass (*m/z*): 365. Analysis found: C, 65.42; H, 5.09; N, 11.31%. Calcd for $C_{20}H_{19}N_3O_2S$: C, 65.73; H, 5.24; N, 11.50%.

3.2.12. Compound 5f. IR (KBr) $\nu_{C=O}$: 1688 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 2.27 (s, 3H, Ar-*Me*), 4.26 (s, 2H, NH_2, exchanges with D_2O), 6.65 (1H, *J*=4 Hz, 7-H), 6.78 (dd, 1H, *J*=4, 8 Hz, 6-H), 7.11–7.97 (m, $9H_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 20.2 (Me), 61.5, 64.8 (6-C, 7-C), 118.4 (2-C), 126.8, 127.9, 128.7, 129.6, 131.1, 132.0, 132.9, 133.7 (4-MeC_6H_4, 4-ClC_6H_4), 150.2 (3-C), 159.9 (SC=N), 171.9 (C=O). Mass (*m/z*): 369. Analysis found: C, 61.42; H, 4.19; N, 11.18%. Calcd for $C_{19}H_{16}ClN_3OS$: C, 61.70; H, 4.36; N, 11.36%.

3.3. Isolation of 3a, 3c and 3f and their conversion into the corresponding annulated products 4a, 4c and 4f

The procedure followed was the same as described above for the synthesis of **4** except that the time of MW irradiation in this case was 5 min instead of 10–15 min for **4**. The adducts **3** were recrystallised from ethanol to give a diastereomeric mixture (>97:<3; in the crude isolates the ratio was >94:<6 as determined by ^1H NMR spectroscopy) which was again recrystallised from ethanol to obtain an analytical sample of **3a**, **3c** and **3f**. The adducts **3a**, **3c** and **3f** were assigned the *erythro* (*syn*) stereochemistry, as their ^1H NMR spectra exhibited lower values of coupling constant, $J_{cyclic\ NCH,\ acyclic\ NCH}$=4 Hz, than that of the very minor (<3%) diastereomer (*threo* or *anti*), $J_{cyclic\ NCH,\ acyclic\ NCH}$=9 Hz.[4,14–18] Finely powdered intermediate compounds **3a**, **3c** and **3f** were intermittently MW irradiated for 6 min in the same way as described for the synthesis of 4 to give the corresponding annulated products **4a**, **4c** and **4f** quantitatively.

3.3.1. Compound 3a. Yield 45%; mp 178–180°C. IR (KBr) $\nu_{C=O}$: 1795 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 2.14 (s, 3H, Me), 6.67 (d, 1H, J=4 Hz, acyclic NCH), 6.78 (d, 1H, J=4 Hz, cyclic NCH), 7.67–7.86 (m, 11H_{arom}), 8.46 (br s, 1H, NH, exchanges with D_2O). ^{13}C NMR (DMSO-d_6/TMS) δ: 20.2 (Me), 64.6 (Ar′-*C*), 69.52 (O=C–*C*), 118.3 (SCH), 127.0, 127.7, 128.5, 129.8, 130.9, 132.0, 132.8, 133.7 (2×Ph), 150.0 (Ar-*C*), 159.5 (SC=N), 160.5 (Me-*C*), 172.1 (C=O). Mass (*m*/*z*): 363 (M^+). Analysis found: C, 65.84; H, 4.50; N, 11.38%. Calcd for $C_{20}H_{17}N_3O_2S$: C, 66.10; H, 4.71; N, 11.56%.

3.3.2. Compound 3c. Yield 49%; mp 186–188°C. IR (KBr) $\nu_{C=O}$: 1800 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 2.15 (s, 3H, Me), 6.69 (d, 1H, J=4 Hz, acyclic NCH), 6.79 (d, 1H, J=4 Hz, cyclic NCH), 7.11–7.84 (m, 10H_{arom}), 8.49 (br s, 1H, NH, exchanges with D_2O). ^{13}C NMR (DMSO-d_6/TMS) δ: 20.4 (Me), 64.7 (Ar′-*C*), 69.6 (O=C–*C*), 118.4 (SCH), 127.1, 128.5, 129.5, 130.3, 131.0, 132.4, 133.5, 134.6 (Ph, 4-ClC_6H_4), 150.1 (Ar-*C*), 159.7 (SC=N), 160.6 (Me-*C*), 172.2 (C=O). Mass (*m*/*z*): 397 (M^+). Analysis found: C, 60.09; H, 3.89; N, 10.28%. Calcd for $C_{20}H_{16}ClN_3O_2S$: C, 60.37; H, 4.05; N, 10.56%.

3.3.3. Compound 3f. Yield 42%; mp 207–209°C. IR (KBr) $\nu_{C=O}$: 1795 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 2.14 (s, 3H, COMe), 2.25 (s, 3H, Ar′-Me), 6.68 (d, 1H, J=4 Hz, acyclic NCH), 6.78 (d, 1H, J=4 Hz, cyclic NCH), 7.11–7.84 (m, 9H_{arom}), 8.47 (br s, 1H, NH, exchanges with D_2O). ^{13}C NMR (DMSO-d_6/TMS) δ: 20.2 (CO*Me*), 21.3 (Ar-*Me*), 64.6 (Ar′-*C*), 69.5 (O=C–*C*), 118.2 (SCH), 126.7, 127.8, 128.6, 129.6, 131.0, 132.0, 132.8, 133.6 (4-MeC_6H_4, 4-ClC_6H_4), 150.0 (Ar-*C*), 159.6 (SC=N), 160.5 (Me-*C*), 172.1 (C=O). Mass (*m*/*z*): 411 (M^+). Analysis found: C, 60.96; H, 4.26; N, 10.02%. Calcd for $C_{21}H_{18}ClN_3O_2S$: C, 61.23; H, 4.40; N, 10.20%.

3.4. 6-Amino-6,7-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-ones 5. General procedure

Compound **4** (5 mmol) was refluxed in H_2SO_4/H_2O (15 mL, 4:3, v/v) for 0.5 h in an oil bath. The reaction mixture was cooled, the desired product **5** was precipitated by adding concentrated NH_4OH (specific gravity 0.88) under ice-cooling and recrystallised from ethanol to obtain an analytical sample of **5** (Table 1).

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