Studies with heteroaromatic amines. A new route to 2-azolylamino-2-thiazolin-4-ones

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Heteroaromatic chloroacetamides **3a–c** on treatment with potassium thiocyanate afforded the thiazolylamino-thiazolines **6a–c** *via* intermediacy of **4a–c** and **5a–c**. Compounds **6a–c** condensed with dimethylformamide dimethylacetal (DMFDMA) to yield the *Z*–enamines **7a–c**. The enamines **7a** and **7b** could be converted into the enamines **8a–e** and **9a,b** on treatment with amines. However, reacting **10c** with morpholine afforded **11b**. Compounds **9a,b**, as well as **9c**, were also obtained on reacting **6a–c** with triethyl orthoformate and piperidine in DMF. The structures of **6a** and **11b** were confirmed by X-ray crystal structure determination.

Keywords: 2-thiazolin-4-ones, enamines, DMFDMA, Dimroth rearrangements, crystal structures

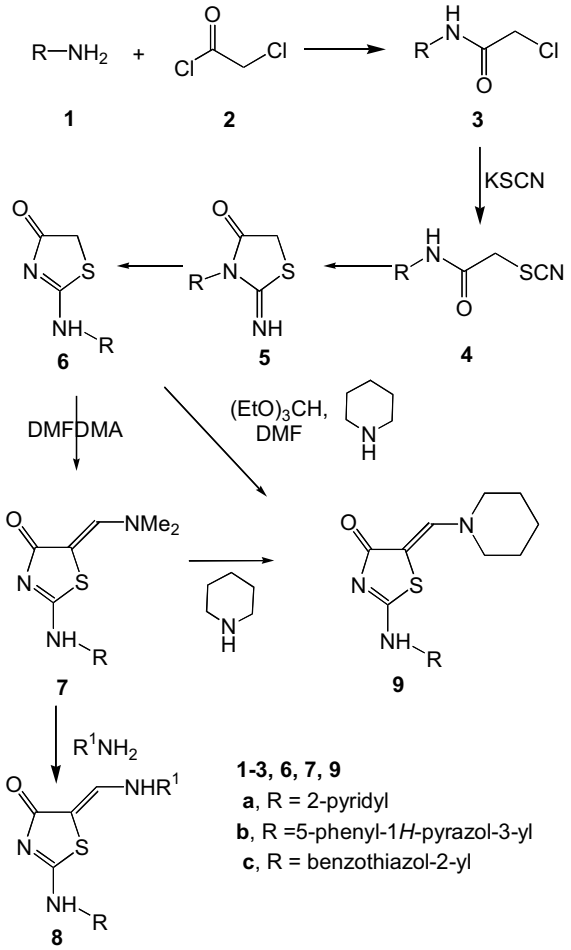
The chemistry of heteroaromatic amines is receiving interest as indicated from the number of recent patents and papers dealing with their synthesis and chemistry.[1-4] As a part of biological chemistry programme in our laboratories, samples of differently substituted azolylamino-2-thiazolin-4-ones were needed for investigation of their antimicrobial activity, in the light of the recently reported activity of 2-thiazolin-4-ones as antibacterial agents.[5] Moreover, enamine derivatives of these products looked potential anticonvulsants in light of anticonvulsant activity recently reported for enaminones.[6-10] The synthetic approach in Scheme 1 was envisaged. A similar reaction scheme has been employed earlier;[11] however, the authors did not acknowledge the possibility of Dimroth rearrangement in their reactions.

Results and discussion

In our laboratories treatment of **1a–c** with chloroacetyl chloride (**2**) afforded the chloroacetyl derivatives **3a–c** in almost quantitative yields. With potassium thiocyanate in refluxing acetonitrile these afforded products that could be formulated as **4, 5** or **6**. Structures **4** were readily ruled out as IR and ^{13}C NMR indicated absence of signals for SCN (IR ~2200 cm^{-1}, ^{13}C NMR ~120 ppm). It was difficult to distinguish between structures **5** and **6** on spectral evidence only although it fitted better structures **6**. An X-ray crystal structure for the product of reaction of **3a** with KSCN was determined (Fig. 1),[12] confirming structure **6a** for this product. Consequently structures **6b,c** are assumed for the products of reacting **3b,c** with KSCN. Clearly **6** resulted from a Dimroth type rearrangement of **5** under the reaction conditions. To our knowledge, this is the first reported rearrangement of this type with N-substituted thiazolidin-4-ones (Scheme 1).

Compounds **6a** and **6b** reacted with DMFDMA to yield the enamines **7a,b** respectively. These reacted with aromatic amines to yield **8a–e**. Similar treatment with piperidine afforded **9a,b**. Also, compounds **9a,b** were obtained when **6a** and **6b** were directly treated with $(EtO)_3CH$ and piperidine in DMF, and the products obtained were found identical with those obtained before (m.p., mixed m.p., TLC).[11] (Scheme 1)**.** We have recently shown that triethylorthoformate/piperidine in DMF forms piperidyl diethylacetal intermediate (nonisolable) that reacts more efficiently than DMFDMA with active methylene groups to form the final isolable products.[12]

When **6c** was similarly treated with DMFDMA, in a general approach to enaminones extensively employed by us in the last 10 years, only **10c** was isolated. It seems that the resulting enamine **7c** is methylated by DMFDMA faster than



Scheme 1

the reaction of DMFDMA with **6c** (Scheme 2). Methylation of heterocycles by DMFDMA has been reported earlier.[13] To form **9c**, compound **6c** was treated with a mixture of $(EtO)_3CH$ and piperidine in DMF. Similarly, compound **10c** reacted with piperidine and morpholine to afford **11a,b** and with *p*-toluidine to yield **12**. The structure of the methylation product **11b** was confirmed by X-ray crystal determination (Fig. 2).[14]

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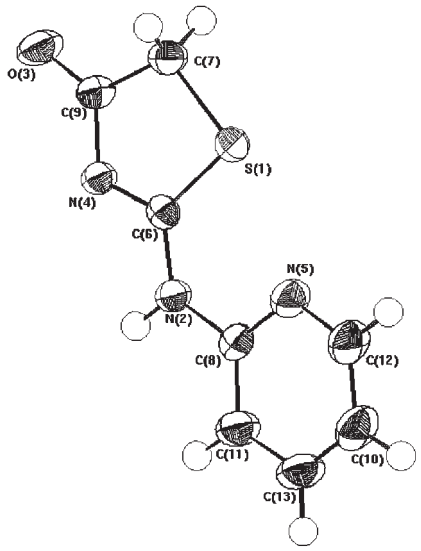


Fig. 1 Molecular structure of **6a** with atom labelling scheme.

Similarly **13** afforded **14** with chloroacetyl chloride, which is converted into **17** on treatment with potassium thiocyanate *via* the intermediacy of **15** and **16**[15] (Scheme 3).

Experimental

All melting points were measured with a Stuart Scientific melting point apparatus. IR spectra were recorded as KBr pellets on a Pye Unicam SP 3-300 Spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded in deuterated dimethylsulfoxide (DMSO-d_6) on a Bruker DPX 400 MHz spectrometer using tetramethylsilane (TMS) as an internal reference; shifts are expressed as δ values. Mass spectra were performed on a Shimadzu GCMS-QP 1000 Ex mass spectrometer at 70 eV. Elemental analyses were carried out at the Microanalytical Centre of Cairo University.

The crystallographic structures were performed on an Enraf Nonius FR 590 diffractometer. The crystals were mounted on a glass fibre. The data were collected at a temperature of 20±1°C using the ω scanning technique to a maximum of 27.12°. The structures were solved by direct methods using SIR 92 and refined by full-matrix least squares.[14] Non hydrogen bond atoms were refined anisotropically. Hydrogen atoms were located geometrically and were refined isotropically. Full data can be obtained on request from the CCDC.[14]

N-Substituted 2-chloroacetamides (**3a–c**, **14**): The heterocyclic amine (**1a–c**, **13**) (0.1 mo1) was suspended in dry dioxan (50 ml). Chloroacetyl chloride (0.1 mol) and anhydrous Na_2CO_3 (0.1 mol) were added and the mixture was left at room temperature for 1 h. The reaction mixture then was poured into ice water, the precipitate collected by filtration, and the crude product recrystallised from ethanol.

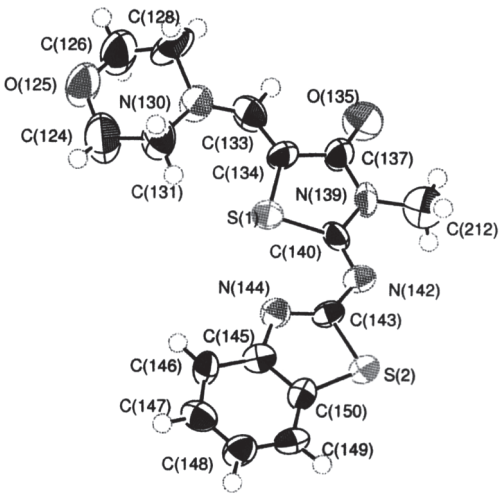
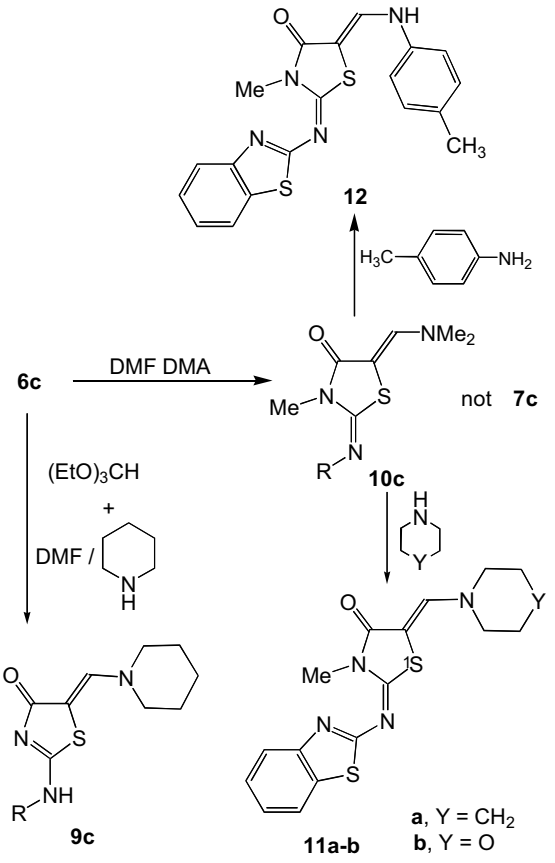


Fig. 2 Molecular structure of **11b** with atom labelling scheme.



Scheme 2

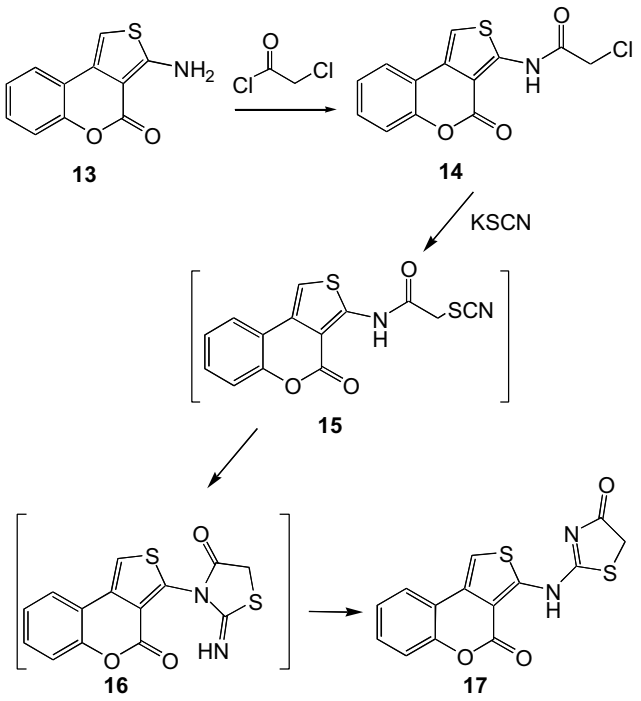
2-Chloro-N-(pyridin-2-yl)acetamide (**3a**): White crystals (84%), m.p. 123–125°C. IR: ν_{max} 3390 (OH), 3224 (NH), 3068 (CH aromatic), 2977 (CH aliphatic) and 1675 cm^{-1} (C=O). ^{1}H NMR: δ 12.85 (s, 1H, NH), 8.67 (d, 1H, pyridine H-6), 7.94 (dd, 1H, pyridine H-3), 7.07(m. 2H, pyridine H-4, H-5), 4.26 ppm (s, 2H, CH_2). MS: *m/z* 170 (M^+, 14%). Anal. calc. for $C_7H_7ClN_2O$: C, 49.28; H, 4.14; N, 16.42. Found: C, 49.45; H, 4.28; N 16.23%.

2-Chloro-N-(5-phenyl-1H-pyrazol-3-yl)acetamide (**3b**): White crystals (52%), m.p. 201–202°C. IR: ν_{max} 3299 (NH), 3221 (NH pyrazole), 3046 (CH aromatic), 2950 (CH aliphatic), 1680 cm^{-1} (C=O). ^{1}H NMR: δ 12.96 (s, 1H, NH), 10.86 (s, 1H, pyrazole NH) 7.41–7.74 (m, 5H, Ar-H), 6.93 (s, 1H, pyrazole H-4), 4.32 (s, 2H, CH_2). ^{13}C NMR: δ 164.53 (C=O), 148.1 (pyrazole C-3), 142.7 (pyrazole C-5), 125.6, 128.7, 129.5, 129.7 (phenyl carbons), 94.3 (pyrazole C-4), 43.3 (CH_2). MS: *m/z* 235 (M^+ 42%). Anal. Calcd for $C_{11}H_{10}ClN_3O$: C, 56.06; H, 4.28; N, 17.83. Found: C 56.28; H, 4.35; N, 17.75%.

N-Benzothiazol-2-yl-2-chloroacetamide (**3c**): White crystals (99%), m.p. 160°C. IR: ν_{max} 3290 (NH), 3050 (CH aromatic), 2944 (CH aliphatic) and 1691 cm^{-1} (C=O). ^{1}H NMR: δ 12.77 (s, 1H, NH), 7.92d, 7.75d, 7.40 m, 7.27 m (each 1H, benzothiazole H-4, H-7, H-6, H-5 resp.), 4.47 (s, 2H, CH_2). ^{13}C NMR: δ 166.5 (C=O), 158.2, 148.9, 132.0, 126.7, 124.3, 122.2, 121.2 (benzothiazole carbons), 43.13 (CH_2). MS: *m/z* 226 (M^+, 18%). Anal. Calcd for $C_9H_7ClN_2O$: C, 47.69; H, 3.11; N, 12.36. Found: C, 47.75; H, 3.33; N, 12.44%.

2-Chloro-N-(4-oxo-4H-thieno[3,4-c][1]benzopyran-3-yl) acetamide (**14**): Pale yellow crystals (70%), m.p. 198–200°C. IR: ν_{max} 3250(NH), 3010(CH aromatic), 2958 (CH aliphatic), 1701(C=O) and 1675 cm^{-1} (C=O ring). ^{1}H NMR: δ 11.39 (s, 1H, NH), 7.81 (s, 1H, thienyl), 7.34–8.08 (m, 4H, Ar–H), 4.73 ppm (s, 2H, CH_2). ^{13}C NMR: δ 165.5 (C=O), 159.1 (C-4), 150.6 (C-5a), 149.0 (C-3), 130.7 (C-9b), 130.2 (C-9a), 127.8 (C-7), 125.5 (C-9), 124.67 (C-8), 117,68(C-6), 117.35(C-3a) 109.82 (C-1), 43.73 ppm (CH_2). MS: *m/z* 293 (M^+, 26%). Anal. Calcd for $C_{13}H_8ClNO_3S$: C, 53.16; H, 2.75; N, 4.77. Found: C, 53.31; H, 2.87; N, 4.91%.

Thiazol-4(5H)-one derivatives (**6a–c**, **17**): The chloroacetamide (**3a–c**, **14**) (0.1 mol) and potassium thiocyanate (0.3 mol) in MeCN (50 ml) was heated to reflux for 3 h. The reaction mixture was cooled and poured into water (150 ml), and after 1 h the crude product was collected by filtration and recrystallised from the indicated solvent.



Scheme 3

2-(Pyridin-2-ylamino)thiazol-4(5H)-one (**6a**): Dark brown crystals (42%), m.p. 275°C, from dimethylformamide. IR: ν_{max} 3200 (NH), 3050 (CH aromatic), 2922 (CH_2) and 1685 cm^{-1} (C=O). ^{1}H NMR: δ 11.94 (s, 1H, NH), 8.39 (d, 1H, pyridyl H-6), 7.82 (dd, 1H, pyridyl H-3), 7.13 (m, 2H, H-4, pyridyl H-5) and 3.82 (s, 2H, CH_2). MS: *m/z* 193 (M^+, 28%). Anal. Calcd for $C_8H_7N_3OS$: C, 49.73; H, 3.65; N, 21.75. Found: C, 49.55; H, 3.73; N, 21.90%.

2-(5-Phenyl-1H-pyrazol-3-ylamino)thiazol-4(5H)-one (**6b**): Dark yellow crystals (88%), m.p. 252°C, from EtOH/DMF (3: 1). IR: ν_{max} 3296 (NH), 3220 (NH pyrazole), 3050 (CH aromatic), 2920 (CH_2), 1719 cm^{-1} (C=O). ^{1}H NMR: δ 13.11 (s, 1H, NH), 11.74 (s, 1H, pyrazole NH), 6.99 (s, 1H, pyrazole H-4), 7.31–7.75 (m, 5H, Ar-H), 4.01 (s, 2H, CH_2). MS: *m/z* 258 (M^+, 100%). Anal. Calcd for $C_{12}H_{10}N_4OS$: C, 55.80; H, 3.90; N, 21.69. Found: C, 55.65; H, 3.80; N, 21.53%.

2-(Benzothiazol-2-ylamino)-thiazol-4(5H)-one (**6c**): Orange crystals (44%), m.p 208–210°C, from ethanol. IR: ν_{max} 3200 (NH), 3061 (CH aromatic), 2966 (CH_2) and 1720 cm^{-1} (C=O). ^{1}H NMR: δ 12.30 (s.1H, NH), 7.95d, 7.78d, 7.47 m, 7.33 m (each 1H, benzothiazole H-4, H-7, H-6, H-5 resp.), 4.06 ppm (s, 2H, CH_2). ^{13}C NMR: δ 174.9 (C=O), 166.7 (thiazolone C-2), 169.4, 151.4, 133.6, 126.9, 124.8, 122.8, 121.9 (benzothiazole carbons), 36.1 pmm (CH_2). MS: *m/z* 249 (M^+, 87%). Anal. Calcd for $C_{10}H_7N_3OS_2$: C, 48.17; H, 2.83; N, 16.85. Found: C, 48.36; H, 2.60; N, 16.79%.

2-[(4-Oxo-4H-thieno[3,4-c][1]benzopyran-3-yl)amino]thiazol-4(5H)-one (**17**): Dark yellow crystals (68%) m.p. 240–241°C, from dioxan. IR: ν_{max} 3265 (NH), 3020 (CH aromatic), 2920 (CH_2), 1700 (N–C=O), 1673 cm^{-1} (C=O ring). ^{1}H NMR: δ 11.40 (s, 1H, NH), 7.83 (s, 1H, thienyl), 7.32–8.06 (m, 4H, Ar–H), 4.44 ppm (s, 2H, CH_2). MS: *m/z* 316 (M^+, 47%). Anal. Calcd for $C_{14}H_8N_2O_3S_2$: C, 53.15; H, 2.55; N, 8.85. Found: C, 53.33; H, 2.76; N, 8.77%.

Dimethylaminomethylene thiazolones (**7a**,**b**, **10c**)

Method A: *N,N*-dimethylformamide dimethylacetal (0.15 mol) was added to each of **6a** and **6b** and the reaction mixture was refluxed for 1 h. The crude product was collected by filtration, washed with petroleum spirit 60–80°C and diethylether, and recrystallised from the indicated solvent.

Method B: A suspension of compound **6c** (0.1 mol) in dry xylene (50 ml), was treated with *N,N*-dimethylformamide dimethylacetal (0.12 mol). The reaction mixture was refluxed for 8 h. The solid products was collected by filtration, washed with petroleum ether 60–80°C, and crystallised from xylene.

5-Dimethylaminomethylene-2-(pyridin-2-ylamino)thiazol-4(5H)-one (**7a**): Yellow crystals (73%), m.p. 263–265°C, from ethanol. IR: ν_{max} 3220 (NH), 3050 (CH aromatic, olefinic), 2910 (CH aliphatic), 1680 cm^{-1} (C=O). ^{1}H NMR: δ 11.56 (s, 1H, NH), 8.37 (d, 1H, pyridine H-6), 7.75 (dd, 1H, pyridine H-3), 7.48 (s, 1H, CH olefin), 7.03 (m, 2H, pyridine H-4 and H-5), 3.14 (s, 3H, CH_3–N), and 3.16 ppm (s, 3H, CH_3–N). MS: *m/z* 248 (M^+, 28%); Anal. Calcd for $C_{11}H_{12}N_4OS$: C, 53.21; H, 4.87; N, 22.56. Found: C, 53,35; H, 4.67; N, 22.33%.

5-Dimethylaminomethylene-2-(5-phenyl-1H-pyrazol-3-ylamino) thiazol-4(5H)-one (**7b**): Orange crystals from ethanol/dioxan (3: 1); m.p 248–249°C; (86%). IR: ν_{max} 3335 (NH), 3196 (NH pyrazol), 3100 (CH aromatic and olefin), 2910 (CH aliphatic) and1650 cm^{-1} (C=O). MS: *m/z* 313 (M^+, 24%); Anal. Calcd for $C_{15}H_{15}N_5OS$: C, 57.49; H, 4.82; N, 22.35. Found: C, 57.60; H, 4.78, N 22.47%.

2-(Benzothiazol-2-ylimino)-5-dimethylaminomethylene-3-methylthiazolidin-4-one (**10c**): Dark red crystals (72%), m.p 204°C. IR: ν_{max} 3050 (CH aromatic and olefin), 2913 (CH aliphatic) 1678 cm^{-1} (C=O). ^{1}H NMR: δ 7.87d, 7.47d, 7.38 m, 7.25 m (each 1H, benzothiazole 4-, 7-, 6-, 5-H, resp.), 7.64 (s, 1H, CH olefin), 3.69 (s, 3H, Me-N) and 3.18 ppm (s, 6H, $2CH_3$-N). MS: *m/z* 318 (M^+, 19%). Anal. Calcd for $C_{14}H_{14}N_4OS_2$: C, 52.81; H, 4.43; N, 17.60. Found: C, 52.68; H, 4.62; N, 17.47%.

Reaction of **7a,b** *and* **10c** *with aromatic amines:* The dimethylaminomethylene compound (**7a**,**b**, **10c**) (0.1 mol) was heated in acetic acid (20 ml) with aromatic amines (0.1 mol) for 1 h. The removal of excess for acetic acid under reduced pressure, and the solid was collected by filtration and recrystallised.

5-Phenylaminomethylene-2-(pyridin-2-ylamino)thiazol-4(5H)-one (**8a**): Pale brown crystals (17%), m.p 294–296°C, from methanol/dioxan (3: 1). IR: ν_{max} 3151, 3200 (2NH), 3099 (CH aromatic), 3042 (CH, olefin), 1647 cm^{-1} (C=O). ^{1}H NMR: δ 11.83 (s, 1H, NH), 9.76 (d, 1H, NH), 8.41 (d, 1H pyridine H-6), 8.03 (d, 1H pyridine H-3), 7.93 (d, 1H, CH olefin), 7.00–7.80 (m, 7H, Ar-H and pyridyl H-4, H-5). MS: *m/z* 296 (M^+, 24%). Anal. Calcd for $C_{15}H_{12}N_4OS$: C, 60.79; H, 4.08; N, 18.91. Found: C, 60.93; H, 4.25; N, 18.84%.

5-[(4-Nitrophenylamino)methylene]-2-(pyridin-2-ylamino)thiazol-4(5H)-one (**8b**): Dark red crystals (41%) m.p. 283°C, from ethanol/dioxan (3: 1). IR: ν_{max} 3240, 3180 (2NH), 3093 (CH aromatic), 3050 (CH, olefin) and 1678 cm^{-1} (C=O). ^{1}H NMR: δ 11.83 (s, 1H, NH), 10.27 (d, 1H, NH), 8.43 (d, 1H, pyridine H-6), 8.15 (dd, 1H, pyridine H-3), 7.99 (d, 1H, CH olefin), 7.13–7.84 (m, 6H, Ar-H and pyridine H-4, H-5). MS: *m/z* 341 (M^+, 14%). Anal. Calcd for $C_{15}H_{11}N_5O_3S$: C, 52.78; H, 3.25; N, 20.52. Found: C, 52.98; H, 3.05; N, 20.35%.

2-*(Pyridin-2-ylamino)-5-(p-tolylaminomethylene)thiazol-4(5H)-one* (**8c**): Yellow crystals (29%), m.p. 296–298°C, from dioxan. IR: ν_{max} 3200, 3174 (2NH), 3045 (CH aromatic and olefin), 2967 (CH aliphatic), 1649 cm^{-1} (C=O). ^{1}H NMR: δ 11.83 (s, 1H, NH), 9.73 (d, 1H, NH), 8.43 (d, 1H, pyridine H-6), 8.08 (d, 1H, pyridine H-3), 7.89 (d, 1H, CH olifin), 7.13–7.89 (m, 7H, Ar–H and H-3, H-4, H-5 pyridine), 2.24 ppm (s, 3H, CH_3). MS: *m/z* 310 (M^+, 37%). Anal. Calcd for $C_{16}H_{14}N_4OS$: C, 61.92; H, 4.55; N, 18.05. Found: C, 61.76; H, 4.35; N, 18.26%.

5-Phenylaminomethylene-2-(5-phenyl-1H-pyrazol-3-ylamino) thiazol-4(5H)-one (**8d**): Yellow crystals (44%) m.p. >300°C, from dioxan. IR: ν_{max} 3220–3278 (3NH), 3090 (CH aromatic and CH olefin), 1624 cm^{-1} (C=O). MS: *m/z* 361 (M^+, 82%). Anal. Calcd for $C_{19}H_{15}N_5OS$: C, 63.14; H, 4.18; N, 19.38. Found: C, 63.36; H, 4.30; N 19.45%.

2-(5-Phenyl-1H-pyrazol-3-ylamino)-5-(p-tolylaminomethylene) thiazol-4(5H)-one (**8e**): Orange crystals (26%), m.p. 298–300°C, from aqueous dimethylformamide (1: 1). IR: ν_{max} 3100–3250 (3NH), 3060 (CH aromatic), 3024 (CH, olefin), 2986 (CH aliphatic), 1697 cm^{-1} (C=O). ^{1}H NMR: δ 12.45 (s, 1H, NH), 11.64 (1H, NH pyrazole), 9.57 (d, 1H, NH), 7.77 (d, 1H, CH olefin), 7.10–7.46 (m, 9H. Ar–H), 6.50 (s, pyrazole H-4), 2.22 (s, 3H, CH_3). MS: *m/z* 375 (M^+, 85%). Anal. Calcd for $C_{20}H_{17}N_5OS$: C, 63.98; H, 4.56; N, 18.65. Found: C, 63.76; H, 4.32; N, 18.88%.

2-(Benzothiazol-2-ylimino)-3-methyl-5-(p-tolylaminomethylene)-thiazolidin-4-one (**12**): Green crystals (29%), m.p. 120–121°C, from ethanol. IR: ν_{max} 3250 (NH), 3055 (CH aromatic and olefin), 2921 (CH, aliphatic), 1689 cm^{-1} (C=O). ^{1}H NMR: δ 9.70 (d, 1H, NH), 7.77 (d, 1H, CH olefin), 7.13–8.16 (m, 8H, Ar–H), 4.06 (s, 3H, N-CH_3), 2.2 (s, 3H, CH_3). MS: *m/z* 380 (M^+, 64%). Anal. Calcd for $C_{19}H_{16}N_4OS_2$: C, 59.98; H 4.24; N, 14.72. Found: C, 59.77; H, 4.02; N, 14. 94%.

Reaction of **7a,b** *and* **10c** *with secondary amines:* The dimethylaminomethylene compound (**7a**,**b**, **10c**) (0.1 mol) in EtOH (20 ml) was heated for 7 h with the appropriate secondary amine (0.1 mol). The removal of solvent under reduced pressure yielded the crude product which was collected by filtration and washed with ethanol.

5-Piperidinomethylene-2-(pyridine-2-ylamino)thiazol-4(5H)-one (**9a**): Orange crystals (10%), m.p. 246°C, from ethanol. IR: ν_{max} 3300 (NH), 3100 (CH aromatic, olefin), 2936 (CH_2), 1663 cm^{-1} (C=O). ^{1}H NMR: δ 11.57 (s, 1H, NH), 8.39 (d, 1H pyridine H-6), 7.76 (dd, 1H pyridine H-3), 7.46 (s, 1H, CH olefin), 7. 03 (m, 2H pyridine H-4, H-5), 3.50 (m, 4H, $2NCH_2$) and 1.59 ppm (m, 6H, $3CH_2$). ^{13}C NMR: δ 172 (C=O), 159.6 (thiazole C-2), 156.6 (thiazole C-5), 147.1 (C-2 pyridine), 144.1 (C-6 pyridine), 138.7 (C-4 pyridine), 118.8 (C-5 pyridine), 118.0 (C-3 pyridine), 89.6 (CH olefin), 51.9 (C-2 and C-6 piperidine), 26.40 (C-4 piperidine) and 23.86 (C-3 and C-5 piperidine). MS: *m/z* 288 (M^+, 30%). Anal. Calcd for $C_{14}H_{16}N_4OS$: C, 58.31; H, 5.59; N, 19.43. Found: C, 58.17; H, 5.39; N,19.66%.

2-(5-Phenyl-1H-pyrazol-3-ylamino)-5-piperidinomethylene-thiazol-4(5H)-one (**9b**): Pale brown crystals (16%), m.p. 270–271°C, from ethanol. IR: ν_{max} 3100–3200 (2NH), 3050 (CH aromatic and olefin), 2933 (CH_2) 1650 cm^{-1} (C=O). ^{1}H NMR: δ 13.11 (s, 1H, NH), 11,33 (s, 1H, pyrazole NH), 7.32–7.73 (m, 6H, Ar-H and CH olefin), 6.41 (s, 1H pyrazole H-4), 3.45 (m, 4H, $2NCH_2$), 1.58 ppm (m, 6H, $3CH_2$). MS: *m/z* 353 (M^+, 35%). Anal. Calcd for $C_{18}H_{19}N_5OS$: C, 61.17; H, 5.42; N, 19.8. Found: C, 61.07; H, 5.33; N, 19.9%.

2-(Benzothiazol-2-ylamino)-5-piperidinomethylenethiazol-4(5H)-one (**9c**): Orange crystals (70%) m.p. 183–185°C, from ethanol. IR: ν_{max} 3350 (NH), 3090 (CH aromatic and olefin), 2995 (CH_2), 1680 cm^{-1} (C=O). ^{1}H NMR: δ 12.30 (s.1H, NH), 7.74 (s, 1H, CH olefin), 7.97–7.30 (m. 4H, Ar–H) 3.50 (m, 4H, $2NCH_2$) 1.63 ppm (m, 6H, $3CH_2$). MS: *m/z* 344 (M^+, 19%). Anal. Calcd for $C_{16}H_{16}N_4OS_2$. C, 55.79; H, 4.68; N, 16.27. Found: C, 94.84; H, 4.45; N, 16.48%.

2-(Benzothiazol-2-ylimino)-3-methyl-5-piperidinomethylene-thiazolidin-4-one (**11a**): Pale rose crystals (20%), m.p. 185°C, from ethanol. IR: ν_{max} 3050 (CH aromatic, olefin), 2982 (CH aliphatic), 1682 cm^{-1} (C=O). ^{1}H NMR: δ 7.93d, 7,79d, 7.40 m, 7.27 m (each 1H, benzothiazole H-4, H-7, H-6, H-5, resp.), 7.74 (s, 1H, CH olefin), 3.58 (m, 4H, $2NCH_2$), 3.28 (s, 3H, N-CH_3), 1.63 ppm (m, 6H, $3CH_2$). ^{13}C NMR: δ 169.2 (C=O), 159.2 (thiazole C-2), 151.6 (thiazole C-5), 166.9, 145.6, 133.3, 126.6, 124.2, 122.3, 121.6 (benzothiazole carbons), 85.5 (CH olefin), 30.0 (CH_3), 51.9 (C-2 and C-6 piperidine), 26.5 (C-4 piperidine) and 23.7 ppm (C-3, C-5 piperidine). MS: *m/z* 358 (M^+, 84%). Anal. Calcd for $C_{17}H_{18}N_4OS_2$: C, 56.96; H, 5.06; N, 15.63. Found: C, 56.73; H, 5.23; N, 15.85%.

2-(Benzothiazol-2-ylimino)-3-methyl-5-morpholinomethylene-thiazolidin-4-one (**11b**): Dark red crystals (17%) m.p. 220°C, from ethanol. IR: ν_{max} 3050 (CH aromatic, olefin), 2968 (CH aliphatic), 1685 cm^{-1} (C=O). MS: *m/z* 360 (M^+, 75%); Anal. Calcd for $C_{16}H_{16}N_4O_2S_2$: C, 53.31; H, 4.47; N, 15.54. Found: C, 53.56; H, 4.63; N, 15.32%.

Received 16 October 2005; accepted 31 January 2006
Paper 05/3551

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