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NOTE

Synthesis and biological evaluation of 3-aryl-2-(2-chloro-7-methoxyquinolin-3-yl)-4-thiazolidinones

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3-Aryl-2-(2-chloro-7-methoxyquinolin-3-yl)-4-thiazolidinones (3a-m, 4a-m) have been synthesised by the condensation of thioglycolic acid/thiolactic acid with *N*-aryl-(2-chloro-7-methoxyquinolin-3-yl)azomethine (2a-m) which in turn are prepared from arylamine and 2-chloro-7-methoxyquinoline-3-carboxaldehyde (1). The products have been evaluated for their antibacterial and antifungal activities.

4-Thiazolidinones have attracted considerable attention due to their pharmacological activity[1] and industrial importance as stabilizers for polymeric materials. The key intermediate 2-chloro-7-methoxyquinoline-3-carboxaldehyde also possesses pharmacological activity[2]. These observations led us to synthesise some new thiazolidinone derivatives bearing 2-chloro-7-methoxyquinoline moiety.

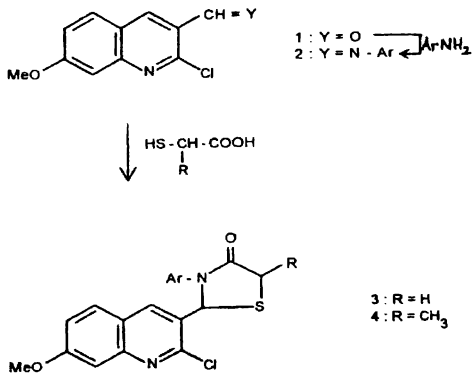
Table 1. M.p. and ^{1}H NMR data of compounds **3a-m** and **4a-m***

Compd. no.	M.p. °C	Ar-Me(s)/ OCH_2CH_3 (q) (t)	OCH_3 (s)	CH_2 (s)	CH Thiazolidinone (s)	ArH (m)
3a C_6H_5-	162		4.0	4.2	6.5	7.1–8.2
b 4-Antipyrine	70	2.8, 3.9	4.0	4.2	6.4	7.0–7.8
c 4-$ASO(OH)_2$-C_6H_4-	100	–	4.0	4.2	6.5	7.0–7.7
d 4-$COOC_2H_5$-C_6H_4-	122	1.5, 4.3	3.9	4.2	6.5	6.8–7.6
e 3-Cl-C_6H_4-	102	–	4.0	4.2	6.5	7.1–8.6
f 3-Cl,4-F-C_6H_3-	126	–	4.0	4.2	6.5	6.8–8.2
g 2,6-$(Cl)_2$-C_6H_3-	138	–	4.0	4.2	6.5	6.9–7.8
h 2,3-$(CH_3)_2$-C_6H_3-	162	2.5, 2.6	4.0	4.2	6.5	7.0–7.9
i 2-C_4H_3O-	175	–	4.0	4.2	6.5	6.9–7.7
j 2-OCH_3-C_6H_4-	148(d)	–	4.0	4.2	6.5	7.0–7.6
k 4-CH_3-C_6H_4-	192	2.7	4.0	4.2	6.5	7.0–7.8
l 2-NO_2-C_6H_4-	176	–	4.0	4.2	6.5	7.2–7.8
m 4-NO_2-C_6H_4-	162	–	4.0	4.2	6.5	7.0–8.1

		CH_3 (d, *J* 6.6 Hz)	Ar-Me(s)/ Ar-Et	OCH_3 (s)	CH (q)	CH Thiazolidinone	ArH (m)
4a C_6H_5-	150	1.6	–	3.97	4.3	6.5	6.9–8.3
b 4-Antipyrine	130	1.6	2.5, 3.9	4.0	4.2	6.5	7.1–7.9
c 4-$ASO(OH)_2$-C_6H_4-	120	1.6	–	4.0	4.2	6.5	7.1–7.7
d 4-$COOC_2H_5$-C_6H_4-	115	1.6	1.6, 4.1	4.0	4.2	6.5	6.8–7.4
e 3-Cl-C_6H_4-	170	1.6	–	4.0	4.3	6.5	6.8–7.3
f 3-Cl, 4-F-C_6H_3-	110	1.7	–	4.1	4.2	6.5	7.1–7.7
g 2.6-$(Cl)_2$-C_6H_3-	112	1.6	–	4.1	4.2	6.5	7.2–8.4
h 2,3-$(CH_3)_2$-C_6H_3-	178	1.6	2.5, 2.6	4.0	4.2	6.5	7.1–7.7
i 2-C_4H_3O-	168	1.6	–	4.0	4.2	6.5	6.8–7.6
j 2-OCH_3-C_6H_4-	115	1.6	3.9	4.0	4.2	6.5	6.9–8.2
k 4-CH_3-C_6H_4-	158	1.6	2.7	4.1	4.2	6.6	7.2–8.4
l 2-NO_2-C_6H_4-	110	1.6	–	4.1	4.2	6.5	7.1–8.4
m 4-NO_2-C_6H_4-	180	1.7	–	4.0	4.2	6.6	7.1–8.5

*All compounds gave satisfactory nitrogen analysis.

The key intermediate 2-chloro-7-methoxyquinoline-3-carboxaldehyde[3] (**1**) was prepared by the action of *m*-methoxyacetanilide with DMF and $POCl_3$. The reaction of **1** with different arylamine furnished the corresponding *N*-aryl-(2-chloro-7-methoxyquinolin-3-yl)azomethines (**2**). The latter (**2**) on cyclocondensation with thioglycolic acid and thiolactic acid formed 4-thiazolidinones **3** and **4** (Scheme 1) respectively.



Scheme 1

The structures of the compounds synthesised were established on the basis of elemental analysis, IR and ^1H NMR spectral data. The ^1H NMR data of all the compounds are recorded in Table 1.

The compounds were evaluated for their antimicrobial screening[4] against gram +ve and –ve microbes and antifungal screening against *A. niger*. The zone of inhibition of the controls were ampicillin 14–22, chloramphenicol 15–18, penicillin 14–22 mm against the bacterial strains, and greseofulvin 20 mm against *A. niger*. Compounds **3b-m** and **4b-d**, **f-i** (zone of inhibition 16–22 mm) were highly active against *B. megaterium*. Compounds **3c, g, i, k, l** and **4a, e, f, i** (17–24 mm) exhibited significant activity against *S. aureus*. Compounds **3c** and **4c** displayed highest activity (17–21 mm) against *S. typhosa*. Compounds **3d, g, l, m** and **4i-l** (18–28 mm) against *E. coli*. Compounds **3c, e, f, i, j, l-n** and **4a, c, e, g, i** showed maximum activity (22–28 mm) against *A. niger*.

Experimental

All the m.ps. were determined in open capillary tubes and are uncorrected. IR spectra (KBr) were recorded on a Nicolet-Megna-IR 550 Series-II spectrophotometer and ^1H NMR spectra (TFA; 60 MHz) on a Hitachi spectrometer using TMS as internal reference.

N-Aryl-(2-chloro-7-methoxyquinolin-3-yl)azomethine (**2**): A mixture of **1** (0.01 mol) and 4-methylaniline (0.01 mol) in alcohol was refluxed for 4 h. It was then cooled and the resulting solid was crystallized from dioxan to give **2** (Y = 4-CH_3-C_6H_4; 65%), m.p. 170° (Found : C, 69.00; H, 5.2; N, 8.89. $C_{18}H_{17}ON_2Cl$ reqd : C, 69.09; H, 5.4; N, 8.96%); ν_{max} 2927 (CH), 1541 (C=C), 1649 (C=N), 1239, 1027 (C–O–C), 714 cm^{-1} (C–Cl); δ 2.7 (3H, s, Ar-Me), 3.95 (3H, s, OMe), 6.5–8.5 (8H, m, ArH). The other azomethines (**2**) were smimilarly derived from **1** and the appropriate arylamines were utilised without further purification for **3** and **4**.

3-Aryl-2-(chloro-7-methoxyquinolin-3-yl)-4-thiazolidinone (**3** *and* **4**) : A mixture of **2** (0.01 mol) and thioglycolic acid or thiolactic acid (0.01 mol) was heated on an oil-bath at 115–120° for 12 h, then treated with 10% sodium carbonate solution and the resulting solid was crystallised from dioxan to give **3** or **4** (Table 1).

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