

ORIGINAL RESEARCH

Synthesis and in vitro microbial activities of amides of pyridoquinolone

Navin B. Patel · Sarvil D. Patel · Hiren I. Chauhan

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Abstract In this study, we report the antimicrobial evaluation of newly synthesized amides of pyridoquinolones from substituted aniline, substituted phenyl thioureas and 4-amino-*N*-(substitutedphenyl)benzenesulfonamide. Structures of selected compounds have been established by IR and ¹H NMR spectra and elemental analysis. The structure–activity relationships have been studied by screening of antimicrobial activity over *S. aureus*, *B. subtilis*, *E. coli*, *P. aeruginosa*, and *C. albicans* using cup–plate method.

Keywords Pyridoquinolone · Phenyl thioureas · Sulfonamides · Antimicrobial activity

Introduction

Discovery of nalidixic acid gave an important class of antibacterial known as fluoroquinolones. They can inhibit DNA gyrase and topoisomerase IV enzymes, essential for DNA supercoiling. Phenyl thiourea derivatives possess significant pharmacological importance, e.g., antiviral (Yan *et al.*, 2009), antimicrobial (Turan-Zitouni *et al.*, 2002), antidiabetic (Maruyama *et al.*, 2009), antitubercular (Sycheva *et al.*, 1966) etc. Sulfonamides demonstrated bacteriostatic activity by inhibiting the bio-synthesis of folic acid (Brown, 1962). Its derivatives possess versatile activity, e.g., carbonic anhydrase inhibitors (Supuran *et al.*, 1998), anticancer (Reddy *et al.*, 2004), anti-inflammatory (Li *et al.*, 1995), anti-HIV (Selvam *et al.*, 2001), COX-2 inhibitors (Dannhardt *et al.*, 2002), selective 5-HT receptor

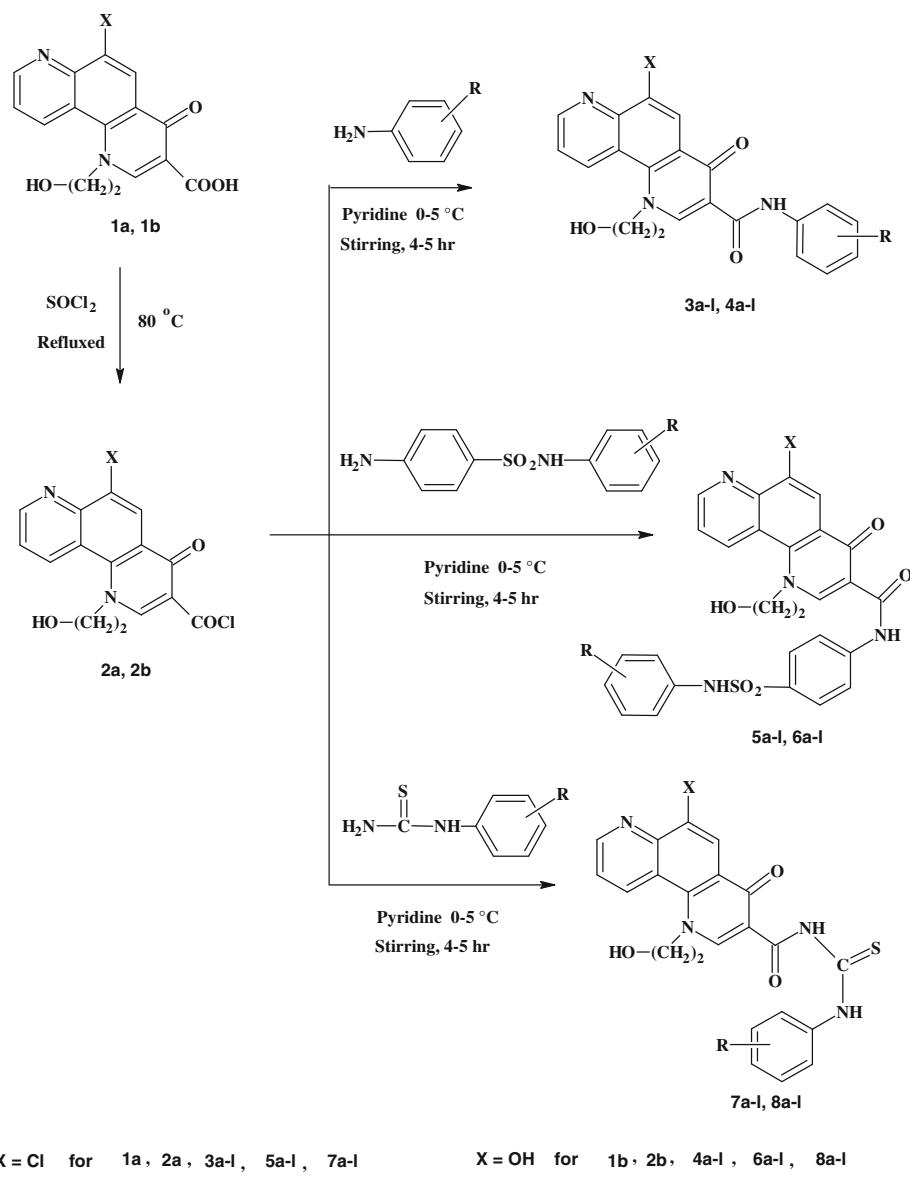
antagonist (Bromidge *et al.*, 2002), antitubercular (Kamal *et al.*, 2007) and antifungal (Briganti *et al.*, 1997) etc. Pyridoquinolones were synthesized and evaluated for antimicrobial activity (Lee *et al.*, 1992; Lee and Chang, 1994, 1996), in which pyridine ring was fused with quinazoline ring, and generally known as phenanthroline. The structure–activity relationships of fluoroquinolone have been studied in some reviews (Mitscher, 2005; Bhanot *et al.*, 2001); consideration of the above facts and the presence of fused pyrido ring in nalidixic acid urged us to synthesize structurally similar compounds to fluoroquinolone by replacing fluoro group with chloro and hydroxy groups at C-6 position with fused pyrido ring; the carboxylic acid group was further converted to amides for enhanced antimicrobial activity.

Results and discussion

Chemistry

We have synthesized amides of pyridoquinolone **3a–l**, **4a–l**, **5a–l**, **6a–l**, **7a–l**, and **8a–l** from substituted aniline, substituted phenyl thioureas, and 4-amino-*N*-(substitutedphenyl)benzenesulfonamide as illustrated in Scheme 1: their structures were confirmed by elemental analysis, IR, and ¹H NMR spectral data. IR absorption bands in cm⁻¹ were observed at 3412 (NH), 3360 (OH), 2942, 2865 (CH), 1739 (>C=O of quinolone), 1640 (amide-I), 1535 (amide-II), 1305 (C–N), 1250 (amide-III), 810 (C–Cl), 1325, 1180 (S=O, sym, asym), and 1160 (>C=S), 1075 (S–N); some additional peaks appeared due to substitution in aromatic ring at 1512, 1352 (N=O sym, asym), 1265, 1046 (C–O–C), and 2236 (>C≡N). In ¹H NMR spectra, the following common signals appeared at δ_H (ppm) values: a singlet

N. B. Patel (✉) · S. D. Patel · H. I. Chauhan
Department of Chemistry, Veer Narmad South Gujarat
University, Surat, Gujarat 395 007, India
e-mail: drnavin@satyam.net.in



	a	b	c	d	e	f	g	h	i	j	K	I
3	-H	3-Cl	4-Cl	2-OCH ₃	4-OCH ₃	2-NO ₂	3-NO ₂	4-NO ₂	2-CH ₃	3-CH ₃	4-CH ₃	2,5-di-CH ₃
4	-H	3-Cl	4-Cl	2-OCH ₃	4-OCH ₃	2-NO ₂	3-NO ₂	4-NO ₂	2-CH ₃	3-CH ₃	4-CH ₃	2,5-di-CH ₃
5	-H	3-Cl	4-Cl	2-OCH ₃	4-OCH ₃	3-NO ₂	4-NO ₂	2-CH ₃	3-CH ₃	4-CH ₃	2,5-di-CH ₃	2-CN, 4-NO ₂
6	-H	3-Cl	4-Cl	2-OCH ₃	4-OCH ₃	3-NO ₂	4-NO ₂	2-CH ₃	3-CH ₃	4-CH ₃	2,5-di-CH ₃	2-CN, 4-NO ₂
7	-H	3-OH	4-OH	2-OCH ₃	4-OCH ₃	2-NO ₂	3-NO ₂	4-NO ₂	2-CH ₃	3-CH ₃	4-CH ₃	3-Cl
8	-H	3-OH	4-OH	2-OCH ₃	4-OCH ₃	2-NO ₂	3-NO ₂	4-NO ₂	2-CH ₃	3-CH ₃	4-CH ₃	3-Cl

Scheme 1 Synthetic route of compounds 3a-l, 4a-l, 5a-l, 6a-l, 7a-l, 8a-l

signal at δ 7.80, and 8.50 corresponding to H-2 and H-5 of quinolone ring, respectively; a multiplet at δ 3.20 corresponding to $>\text{N}-(\text{CH}_2)_2-\text{O}$; a singlet at δ 4.25 corresponding to CH₂OH; a multiplet at δ 8.75–9.50 corresponding to pyrido ring; a singlet at δ 5.40 corresponding to Ar-OH; a singlet at δ 10.10 corresponding to >CO.NH; and a singlet single at δ 10.20 and 10.28 corresponding to –SONH₂ and

$>\text{CS.NH}$, respectively. Due to the substitution on aromatic ring, a singlet appeared at δ 6.56 and 3.85 corresponding to Ar-OH and Ar-OCH₃, respectively. Substituted phenyl thiourea derivatives (Venkatesh and Pandeya, 2009; Bhusari *et al.*, 2008) and substituted 4-amino-N-(substitutedphenyl)benzenesulfonamide (Hirpara *et al.*, 2004) have been synthesized as per the previously reported methods (Table 1).

Table 1 Antibacterial and antifungal activity of synthesized compounds

Zone of inhibition in mm at 100 µg/ml

Compd.	Gram negative				Gram positive				Fugal species	
	<i>E. coli</i>		<i>P. aeruginosa</i>		<i>S. aureus</i>		<i>B. subtilis</i>		<i>C. albicans</i>	
	Z.I.	A.I.	Z.I.	A.I.	Z.I.	A.I.	Z.I.	A.I.	Z.I.	A.I.
3a	12	0.8	09	0.52	12	0.7	11	0.68	05	0.55
3b	07	0.46	07	0.41	08	0.47	09	0.6	03	0.33
3c	06	0.4	06	0.35	05	0.29	07	0.43	02	0.22
3d	08	0.53	08	0.47	09	0.52	10	0.62	03	0.33
3e	00	–	06	0.35	06	0.66	06	0.35	02	0.22
3f	11	0.73	11	0.64	08	0.47	10	0.62	04	0.44
3g	09	0.6	09	0.52	09	0.52	06	0.35	03	0.33
3h	09	0.6	10	0.58	10	0.66	06	0.35	04	0.44
3i	07	0.46	04	0.23	00	–	05	0.31	00	–
3j	10	0.66	10	0.58	10	0.66	09	0.6	04	0.44
3k	04	0.26	05	0.29	05	0.29	07	0.43	00	–
3l	10	0.66	08	0.47	08	0.47	09	0.6	00	–
4a	08	0.53	08	0.47	07	0.41	06	0.35	01	0.11
4b	04	0.26	04	0.23	00	–	06	0.35	00	–
4c	10	0.66	08	0.47	12	0.7	10	0.62	05	0.55
4d	06	0.4	00	–	06	0.66	08	0.5	01	0.11
4e	11	0.73	10	0.58	10	0.58	12	0.75	05	0.55
4f	09	0.6	09	0.52	10	0.58	11	0.68	04	0.44
4g	08	0.53	10	0.58	07	0.41	08	0.5	02	0.22
4h	06	0.4	06	0.35	08	0.47	07	0.43	00	–
4i	09	0.6	10	0.58	06	0.66	06	0.35	00	–
4j	00	–	06	0.35	05	0.29	06	0.35	01	0.11
4k	10	0.66	09	0.52	09	0.52	08	0.5	03	0.33
4l	09	0.6	08	0.47	08	0.47	09	0.6	02	0.22
5a	06	0.4	07	0.41	08	0.47	10	0.62	02	0.22
5b	10	0.66	10	0.58	11	0.64	09	0.6	04	0.44
5c	08	0.53	00	–	06	0.66	07	0.43	01	0.11
5d	05	0.33	05	0.29	06	0.66	06	0.35	02	0.22
5e	09	0.6	10	0.58	09	0.52	10	0.62	03	0.33
5f	07	0.46	05	0.29	06	0.66	08	0.5	02	0.22
5g	11	0.73	09	0.52	09	0.52	10	0.62	03	0.33
5h	09	0.6	09	0.52	09	0.52	10	0.62	03	0.33
5i	00	–	04	0.23	00	–	06	0.35	00	–
5j	05	0.33	07	0.41	05	0.29	06	0.35	01	0.11
5k	10	0.66	10	0.58	10	0.58	09	0.6	04	0.44
5l	08	0.53	08	0.47	08	0.47	09	0.6	02	0.22
6a	09	0.6	10	0.58	09	0.52	08	0.5	03	0.33
6b	09	0.6	08	0.47	08	0.47	09	0.6	03	0.33
6c	04	0.26	04	0.23	00	–	06	0.35	00	–
6d	00	–	06	0.35	06	0.66	08	0.5	01	0.11
6e	08	0.53	08	0.47	10	0.58	11	0.68	04	0.44
6f	08	0.53	07	0.41	08	0.47	08	0.5	02	0.22
6g	12	0.8	10	0.58	10	0.58	11	0.68	04	0.44
6h	00	–	04	0.23	04	0.26	06	0.35	00	–
6i	10	0.66	11	0.64	11	0.64	12	0.75	05	0.55

Table 1 continued

Zone of inhibition in mm at 100 µg/ml

Compd.	Gram negative				Gram positive				Fugal species	
	<i>E. coli</i>		<i>P. aeruginosa</i>		<i>S. aureus</i>		<i>B. subtilis</i>		<i>C. albicans</i>	
	Z.I.	A.I.	Z.I.	A.I.	Z.I.	A.I.	Z.I.	A.I.	Z.I.	A.I.
6j	05	0.33	00	—	05	0.29	06	0.35	00	—
6k	10	0.66	11	0.64	11	0.64	09	0.6	04	0.44
6l	06	0.4	08	0.47	08	0.47	06	0.35	02	0.22
7a	10	0.66	09	0.52	09	0.52	11	0.68	03	0.33
7b	08	0.53	06	0.35	08	0.47	09	0.6	02	0.22
7c	12	0.80	11	0.64	12	0.7	11	0.68	05	0.55
7d	05	0.33	03	0.17	00	—	06	0.35	00	—
7e	08	0.53	06	0.35	08	0.47	09	0.6	02	0.22
7f	10	0.66	08	0.47	12	0.7	09	0.6	04	0.44
7g	00	—	08	0.47	08	0.47	06	0.35	01	0.11
7h	10	0.66	09	0.52	11	0.64	12	0.75	05	0.55
7i	00	—	04	0.23	06	—	08	0.5	02	0.22
7j	11	0.73	10	0.58	10	0.58	09	0.6	04	0.44
7k	06	0.4	00	—	06	0.66	06	0.35	00	—
7l	09	0.6	09	0.52	08	0.47	10	0.62	03	0.33
8a	11	0.73	10	0.58	11	0.64	15	0.93	04	0.44
8b	09	0.6	07	0.41	08	0.47	10	0.66	03	0.33
8c	06	0.4	06	0.35	06	0.66	07	0.43	00	—
8d	00	—	04	0.23	04	0.26	00	—	00	—
8e	08	0.53	08	0.47	08	0.47	06	0.35	02	0.22
8f	05	0.33	04	0.23	00	—	05	0.31	01	0.11
8g	09	0.6	10	0.58	07	0.41	07	0.43	00	—
8h	12	0.8	10	0.58	10	0.58	09	0.6	04	0.44
8i	06	0.4	00	—	05	0.29	07	0.43	00	—
8j	09	0.6	09	0.52	09	0.52	08	0.5	03	0.33
8k	06	0.4	04	0.23	00	—	06	0.35	01	0.11
8l	10	0.66	09	0.52	09	0.52	10	0.62	03	0.33
Ciprofloxacin	15	1	17	1	17	1	16	1	9	1
Amphotericin-B										

Z.I Zone of inhibition in mm, A.I. Activity index

A.I. = Zone of inhibition of compounds/Zone of inhibition of standard drug

Antimicrobial activity

Antibacterial and antifungal activity of all the synthesized compounds have been screened against five different strains, e.g., two Gram-positive *S. aureus*, *B. subtilis*, two Gram-negative *E. coli*, *P. aeruginosa* bacteria and fungi *C. albicans* by cup-plate method (Collee *et al.*, 1996) at 100 µg/mL concentration, compared with standard drug ciprofloxacin and amphotericin-B.

Amides **3d**, **3g**, **3h**, **3j**, **3l**, **4a**, **4f**, **4c**, **4g**, **4i**, **4k**, **4l**, sulfonamides **5b**, **5c**, **5e**, **5k**, **5l**, **6a**, **6b**, **6e**, **6f**, **6k**, and thioureido amides **7a**, **7b**, **7e**, **7f**, **7h**, **7l**, **8b**, **8e**, **8g**, **8j**, **8l**;

demonstrated good activity against *E. coli*; whereas amides **3a**, **3f**, **4e**, sulfonamides **5g**, **6g** and thioureido amides **7c**, **7j**, **8a**, **8h** demonstrated strong activity against *E. coli*.

Amides **3a**, **3f**, **3g**, **3h**, **3j**, **4e**, **4g**, **4i**, **4f**, **4k**, sulfonamides **5b**, **5e**, **5g**, **5h**, **5k**, **6a**, **6g**, **6i**, **6k**, and thioureido amides **7c**, **7j**, **7l**, **8a**, **8g**, **8h**, **8j**, **8l** demonstrated good activity against *P. aeruginosa*. Amides **3a**, **3d**, **3e**, **3g–j**, **4c–f**, **4i**, **4k**, sulfonamides **5b–h**, **5k**, **6a**, **6d**, **6e**, **6g**, **6i**, **6k** and thioureido amides **7a**, **7c**, **7f**, **7h**, **7j**, **7k**, **8a**, **8c**, **8h**, **8j**, **8l** showed good activity against *S. aureus*.

Amides **3a**, **3b**, **3d**, **3f**, **3j**, **3l**, **4c**, **4d**, **4f**, **4g**, **4k**, **4l**, sulfonamides **5a**, **5b**, **5e–h**, **5l**, **6a**, **6b**, **6e**, **6f**, **6g**, **6k**, and

thioureido amides **7a–c**, **7e**, **7f**, **7j**, **7l**, **8b**, **8h**, **8j**, **8l** demonstrated good activity against *B. substillis*; whereas amide **4e**, sulfonamides **6i**, and thioureido amides **7h**, **8a** demonstrated strong activity against *B. substillis*.

Amides **3a**, **4c**, **4e**; sulfonamide **6i**, and thioureido amides **7c**, **7h**, showed good activity against *C. albicans*.

Conclusion

The structure–activity relationship study demonstrated that electron withdrawing as well as electrodonating groups at phenyl ring were active; whereas chloro and hydroxyl groups at C–6 position showed similar activity. Variations in antimicrobial activities of amides were observed.

Activities of amides in increasing order:

Thioureido amides < Sulfonamides < Amide

Activities against bacteria in increasing order:

P. aeruginosa < *S. aureus* < *B. substillis* < *E. coli*

Experimental

General

Melting points (m.p.) were determined in open capillaries and left uncorrected. The IR spectra were recorded on Shimadzu FTIR spectrophotometer, using KBr pallets. ¹H NMR spectra were recorded in (DMSO-d₆) using Bruker DRX-300 spectrometer at 300 MHz; the chemical shifts are reported in part per million (δ ppm) using tetramethylsilane (TMS) as an internal standard. Elemental analysis (C, H, and N) of compounds was performed on Carlo Erba 1108.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (**1a**)

The parent molecule was prepared from 5-amino-8-chloro quinoline on reaction with diethyl ethoxymethylene malonate and cyclized in diethyl ether; further condensation with chloroethanol gave ester, which finally hydrolyzed to title compounds (Lee *et al.*, 1992). ¹H NMR (DMSO-d₆): δ 3.61 (m, 4H, >N(CH₂)₂O), 4.25 (s, 1H, CH₂OH), 8.50 (s, H-2, quinolone), 7.80 (s, H-5, quinolone), 8.75–9.40 (m, 3H, pyrido), and 13.00 (s, 1H, COOH).

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (**1b**)

The parent molecule was prepared from 5-amino-8-hydroxy quinoline on reaction with diethyl ethoxymethylene

malonate and cyclized in diethyl ether; further condensation with chloroethanol gave ester, which finally hydrolyzed to title compounds (Lee *et al.*, 1992). ¹H NMR (DMSO-d₆): δ 3.61 (m, 4H, >N(CH₂)₂O), 4.25 (s, 1H, CH₂OH), 8.50 (s, H-2, quinolone), 7.80 (s, H-5, quinolone), 5.65 (s, 1H, Ar-OH), 8.75–9.40 (m, 3H, pyrido), and 13.00 (s, 1H, COOH).

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxyl chloride (**2a**)

The mixture of 6-chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (**1a**) (0.01 mol) and thionyl chloride (0.01 mol) was refluxed using chloroform as a solvent in water bath at 80°C for 5–6 h in anhydrous condition with the help of calcium chloride guard tube, until the HCl gas evolution ceased, and then solvent was removed by distillation. The solid material of the title compound was obtained and used in next step.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxyl chloride (**2b**)

The mixture of 6-hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (**1b**) (0.01 mol) and thionyl chloride (0.01 mol) was refluxed using chloroform as a solvent in water bath at 80°C for 5–6 h in anhydrous condition with the help of calcium chloride guard tube, until the HCl gas evolution ceased, and then solvent was removed by distillation. The solid material of the title compound was obtained and used in next step.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (substitutedphenyl)amide (**3a–l**)

Substituted aniline (0.005 mol) was dissolved in dry pyridine and added dropwise in solution of carbonyl chloride (**2a**) (0.005 mol) in pyridine within 1.5 h with constant stirring at 0–5°C and refluxed for 8 h; then, material was poured into acidic crushed ice, and the solid mass was filtered and washed thoroughly with NaHCO₃ solution for neutralization. The purity of the compounds was monitored by TLC on silica gel glass plate using benzene:ethylacetate (1:1) as mobile phase.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid phenylamide (**3a**)

Yield = 62%, m.p. 256–258°C. IR (KBr) cm⁻¹: 3412 (NH); 3360 (OH); 2942, 2865 (CH); 1739 (>C=O of quinolone); 1640 (amide-I); 1535 (amide-II); 1305 (C–N); 1250 (amide-III); and 810 (C–Cl). ¹H NMR (DMSO-d₆):

δ 3.25 (m, 4H, $>\text{N}(\text{CH}_2)_2\text{O}$); 4.45 (s, 1H, CH_2OH); 8.71 (s, H-2, quinolone); 8.88 (s, H-5, quinolone); 8.94–9.55 (m, 3H, pyrido); 10.10 (s, 1H, CO.NH); and 7.28–7.92 (m, 5H, Ar-H). Anal. Calcd. for $\text{C}_{21}\text{H}_{16}\text{O}_3\text{N}_3\text{Cl}$: C, 64.11; H, 4.10; and N, 10.69. Found: C, 64.12; H, 4.12; and N, 10.65.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (3b)

Yield = 53%, m.p. 278–280°C.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (4-chlorophenyl)amide (3c)

Yield = 65%. m.p. 247–249°C. IR (KBr) cm^{-1} : 3425 (NH); 3365 (OH); 2937; 2864 (CH); 1745 ($>\text{C=O}$ of quinolone); 1645 (amide-I); 1525 (amide-II); 1315 (C–N); 1254 (amide-III); and 786 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.20 (m, 4H, $>\text{N}(\text{CH}_2)_2\text{O}$); 4.35 (s, 1H, CH_2OH); 8.70 (s, H-2, quinolone); 8.84 (s, H-5, quinolone); 8.95–9.55 (m, 3H, pyrido); 10.15 (s, 1H, CO.NH); and 7.20–7.95 (m, 4H, Ar-H). Anal. Calcd. for $\text{C}_{21}\text{H}_{15}\text{O}_3\text{N}_3\text{Cl}_2$: C, 59.01; H, 3.54; and N, 9.84. Found: C, 59.05; H, 3.56; and N, 9.82.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (2-methoxyphenyl)amide (3d)

Yield = 67%, m.p. 255–257°C.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (4-methoxyphenyl)amide (3e)

Yield = 62%, m.p. 271–272°C. IR (KBr) cm^{-1} : 3427 (NH); 3360 (OH); 2935, 2861 (CH); 1752 ($>\text{C=O}$ of quinolone); 1652 (amide-I); 1535 (amide-II); 1312 (C–N); 1245 (amide-III); 1235, 1040 (C–O–C); and 786 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.21 (m, 4H, $>\text{N}(\text{CH}_2)_2\text{O}$); 4.27 (s, 1H, CH_2OH); 8.65 (s, H-2, quinolone); 8.88 (s, H-5, quinolone); 8.97–9.61 (m, 3H, pyrido); 10.25 (s, 1H, CONH); 7.21–7.79 (m, 4H, Ar-H); and 3.85 (s, 3H, Ar-OCH₃). Anal. Calcd. for $\text{C}_{22}\text{H}_{18}\text{O}_4\text{N}_3\text{Cl}$: C, 62.40; H, 4.29; and N, 9.93. Found: C, 62.38; H, 4.27; and N, 9.90.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (2-nitrophenyl)amide (3f)

Yield = 55%, m.p. 260–262°C.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (3-nitrophenyl)amide (3g)

Yield = 66%, m.p. 277–279°C. IR (KBr) cm^{-1} : 3433 (NH); 3355 (OH); 2937, 2865 (CH); 1745 ($>\text{C=O}$ of quinolone); 1645 (amide-I); 1525 (amide-II); 1510, 1330 (N=O sym, asym); 1320 (C–N); 1235 (amide-III); and 792 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.28 (m, 4H, $>\text{N}(\text{CH}_2)_2\text{O}$); 4.25 (s, 1H, CH_2OH); 8.61 (s, H-2, quinolone); 8.87 (s, H-5, quinolone); 8.81–9.65 (m, 3H, pyrido); 10.21 (s, 1H, CO.NH); and 7.18–7.65 (m, 4H, Ar-H). Anal. Calcd. for $\text{C}_{21}\text{H}_{15}\text{O}_3\text{N}_4\text{Cl}$: C, 57.52; H, 3.45; and N, 12.79. Found: C, 57.51; H, 3.42; and N, 12.77.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (4-nitrophenyl)amide (3h)

Yield = 62%, m.p. 250–252°C.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (2-methylphenyl)amide (3i)

Yield = 53%, m.p. 247–249°C. IR (KBr) cm^{-1} : 3435 (NH); 3358 (OH); 2925, 2861 (CH); 1745 ($>\text{C=O}$ of quinolone); 1645 (amide-I); 1525 (amide-II); 1308 (C–N); 1232 (amide-III); and 798 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.27 (m, 4H, $>\text{N}(\text{CH}_2)_2\text{O}$); 4.25 (s, 1H, CH_2OH); 8.61 (s, H-2, quinolone); 8.79 (s, H-5, quinolone); 8.85–9.61 (m, 3H, pyrido); 10.14 (s, 1H, CO.NH); 7.22–7.80 (m, 4H, Ar-H); and 2.22 (s, 3H, Ar-CH₃). Anal. Calcd. for $\text{C}_{22}\text{H}_{18}\text{O}_3\text{N}_3\text{Cl}$: C, 64.85; H, 4.46; and N, 10.32. Found: C, 64.81; H, 4.42; and N, 10.37.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (3-methylphenyl)amide (3j)

Yield = 58%, m.p. 268–270°C.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (4-methylphenyl)amide (3k)

Yield = 64%, m.p. 241–243°C. IR (KBr) cm^{-1} : 3425 (NH); 3345 (OH); 2935, 2865 (CH); 1752 ($>\text{C=O}$ of quinolone); 1648 (amide-I); 1521 (amide-II); 1315 (C–N); 1237 (amide-III); and 788 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.29 (m, 4H, $>\text{N}(\text{CH}_2)_2\text{O}$); 4.21 (s, 1H, CH_2OH); 8.56 (s, H-2, quinolone); 8.85 (s, H-5, quinolone); 8.90–9.62 (m, 3H, pyrido); 10.15 (s, 1H, CO.NH); 7.21–7.82 (m, 4H,

Ar–H); 2.25 (s, 3H, Ar–CH₃). Anal. Calcd. for C₂₂H₁₈O₃N₃Cl: C, 64.85; H, 4.46; and N, 10.32. Found: C, 64.82; H, 4.41; and N, 10.35.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (2,5-dimethylphenyl)amide (3l)

Yield = 60%, m.p. 265–267°C.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (substitutedphenyl)amide (4a–l)

Substituted aniline (0.005 mol) was dissolved in dry pyridine and added dropwise in solution of carbonyl chloride (**2b**) (0.005 mol) in pyridine within 1.5 h with constant stirring at 0–5°C and refluxed for 8 h, then refluxed material was poured into acidic crushed ice, the solid mass was filtered and washed thoroughly with NaHCO₃ solution for neutralization. The purity of the compounds was monitored by TLC on silica gel glass plate using benzene:ethylacetate (1:1) as mobile phase.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid phenylamide (4a)

Yield = 58%, m.p. 244–246°C. IR (KBr) cm^{−1}: 3425 (NH); 3345 (OH); 2965, 2854 (CH); 1749 (>C=O of quinolone); 1668 (amide-I); 1565 (amide-II); 1315 (C–N); and 1258 (amide-III). ¹H NMR (DMSO-d₆): δ 3.60 (m, 4H, >N(CH₂)₂O); 4.35 (s, 1H, CH₂OH); 8.70 (s, H-2, quinolone); 8.15 (s, H-5, quinolone); 9.10–9.60 (m, 3H, pyrido); 10.10 (s, 1H, CO.NH); 5.65 (s, 1H, Ar–OH); and 6.95–7.40 (m, 5H, Ar–H). Anal. Calcd. for C₂₁H₁₇O₄N₃: C, 67.18; H, 4.57; and N, 11.20. Found: C, 67.15; H, 4.55; and N, 11.18.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (3-chlorophenyl)amide (4b)

Yield = 64%, m.p. 265–267°C.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (4-chlorophenyl)amide (4c)

Yield = 62%, m.p. 261–263°C. IR (KBr) cm^{−1}: 3421 (NH); 3335 (OH); 2961, 2851 (CH); 1751 (>C=O of quinolone); 1665 (amide-I); 1569 (amide-II); 1312 (C–N); 1252 (amide-III); and 788 (C–Cl). ¹H NMR (DMSO-d₆): δ 3.61 (m, 4H, >N(CH₂)₂O); 4.25 (s, 1H, CH₂OH); 8.65 (s, H-2, quinolone); 8.10 (s, H-5, quinolone); 9.12–9.65

(m, 3H, pyrido); 10.15 (s, 1H, CO.NH); 5.62 (s, 1H, Ar–OH); and 6.85–7.45 (m, 4H, Ar–H). Anal. Calcd. for C₂₁H₁₆O₄N₃Cl: C, 61.60; H, 3.94; and N, 10.27. Found: C, 61.62; H, 3.92; and N, 10.22.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (2-methoxyphenyl)amide (4d)

Yield = 62%, m.p. 261–263°C.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (4-methoxyphenyl)amide (4e)

Yield = 65%, m.p. 258–260°C. IR (KBr) cm^{−1}: 3422 (NH); 3339 (OH); 2961, 2852 (CH); 1752 (>C=O of quinolone); 1664 (amide-I); 1561 (amide-II); 1310 (C–N); 1245 (amide-III) 1225, and 1038 (C–O–C). ¹H NMR (DMSO-d₆): δ 3.68 (m, 4H, >N(CH₂)₂O); 4.37 (s, 1H, CH₂OH); 8.68 (s, H-2, quinolone); 8.25 (s, H-5, quinolone); 9.15–9.65 (m, 3H, pyrido); 10.15 (s, 1H, CO.NH); 5.61 (s, 1H, Ar–OH); 6.85–7.45 (m, 4H, Ar–H); and 3.95 (s, 3H, Ar–OCH₃). Anal. Calcd. for C₂₂H₁₉O₅N₃: C, 65.16; H, 4.73; and N, 10.37. Found: C, 65.15; H, 4.51; and N, 10.35.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (2-nitrophenyl)amide (4f)

Yield = 60%, m.p. 266–267°C.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (3-nitrophenyl)amide (4g)

Yield = 66%, m.p. 235–237°C. IR (KBr) cm^{−1}: 3428 (NH); 3325 (OH); 2965, 2858 (CH); 1745 (>C=O of quinolone); 1662 (amide-I); 1565 (amide-II); 1512, 1339 (N=O sym, asym); 1307 (C–N); and 1252 (amide-III). ¹H NMR (DMSO-d₆): δ 3.65 (m, 4H, >N(CH₂)₂O); 4.32 (s, 1H, CH₂OH); 8.71 (s, H-2, quinolone); 8.15 (s, H-5, quinolone); 9.10–9.62 (m, 3H, pyrido); 10.12 (s, 1H, CO.NH); 5.62 (s, 1H, Ar–OH); and 6.79–7.35 (m, 4H, Ar–H). Anal. Calcd. for C₂₁H₁₆O₆N₄: C, 59.98; H, 3.84; and N, 13.33. Found: C, 59.95; H, 3.82; and N, 13.31.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (4-nitrophenyl)amide (4h)

Yield = 64%, m.p. 255–258°C.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (2-methylphenyl)amide (4i**)**

Yield = 55%, m.p. 247–249°C. IR (KBr) cm^{-1} : 3435 (NH); 3320 (OH); 2955, 2854 (CH); 1751 (>C=O of quinolone); 1665 (amide-I); 1561 (amide-II); 1310 (C–N); and 1245 (amide-III). ^1H NMR (DMSO-d₆): δ 3.67 (m, 4H, >N(CH₂)₂O); 4.21 (s, 1H, CH₂OH); 8.65 (s, H-2, quinolone); 8.05 (s, H-5, quinolone); 9.12–9.55 (m, 3H, pyrido); 10.18 (s, 1H, CO.NH); 5.65 (s, 1H, Ar–OH); 6.71–7.25 (m, 4H, Ar–H); and 2.14 (s, 3H, Ar–CH₃). Anal. Calcd. for C₂₂H₁₉O₄N₃: C, 67.84; H, 4.92; and N, 10.80. Found: C, 67.82; H, 4.91; and N, 10.78.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (3-methylphenyl)amide (4j**)**

Yield = 67%, m.p. 270–271°C.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (4-methylphenyl)amide (4k**)**

Yield = 62%, m.p. 261–263°C.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid (2,5-dimethylphenyl)amide (4l**)**

Yield = 57%, m.p. 255–257°C.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(phenylsulfamoyl)phenyl]amide (5a–l**)**

4-Amino-N-(substitutedphenyl)benzenesulfonamides (0.005 mol) was dissolved in dry pyridine and added dropwise in solution of carbonyl chloride **2a** (0.005 mol) in pyridine within 1.5 h with constant stirring at 0–5°C and refluxed for 8 h, then refluxed material was poured into acidic crushed ice, the solid mass was filtered and washed thoroughly with NaHCO₃ solution for neutralization. The purity of the compounds was monitored by TLC on silica gel glass plate using benzene:ethylacetate (1:1) as mobile phase.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(phenylsulfamoyl)phenyl]amide (5a**)**

Yield = 66%, m.p. 241–243°C.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(3-chlorophenylsulfamoyl)phenyl]amide (5b**)**

Yield = 60%, m.p. 239–240°C. IR (KBr) cm^{-1} : 3425 (NH); 3365 (OH); 2945, 2850 (CH); 1742 (>C=O of quinolone); 1680 (amide-I); 1565 (amide-II); 1325, 1180 (S=O, sym, asym); 1310 (C–N); 1255 (amide-III); 1075 (S–N); and 798 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.58 (m, 4H, >N(CH₂)₂O); 4.44 (s, 1H, CH₂OH); 8.68 (s, H-2, quinolone); 7.95 (s, H-5, quinolone); 8.98–9.75 (m, 3H, pyrido); 10.10 (s, 1H, CO.NH); 10.32 (s, 1H, SO₂NH); and 7.15–7.70 (m, 4H, Ar–H). Anal. Calcd. for C₂₇H₂₀O₅N₄SCl₂: C, 55.67; H, 3.46; and N, 9.62. Found: C, 55.62; H, 3.42; and N, 9.60.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(4-chlorophenylsulfamoyl)phenyl]amide (5c**)**

Yield = 56%, m.p. 260–262°C.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(2-methoxyphenylsulfamoyl)phenyl]amide (5d**)**

Yield = 64%, m.p. 257–259°C. IR (KBr) cm^{-1} : 3431 (NH); 3361 (OH); 2937, 2848 (CH); 1748 (>C=O of quinolone); 1665 (amide-I); 1557 (amide-II); 1325, 1180 (S=O, sym, asym); 1310 (C–N); 1255 (amide-III); 1212, 1035 (C–O–C); 1075 (S–N); and 798 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.62 (m, 4H, >N(CH₂)₂O); 4.47 (s, 1H, CH₂OH); 8.61 (s, H-2, quinolone); 7.90 (s, H-5, quinolone); 8.91–9.72 (m, 3H, pyrido); 10.15 (s, 1H, CO.NH); 9.95 (s, 1H, SO₂NH); 7.01–7.65 (m, 4H, Ar–H); and 3.82 (s, 3H, Ar–OCH₃). Anal. Calcd. for C₂₈H₂₃O₆N₄SCl: C, 58.12; H, 4.01; and N, 9.69. Found: C, 58.10; H, 4.06; and N, 9.64.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(4-methoxyphenylsulfamoyl)phenyl]amide (5e**)**

Yield = 52%, m.p. 274–276°C.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(3-nitrophenylsulfamoyl)phenyl]amide (5f**)**

Yield = 55%, m.p. 247–249°C. IR (KBr) cm^{-1} : 3426 (NH); 3358 (OH); 2928, 2835 (CH); 1751 (>C=O of quinolone); 1671 (amide-I); 1562 (amide-II); 1528, 1332 (N=O sym, asym); 1335, 1182 (S=O, sym, asym); 1315

(C–N); 1265 (amide-III); and 1065 (S–N); 795 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.62 (m, 4H, >N(CH₂)₂O); 4.47 (s, 1H, CH₂OH); 8.61 (s, H-2, quinolone); 7.90 (s, H-5, quinolone); 8.91–9.72 (m, 3H, pyrido); 10.15 (s, 1H, CO.NH); 9.95 (s, 1H, SO₂NH); and 7.01–7.65 (m, 4H, Ar–H). Anal. Calcd. for C₂₇H₂₀O₇N₅SCl: C, 54.63; H, 3.40; and N, 11.81. Found: C, 54.60; H, 3.38; and N, 11.78.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(4-nitrophenylsulfamoyl)phenyl]amide (5g)

Yield = 61%, m.p. 259–261°C.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(2-methyphenylsulfamoyl)phenyl]amide (5h)

Yield = 63%, m.p. 236–237°C. IR (KBr) cm^{−1}: 3420 (NH); 3345 (OH); 2932, 2821 (CH); 1741 (>C=O of quinolone); 1665 (amide-I); 1565 (amide-II); 1325, 1179 (S=O, sym, asym); 1310 (C–N); 1262 (amide-III); 1062 (S–N); and 805 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.62 (m, 4H, >N(CH₂)₂O); 4.47 (s, 1H, CH₂OH); 8.69 (s, H-2, quinolone); 7.91 (s, H-5, quinolone); 8.85–9.68 (m, 3H, pyrido); 10.10 (s, 1H, CO.NH); 9.91 (s, 1H, SO₂NH); 7.15–7.70 (m, 4H, Ar–H); and 2.10 (s, 3H, Ar–CH₃). Anal. Calcd. for C₂₇H₂₀O₇N₅SCl: C, 59.78; H, 4.12; and N, 9.96. Found: C, 59.75; H, 4.10; and N, 9.95.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(3-methyphenylsulfamoyl)phenyl]amide (5i)

Yield = 59%, m.p. 231–233°C.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(4-methyphenylsulfamoyl)phenyl]amide (5j)

Yield = 67%, m.p. 255–257°C. IR (KBr) cm^{−1}: 3425 (NH); 3341 (OH); 2935, 2825 (CH); 1745 (>C=O of quinolone); 1670 (amide-I); 1562 (amide-II); 1321, 1175 (S=O, sym, asym); 1315 (C–N); 1265 (amide-III); 1058 (S–N); and 795 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.67 (m, 4H, >N(CH₂)₂O); 4.42 (s, 1H, CH₂OH); 8.65 (s, H-2, quinolone); 7.88 (s, H-5, quinolone); 8.81–9.65 (m, 3H, pyrido); 10.15 (s, 1H, CO.NH); 9.95 (s, 1H, SO₂NH); 7.19–7.65 (m, 4H, Ar–H); and 2.10 (s, 3H, Ar–CH₃). Anal. Calcd. for C₂₇H₂₀O₇N₅SCl: C, 59.78; H, 4.12; and N, 9.96. Found: C, 59.74; H, 4.09; and N, 9.92.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(2,5-dimethyphenylsulfamoyl)phenyl]amide (5k)

Yield = 60%, m.p. 258–260°C.

6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(2-cyno-4-nitrophenylsulfamoyl)phenyl]amide (5l)

Yield = 64%, m.p. 233–235°C. IR (KBr) cm^{−1}: 3428 (NH); 3335 (OH); 2925, 2818 (CH); 2236 (>C≡N); 1755 (>C=O of quinolone); 1665 (amide-I); 1565 (amide-II); 1528, 1332 (N=O sym, asym); 1325, 1174 (S=O, sym, asym); 1304 (C–N); 1260 (amide-III); 1062 (S–N); and 795 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.67 (m, 4H, >N(CH₂)₂O); 4.42 (s, 1H, CH₂OH); 8.65 (s, H-2, quinolone); 7.88 (s, H-5, quinolone); 8.81–9.65 (m, 3H, pyrido); 10.15 (s, 1H, CO.NH); 9.95 (s, 1H, SO₂NH); and 7.19–7.65 (m, 3H, Ar–H). Anal. Calcd. for C₂₇H₂₀O₇N₅SCl: C, 59.78; H, 4.12; and N, 9.96. Found: C, 59.74; H, 4.09; and N, 9.92.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(substitutedphenylsulfamoyl)phenyl]amide (6a–l)

4-Amino-N-(substitutedphenyl)benzenesulfonamides (0.005 mol) was dissolved in dry pyridine and added dropwise in solution of carbonyl chloride **2b** (0.005 mol) in pyridine within 1.5 h with constant stirring at 0–5°C and refluxed for 8 h. Then, refluxed material was poured into acidic crushed ice, and the solid mass was filtered and washed thoroughly with NaHCO₃ solution for neutralization. The purity of the compounds was monitored by TLC on silica gel glass plate using benzene:ethylacetate (1:1) as mobile phase.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(phenylsulfamoyl)phenyl]amide (6a)

Yield = 62%, m.p. 235–237°C.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(3-chlorophenylsulfamoyl)phenyl]amide (6b)

Yield = 65%, m.p. 271–273°C. IR (KBr) cm^{−1}: 3432 (NH); 3395 (OH); 2945, 2858 (CH); 1746 (>C=O of quinolone); 1668 (amide-I); 1528 (amide-II); 1352, 1165 (S=O, sym, asym); 1314 (C–N); 1265 (amide-III); 1075 (S–N); and 795 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.67

(m, 4H, $>\text{N}(\text{CH}_2)_2\text{O}$); 4.42 (s, 1H, CH_2OH); 8.65 (s, H-2, quinolone); 7.88 (s, H-5, quinolone); 8.81–9.65 (m, 3H, pyrido); 10.15 (s, 1H, CO.NH); 9.95 (s, 1H, SO_2NH); 5.60 (s, 1H, Ar-OH); 7.19–7.65 (m, 4H, Ar-H). Anal. Calcd. for $\text{C}_{27}\text{H}_{21}\text{O}_6\text{N}_4\text{SCl}$: C, 57.44; H, 3.75; and N, 9.93. Found: C, 57.42; H, 3.72; and N, 9.90.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(4-chlorophenylsulfamoyl)phenyl]amide (6c)

Yield = 54%, m.p. 258–260°C.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(2-methoxyphenylsulfamoyl)phenyl]amide (6d)

Yield = 66%, m.p. 245–248°C. IR (KBr) cm^{-1} : 3435 (NH); 3385 (OH); 2942, 2848 (CH); 1755 ($>\text{C=O}$ of quinolone); 1674 (amide-I); 1532 (amide-II); 1345, 1166 (S=O, sym, asym); 1320 (C-N); 1261 (amide-III); 1269, 1040 (C-O-C); and 1065 (S-N). ^1H NMR (DMSO-d₆): δ 3.61 (m, 4H, $>\text{N}(\text{CH}_2)_2\text{O}$); 4.47 (s, 1H, CH_2OH); 8.69 (s, H-2, quinolone); 7.85 (s, H-5, quinolone); 8.79–9.62 (m, 3H, pyrido); 10.25 (s, 1H, CO.NH); 10.12 (s, 1H, SO_2NH); 5.64 (s, 1H, Ar-OH); 7.20–7.52 (m, 4H, Ar-H); and 3.78 (s, 3H, Ar-OCH₃). Anal. Calcd. for $\text{C}_{28}\text{H}_{24}\text{O}_7\text{N}_4\text{S}$: C, 59.99; H, 4.32; and N, 10.00. Found: C, 59.96; H, 4.30; and N, 10.02.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(4-methoxyphenylsulfamoyl)phenyl]amide (6e)

Yield = 59%, m.p. 275–277°C.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(3-nitrophenylsulfamoyl)phenyl]amide (6f)

Yield = 67%, m.p. 263–265°C. IR (KBr) cm^{-1} : 3441 (NH); 3387 (OH); 2937, 2845 (CH); 1749 ($>\text{C=O}$ of quinolone); 1672 (amide-I); 1535 (amide-II); 1525, 1325 (N=O sym, asym); 1335, 1162 (S=O, sym, asym); 1315 (C-N); 1265 (amide-III); and 1065 (S-N). ^1H NMR (DMSO-d₆): δ 3.65 (m, 4H, $>\text{N}(\text{CH}_2)_2\text{O}$); 4.48 (s, 1H, CH_2OH); 8.65 (s, H-2, quinolone); 7.84 (s, H-5, quinolone); 8.75–9.61 (m, 3H, pyrido); 10.15 (s, 1H, CO.NH); 10.15 (s, 1H, SO_2NH); 5.65 (s, 1H, Ar-OH); and 7.15–7.45 (m, 4H, Ar-H). Anal. Calcd. for $\text{C}_{27}\text{H}_{21}\text{O}_8\text{N}_5\text{S}$: C, 56.34; H, 3.68; and N, 12.17. Found: C, 56.32; H, 3.65; and N, 12.15.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(4-nitrophenylsulfamoyl)phenyl]amide (6g)

Yield = 63%, m.p. 255–257°C.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(2-methylphenylsulfamoyl)phenyl]amide (6h)

Yield = 60%, m.p. 275–277°C. IR (KBr) cm^{-1} : 3438 (NH); 3375 (OH); 2939, 2852 (CH); 1752 ($>\text{C=O}$ of quinolone); 1665 (amide-I); 1538 (amide-II); 1338, 1165 (S=O, sym, asym); 1305 (C-N); 1261 (amide-III); and 1060 (S-N). ^1H NMR (DMSO-d₆): δ 3.66 (m, 4H, $>\text{N}(\text{CH}_2)_2\text{O}$); 4.45 (s, 1H, CH_2OH); 8.60 (s, H-2, quinolone); 7.89 (s, H-5, quinolone); 8.74–9.69 (m, 3H, pyrido); 10.10 (s, 1H, CO.NH); 9.95 (s, 1H, SO_2NH); 5.62 (s, 1H, Ar-OH); 7.05–7.41 (m, 4H, Ar-H); and 2.21 (s, 3H, Ar-CH₃). Anal. Calcd. for $\text{C}_{28}\text{H}_{24}\text{O}_6\text{N}_4\text{S}$: C, 61.75; H, 4.45; and N, 10.29. Found: C, 61.72; H, 4.42; and N, 10.27.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(3-methylphenylsulfamoyl)phenyl]amide (6i)

Yield = 58%, m.p. 240–241°C.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(4-methylphenylsulfamoyl)phenyl]amide (6j)

Yield = 62%, m.p. 264–266°C. IR (KBr) cm^{-1} : 3435 (NH); 3371 (OH); 2935, 2845 (CH); 1745 ($>\text{C=O}$ of quinolone); 1668 (amide-I); 1535 (amide-II); 1340, 1168 (S=O, sym, asym); 1315 (C-N); 1265 (amide-III); and 1065 (S-N). ^1H NMR (DMSO-d₆): δ 3.60 (m, 4H, $>\text{N}(\text{CH}_2)_2\text{O}$); 4.48 (s, 1H, CH_2OH); 8.62 (s, H-2, quinolone); 7.88 (s, H-5, quinolone); 8.65–9.65 (m, 3H, pyrido); 10.15 (s, 1H, CO.NH); 9.98 (s, 1H, SO_2NH); 5.68 (s, 1H, Ar-OH); 7.15–7.48 (m, 4H, Ar-H); and 2.15 (s, 3H, Ar-CH₃). Anal. Calcd. for $\text{C}_{28}\text{H}_{24}\text{O}_6\text{N}_4\text{S}$: C, 61.75; H, 4.45; and N, 10.29. Found: C, 61.70; H, 4.44; and N, 10.31.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(2,5-dimethylphenylsulfamoyl)phenyl]amide (6k)

Yield = 67%, m.p. 277–279°C.

6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carboxylic acid [4-(2-cyno-4-nitrophenylsulfamoyl)phenyl]amide (6l)

Yield = 65%, m.p. 280–282°C. IR (KBr) cm^{-1} : 3428 (NH); 3365 (OH); 2925, 2832 (CH); 2236 (>C≡N); 1751 (>C=O of quinolone); 1665 (amide-I); 1532 (amide-II); 1528, 1332 (N=O sym, asym); 1345, 1160 (S=O, sym, asym); 1325 (C–N); 1262 (amide-III); and 1056 (S–N). ^1H NMR (DMSO-d₆): δ 3.68 (m, 4H, >N(CH₂)₂O); 4.47 (s, 1H, CH₂OH); 8.65 (s, H-2, quinolone); 7.85 (s, H-5, quinolone); 8.62–9.62 (m, 3H, pyrido); 10.10 (s, 1H, CO.NH); 9.95 (s, 1H, SO₂NH); 5.69 (s, 1H, Ar–OH); and 7.10–7.52 (m, 3H, Ar–H). Anal. Calcd. for C₂₈H₂₀O₈N₄S: C, 58.73; H, 3.52; and N, 9.79. Found: C, 58.70; H, 3.50; and N, 9.76.

1-[6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(substitutedphenyl)thiourea (7a–l)

Substitutedphenyl thioureas (0.005 mol) was dissolved in dry pyridine and added dropwise in solution of carbonyl chloride **2a** (0.005 mol) in pyridine within 1.5 h with constant stirring at 0–5°C and refluxed for 8 h. Then, refluxed material was suspended into acidic crushed ice, and the solid mass was filtered and washed thoroughly with NaHCO₃ solution for neutralization. The purity of the compounds were monitored by TLC on silica gel glass plate using benzene:ethylacetate (1:1) as mobile phase.

1-[6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-phenylthiourea (7a)

Yield = 55%, m.p. 257–258°C. IR (KBr) cm^{-1} : 3434 (NH); 3322 (OH); 2950, 2860 (CH); 1735 (>C=O of quinolone); 1650 (amide-I); 1540 (amide-II); 1300 (C–N); 1256 (amide-III); 1190 (>C=S); and 766 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.31 (m, 4H, >N(CH₂)₂O); 4.35 (s, 1H, CH₂OH); 8.70 (s, H-2, quinolone); 8.14 (s, H-5, quinolone); 8.88–9.45 (m, 3H, pyrido); 10.05 (s, 1H, CO.NH); 10.25 (s, 1H, CS.NH); and 7.30–7.92 (m, 5H, Ar–H). Anal. Calcd. for C₂₂H₁₇O₃N₄SCl: C, 58.40; H, 3.79; and N, 12.39. Found: C, 58.38; H, 3.76; and N, 12.36.

1-[6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(3-hydroxyphenyl)thiourea (7b)

Yield = 65%, m.p. 244–246°C.

1-[6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(4-hydroxyphenyl)thiourea (7c)

Yield = 60%, m.p. 275–276°C. IR (KBr) cm^{-1} : 3445 (NH); 3315 (OH); 2945, 2865 (CH); 1741 (>C=O of quinolone); 1645 (amide-I); 1540 (amide-II); 1305 (C–N); 1258 (amide-III); 1165 (>C=S); and 766 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.45 (m, 4H, >N(CH₂)₂O); 4.25 (s, 1H, CH₂OH); 8.85 (s, H-2, quinolone); 8.24 (s, H-5, quinolone); 8.85–9.35 (m, 3H, pyrido); 10.10 (s, 1H, CO.NH); 10.35 (s, 1H, CS.NH); 7.25–7.85 (m, 4H, Ar–H); and 5.65 (s, 1H, Ar–OH). Anal. Calcd. for C₂₂H₁₇O₄N₄SCl: C, 56.40; H, 3.66; and N, 11.97. Found: C, 56.37; H, 3.64; and N, 11.95.

1-[6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(2-methoxyphenyl)thiourea (7d)

Yield = 57%, m.p. 277–279°C.

1-[6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(4-methoxyphenyl)thiourea (7e)

Yield = 60%, m.p. 255–256°C. IR (KBr) cm^{-1} : 3452 (NH); 3325 (OH); 2935, 2860 (CH); 1748 (>C=O of quinolone); 1656 (amide-I); 1535 (amide-II); 1315 (C–N); 1269, 1040 (C–O–C); 1255 (amide-III); 1160 (>C=S); and 769 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.52 (m, 4H, >N(CH₂)₂O); 4.30 (s, 1H, CH₂OH); 8.78 (s, H-2, quinolone); 8.30 (s, H-5, quinolone); 8.75–9.25 (m, 3H, pyrido); 10.05 (s, 1H, CO.NH); 10.15 (s, 1H, CS.NH); 7.26–7.75 (m, 4H, Ar–H); and 3.85 (s, 3H, Ar–OCH₃). Anal. Calcd. for C₂₃H₁₉O₄N₄SCl: C, 57.25; H, 3.62; and N, 11.93. Found: C, 57.25; H, 3.64; and N, 11.95.

1-[6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(2-nitrophenyl)thiourea (7f)

Yield = 67%, m.p. 284–286°C.

1-[6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(3-nitrophenyl)thiourea (7g)

Yield = 56%, m.p. 261–263°C. IR (KBr) cm^{-1} : 3456 (NH); 3330 (OH); 2925, 2865 (CH); 1755 (>C=O of quinolone); 1665 (amide-I); 1520 (amide-II); 1528, 1332

(N=O); 1325 (C–N); 1245 (amide-III); 1165 (>C=S); and 777 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.51 (m, 4H, >N(CH₂)₂O); 4.41 (s, 1H, CH₂OH); 8.80 (s, H-2, quinolone); 8.25 (s, H-5, quinolone); 8.68–9.20 (m, 3H, pyrido); 10.00 (s, 1H, CO.NH); 10.22 (s, 1H, CS.NH); and 7.24–7.71 (m, 4H, Ar–H). Anal. Calcd. for C₂₂H₁₆O₃N₅ SCl: C, 53.11; H, 3.24; and N, 14.09. Found: C, 53.09; H, 3.24; and N, 14.07.

1-[6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(4-nitrophenyl)thiourea (7h)

Yield = 61%, m.p. 249–251°C. IR (KBr) cm⁻¹: 3445 (NH); 3325 (OH); 2920, 2862 (CH); 1748 (>C=O of quinolone); 1662 (amide-I); 1528 (amide-II); 1535, 1340 (N=O); 1320 (C–N); 1235 (amide-III); 1160 (>C=S); and 772 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.55 (m, 4H, >N(CH₂)₂O); 4.47 (s, 1H, CH₂OH); 8.75 (s, H-2, quinolone); 8.15 (s, H-5, quinolone); 8.65–9.15 (m, 3H, pyrido); 10.05 (s, 1H, CO.NH); 10.28 (s, 1H, CS.NH); and 7.14–7.65 (m, 4H, Ar–H). Anal. Calcd. for C₂₃H₁₉O₃N₄ SCl: C, 59.22; H, 4.11; and N, 12.02. Found: C, 59.20; H, 4.09; and N, 12.04.

1-[6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(2-methylphenyl)thiourea (7i)

Yield = 67%, m.p. 243–244°C.

1-[6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(3-methylphenyl)thiourea (7j)

Yield = 62%, m.p. 241–243°C.

1-[6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(4-methylphenyl)thiourea (7k)

Yield = 63%, m.p. 263–265°C. IR (KBr) cm⁻¹: 3452 (NH); 3330 (OH); 2922, 2865 (CH); 1752 (>C=O of quinolone); 1665 (amide-I); 1522 (amide-II); 1325 (C–N); 1231 (amide-III); 1165 (>C=S); and 762 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.57 (m, 4H, >N(CH₂)₂O); 4.51 (s, 1H, CH₂OH); 8.65 (s, H-2, quinolone); 8.20 (s, H-5, quinolone); 8.62–9.20 (m, 3H, pyrido); 10.12 (s, 1H, CO.NH); 10.22 (s, 1H, CS.NH); 7.25–7.74 (m, 4H, Ar–H); and 2.22 (s, 1H, Ar–CH₃). Anal. Calcd. for C₂₃H₁₉O₃N₄ SCl: C, 59.22; H, 4.11; and N, 12.02. Found: C, 59.24; H, 4.13; and N, 12.00.

1-[6-Chloro-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(3-chlorophenyl)thiourea (7l)

Yield = 60%, m.p. 251–253°C. IR (KBr) cm⁻¹: 3435 (NH); 3325 (OH); 2945, 2845 (CH); 1745 (>C=O of quinolone); 1665 (amide-I); 1562 (amide-II); 1312 (C–N); 1245 (amide-III); 1160 (>C=S); and 764 (C–Cl). ^1H NMR (DMSO-d₆): δ 3.35 (m, 4H, >N(CH₂)₂O); 4.37 (s, 1H, CH₂OH); 8.75 (s, H-2, quinolone); 8.10 (s, H-5, quinolone); 8.90–9.52 (m, 3H, pyrido); 9.90 (s, 1H, CO.NH); 10.22 (s, 1H, CS.NH); and 7.18–7.95 (m, 4H, Ar–H). Anal. Calcd. for C₂₂H₁₈O₄N₄S: C, 60.81; H, 4.18; and N, 12.90. Found: C, 60.78; H, 4.15; and N, 12.85.

1-[6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(substitutedhydroxyphenyl)thiourea (8a–l)

Substitutedphenyl thioureas (0.005 mol) was dissolved in dry pyridine and added dropwise the solution of carbonyl chloride **2b** (0.005 mol) in pyridine within 1.5 h with constant stirring at 0–5°C and refluxed for 8 h; then, refluxed material was poured into acidic crushed ice; and the solid mass was filtered and was washed thoroughly with NaHCO₃ solution for neutralization. The purity of the compounds was monitored by TLC on silica gel glass plate using benzene:ethylacetate (1:1) as mobile phase.

1-[6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-phenylthiourea (8a)

Yield = 66%, m.p. 246–247°C.

1-[6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(3-hydroxyphenyl)thiourea (8b)

Yield = 62%, m.p. 281–283°C.

1-[6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(4-hydroxyphenyl)thiourea (8c)

Yield = 56%, m.p. 246–248°C. IR (KBr) cm⁻¹: 3425 (NH); 3315 (OH); 2952, 2838 (CH); 1745 (>C=O of quinolone); 1662 (amide-I); 1562 (amide-II); 1315 (C–N); 1248 (amide-III); and 1165 (>C=S). ^1H NMR (DMSO-d₆): δ 3.42 (m, 4H, >N(CH₂)₂O); 4.35 (s, 1H, CH₂OH); 8.74 (s, H-2, quinolone); 8.15 (s, H-5, quinolone); 8.88–9.45 (m, 3H, pyrido); 9.95 (s, 1H, CO.NH); 10.15 (s, 1H, CS.NH); 7.18–7.95 (m, 4H, Ar–H); and 5.40, 6.20 (s, 1H,

Ar–OH). Anal. Calcd. for $C_{22}H_{18}O_5N_4S$: C, 58.65; H, 4.03; and N, 12.44. Found: C, 58.62; H, 4.01; and N, 12.42.

1-[6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(2-methoxyphenyl)thiourea (8d)

Yield = 56%, m.p. 241–243°C.

1-[6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(4-methoxyphenyl)thiourea (8e)

Yield = 60%, m.p. 233–235°C. IR (KBr) cm^{-1} : 3445 (NH); 3324 (OH); 2945, 2825 (CH); 1748 ($>\text{C=O}$ of quinolone); 1665 (amide-I); 1565 (amide-II); 1323 (C–N); 1252 (amide-III); 1235, 1020 (C–O–C); and 1161 ($>\text{C=S}$). ^1H NMR (DMSO-d₆): δ 3.44 (m, 4H, $>\text{N}(\text{CH}_2)_2\text{O}$); 4.45 (s, 1H, CH₂OH); 8.78 (s, H-2, quinolone); 8.05 (s, H-5, quinolone); 8.08–9.35 (m, 3H, pyrido); 9.98 (s, 1H, CO.NH); 10.18 (s, 1H, CS.NH); 7.28–7.85 (m, 4H, Ar–H); and 3.85 (s, 1H, Ar–OCH₃). Anal. Calcd. for $C_{23}H_{20}O_5N_4S$: C, 59.47; H, 4.34; and N, 12.07. Found: C, 59.45; H, 4.24; and N, 12.05.

1-[6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(2-nitrophenyl)thiourea (8f)

Yield = 63%, m.p. 253–254°C.

1-[6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(3-nitrophenyl)thiourea (8g)

Yield = 56%, m.p. 244–246°C. IR (KBr) cm^{-1} : 3450 (NH); 3314 (OH); 2948, 2828 (CH); 1748 ($>\text{C=O}$ of quinolone); 1675 (amide-I); 1564 (amide-II); 1315 (C–N); 1248 (amide-III); 1512, 1352 (N=O sym, asym); and 1168 ($>\text{C=S}$). ^1H NMR (DMSO-d₆): δ 3.48 (m, 4H, $>\text{N}(\text{CH}_2)_2\text{O}$); 4.42 (s, 1H, CH₂OH); 8.88 (s, H-2, quinolone); 8.11 (s, H-5, quinolone); 8.15–9.25 (m, 3H, pyrido); 9.92 (s, 1H, CO.NH); 10.15 (s, 1H, CS.NH); and 7.25–7.75 (m, 4H, Ar–H). Anal. Calcd. for $C_{23}H_{20}O_5N_4S$: C, 55.10; H, 3.58; and N, 14.61. Found: C, 55.05; H, 3.45; and N, 14.59.

1-[6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(4-nitrophenyl)thiourea (8h)

Yield = 58%, m.p. 251–253°C. IR (KBr) cm^{-1} : 3445 (NH); 3310 (OH); 2958, 2818 (CH); 1752 ($>\text{C=O}$ of

quinolone); 1665 (amide-I); 1562 (amide-II); 1321 (C–N); 1352 (N=O sym, asym); 1252 (amide-III); and 1168 ($>\text{C=S}$). ^1H NMR (DMSO-d₆): δ 3.52 (m, 4H, $>\text{N}(\text{CH}_2)_2\text{O}$); 4.40 (s, 1H, CH₂OH); 8.85 (s, H-2, quinolone); 8.14 (s, H-5, quinolone); 8.01–9.15 (m, 3H, pyrido); 9.85 (s, 1H, CO.NH); 10.25 (s, 1H, CS.NH); and 7.15–7.85 (m, 4H, Ar–H). Anal. Calcd. for $C_{23}H_{20}O_4N_4S$: C, 61.59; H, 4.50; and N, 12.50. Found: C, 61.55; H, 4.48; and N, 12.47.

1-[6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(2-methylphenyl)thiourea (8i)

Yield = 60%, m.p. 235–237°C.

1-[6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(3-methylphenyl)thiourea (8j)

Yield = 52%, m.p. 237–239°C.

1-[6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(4-methylphenyl)thiourea (8k)

Yield = 60%, m.p. 251–253°C. IR (KBr) cm^{-1} : 3452 (NH); 3315 (OH); 2945, 2810 (CH); 1742 ($>\text{C=O}$ of quinolone); 1675 (amide-I); 1565 (amide-II); 1328 (C–N); 1245 (amide-III); and 1160 ($>\text{C=S}$). ^1H NMR (DMSO-d₆): δ 3.47 (m, 4H, $>\text{N}(\text{CH}_2)_2\text{O}$); 4.35 (s, 1H, CH₂OH); 8.75 (s, H-2, quinolone); 8.18 (s, H-5, quinolone); 8.05–9.25 (m, 3H, pyrido); 9.88 (s, 1H, CO.NH); 10.28 (s, 1H, CS.NH); 7.05–7.78 (m, 4H, Ar–H); and 2.44 (s, 3H, Ar–CH₃). Anal. Calcd. for $C_{23}H_{20}O_4N_4S$: C, 61.59; H, 4.50; and N, 12.50. Found: C, 61.54; H, 4.47; and N, 12.46.

1-[6-Hydroxy-1-(2-hydroxyethyl)-4-oxo-1,4-dihydro-[1,7]phenanthroline-3-carbonyl]-3-(3-chlorophenyl)thiourea (8l)

Yield = 51%, m.p. 246–248°C.

References

- Bhanot SK, Singh M, Chatterjee NR (2001) The chemical and biological aspects of fluoroquinolone: reality and dreams. Current Pharma Design 7:313–317
- Bhusari KP, Amnerkar ND, Khedekar PB, Kale MK, Bhole RP (2008) Synthesis and invitro antimicrobial activity of some new 4-amino-N-(1,3-benzothiazol-2-yl)benzenesulphonamide derivatives. Asian J Res Chem 1:53–57
- Briganti F, Scozzafava A, Supuran CT (1997) Sulfonylamido derivatives of aminoglutethimide and their copper(II) complexes: a

- novel class of antifungal compounds. *Eur J Med Chem* 32: 901–910
- Bromidge SM, Clarke SE, King FD, Lovell PJ, Newman H, Riley G, Routledge C, Serafinowska HT, Smith DR, Thomas DR (2002) Bicyclic piperazinylbenzenesulphonamides are potent and selective 5-HT₆ receptor antagonists. *Bioorg Med Chem Lett* 12: 1357–1360
- Brown GM (1962) Biosynthesis of folic acid. *J Bio Chem* 237:536–540
- Collee GJ, Fraser GA, Marmion PB, Simmon A (1996) Practical medical microbiology. Churcill Livinstone, Edinburg, pp 163–174
- Dannhardt G, Fiebich BL, Schweppenhäuser J (2002) COX-1/COX-2 inhibitors based on the methanone moiety. *Eur J Med Chem* 37:147–161
- Hirpara KV, Patel SP, Parikh KA, Bhimani AS, Parekh HH (2004) Preparation, characterisation and antimicrobial activities of some novel nitriles and imidazolines. *J Sci Islamic Rep Iran* 15(2):135–138
- Kamal A, Ahmed SK, Reddy KS, Khan MA, Shetty R, Siddhardha B, Murthy USN, Khan IA, Kumar M, Sharma S, Ram AB (2007) Anti-tubercular agents. Part IV: synthesis and antimycobacterial evaluation of nitroheterocyclic-based 1,2,4-benzothiadiazines. *Bioorg Med Chem Lett* 17:5419–5422
- Lee JK, Chang SJ (1994) Quinolone(II): synthesis of Fluoro-substituted pyrido[3,2-h] quinolone derivatives as potential antibacterials. *Korean J Med Chem* 4(2):92–100
- Lee JK, Chang SJ (1996) Quinolone(III): synthesis of pyrido[2,3-h] quinolone and pyrido [2,3-g] quinolone-3 carboxilic acid derivatives as potential antibacterials. *Bull Korean Chem Soc* 17:90–93
- Lee JK, Lee SH, Chang SJ (1992) New quinolones(I); Synthesis of new pyrido[3,2-h] quinoline derivatives and their antibacterial activity. *Bull Korean Chem Soc* 13(5):571–573
- Li JJ, Anderson GD, Burton EG, Cogburn JN, Collins JT, Garland DJ, Gregory SA, Huang H, Isakson PC (1995) 1,2-Diarylcyclopentenes as selective Cyclooxygenase-2 Inhibitors and orally active anti-inflammatory agents. *J Med Chem* 38:4570–4578
- Maruyama T, Seki N, Onda K, Suzuki T, Kawazoe S, Hayakawa M, Matsui T, Takasu T, Ohta M (2009) Discovery of novel thiourea derivatives as potent and selective β 3-adrenergic receptor agonists. *Bioorg Med Chem* 17:5510–5519
- Mitscher LA (2005) Bacterial topoisomerase inhibitors: quinolone and pyridone antibacterial agents. *Chem Rev* 105:559–592
- Reddy NS, Mallireddigari MR, Stephen C, Kiranmai G, Stanley B, Reddy P, Reddy R (2004) Synthesis of new coumarin 3-(N-aryl) sulfonamides and their anticancer activity. *Bioorg Med Chem Lett* 14:4093–4097
- Selvam P, Chandramohan M, De Clercq E, Witvrouw M, Pannecouque C (2001) Synthesis and anti-HIV activity of 4-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene) amino]-N(4,6-dimethyl-2-pyrimidinyl)-benzene sulfonamide and its derivatives. *Eur J Pharma Sci* 14:313–316
- Supuran CT, Scozzafava A, Jurca BC, Ilies MA (1998) Carbonic anhydrase inhibitors Carbonic anhydrase inhibitors—part 49: synthesis of substituted ureido and thioureido derivatives of aromatic/heterocyclic sulfonamides with increased affinities for isozyme. *Eur J Med Chem* 33:83–93
- Sycheva TP, Kiseleva ID, Shchukina MN (1966) The synthesis of compounds with potential antitubercular activity. *Chem Hetero Com* 2:526–528
- Turan-Zitouni G, Sivaci DM, Kaplancikli ZA, Ozdemir A (2002) Synthesis and antimicrobial activity of some pyridinylimino-thiazoline derivatives. *Farmacol* 57:569–572
- Venkatesh P, Pandeya SN (2009) Synthesis, characterisation and anti-inflammatory activity of some 2-amino benzothiazole derivatives. *Int J Chemtech Res* 1:1354–1358
- Yan Z, Cai X, Yang X, Song B, Chen Z, Bhadury P, Hu D, Jin L, Xue W, Lu P (2009) Synthesis and antiviral activities of chiral thiourea derivatives. *Chin J Chem* 27(3):593–601