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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Pyridoquinolones containing azetidinones: synthesis and their biological evaluation

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Abstract A series of pyridoquinolone 4-oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])quinoline-3-[*N*-(substituted phenyl methylidine)]carbohydrazide **3a–j** and 4-oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])-3-[*N*-{(3-chloro-2-oxo-4-(substituted phenyl) azetidine-1-yl)amino}carbonyl] quinoline **4a–j** have been synthesized via 4-oxo-1,4-dihydro-(4′-methyl-6′-chloropyrido[2,3-h])quinoline carboxylate **1**. All the compounds were proved by IR, ^{1}H-NMR, ^{13}C-NMR spectral studies and elemental analysis. Antibacterial activities (MIC) against *E. coli, P. aeruginosa, S. aureus* and *S. pyogenes,* and antifungal activities against *C. albicans, A. niger* and *A. clavatus* were screened, whereas selected compounds were screened against *Mycobacterium tuberculosis* $H_{37}Rv$ and compared with standard drugs.

Keywords Pyridoquinolone · Schiff base · Azetidinone · Antibacterial · Antifungal · Antitubarcular activity

Introduction

Quinolones are very important family of antibacterial agents that are widely prescribed for the treatment of infections in humans. The 4-pyridone-3-carboxylic acid associated with a 5, 6-fused aromatic ring is the common chemical feature of bactericidal quinolones. In the resulting bicyclic ring, the 1-, 5-, 6-, 7- and 8-positions are the major targets of chemical variation (Emami *et al.*, 2005). The first quinolone, nalidixic acid was introduced in 1962. The substance was discovered by George Lesher and coworkers in a distillate during chloroquine synthesis (Norris and Mandell, 1988; Leverkusan, 1999). Since then structural modifications have resulted in an important class of fluoroquinolones, which have improved coverage of gram-positive organisms. Quinolones rapidly inhibit DNA synthesis by promoting cleavage of bacterial DNA in the DNA-enzyme complexes of DNA gyrase and type IV topoisomerase, resulting in rapid bacterial death (Hooper, 1999).

Various substituted quinolone drugs like ciprofloxacin, norfloxacin, ofloxacin, levofloxacin, sparfloxacin, gatifloxacin, moxifloxacin, trovafloxacin, etc. have clinical applications in the disease of genitourinary tract infections, upper and lower respiratory infections, gastrointestinal infections, gynaecological infections, sexually transmitted diseases, some skin and soft tissue infections (Oliphant, 2002; Wolfson and Hooper, 1989; Hooper and Wolfson, 1991; Fang *et al*., 1991; Sabbaj *et al*., 1986; Hooper, 2000; Centers for diesease control and prevention, 1998).

Fluorinated pyridoquinolones have been synthesized by Lee and Chang (Lee *et al*., 1992) and their biological activity has been studied. We have concentrated on non-fluorinated pyridoquinolones, synthesized several compounds by incorporating various substituted urea, thiourea and piperazine compounds at C-3 position and studied their antimicrobial activities (Patel and Chauhan, 2005; Patel and Patel, 2010; Patel *et al.,* 2010a; Patel and Modi, 2010; Patel *et al*., 2010b), and found that these compounds showed good antimicrobial activities.

Furthermore the 2-azetidinones, commonly known as β-lactam unit is a crucial structural feature of one class of significant antibiotics and its stereo chemistry is very important to their biological activities. Traditionally, β-lactam is a part of the structure of broad spectrum antibiotic class of drugs: penicillins and cephalosporins (Toraskar *et al.*, 2010). Azetidinones were reported to posses antibacterial

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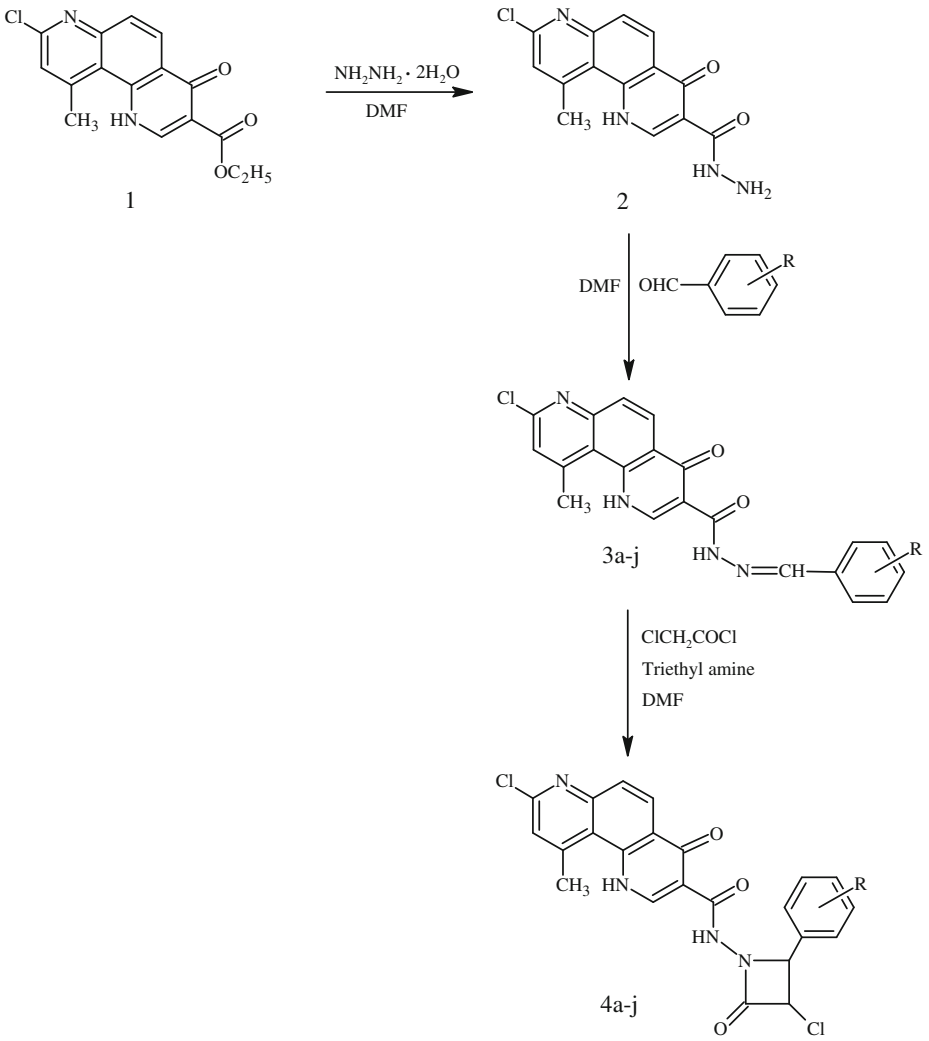

	a	b	c	d	e	f	g	h	i	j
3	-H	2-Cl	4-Cl	4-CH_3	2-OCH_3	4-OCH_3	3-OCH_3, 4-OH	2-O	2-OH, 3-NO_2	2-OH, 5-NO_2,
4	-H	2-Cl	4-Cl	4-CH_3	2-OCH_3	4-OCH_3	3-OCH_3, 4-OH	2-OH	2-OH, 3-NO_2	2-OH, 5-NO_2,

Scheme 1 Synthetic route of compounds 3a–j and 4a–j

(Patel and Patel, 2011), antifungal (Bhat *et al.*, 2007), antitubercular (Chikhalia *et al.*, 2006; Rajasekaran *et al.*, 2010), anticancer (Veinberg *et al.*, 2003), anticonvulsant (Kumar *et al.*, 2009a), anti-HIV (Mukund *et al.*, 1998), anti-inflammatory (Kumar *et al.* 2009b), ACAT and cholesterol absorption inhibitor (Burnett *et al.*, 1994) activities.

Limited study has been carried out on pyridoquinolone-based azetidinone scaffold, in view of this, we have selected this scaffold for further studies and enhanced our study to prepare pyridoquinolone analogues incorporating various azetidinones via substituted Schiff bases at C-3 position, which were screened for antibacterial and antifungal activities as well as antitubercular activity against *$H_{37}Rv$*.

Result and discussion

Chemistry

Schiff base derivatives 4-oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])quinoline-3-[*N*-(substituted phenyl methylidine)]carbohydrazide **3a–j** and azetidinones; 4-oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])-3-[*N*{(3-chloro-2-oxo-4-(substituted phenyl) azetidine-1-yl) amino}carbonyl]quinoline **4a–j** were synthesized; which is illustrated in the Scheme 1. The structures of all the compounds were confirmed by elemental analysis, IR, ^{1}H-NMR and ^{13}C-NMR spectral data.

Compounds **3a–j** and **4a–j** were confirmed by IR-spectra (cm^{-1}) absorption bands at 3424 (NH), 2925, 2842 (C–H), 1725 (>C=O), 1638 (amide-I), 1620 (–N=CH–), 1536 (amide-II), 1317 (C–N), 1240 (amide-III), 790 (C–Cl); other bands at 3230 (O–H), 1536, 1357 (NO_2, sym, asym), 1228, 1012 (C–O–C) were also observed due to substituted aldehydes. When compound **2** was reacted with substituted aldehydes, Schiff bases **3a–j** were formed which was confirmed by strong –N=CH– stretching band at 1620 cm^{-1}. The ^{1}H-NMR showed singlet at δ 8.66, 7.46, 2.72 of H_2, H_5 and -CH_3; whereas doublet at δ 12.40, 8.32 and 7.84 of >NH, H_5 and H_6 of pyridoquinolone ring, respectively, singlet at δ 7.5 of –N=CH– showed the presence of Schiff base in **3a–j**, which disappeared when it was converted to azetidinones **4a–j** and which was confirmed by doublet at δ 3.32 and 3.23 due to H_3 and H_4 of β-lactam ring, respectively. This was also confirmed by the ^{13}C-NMR for azetidinone ring signal of C=O at 166.6 the.

Antimicrobial activity

In vitro antimicrobial activities of all compounds were carried out by broth dilution method (Rattan, 2000), and MIC were screened against two gram-negative *E. coli*, *P. aeruginosa*; two gram-positive *S. aureus*, *S. pyogenes* bacteria, three fungal species *C. albicans*, *A. niger*, *A. clavatus*, and the selected compounds were screened against *Mycobacterium tuberculosis* $H_{37}Rv$. Ampicillin, chloramphenicol, ciprofloxacin and norfloxacin for antibacterial; nystatin and griseofulvin for antifungal and isoniazide for antitubercular were used as standard drugs.

From the results (Table 1), the activity of **2** increased against both gram-negative, while decreased against both gram-positive bacteria. Compounds **3e** (R=2-OCH_3), and **3j** (R=2-OH, 5-NO_2) showed relatively strong activity against both *E. coli* and *P. aeruginosa*; however, **3g** (R=3-OCH_3, 4-OH), **3h** (R=2–OH) showed relatively strong activity against *S. aureus* compared with ampicillin. All the Schiff bases showed relatively poor activity against *S. pyogenes*.

Compounds **4a** (R=–H), **4c** (R=4-Cl), **4 h** (R=2-OH), **4i** (R=2-OH, 3-NO_2) showed relatively strong activity against *E. coli*; however, **4c** (R=4-Cl) showed relatively strong activity against *P. aeruginosa* compared with ampicillin. Remaining compounds were poor in activity compared with other drugs.

Activity of **2** decreased against all fungal species *C. albicans*, *A. niger* and *A. clavatus*. Compounds **3a** (R=-H), **3b** (R=2-Cl), **3d** (R=4-CH_3), **3g** (R=3-OCH_3, 4-OH), **3i** (R=2-OH, 3-NO_2) and **3j** (R=2-OH, 5-NO_2) showed relatively strong activity against *C. albicans* compared with nystatin; however, **3h** (R=2-OH) showed relatively strong activity against *C. albicans* compared with griseofulvin. **3c** (R=4-Cl) showed relatively strong activity against *A. niger* and *A. clavatus* compared with both nystatin and griseofulvin.

Compounds **4c** (R=4-Cl), **4d** (R=4-CH_3), **4e** (R=2-OCH_3) and **4j** (R=2-OH, 5-NO_2) showed relatively strong activity against *C. albicans* compared with griseofulvin; however, **4b** (R=2-Cl) showed relatively strong activity against *C. albicans* compared with nystatin and showed relatively strong activity against *A. niger*, and *A. clavatus* compared with griseofulvin.

Selected compounds were screened against *Mycobacterium tuberculosis (*Table 2). Compounds **3i** (R=2-OH, 3-NO_2) and **4c** (R=4-Cl) showed better activity among all the compounds, but poorer activity with isoniazide.

Conclusions

- When parent compound was converted into hydrazide, activity increased against gram-negative bacteria but decreased against gram-positive bacteria.
- Schiff base derivatives with 4-methoxy and 2-hydroxy-5-nitro substitution displayed strong activity against *E. coli* compared with ampicillin; with 2-chloro, 3-methoxy-4-hydroxy and 2-hydroxy substitution displayed strong activity against *S. aureus*.
- Azetidinones with 4-chloro, 2-hydroxy and 2-hydroxy-3-nitro substitution displayed strong activity against *E. coli*; however, 4-chloro substitution displayed relatively strong activity against *P. aeruginosa*.
- All the Schiff bases showed relatively strong activity against fungal species *C. albicans* and retained its activity when converted into azetidinones but poor against *A. niger* and *A. clavatus*.

Experimental

General

Melting points were determined on a Kofler melting point apparatus and are uncorrected. Conversions of reactions were monitored by TLC using Merck silica gel 60 F254 plates, and spots were visualized under UV radiation. ^{1}H and ^{13}C-NMR spectra were recorded in DMSO-d_6 solvent on Bruker Avance II-400 spectrometer at 400 MHz and 100 MHz, respectively, the chemical shifts are reported in part per million (δ ppm) using tetramethylsilane (TMS) as an internal standard. IR spectra were recorded in the range of 4000–600 cm^{-1} on a Thermo Scientific Nicolet iS10 FT-IR spectrometer using KBr pellets. Elemental analyses were performed on a Heraeus Carlo Erba 1180 CHN analyzer.

Table 1 Antibacterial and antifungal activity of synthesized compounds

Compd.	Antibacterial activity Minimal inhibition concentration (μg/ml)						
	Gram negative		Gram positive		Fungal species		
	E. coli	*P. aeruginosa*	*S. aureus*	*S. pyogenes*	*C. albicans*	*A. niger*	*A. clavatus*
1	250	250	150	100	200	1000	1000
2	100	200	250	200	500	>1000	>1000
3_a	250	250	200	250	250	>1000	>1000
3_b	500	500	100	200	250	500	>1000
3_c	500	1000	250	250	500	250	250
3_d	200	250	250	250	250	500	500
3_e	100	250	250	250	500	1000	1000
3_f	250	500	500	500	500	500	500
3_g	500	500	100	200	250	1000	1000
3_h	250	250	100	200	100	500	500
3_i	150	200	500	500	200	500	500
3_j	62.5	100	200	250	200	1000	1000
4_a	100	250	250	250	500	>1000	>1000
4_b	200	250	200	200	100	250	250
4_c	100	100	500	500	200	500	500
4_d	250	250	250	250	200	>1000	>1000
4_e	500	1000	250	500	250	>1000	>1000
4_f	250	250	500	500	500	>1000	>1000
4_g	250	500	1000	1000	1000	500	500
4_h	100	200	500	500	500	1000	1000
4_i	62.5	200	500	500	500	>1000	>1000
4_j	250	500	500	500	250	500	500
Ampicillin	100	100	250	100			
Chloramphenicol	50	50	50	50			
Ciprofloxacin	25	25	50	50			
Norfloxacin	10	10	10	10			
Nystatin					100	100	100
Griseofulvin					500	100	100

Table 2 Anti tubercular activity table

Compds	MIC values μg/ml of *M. tuberculosis* $H_{37}Rv$
1	500
2	200
3_e	250
3_g	500
3_h	200
3_i	62.5
3_j	500
4_a	250
4_c	100
4_h	500
4_i	200

Isoniazide was considered as a standard drug: 0.20 μg/ml 99% inhibition

General procedure for synthesis of compound 3a–j and 4a–j

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido [2,3-h])quinolone-3-carboxylate (**1**)*

The parent compound **1** was prepared from 2-chloro-4-methyl quinoline which underwent a nitration (Krahler and Burger, 1941), and reduction (Gamble *et al.,* 2007) was followed by condensation (Lee and Chang, 1994) with diethyl ethoxy methylene malonate and cyclization (Lee and Chang, 1996) in diphenyl ether.

2-Chloro-4-methyl quinoline under nitration using fuming HNO_3 and conc. H_2SO_4 (98%) formed 2-chloro-4-methyl-5-nitro quinoline, which on reduction by using Fe/

CH_3COOH formed 2-chloro-4-methyl-5-amino quinoline, followed by condensation with diethyl ethoxy methylene malonate to give (2-chloro-4-methyl quinolin-5-yl)amino] methylenemalonate; 0.01 mol of the obtained product was suspended in 30 ml of diphenyl ether and refluxed for 3 h at 250°C, the reaction mixture was cooled to room temperature and kept it to settle for one day. The resulting solid was filtered and washed with petroleum ether and recrystallized from DMF to give pure product of **1**.

Yield = 60%, m.p. 280–282°C; IR (KBr) cm^{-1}: 3417 (NH), 2920, 2845 (C–H), 1725 (>C=O), 1340 (C–N), 780 (C–Cl); ^1H NMR (DMSO-d_6): δ 12.40 (d, 1H, NH), 8.66 (s, 1H, H_2), 8.35 (d, 1H, H_5), 7.80 (d, 1H, H_6), 7.46 (s, 1H, H_5, of pyrido), 4.32 (q, 2H, CH_2), 2.74 (s, 3H, CH_3 of pyrido), 1.40 (t, 3H, CH_3); ^{13}C NMR (DMSO-d_6): δ 187, 172.7, 154.2, 148, 145.5, 138.1, 136.6, 129, 122, 120.2, 117.1, 110.1, 108.7, 40.1, 18, 13.4; Anal. Calcd. for $C_{16}H_{13}ClN_2O_3$: C 60.67, H 4.14, N 8.84. Found: C 60.62, H 4.10, N 8.81.

4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido [2,3-h])quinolone-3-carbohydrazide (2)

A mixture of **1** (0.005 mol) and hydrazine hydrate (0.01 mol) in 30 ml DMF was refluxed on water bath for 6 h. Conversion of reaction was periodically observed by TLC using mobile phase toluene to methanol (9:1). The reaction mixture was concentrated by distilled-off solvent and poured into crushed ice. The solid separated, was washed with water, dried and recrystallized from DMF, and the crystals of **2** were obtained.

Yield = 64%, m.p. 250–252°C; IR (KBr) cm^{-1}: 3410 (NH), 2915, 2847 (C–H), 1719 (>C=O), 1645 (amide-I), 1530 (amide-II), 1320 (C–N), 1244 (amide-III), 784 (C–Cl); ^1H NMR (DMSO-d_6): δ 12.42 (d, 1H, NH), 8.84 (s, 1H, >CO–NH), 8.62 (s, 1H, H_2), 8.33 (d, 1H, H_5), 7.82 (d, 1H, H_6), 7.44 (s, 1H, H_5, of pyrido), 4.36 (s, 2H, $–NH_2$), 2.75 (s, 3H, CH_3 of pyrido); ^{13}C NMR (DMSO-d_6): δ 185.5, 170.6, 153.3, 149.9, 144.4, 137, 136.1, 127.2, 122.3, 120.1, 117.7, 109.9, 108.4, 18.2; Anal. Calcd. for $C_{14}H_{11}ClN_4O_2$: C 55.55, H 3.66 N 18.51. Found: C 55.50, H 3.62, N 18.48.

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido [2,3-h])quinoline-3-[N-(substituted phenyl methylidine)]carbohydrazide (**3a–j**)*

An equimolar amount of **2** (0.005 mol) and substituted aromatic aldehyde (0.005 mol), along with 2–3 drops of glacial acetic acid were taken in 10 ml of dry DMF, and the reaction mixture was refluxed for 4–6 h on water bath. Conversion of reaction was periodically observed by TLC using mobile phase toluene to methanol (9:1). After the completion of the reaction mixture, it was poured into crushed ice, and the product was filtered, washed with water and recrystallized from DMF to give **3**.

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])quinoline-3-[N-(phenyl methylidine)] carbohydrazide (**3a**)* Yield = 60%, m.p. 256–258°C; IR (KBr) cm^{-1}: 3424 (NH), 2925, 2842 (C–H), 1725 (>C=O), 1638 (amide-I), 1620 (–N=CH–), 1536 (amide-II), 1317 (C–N), 1240 (amide-III), 790 (C–Cl); ^1H NMR (DMSO-d_6): δ 12.40 (d, 1H, NH), 8.80 (s, 1H, >CONH), 8.66 (s, 1H, H_2), 8.32 (d, 1H, H_5), 7.84 (d, 1H, H_6), 7.5 (s, 1H, –N=CH–), 7.46 (s, 1H, H_5, of pyrido), 7.2–8.4 (m, 5H, Ar–H), 2.72 (s, 3H, CH_3 of pyrido); ^{13}C NMR (DMSO-d_6): δ 185.7, 171.4, 155.9, 154.1, 149.7, 144.1, 138, 136.2, 131.1, 130.4, 129, 128.2, 127.6, 122.1, 120, 116.9, 109.2, 108.7, 18.4; Anal. Calcd. for $C_{21}H_{15}ClN_4O_2$: C 64.54, H 3.87, N 14.34. Found: C 64.58, H 3.82, N 14.30.

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])quinoline-3-[N-(2-chlorophenyl methylidine)]carbohydrazide **(3b)*** Yield = 62%, m.p. 251–253°C; IR (KBr) cm^{-1}: 3415 (NH), 2922, 2830 (C–H), 1717 (>C=O), 1670 (amide-I), 1627 (–N=CH–), 1525 (amide-II), 1317 (C–N), 1250 (amide-III), 778 (C–Cl); ^1H NMR (DMSO-d_6): δ 12.42 (d, 1H, NH), 8.82 (s, 1H, >CONH), 8.65 (s, 1H, H_2), 8.33 (d, 1H, H_5), 7.86 (d, 1H, H_6), 7.46 (s, 1H, –N=CH–), 7.41 (s, 1H, H_5, of pyrido), 7.30–8.55 (m, 4H, Ar–H), 2.70 (s, 3H, CH_3 of pyrido); ^{13}C NMR (DMSO-d_6): δ 180.7, 172.4, 155.1, 154.2, 149.3, 144.4, 138.2, 136.3, 134.4, 131.4, 130.3, 129, 128.3, 127.9, 122.4, 119.7, 116.7, 108.9, 108.1, 17.7; Anal. Calcd. for $C_{21}H_{14}Cl_2N_4O_2$: C 59.31, H 3.32, N 13.17. Found: C 59.35, H 3.37, N 13.12.

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])quinoline-3-[N-(4-chlorophenyl methylidine)]carbohydrazide **(3c)*** Yield = 56%, m.p. 255–257°C; IR (KBr) cm^{-1}: 3395 (NH), 2928, 2842 (C–H), 1719 (>C=O), 1637 (amide-I), 1620 (–N=CH–), 1531 (amide-II), 1322 (C–N), 1254 (amide-III), 796 (C–Cl); ^1H NMR (DMSO-d_6): δ 12.46 (d, 1H, NH), 8.70 (s, 1H, >CONH), 8.60 (s, 1H, H_2), 8.38 (d, 1H, H_5), 7.80 (d, 1H, H_6), 7.50 (s, 1H, –N=CH–), 7.45 (s, 1H, H_5, of pyrido), 7.42-8.45 (m, 4H, Ar–H), 2.72 (s, 3H, CH_3 of pyrido); ^{13}C NMR (DMSO-d_6): δ 182.6, 172.9, 154.4, 153.2, 148.7, 144.1, 138.6, 135.3, 131.9, 130.1, 129.2, 128.4, 126.4, 120.9, 119.4, 117.6, 108.9, 108, 17.9; Anal. Calcd. for $C_{21}H_{14}Cl_2N_4O_2$: C 59.31, H 3.32, N 13.17. Found: C 59.37, H 3.25, N 13.22.

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])quinoline-3-[N-(4-methylphenyl methylidine)]carbohydrazide **(3d)*** Yield = 58%, m.p. 262-264°C; IR (KBr) cm^{-1}: 3414 (NH), 2917, 2845 (C–H), 1717 (>C=O), 1645 (amide-I), 1617 (–N=CH–), 1531 (amide-II), 1321 (C–N), 1238

(amide-III), 782 (C–Cl); ^{1}H NMR (DMSO-d_6): δ 12.40 (d, 1H, NH), 8.74 (s, 1H, >CONH), 8.63 (s, 1H, H_2), 8.29 (d, 1H, H_5), 7.85 (d, 1H, H_6), 7.48 (s, 1H, –N=CH–), 7.40 (s, 1H, $H_{5'}$ of pyrido), 7.0–8.55 (m, 4H, Ar–H), 2.74 (s, 3H, CH_3 of pyrido), 1.6 (s, 3H, -CH_3);); ^{13}C NMR (DMSO-d_6): δ 182.2, 171.4, 154.9, 153.1, 147.6, 144, 138.2, 134.3, 130.7, 130, 129.1, 127.9, 126.2, 120.4, 119, 116.9, 110.1, 108, 22.4, 18.1; Anal. Calcd. for $C_{22}H_{17}ClN_4O_2$: C 65.27, H 4.23, N 13.84. Found: C, 65.32, H 4.27, N 13.90.

4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])quinoline-3-[N-(-2-methoxy phenyl methylidine)]carbohydrazide ***(3e)*** Yield = 62%, m.p. 270–272°C; IR (KBr) cm^{-1}: 3410 (NH), 2924, 2850 (C–H), 1721 (>C=O), 1639 (amide-I), 1629 (–N=CH–), 1533 (amide-II), 1322 (C–N), 1237 (amide-III), 1230, 1025 (C–O–C), 792 (C–Cl); ^{1}H NMR (DMSO-d_6): δ 12.48 (d, 1H, NH), 8.80 (s, 1H, >CONH), 8.60 (s, 1H, H_2), 8.33 (d, 1H, H_5), 7.82 (d, 1H, H_6), 7.46 (s, 1H, –N=CH–), 7.41 (s, 1H, $H_{5'}$ of pyrido), 7.25–8.40 (m, 4H, Ar–H), 3.77 (s, 3H, –OCH_3), 2.75 (s, 3H, CH_3 of pyrido); ^{13}C NMR (DMSO-d_6): δ 180.4, 172.6, 164.4, 155.5, 152.4, 147.1, 143.8, 137.2, 136.2, 134.1, 130.4, 129.4, 128.1, 126.7, 120.1, 119, 117.7, 110, 108.2, 54.2, 18.2; Anal. Calcd. for $C_{22}H_{17}ClN_4O_3$: C 62.79, H 4.07, N 13.31. Found: C 62.70, H 4.02, N 13.35.

4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])quinoline-3-[N-(-4-methoxy phenyl methylidine)]carbohydrazide ***(3f)*** Yield = 62%, m.p. 263–265°C; IR (KBr) cm^{-1}: 3405 (NH), 2924, 2856 (C–H), 1725 (>C=O), 1644 (amide-I), 1622 (–N=CH–), 1531 (amide-II), 1319 (C–N), 1240 (amide-III), 1228, 1012 (C–O–C), 786 (C–Cl); ^{1}H NMR (DMSO-d_6): δ 12.50 (d, 1H, NH), 8.78 (s, 1H, >CONH), 8.63 (s, 1H, H_2), 8.30 (d, 1H, H_5), 7.84 (d, 1H, H_6), 7.48 (s, 1H, –N=CH–), 7.40 (s, 1H, $H_{5'}$ of pyrido), 7.42–8.48 (m, 4H, Ar–H), 3.70 (s, 3H, –OCH_3), 2.68 (s, 3H, CH_3 of pyrido); ^{13}C NMR (DMSO-d_6): δ 186.2, 172.1,166.5, 155.2, 152.1, 146.1, 142.9, 137.7, 136.4, 134, 130.2, 128.9, 126.5, 120.3, 119.4, 117.1, 109.9, 108.4, 56.3, 18.7; Anal. Calcd. for $C_{22}H_{17}ClN_4O_3$: C 62.79, H 4.07, N 13.31. Found: C 62.82, H 4.12, N 13.36.

4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])quinoline-3-[N-(3-methoxy-4-hydroxy phenyl methylidine)]carbohydrazide ***(3g)*** Yield = 65%, m.p. 254–256°C; IR (KBr) cm^{-1}: 3407 (NH), 3230 (O–H), 2930, 2849 (C–H), 1720 (>C=O), 1641 (amide-I), 1619 (–N=CH–), 1533 (amide-II), 1324 (C–N), 1236 (amide-III), 1223, 1017 (C–O–C), 790 (C–Cl); ^{1}H NMR (DMSO-d_6): δ 12.40 (d, 1H, NH), 8.76 (s, 1H, >CONH), 8.64 (s, 1H, H_2), 8.36 (d, 1H, H_5), 7.82 (d, 1H, H_6), 7.47 (s, 1H, –N=CH–), 7.39 (s, 1H, $H_{5'}$ of pyrido), 7.25–8.30 (m, 3H, Ar–H), 4.90 (s, 1H, –OH), 3.72 (s, 3H, –OCH_3), 2.72 (s, 3H, CH_3 of pyrido); ^{13}C NMR (DMSO-d_6): δ 185.3, 172.5, 160.2, 155.5, 152.4, 145.4, 141.7, 138.2, 136, 134.5, 133.9, 130.7, 128.4, 125.9, 120.1, 119.1, 117.3, 110.4, 108.1, 55.7, 18.1; Anal. Calcd. for $C_{22}H_{17}ClN_4O_4$: C 60.49, H 3.92, N 12.83. Found: C 60.55, H 3.88, N 12.80.

4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])quinoline-3-[N-(2-hydroxy phenyl methylidine)]carbohydrazide ***(3h)*** Yield = 62%, m.p. 258–260°C; IR (KBr) cm^{-1}: 3399 (NH), 3222 (O–H), 2928, 2830 (C–H), 1725 (>C=O), 1647 (amide-I), 1624 (–N=CH–), 1527 (amide-II), 1319 (C–N), 1242 (amide-III), 792 (C–Cl); ^{1}H NMR (DMSO-d_6): δ 12.44 (d, 1H, NH), 8.78 (s, 1H, >CONH), 8.63 (s, 1H, H_2), 8.41 (d, 1H, H_5), 7.78 (d, 1H, H_6), 7.51 (s, 1H, –N=CH–), 7.38 (s, 1H, $H_{5'}$ of pyrido), 7.30–8.50 (m, 4H, Ar–H), 4.95 (s, 1H, –OH), 2.68 (s, 3H, CH_3 of pyrido); ^{13}C NMR (DMSO-d_6): δ 184.2, 169.4, 158.1, 154.7, 152.1, 146.1, 141.4, 138.9, 136.2, 134.6, 133.2, 131.2, 128.9, 126.2, 120.4, 119, 117.7, 110, 108.7, 18.9; Anal. Calcd. for $C_{21}H_{15}ClN_4O_3$: C 62.00, H 3.72, N 13.77. Found: C 62.10, H 3.76, N 13.71 (Fig. 1).

4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])quinoline-3-[N-(2-hydroxy-3-nitro phenyl methylidine)]carbohydrazide ***(3i)*** Yield = 60%, m.p. 255-257°C; IR (KBr) cm^{-1}: 3417 (NH), 3224 (O–H), 2922, 2844 (C–H), 1717 (>C=O), 1645 (amide-I), 1621 (–N=CH–), 1529 (amide-II), 1536, 1357 (NO_2, sym, asym), 1317 (C–N), 1246 (amide-III), 793 (C–Cl); ^{1}H NMR (DMSO-d_6): δ 12.38 (d, 1H, NH), 8.70 (s, 1H, >CONH), 8.61 (s, 1H, H_2), 8.38 (d, 1H, H_5), 7.75 (d, 1H, H_6), 7.49 (s, 1H, –N=CH–), 7.42 (s, 1H, $H_{5'}$ of pyrido), 7.38–8.40 (m, 3H, Ar–H), 4.92 (s, 1H, –OH), 2.72 (s, 3H, CH_3 of pyrido); ^{13}C NMR (DMSO-d_6): δ 183.1, 170.5, 159.2, 155.5, 151, 146.4, 141.7, 139.2, 136, 134.1, 133.6, 132.1, 130.7, 128.4, 126.5, 121.5, 120.1, 117.6, 110.4, 108.6, 18.7; Anal. Calcd. for $C_{21}H_{14}ClN_5O_5$: C 55.82, H 3.12, N 15.50. Found: C 55.90, H 3.18, N 15.42.

Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])quinoline-3-[N-(2-hydroxy-5-nitro phenyl methylidine)]carbohydrazide ***(3j)*** Yield = 58%, m.p. 250–252°C; IR (KBr) cm^{-1}: 3422 (NH), 3217 (O–H), 2920, 2837 (C–H), 1721 (>C=O), 1648 (amide-I), 1617 (–N=CH–), 1533 (amide-II), 1532, 1352 (NO_2, sym, asym), 1322 (C–N), 1248 (amide-III), 787 (C–Cl); ^{1}H NMR (DMSO-d_6): δ 12.44 (d, 1H, NH), 8.75 (s, 1H, >CONH), 8.64 (s, 1H, H_2), 8.34 (d, 1H, H_5), 7.80 (d, 1H, H_6), 7.51 (s, 1H, –N=CH–), 7.43 (s, 1H, $H_{5'}$ of pyrido), 7.25-8.35 (m, 3H, Ar–H), 4.90 (s, 1H, –OH), 2.68 (s, 3H, CH_3 of pyrido); ^{13}C NMR (DMSO-d_6): δ 184.2, 171.6, 161.1, 154.9, 151.2, 146.7, 142.4, 139.7, 136.2, 134.5, 133.4, 132, 130.4, 127.2, 126.9, 121.4, 119.7, 117.1, 110.2, 109.1, 18.2; Anal. Calcd. for $C_{21}H_{14}ClN_5O_5$: C 55.82, H 3.12, N 15.50. Found: C 55.86, H 3.17, N 15.61.

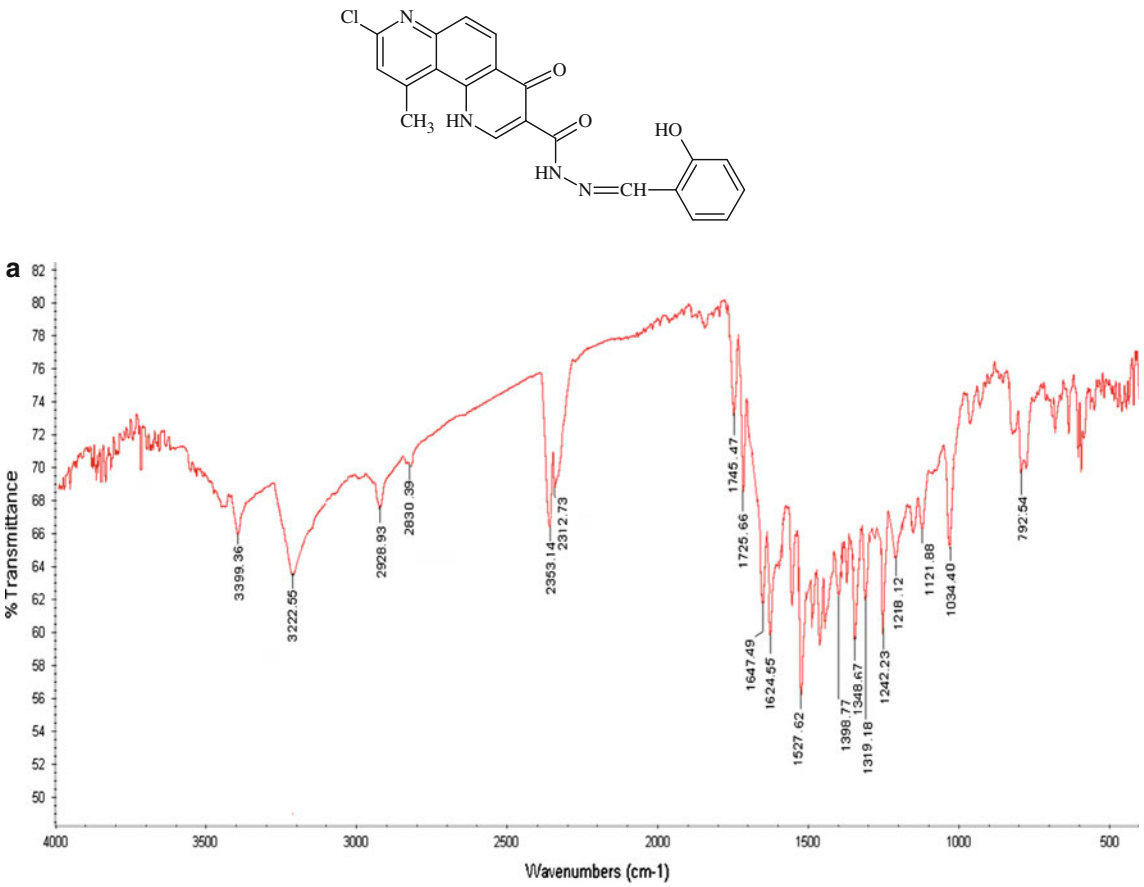

Fig. 1 **a** IR, **b** ^{1}H-NMR, **c** ^{13}C-NMR spectra of compound (**3h**)

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])-3-[N-{(3-chloro-2-oxo-4-(substituted phenyl) azetidine-1-yl) amino}carbonyl]quinoline (**4a–j**)*

Chloroacetyl chloride (0.0025 mol) was added drop wise into the solution of **3** (0.0025 mol) in DMF (50 ml) under stirring below 10°C, and triethyl amine (0.0025 mol) was added into reaction mixture and refluxed for 14–18 h. Conversion of reaction was periodically observed by TLC using mobile phase toluene to methanol (9:1). Reaction mixture was concentrated by distilled-off solvent and poured into crushed ice. The product filtered, washed with water and recrystallized from DMF to give **4**.

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])-3-[N-{(3-chloro-2-oxo-4-phenyl azetidine-1-yl)amino}carbonyl]quinoline **(4a)*** Yield = 62%, m.p. 265–267°C; IR (KBr) cm^{-1}: 3418 (NH), 2922, 2840 (C–H), 1719 (>C=O), 1646 (amide-I), 1525 (amide-II), 1327 (C–N), 1239 (amide-III), 790 (C–Cl); ^{1}H NMR (DMSO-d$_6$): δ 12.40 (d, 1H, NH), 8.64 (s, 1H, >CONH), 8.67 (s, 1H, H$_2$), 8.34 (d, 1H, H$_5$), 7.81 (d, 1H, H$_6$), 7.47 (s, 1H, H$_5$, of pyrido), 7.24–8.45 (m, 5H, Ar–H), 3.32 (d, 1H, CH of azetidinone), 3.23 (d, 1H, CH–Cl of azetidinone), 2.70 (s, 3H, CH$_3$ of pyrido); ^{13}C NMR (DMSO-d$_6$): δ 184.2, 169.4, 166.6, 156.1, 150.5, 144.2, 142.2, 138, 136.4, 129.6, 128.2,127, 125.5, 122.1, 120.6, 117.9, 110.2, 108.4, 65.3, 62.4, 18; Anal. Calcd. for $C_{23}H_{16}Cl_2N_4O_3$: C 59.11, H 3.45, N 11.99. Found: C 59.17, H 3.40, N 11.80.

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])-3-[N-{(3-chloro-2-oxo-4-(2-chloro phenyl)azetidine-1-yl)amino} carbonyl]quinoline (**4b**)* Yield = 65%, m.p. 260–262°C; IR (KBr) cm^{-1}: 3421 (NH), 2930, 2850 (C–H), 1717 (>C=O), 1668 (amide-I), 1526 (amide-II), 1323 (C–N), 1243 (amide-III), 786 (C–Cl); ^{1}H NMR (DMSO-d$_6$): δ 12.50 (d, 1H, NH), 8.70 (s, 1H, >CONH), 8.60 (s, 1H, H$_2$), 8.37 (d, 1H, H$_5$), 7.85 (d, 1H, H$_6$), 7.46 (s, 1H, H$_5$, of pyrido), 7.4-8.40 (m, 4H, Ar–H), 3.30 (d, 1H, CH of azetidinone), 3.21 (d, 1H, CH–Cl of azetidinone), 2.68 (s, 3H, CH$_3$ of pyrido); ^{13}C NMR (DMSO-d$_6$): δ 184.6, 169.1, 166.2, 155.9, 150.9, 143.7, 141.5, 138.7, 136.1, 134.7, 129.5, 128.7, 127.1, 124.6, 121.7, 120.1, 117.2, 109.7, 108.1, 65.5, 62.7, 18.4; Anal. Calcd. for $C_{23}H_{15}Cl_3N_4O_3$: C 55.06, H 3.01, N 11.17. Found: C 55.01, H 3.07, N 11.12.

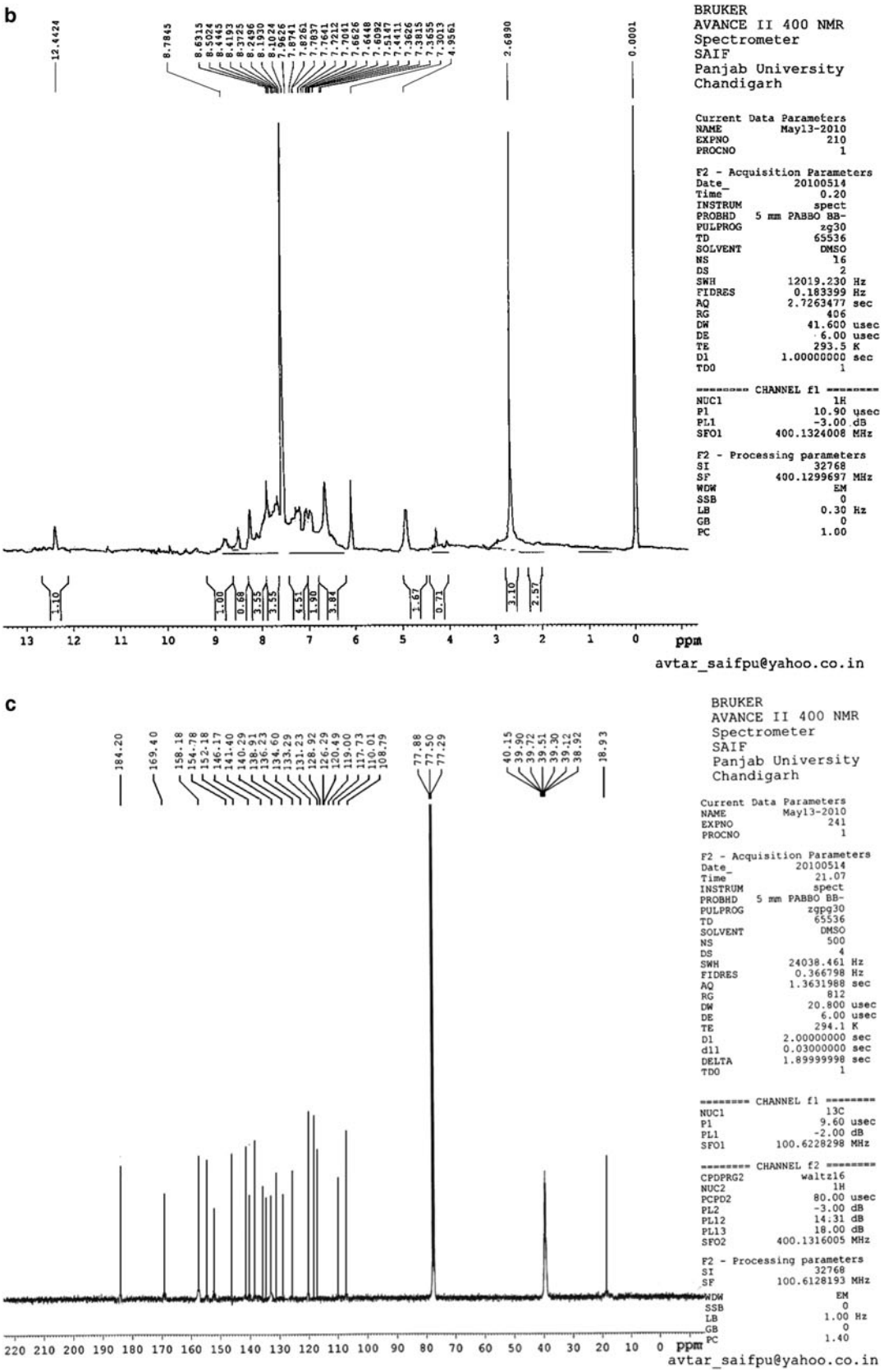

Fig. 1 contiuned

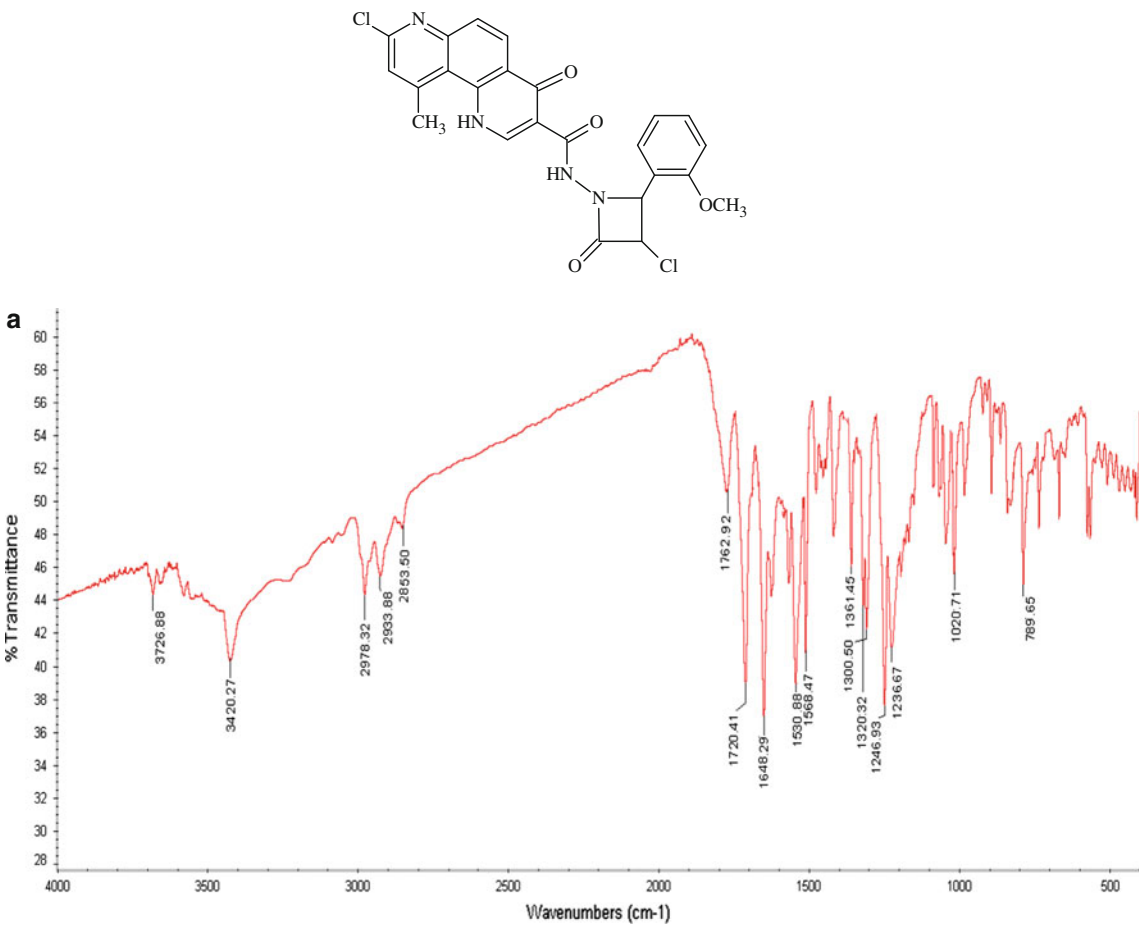

Fig. 2 **a** IR, **b** ^{1}H-NMR **c** ^{13}C-NMR spectra of compound (**4e**)

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])-3-[N-{(3-chloro-2-oxo-4-(4-chloro phenyl)azetidine-1-yl)amino} carbonyl]quinoline (**4c**)* Yield = 58%, m.p. 256–258°C; IR (KBr) cm^{-1}: 3405 (NH), 2918, 2836 (C–H), 1722 (>C=O), 1637 (amide-I), 1534 (amide-II), 1318 (C–N), 1245 (amide-III), 787 (C–Cl); ^{1}H NMR (DMSO-d$_6$): δ 12.55 (d, 1H, NH), 8.75 (s, 1H, >CONH), 8.64 (s, 1H, H$_2$), 8.30 (d, 1H, H$_5$), 7.80 (d, 1H, H$_6$), 7.41 (s, 1H, H$_{5'}$ of pyrido), 7.45-8.40 (m, 4H, Ar–H), 3.31 (d, 1H, CH of azetidinone), 3.19 (d, 1H, CH-Cl of azetidinone), 2.71 (s, 3H, CH$_3$ of pyrido); ^{13}C NMR (DMSO-d$_6$): δ 185.1, 169.4, 165.5, 155.4, 150.1, 144.5, 141.6, 137.5, 136.2, 129.1, 128.4, 126.7, 124.5, 120.5, 119.9, 117.1, 110.2, 108.2, 64.7, 63.1, 17.9; Anal. Calcd. for $C_{23}H_{15}Cl_3N_4O_3$: C 55.06, H 3.01, N 11.17. Found: C 55.10, H 3.07, N 11.25.

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])-3-[N-{(3-chloro-2-oxo-4-(4-methyl phenyl)azetidine-1-yl)amino} carbonyl]quinoline (**4d**)* Yield = 61%, m.p. 261–263°C; IR (KBr) cm^{-1}: 3407 (NH), 2927, 2834 (C–H), 1725 (>C=O), 1640 (amide-I), 1536 (amide-II), 1319 (C–N), 1243 (amide-III), 790 (C–Cl); ^{1}H NMR (DMSO-d$_6$): δ 12.58 (d, 1H, NH), 8.76 (s, 1H, >CONH), 8.66 (s, 1H, H$_2$), 8.28 (d, 1H, H$_5$), 7.77 (d, 1H, H$_6$), 7.39 (s, 1H, H$_{5'}$ of pyrido), 7.45–8.30 (m, 4H, Ar–H), 3.34 (d, 1H, CH of azetidinone), 3.24 (d, 1H, CH-Cl of azetidinone), 2.75 (s, 3H, CH$_3$ of pyrido), 1.48 (s, 3H, -CH$_3$); ^{13}C NMR (DMSO-d$_6$): δ 185.4, 168.9, 164.7, 155.6, 150.5, 145.1, 141.3, 138.2, 136.1, 129.3, 127.9, 126.1, 125.1, 120.1, 119.7, 117.2, 110, 108.1, 64.5, 63.4, 22.4, 18.1; Anal. Calcd. for $C_{24}H_{18}Cl_2N_4O_3$: C 59.89, H 3.77, N 11.64. Found: C 59.80, H 3.72, N 11.69.

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])-3-[N-{(3-chloro-2-oxo-4-(2-methoxy-phenyl)azetidine-1-yl)amino} carbonyl]quinoline (**4e**)* Yield = 62%, m.p. 272–274°C; IR (KBr) cm^{-1}: 3420 (NH), 2933, 2853 (C–H), 1720 (>C=O), 1648 (amide-I), 1530 (amide-II), 1320 (C–N), 1246 (amide-III), 1236, 1020 (C–O–C), 789 (C–Cl); ^{1}H NMR (DMSO-d$_6$): δ 12.55 (d, 1H, NH), 8.80 (s, 1H, >CONH), 8.68 (s, 1H, H$_2$), 8.30 (d, 1H, H$_5$), 7.80 (d, 1H, H$_6$), 7.41 (s, 1H, H$_{5'}$ of pyrido), 7.45–8.40 (m, 4H, Ar–H), 3.31 (d, 1H, CH of azetidinone), 3.70 (s, 3H, -OCH$_3$), 3.19 (d, 1H, CH-Cl of azetidinone), 2.71 (s, 3H, CH$_3$ of

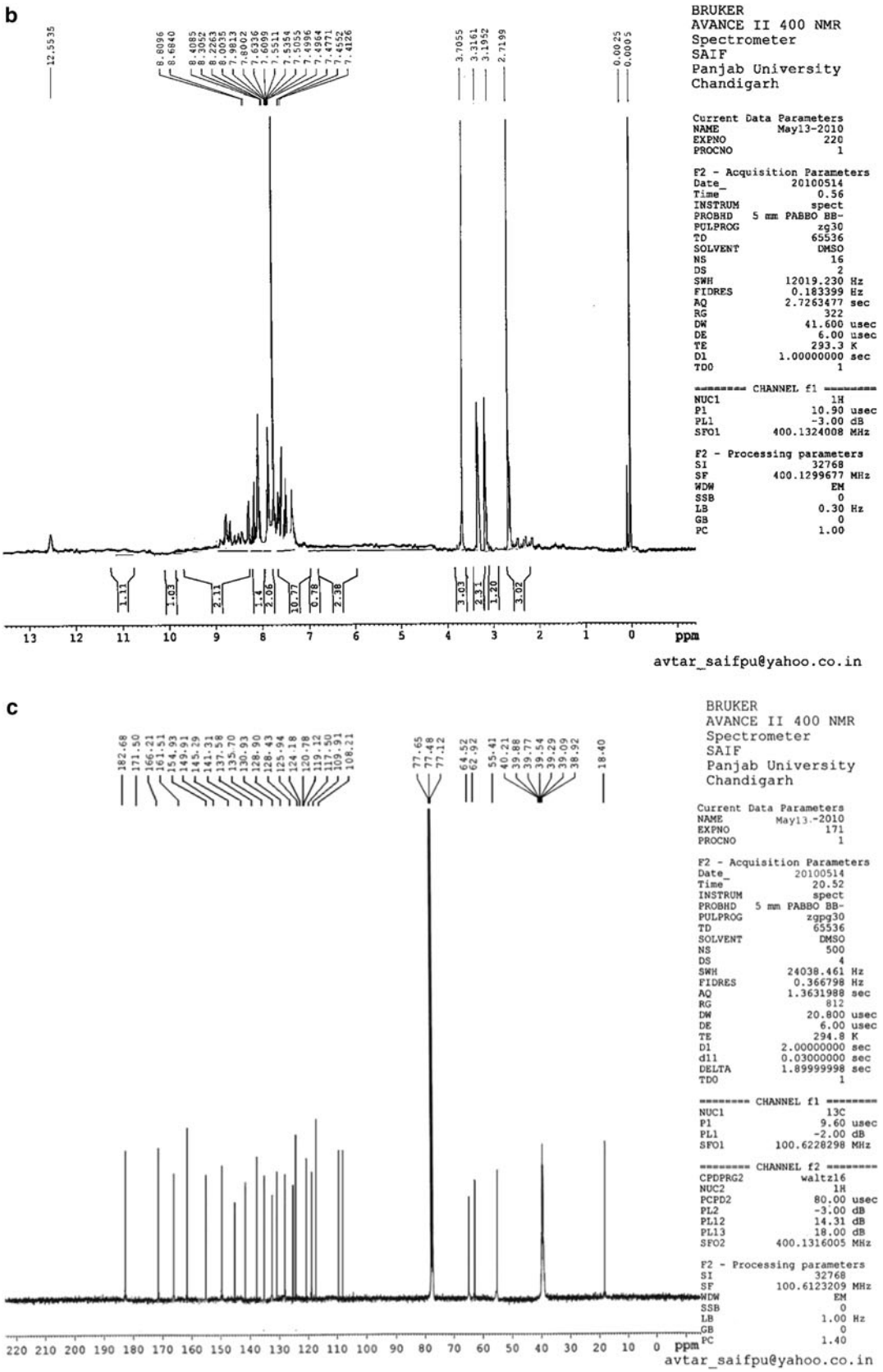

Fig. 2 continued

pyrido);); ^{13}C NMR (DMSO-d_6): δ 182.6, 171.5, 166.2, 161.5, 154.9, 149.9, 145.2, 141.3, 137.5, 135.7, 130.9, 128.4, 125.9, 124.1, 120.7, 119.1, 117.5, 109.9, 108.2, 64.5, 62.9, 55.4, 18.4; Anal. Calcd. for $C_{24}H_{18}Cl_2N_4O_4$: C 57.96, H 3.65, N 11.27. Found: C 57.99, H 3.60, N 11.22 (Fig. 2).

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])-3-[N-{(3-chloro-2-oxo-4-(4-methoxy phenyl)azetidine-1-yl)amino} carbonyl]quinoline (**4f**)* Yield = 56%, m.p. 271–273°C; IR (KBr) cm^{-1}: 3418 (NH), 2933, 2850 (C–H), 1721 (>C=O), 1647 (amide-I), 1534 (amide-II), 1319 (C–N), 1248 (amide-III), 1231, 1030 (C–O–C), 791 (C–Cl); ^{1}H NMR (DMSO-d_6): δ 12.40 (d, 1H, NH), 8.71 (s, 1H, >CONH), 8.66 (s, 1H, H_2), 8.37 (d, 1H, H_5), 7.80 (d, 1H, H_6), 7.44 (s, 1H, $H_{5'}$ of pyrido), 7.35–8.48 (m, 4H, Ar–H), 3.28 (d, 1H, CH of azetidinone), 3.17 (d, 1H, CH–Cl of azetidinone), 3.74 (s, 3H, –OCH_3), 2.66 (s, 3H, CH_3 of pyrido); ^{13}C NMR (DMSO-d_6): δ 184.1, 170.7, 165.7, 160.1, 155.1, 150.1, 145.4, 140.9, 137.7, 135.2, 131.5, 128.9, 125.2, 120.7, 119.2, 117.1, 110.2, 108.4, 64.6, 62.4, 56.1, 18.1; Anal. Calcd. for $C_{24}H_{18}Cl_2N_4O_4$: C 57.96, H 3.65, N 11.27. Found: C 58.02, H 3.60, N 11.21.

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])-3-[N-{(3-chloro-2-oxo-4-(3-methoxy-4-hydroxy phenyl)azetidine-1-yl)amino}carbonyl]quinoline (**4g**)* Yield = 62%, m.p. 276-278°C; IR (KBr) cm^{-1}: 3425 (NH), 3234 (O–H), 2930, 2855 (C–H), 1717 (>C=O), 1640 (amide-I), 1529 (amide-II), 1323 (C–N), 1243 (amide-III), 1225, 1022 (C–O–C), 787 (C–Cl); ^{1}H NMR (DMSO-d_6): δ 12.50 (d, 1H, NH), 8.80 (s, 1H, >CONH), 8.62 (s, 1H, H_2), 8.31 (d, 1H, H_5), 7.76 (d, 1H, H_6), 7.38 (s, 1H, $H_{5'}$ of pyrido), 7.48-8.40 (m, 3H, Ar–H), 4.95 (s, 1H, -OH), 3.76 (s, 3H, –OCH_3), 3.32 (d, 1H, CH of azetidinone), 3.20 (d, 1H, CH-Cl of azetidinone), 2.70 (s, 3H, CH_3 of pyrido); ^{13}C NMR (DMSO-d_6): δ 184.2, 172.4, 166.2, 160.4, 156.4, 151.2, 150.4, 145.3, 141.4, 138.3, 134.9, 131.1, 129.2, 125.1, 120.2, 119.6, 117.2, 110.7, 108.1, 64.2, 62.1, 55.7, 18.9; Anal. Calcd. for $C_{24}H_{18}Cl_2N_4O_5$: C 56.15, H 3.53, N 10.91. Found: C 56.22, H 3.45, N 10.84.

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])-3-[N-{(3-chloro-2-oxo-4-(2-hydroxy phenyl)azetidine-1-yl)amino} carbonyl]quinoline (**4h**)* Yield = 65%, m.p. 275-277°C; IR (KBr) cm^{-1}: 3422 (NH), 3240 (O–H), 2910, 2830 (C–H), 1716 (>C=O), 1648 (amide-I), 1527 (amide-II), 1320 (C–N), 1242 (amide-III), 789 (C–Cl); ^{1}H NMR (DMSO-d_6): δ 12.42 (d, 1H, NH), 8.76 (s, 1H, >CONH), 8.64 (s, 1H, H_2), 8.35 (d, 1H, H_5), 7.78 (d, 1H, H_6), 7.46 (s, 1H, $H_{5'}$ of pyrido), 7.40–8.50 (m, 4H, Ar–H), 4.92 (s, 1H, –OH), 3.32 (d, 1H, CH of azetidinone), 3.22 (d, 1H, CH-Cl of azetidinone), 2.74 (s, 3H, CH_3 of pyrido); ^{13}C NMR (DMSO-d_6): δ 185.1, 173.2, 166.7, 156.7, 151.9, 150.1, 144.7, 142.5, 138.9, 136.6, 135.1, 131.4, 129.5, 124.7, 120.1, 119.1, 117.7, 110.1, 108.7, 64.7, 62.2, 18.1; Anal. Calcd. for $C_{23}H_{16}Cl_2N_4O_4$: C 57.16, H 3.34, N 11.59. Found: C 57.22, H 3.30, N 11.51.

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])-3-[N-{(3-chloro-2-oxo-4-(2-hydroxy-3-nitro phenyl(azetidine-1-yl)amino}carbonyl]quinoline (**4i**)* Yield = 55%, m.p. 266-268°C; IR (KBr) cm^{-1}: 3417 (NH), 3236 (O–H), 2920, 2841 (C–H), 1723 (>C=O), 1643 (amide-I), 1530 (amide-II), 1540, 1351 (NO_2, sym, asym), 1318 (C–N), 1243 (amide-III), 792 (C–Cl); ^{1}H NMR (DMSO-d_6): δ 12.58 (d, 1H, NH), 8.82 (s, 1H, >CONH), 8.66 (s, 1H, H_2), 8.30 (d, 1H, H_5), 7.74 (d, 1H, H_6), 7.38 (s, 1H, $H_{5'}$ of pyrido), 7.44–8.52 (m, 3H, Ar–H), 4.90 (s, 1H, -OH), 3.33 (d, 1H, CH of azetidinone), 3.20 (d, 1H, CH-Cl of azetidinone), 2.66 (s, 3H, CH_3 of pyrido); ^{13}C NMR (DMSO-d_6): δ 183.5, 171.7, 166.2, 155.5, 152.2, 150.4, 144.2, 141.7, 138.3, 136.5, 135.1, 131.3, 128.9, 126.6, 125.2, 120.2, 119.7, 117.2, 110.2, 108.5, 65.1, 62.6, 18.9; Anal. Calcd. for $C_{23}H_{15}Cl_2N_5O_6$: C 52.29, H 2.86, N 13.26. Found: C 52.34, H 2.80, N 13.31.

*4-Oxo-1,4-dihydro(4′-methyl-6′-chloropyrido[2,3-h])-3-[N-{(3-chloro-2-oxo-4-(2-hydroxy-5-nitro phenyl)azetidine-1-yl)amino}carbonyl]quinoline (**4j**)* Yield = 58%, m.p. 268–270°C; IR (KBr) cm^{-1}: 3420 (NH), 3240 (O–H), 2933, 2841 (C–H), 1723 (>C=O), 1640 (amide-I), 1534 (amide-II), 1538, 1360 (NO_2, sym, asym), 1317 (C–N), 1246 (amide-III), 794 (C–Cl); ^{1}H NMR (DMSO-d_6): δ 12.56 (d, 1H, NH), 8.62 (s, 1H, >CONH), 8.61 (s, 1H, H_2), 8.36 (d, 1H, H_5), 7.78 (d, 1H, H_6), 7.40 (s, 1H, $H_{5'}$ of pyrido), 7.40–8.55 (m, 3H, Ar–H), 4.96 (s, 1H, –OH), 3.30 (d, 1H, CH of azetidinone), 3.23 (d, 1H, CH-Cl of azetidinone), 2.68 (s, 3H, CH_3 of pyrido); ^{13}C NMR (DMSO-d_6): δ 184.4, 172.6, 166.4, 156.1, 152.7, 150.1, 145.1, 142.4, 138.5, 136.1, 135.1, 131.2, 129.1, 126.9, 125.1, 120.7, 120.1, 117.5, 110.1, 108.7, 64.4, 62.5, 18.5; Anal. Calcd. for $C_{23}H_{15}Cl_2N_5O_6$: C 52.29, H 2.86, N 13.26. Found: C 52.36, H 2.79, N 13.18.

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