J. Indian Chem. Soc.,
Vol. 86, October 2009, pp. 1072-1078

Synthesis and pharmacological studies on some phthalimidoxy substituted quinoline derivatives

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Manuscript received 30 September 2008, revised 1 April 2009, accepted 26 June 2009

Abstract : Synthesis of novel *N'*-[2-(4-substitutedphenyl)-3-*N*-ethoxyphthalimido-5-oxoimidazolidene-1-yl]-2-(quinoline-8-yloxy)acetamide derivatives (6a-e) with potential biological activities were carried out by adopting the reaction scheme given below. Compound ethyl-(quinoline-8-yloxy)acetate (2) was synthesized by refluxing 8-hydroxyquinoline with ethylchloroacetate in presence of K_2CO_3 . Ethyl-(quinoline-8-yloxy)acetate (2) was converted to corresponding hydrazide (3) on treatment with hydrazine hydrate which on further condensation with various araldehydes gave respective Schiff's bases (4a-e). These on cyclisation with glycine yielded corresponding oxoimidazolidenes (5a-e). Active H of imidazolidinones (5a-e) was replaced by ethoxy phthalimide to yield final products (6a-e).

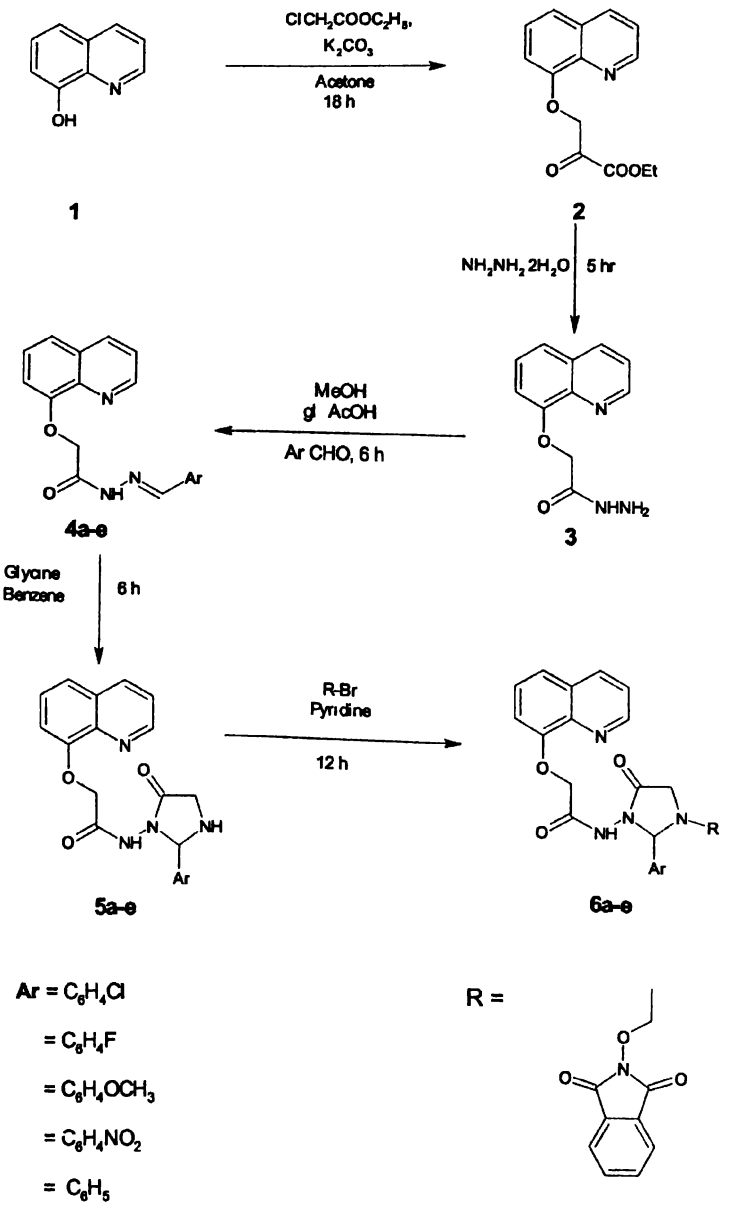
Keywords : 8-Hydroxyquinoline, oxoimidazolidene, ethoxy phthalimide.

Introduction

The diverse biological activities of various functional derivatives of quinolines are well known. Some of the quinoline derivatives have found application in clinical medicine due to there pronounced antiHIV[1], antitumor[2], antiasthamatic[3], antibacterial[4], antifungal[5], antiviral[6], anti-inflammatory[7] and antimalarial[8-11] activities. Interest in the synthesis of many substituted quinolines has been reviewed due to their use as general synthetic building blocks and their wide occurrence in natural products[12] as well as biologically active compounds[13]. Substituted imidazoles are reported to possess interesting pharmacological activities such as antimicrobial[14], antiviral[15], antineoplastic[16], analgesic[17], antiinflammatory[18], antihypertensive[19], vasodilating[20] etc. In view of above mentioned facts and in connection with our on going work on the synthesis of alkoxyphthalimide derivatives of heterocycles, it appeared expedient to synthesize *N'*-[2-(4-substitutedphenyl)-3-*N*-ethoxyphthalimido-5-oxoimidazolidene-1-yl]-2-(quinoline-8-yloxy)acetamides (**6a-e**) via a series of reactions.

Results and discussion

Ethyl-(quinolin-8-yloxy)acetate (**2**) has been synthesized by condensation of 8-hydroxyquinoline (**1**) with ethylchloroacetate in dry acetone. In the IR spectrum of compound **2**, bands in the range of 1745 cm^{-1} were obtained due to C=O stretching. Signals at 4.97 (singlet), 3.22 (quartet) and 2.28 ppm (triplet) in ^1H NMR spectrum, proved the presence of $-CH_2COOC_2H_5$ group. Compound **2** on refluxing with hydrazine hydrate, yielded 2-(quinoline-8-yloxy)acetohydrazide (**3**). N-H stretching in IR spectrum of **3** was observed at 3435 cm^{-1}, which was absent in precursor. In the ^1H NMR spectrum the characteristic proton of CONH group was observed at 8.40 ppm as a singlet. Compound **3** on reaction with various aromatic aldehydes gave *N'*-[(4-substitutedphenyl)-methylidene]-2-(quinoline-8-yloxy)acetohydrazide derivatives (**4a-e**), which on cyclisation with glycine in benzene afforded *N*-[2-(4-substitutedphenyl)-5-oxoimidazolidene-1-yl]-2-(quinoline-8-yloxy)acetamide (**5a-e**). Structure of the product was elucidated further on the basis of IR and ^1H NMR spectra. In IR spectra characteristic C=O group was observed as a strong band at 1705 cm^{-1} in all these compounds. Signals of NH, CH and CH_2 protons of imidazolidinone in ^1H NMR were observed at 10.05, 5.60 and 4.38 ppm as singlet respectively, which indicates the formation of imidazolidinoquinoline (**5a**). *N'*-[2-(4-Substitutedphenyl)-3-*N*-ethoxyphthalimido-5-oxoimidazoli-



Reaction Scheme

dene-1-yl]-2-(quinoline-8-yloxy)acetamide (**6a-e**) were prepared by reaction of imidazolidinoquinolines and phthalimidoxyethyl bromide in alcohol using pyridine as base. Disappearance of NH singlet of imidazolidinone group and appearance of two new triplets attributed to phthalimidoxy group confirmed the completion of the reaction, which was further supported by molecular ion peak in the mass spectra.

Antimicrobial activity :

Five synthesized compounds **6a-e** were *in vitro* screened for their antibacterial and antifungal activity using 100 µg/ml concentration in DMF by cup and well method[21]. The micro-organisms *Proteus mirabilis*, *Bacillus subtilis*, *Klebsiella pneumoniae*, *Escherichia coli* were used as bacterial strains, *Candida albicans* (MTCC 227),

Aspergillus fumigatus (MTCC 2550) were used as fungal strains. Drugs, Ciprofloxacin, Roxithromycin for antibacterial and Amphotericin B, Flucanozole for antifungal were used as reference drugs for comparison. By visualizing the antimicrobial data given in Table 2 it could be observed that most of the synthesized compounds **6a-e** show poor activity against *K. pneumoniae* as compared to both standard drugs except compound **6e** which shows stronger activity compared to standard drug Roxithromycin. All synthesized compounds show moderate activity against *P. mirabilis*. Compound **6c** shows moderate to stronger activity against all bacterial strains used for testing but shows stronger activity against both the fungal strains. Compound **6e** shows good activity against *E. coli* but very poor activity against fungal strains compared to standard drugs.

Conclusively, **6c** and **6e** may be considered as important compounds in pharmacological research against fungal and bacterial strains respectively.

Experimental

Melting points of all synthesized compounds were taken (in open capillaries) and are uncorrected. Percentages of nitrogen were determined on Elementar Vario EL III Carlo Alba 1108. IR spectra (KBr) were recorded on FT-IR RX1 Perkin-Elmer spectrophotometer and ^{1}H NMR were determined on Bruker DRX 300 MHz spectrometer using TMS as internal standard. The FAB mass spectra were recorded on JEOL SX-102/DA-6000 mass spectrometer. Purity of the synthesized compounds was checked by TLC using silica gel-G plates using *n*-hexane-ethylacetate as developing solvent and the spots were exposed in iodine chamber. Phthalimidoxyethyl bromide was synthesized by literature method[22]. Physical and analytical data are given in Table 1.

Table 1. Physical and analytical data of synthesized compounds

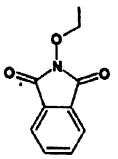
Compd.	Mol. formula	Mol. weight	Ar	R	Yield (%)	M.p. (°C)	Analysis of N (%) : Calcd.	Found.
2	$C_{14}H_{13}NO_4$	249	-	-	80	60	5.40	5.32
3	$C_{11}H_{11}N_3O_2$	217	-	-	84	140	19.34	19.24
4a	$C_{18}H_{14}ClN_3O_2$	339.5	4-Chlorophenyl	-	70	132	12.38	12.31
4b	$C_{18}H_{14}FN_3O_2$	323	4-Fluorophenyl	-	67	128	13.00	12.91
4c	$C_{19}H_{17}N_3O_3$	335	4-Methoxyphenyl	-	63	149	12.53	12.46
4d	$C_{18}H_{14}N_4O_4$	350	4-Nitrophenyl	-	62	172	16.00	15.93
4e	$C_{18}H_{15}N_3O_2$	305	Phenyl	-	65	108	13.77	13.69
5a	$C_{20}H_{17}ClN_4O_3$	396.5	4-Chlorophenyl	-	67	272	14.14	14.02
5b	$C_{20}H_{17}FN_4O_3$	380	4-Fluorophenyl	-	61	278	14.73	14.66
5c	$C_{21}H_{20}N_4O_4$	392	4-Methoxyphenyl	-	58	258	14.28	14.20
5d	$C_{20}H_{17}N_5O_5$	407	4-Nitrophenyl	-	54	298	17.19	17.11
5e	$C_{20}H_{18}N_4O_3$	362	Phenyl	-	60	262	15.46	15.40
6a	$C_{30}H_{24}ClN_5O_6$	585.5	4-Chlorophenyl		61	210	11.96	11.91
6b	$C_{30}H_{24}FN_5O_6$	569	4-Fluorophenyl		57	218	12.30	12.24
6c	$C_{31}H_{27}N_5O_7$	581	4-Methoxyphenyl		56	192	12.04	11.92
6d	$C_{30}H_{24}N_6O_8$	596	4-Nitrophenyl		50	222	14.09	13.98
6e	$C_{30}H_{25}N_5O_6$	551	Phenyl		53	207	12.70	12.62

Table 2. Antimicrobial activity of compounds (**6a-e**)

Compd.	Zone of inhibition (mm) (activity index)[a]					
	Antibacterial activity			Antifungal activity		
	P. mirabilis	*B. subtilis*	*K. pneumoniae*	*E. coli*	*C. albicans*	*A. fumigatus*
	13	6		11	10	7
6a	(0.92) C_1	(0.54) C_1	NA	(0.91) C_1	(0.83) C_1	(1.16) C_1
	(1.30) C_2	(1.00) C_2		(1.10) C_2	(1.66) C_2	(2.33) C_2
	15	8	4	11	9	3
6b	(1.07) C_1	(0.72) C_1	(0.32) C_1	(0.91) C_1	(0.75) C_1	(0.50) C_1
	(1.50) C_2	(1.33) C_2	(0.66) C_2	(1.10) C_2	(1.50) C_2	(1.00) C_2
	11	12	7	15	14	11
6c	(0.79) C_1	(1.09) C_1	(0.58) C_1	(1.25) C_1	(1 17) C_1	(1.83) C_1
	(1.10) C_2	(2.00) C_2	(1.17) C_2	(1.50) C_2	(2.33) C_2	(3.67) C_2
	14	13	5	5		8
6d	(1.00) C_1	(1.18) C_1	(0.42) C_1	(0.42) C_1	NA	(1.33) C_1
	(1.40) C_2	(2.17) C_2	(0.83) C_2	(0.83) C_2		(2.67) C_2
	10	3	10	16	6	4
6e	(0.71) C_1	(0.27) C_1	(0.83) C_1	(1.33) C_1	(0.50) C_1	(0.67) C_1
	(1.00) C_2	(0.50) C_2	(1.67) C_2	(1.60) C_2	(1.00) C_2	(1.33) C_2
C_1	14	11	12	12	12	6
C_2	10	6	6	10	6	3

[a]Activity index = Inhibition zone of compound/Inhibition zone of the standard drug.

For antibacterial activity : C_1 = Ciprofloxacin, C_2 = Roxithromycin.

For antifungal activity : C_1 = Amphotericin B, C_2 = flucanazole.

NA = Nil activity.

Synthesis of ethyl-(quinolin-8-yloxy)acetate (**2**) :

A mixture of 8-hydroxyquinoline (**1**) (0.01 mol), ethylchloroacetate (0.01 mol) and anhydrous K_2CO_3 (0.02 mol) in dry acetone was refluxed on a water bath for 18 h. It was then filtered and solvent was removed under reduced pressure, resulting solid was crystallized from ethanol. IR (KBr, cm^{-1}) : 3021 (C-H str., ArH), 2951, 2831 (C-H str., CH_3), 1745 (C=O str.), 1614 (C=N str.), 1095 (C-O str.); ^1H NMR (δ) : 4.97 (2H, s, CH_2), 3.22 (2H, q, CH_2), 2.28 (3H, t, CH_3).

Synthesis of 2-(quinolin-8-yloxy)acetohydrazide (**3**) :

A mixture of compound **2** (0.01 mol) and hydrazine hydrate (0.02 mol) in ethanol was refluxed on a water bath for 5 h. Reaction mixture was cooled. The solid separated was washed with water, dried and recrystallized from ethanol. White needle shaped crystals were obtained. IR (KBr, cm^{-1}) : 3435 (N-H str.), 1690 (C=O str.).

Synthesis of N'-{[(4-chlorophenyl)methylidene]-2-(quinolin-8-yloxy)}acetohydrazide (**4a**) :

An equimolar mixture of compound **3** and 4-chlorobenzaldehyde were dissolved in methanol and refluxed for 6 h using glacial acetic acid in catalytic amount. The solution was concentrated and after cooling obtained solid was filtered off, dried and recrystallized from methanol. IR (KBr, cm^{-1}) : 3421 (N-H str.), 1638 (C=N str.), 776 (C-Cl str.); ^1H NMR (δ) : 8.31 (1H, s, NH), 7.81-7.04 (10H, m, ArH), 6.98 (1H, s, =CH-Ar), 5.35 (2H, s, CH_2-CO).

Similarly, other compounds **4b-e** were also synthesized, their characteristic data are given below :

N'-{[(4-Fluorophenyl)methylidene]-2-(quinolin-8-yloxy)}acetohydrazide (**4b**) :

IR (KBr, cm^{-1}) : 3417 (N-H str.), 1631 (C=N str.), 1156 (C-F str.); ^1H NMR (δ) : 8.27 (1H, s, NH), 7.79-7.10 (10H, m, ArH), 6.96 (1H, s, =CH-Ar), 5.31 (2H, s, CH_2-CO).

N'-{[(4-Methoxyphenyl)methylidene]-2-(quinolin-8-yloxy)}acetohydrazide (**4c**) :

IR (KBr, cm^{-1}) : 3429 (N-H str.), 1623 (C=N str.), 1017 (C-O str.); ^1H NMR (δ) : 8.30 (1H, s, NH), 7.84-7.09 (10H, m, ArH), 6.89 (1H, s, =CH-Ar), 5.29 (2H, s, CH_2-CO), 3.79 (3H, s, CH_3).

N'-{[(4-Nitrophenyl)methylidene]-2-(quinolin-8-yloxy)}acetohydrazide (**4d**) :

IR (KBr, cm^{-1}) : 3408 (N-H str.), 1628 (C=N str.), 1532, 1326 (NO_2 asym. and sym. str.); ^1H NMR (δ) : 8.22 (1H, s, NH), 7.74-7.14 (10H, m, ArH), 6.93 (2H, s, =CH-Ar), 5.30 (2H, s, CH_2-CO).

N'-{[(Phenyl)methylidene]-2-(quinolin-8-yloxy)}-acetohydrazide (**4e**) :

IR (KBr, cm^{-1}) : 3418 (N-H str.), 1632 (C=N str.); ^1H NMR (δ) : 8.29 (1H, s, NH), 7.77-6.98 (11H, m, ArH), 6.93 (1H, s, =CH-Ar), 5.27 (2H, s, CH_2-CO).

Synthesis of N-[2-(4-chlorophenyl)-5-oxoimidazolidene-1-yl]-2-(quinolin-8-yloxy)acetamide (**5a**) :

Equimolar amount of **4a** and glycine in benzene was refluxed for 6 h with azeotropic elimination of water. Excess solvent was evaporated and obtained solid was filtered, dried and recrystallized from dry ethanol.

IR (KBr, cm^{-1}) : 3340 (N-H str.), 1705 (C=O str.), 1690 (C=O str., -CONH), 1640 (C=N str.), 751 (C-Cl str.); ^1H NMR (δ) : 10.05 (1H, s, NH), 8.72 (1H, s, NH-CO), 8.45-7.26 (10H, m, ArH), 5.60 (1H, s, =CH-Ar), 5.25 (2H, s, CH_2-O), 4.38 (2H, s, -CH_2-NH).

Compounds **5b-e** were prepared in similar way with minor changes in reflux time. Their spectral data are given below :

N-[2-(4-Fluorophenyl)-5-oxoimidazolidene-1-yl]-2-(quinolin-8-yloxy)acetamide (**5b**) :

IR (KBr) : 3332 (N-H str.), 1701 (C=O str.), 1691 (C=O str., -CONH), 1631 (C=N str.), 1170 (C-F str.); ^1H NMR (δ) : 10.00 (1H, s, NH), 8.69 (1H, s, NH-CO), 8.40-7.22 (10H, m, ArH), 5.66 (1H, s, =CH-Ar), 5.21 (2H, s, CH_2-O), 4.30 (2H, s, -CH_2-NH).

N-[2-(4-Methoxyphenyl)-5-oxoimidazolidene-1-yl]-2-(quinolin-8-yloxy)acetamide (**5c**) :

IR (KBr, cm^{-1}) : 3337 (N-H str.), 1700 (C=O str.), 1685 (C=O str., -CONH), 1634 (C=N str.), 1090 (C-O str.); ^1H NMR (δ) : 10.11 (1H, s, NH), 8.77 (1H, s, NH-CO), 8.42-7.20 (10H, m, ArH), 5.63 (1H, s, =CH-Ar), 5.18 (2H, s, CH_2-O), 4.34 (2H, s, -CH_2-NH), 3.84 (3H, s, OCH_3).

N-[2-(4-Nitrophenyl)-5-oxoimidazolidene-1-yl]-2-(quinolin-8-yloxy)acetamide (**5d**) :

IR (KBr, cm^{-1}) : 3326 (N-H str.), 1710 (C=O str.), 1690 (C=O str., -CONH), 1630 (C=N str.), 1072 (C-O str.), 1552, 1338 (NO_2 asym. and sym. str.); ^1H NMR (δ) : 9.96 (1H, s, NH), 8.66 (1H, s, NH-CO), 8.41-7.16 (10H, m, ArH), 5.69 (1H, s, =CH-Ar), 5.17 (2H, s, CH_2-O), 4.30 (2H, s, -CH_2-NH).

N-[2-Phenyl-5-oxoimidazolidene-1-yl]-2-(quinolin-8-yloxy)acetamide (**5e**) :

IR (KBr, cm^{-1}) : 3329 (N-H str.), 1703 (C=O str.), 1682 (C=O str., -CONH), 1633 (C=N str.); ^1H NMR (δ) : 9.93 (1H, s, NH), 8.76 (1H, s, NH-CO), 8.40-7.11 (11H, m, ArH), 5.55 (1H, s, =CH-Ar), 5.20 (2H, s, CH_2-O), 4.29 (2H, s, -CH_2-NH).

Synthesis of N'-[2-(4-chlorophenyl)-3-N-ethoxyphthalimido-5-oxoimidazolidene-1-yl]-2-(quinolin-8-yloxy)-acetamide (**6a**) :

To a solution of **5a** (0.01 mol) in absolute ethanol (50 ml), phthalimidoxyethyl bromide (0.01 mol) and a few drops of pyridine were added. The reaction mixture was refluxed for 12 h and poured into water. The resultant solid was filtered, dried and recrystallized from ethanol.

IR (KBr, cm^{-1}) : 1730 (C=O str., CO-N-CO), 1700 (C=O str., -CONH), 1634 (C=N str.), 905 (N-O str.), 824 (Ar-H bend, 1,4-disubs.), 751 (C-Cl str.); ^1H NMR (δ) : 8.78 (1H, s, NH), 7.41-6.73 (14H, m, ArH), 5.89 (1H, s, -CH-N), 5.30 (2H, s, -OCH_2-CO), 4.60 (2H, s, -NCH_2-CO), 4.18 (2H, t, -OCH_2CH_2), 3.69 (2H, t, -NCH_2CH_2); MS : *m/z* 587 $[M+2]^{+\bullet}$, 585 $[M]^{+\bullet}$, 555 $[M-CH_2O]^{+\bullet}$, 543 $[M-C_2H_2O]^{+\bullet}$, 337 $[M-C_{12}H_{12}N_2O_4]^{+\bullet}$, 328 $[M-C_{13}H_{11}N_3O_3]^{+\bullet}$, 310 $[M-C_{13}H_{13}N_3O_4]^{+\bullet}$, 270 $[C_{15}H_{11}ClN_2O]^{+\bullet}$, 202 $[C_{11}H_{10}N_2O_2]^{+\bullet}$, 132 $[C_8H_4O_2]^{+\bullet}$, 111 $[C_6H_4Cl]^{+\bullet}$, 104 $[C_7H_4O]^{+\bullet}$, 76 $[C_6H_4]^{+\bullet}$.

Same procedure was adopted for the synthesis of compounds **6b-e**. Their spectral data are given below :

N'-[2-(4-Fluorophenyl)-3-N-ethoxyphthalimido-5-oxoimidazolidene-1-yl]-2-(quinolin-8-yloxy)acetamide (**6b**) :

IR (KBr, cm^{-1}) : 1723 (C=O str., CO-N-CO), 1692 (C=O str., -CONH), 1630 (C=N str.), 1172 (C-F str.), 901 (N-O str.), 822 (Ar-H bend, 1,4-disubs.); ^1H NMR (δ) : 8.73 (1H, s, NH), 7.40-6.71 (14H, m, ArH), 5.82 (1H, s, -CH-N), 5.27 (2H, s, -OCH_2-CO), 4.57 (2H, s, -NCH_2-CO), 4.08 (2H, t, -OCH_2CH_2), 3.62 (2H, t, -NCH_2CH_2); MS : *m/z* 569 $[M]^{+\bullet}$, 539 $[M-CH_2O]^{+\bullet}$, 527 $[M-C_2H_2O]^{+\bullet}$, 321 $[M-C_{12}H_{12}N_2O_4]^{+\bullet}$, 312

$[M\text{-}C_{13}H_{11}N_3O_3]^{+\bullet}$, 294 $[M\text{-}C_{13}H_{13}N_3O_4]^{+\bullet}$, 257 $[C_{15}H_{11}FN_2O]^{+\bullet}$, 202 $[C_{11}H_{10}N_2O_2]^{+\bullet}$, 132 $[C_8H_4O_2]^{+\bullet}$, 121 $[C_7H_4FN]^{+\bullet}$, 104 $[C_7H_4O]^{+\bullet}$, 95 $[C_6H_4F]^{+\bullet}$, 76 $[C_6H_4]^{+\bullet}$.

N'-[2-(4-Methoxyphenyl)-3-N-ethoxyphthalimido-5-oxoimidazolidene-1-yl]-2-(quinolin-8-yloxy)acetamide (**6c**) :

IR (KBr, cm^{-1}) : 1727 (C=O str., CO-N-CO), 1695 (C=O str., -CONH), 1626 (C=N str.), 896 (N-O str.), 821 (Ar-H bend, 1,4-disubs.); ^1H NMR (δ) : 8.71 (1H, s, NH), 7.45-6.76 (14H, m, ArH), 5.84 (1H, s, -CH-N), 5.23 (2H, s, $-OCH_2-CO$), 4.52 (2H, s, $-NCH_2-CO$), 4.11 (2H, t, $-OCH_2CH_2$), 3.95 (3H, s, OCH_3), 3.57 (2H, t, $-NCH_2CH_2$); MS : *m/z* 581 $[M]^{+\bullet}$, 551 $[M\text{-}CH_2O]^{+\bullet}$, 539 $[M\text{-}C_2H_2O]^{+\bullet}$, 333 $[M\text{-}C_{12}H_{12}N_2O_4]^{+\bullet}$, 324 $[M\text{-}C_{13}H_{11}N_3O_3]^{+\bullet}$, 306 $[M\text{-}C_{13}H_{13}N_3O_4]^{+\bullet}$, 266 $[C_{16}H_{14}N_2O_2]^{+\bullet}$, 257 $[C_{13}H_{11}N_3O_3]^{+\bullet}$, 132 $[C_8H_4O_2]^{+\bullet}$, 133 $[C_8H_7NO]^{+\bullet}$, 104 $[C_7H_4O]^{+\bullet}$, 76 $[C_6H_4]^{+\bullet}$.

N'-[2-(4-Nitrophenyl)-3-N-ethoxyphthalimido-5-oxoimidazolidene-1-yl]-2-(quinolin-8-yloxy)acetamide (**6d**) :

IR (KBr, cm^{-1}) : 1728 (C=O str., CO-N-CO), 1683 (C=O str., -CONH), 1619 (C=N str.), 1556, 1338 (NO_2 asym. and sym. str.), 887 (N-O str.), 816 (Ar-H bend, 1,4-disubs.); ^1H NMR (δ) : 8.69 (1H, s, NH), 7.38-6.70 (14H, m, ArH), 5.82 (1H, s, -CH-N), 5.24 (2H, s, $-OCH_2-CO$), 4.55 (2H, s, $-NCH_2-CO$), 4.13 (2H, t, $-OCH_2CH_2$), 3.64 (2H, t, $-NCH_2CH_2$); MS : *m/z* 596 $[M]^{+\bullet}$, 554 $[M\text{-}C_2H_2O]^{+\bullet}$, 348 $[M\text{-}C_{12}H_{12}N_2O_4]^{+\bullet}$, 339 $[M\text{-}C_{13}H_{11}N_3O_3]^{+\bullet}$, 321 $[M\text{-}C_{13}H_{13}N_3O_4]^{+\bullet}$, 281 $[C_{15}H_{11}N_3O_3]^{+\bullet}$, 257 $[C_{13}H_{11}N_3O_3]^{+\bullet}$, 148 $[C_7H_4N_2O_2]^{+\bullet}$, 132 $[C_8H_4O_2]^{+\bullet}$, 104 $[C_7H_4O]^{+\bullet}$, 76 $[C_6H_4]^{+\bullet}$.

N'-[2-Phenyl-3-N-ethoxyphthalimido-5-oxoimidazolidene-1-yl]-2-(quinolin-8-yloxy)acetamide (**6e**) :

IR (KBr, cm^{-1}) : 1727 (C=O str., CO-N-CO), 1680 (C=O str., -CONH), 1626 (C=N str.), 888 (N-O str.); ^1H NMR (δ) : 8.71 (1H, s, NH), 7.56-6.66 (15H, m, ArH), 5.80 (1H, s, -CH-N), 5.18 (2H, s, $-OCH_2-CO$), 4.53 (2H, s, $-NCH_2-CO$), 4.12 (2H, t, $-OCH_2CH_2$), 3.57 (2H, t, $-NCH_2CH_2$); MS : *m/z* 551 $[M]^{+\bullet}$, 509 $[M\text{-}C_2H_2O]^{+\bullet}$, 303 $[M\text{-}C_{12}H_{12}N_2O_4]^{+\bullet}$, 294 $[M\text{-}C_{13}H_{11}N_3O_3]^{+\bullet}$, 276 $[M\text{-}C_{13}H_{13}N_3O_4]^{+\bullet}$, 257 $[C_{13}H_{11}N_3O_3]^{+\bullet}$, 236 $[C_{15}H_{12}N_2O]^{+\bullet}$, 132 $[C_8H_4O_2]^{+\bullet}$, 103 $[C_7H_5O]^{+\bullet}$, 77 $[C_6H_5]^{+\bullet}$.

Acknowledgement

Authors are thankful to the Head, Department of Chemistry, M. L. Sukhadia University, Udaipur, for providing laboratory facilities and to the Director, RSIC, CDRI, Lucknow, India for providing spectral and analytical data. Authors are grateful to Antimicrobial Research Laboratory, particularly Dr. Kanika Sharma, Department of Botany, M. L. Sukhadia University for evaluating antimicrobial activity. Two of the authors (DB and VS) are thankful to UGC and CSIR, New Delhi respectively for providing necessary financial assistance.

References

1. W. D. Wilson, M. Zhao, S. E. Patterson, R. L. Wydra, L. Janda and L. Strekowski, *Med. Chem. Res.*, 1992, **2**, 102.
2. G. J. Atwell, B. C. Baguley and W. A. Denny, *J. Med. Chem.*, 1989, **32**, 393.
3. Doube, M. Blouin, C. Brideau, C. Chan, C. Desmarais, D. Ethier, J. P. Falgueyret, R. W. Friesen, M. Girard, Y. Girard, J. Guay, P. Tagari and R. N. Young, *Bioorg. Med. Chem. Lett.*, 1998, **8**, 1255.
4. M. Kidwai, K. R. Bhushan, P. Sapra, R. K. Saxena and R. Gupta, *Bioorg. Med. Chem.*, 2000, **8**, 69.
5. I. K. Moissev, M. N. Zemtsova, P. L. Trakhteberg, D. A. Kulikowa, I. Pskobkina, G. N. Neshchadim and N. V. Ostapchuk, *Khim. Fram. Zh.*, 1998, **22**, 1448.
6. D. Narsinh and A. Shah, *Ind. J. Pharm. Sci.*, 2001, **63**, 211.
7. R. D. Dillard, D. E. Pavey and D. N. Benslay, *J. Med. Chem.*, 1973, **16**, 251.
8. G. R. Coatney, W. C. Cooper, N. B. Eddy and J. Greenderg, *Public Health Monogr.*, 1953, **15**, 322.
9. K. H. Rieckmann, M. Trenholme, R. L. Williams, P. E. Carson, H. Frisher and R. E. Desjardines, *Bull. World Health Organ.*, 1974, **51**, 375.
10. P. M. Neill, A. Kukhtar, P. A Stocks, L. E. Randle, S. Hindley, P. G. Bary and B. K. Park, *J. Med. Chem.*, 2003, **46**, 4933.
11. P. A. Stocks, K. J. Raynes, P. G. Bray, B. K. Park and S. A. Ward, *J. Med. Chem.*, 2002, **45**, 4975.
12. M. Balasubramanian and J. G. Keay, in "Comprehensive Heterocyclic Chemistry II", Pergamon Press, Oxford, 1996, **5**, 249.
13. G. Roma, M. D. Braccio, G. Grossi, F. Mattioli and M. Ghia, *Eur. J. Med. Chem.*, 2000, **35**, 1021.
14. R. A. Coburn, M. T. Clarck, R. T. Evans and R. J. Genco, *J. Med. Chem.*, 1987, **30**, 205.
15. B. Insuasty, F. Fernandez, J. Quiroga, R. Martinez, R. Gavino and E. Angeles, *Heterocycl. Commun.*,

2002, **8**, 151.

16. I. Islam, E. B. Skibo, R. T. Dorr and D. S. Alberts, *J. Med. Chem.*, 1991, **34**, 2954.
17. K. Ito, H. Kagaya, T. Fukuda, K. Yoshino and T. Nose, *Arzneim.-Forsch.*, 1982, **32**, 49.
18. A. Mertens, B. Muller-Backmann, W. Kampe, J. P. Holck and W. VonderSall, *J. Med. Chem.*, 1987, **30**, 1279.
19. K. Kubo, Y. Inada, Y. Kohara, Y. Sugiura, M. Ojima, K. Itoh, Y. Furukawa, Y. K. Nishikawa and T. Naka, *J. Med. Chem.*, 1993, **36**, 1772.
20. P. Demenge, G. Carraz, C. L. Duc and C. Silice, *Arzneim.-Forsch.*, 1979, **29**, 628.
21. G. J. Collee, G. A. Fraser, P. B. Marmion and A. Simmon, "Practical Medical Microbiology", 14th, ed., Vol. 11, Churchill Livingstone, Edinburg, 1996, 163.
22. L. Bauer and K. S. Suresh, *J. Org. Chem.*, 1963, **28**, 1604.