ISSN: 0974 - 7516 Volume 9 Issue 12

Organic CHEMISTRY

An Indian Journal

Full Paper

OCAIJ, 9(12), 2013 [509-515]

Synthesis and therapeutic evaluation of α-(4'-acetamido-2'-ethoxybenzoly hydrazino) aryl aceto nitrile

Jayesh V.Padaliya*[1], M.V.Parsania[2], A.V.Kalavadia[3]

[1]H. & H. B. Kotak Institution of Science, Dr. Yagnik Road, Rajkot, Gujrat, (INDIA)

[2]M. M. Science College, Morbi, Gujrat, (INDIA)

[3]Shri M&N Virani Science College, Rajkot, Gujarat, (INDIA)

E-mail: jayeshpatel123@yahoo.com; manharparsania@yahoo.in

ABSTRACT

4-acetanido-2-ethoxy benzoyl hydrazine (2) obtains by reacting hydrazine with methyl 4-acetamido-2-ethoxybenzoate. Further compound **(2)** was condensed with different aldehydes. Cyanohydrin which is obtain by addition reaction between different aromatic aldehyde and potassium cyanide in acidic medium to afforded new α-(4'-acetamido-2'-ethoxybenzoly hydrazino) aryl aceto nitrile derivatives in good yields (65 to 90 %). The structure of newly synthesized compound was confirmed by IR, ^{1}H NMR, Mass spectral studies and elemental analysis. All the synthesized compounds have been screened for antimicrobial activity.

KEYWORDS

4-Acetamido-2-ethoxy benzoyl hydrazine;
Different aromatic aldehyde;
Potassium cyanide;
α-(4'-acetamido-2'-ethoxybenzoly hydrazino) aryl aceto nitrile;
Spectral study;
Antimicrobial activity.

INTRODUCTION

Nitriles with fused pyridine ring were reported as ulcer inhibitor. The 3'-cyano phynylalkanano amines are here found to be sympathomimetic drugs[1]. The benzylidene derivatives of nucleic acid dinitrile show 98 % effectiveness against tetranychus urticase[2]. Cardenolide nitrile shows moderate biological activity in rats by cather method[3].

But now a day acetonitrile represents one of the modest classes of compound possessing wide range of therapeutic activities like Antihypertensive[4,5], centre nervous stimulants[6], Antihypoxic[7], Bacterial[8], Antiarrythemic[9], Anti-inflammatory[10], Fungicidal[11], Pesticidal[12] and Herbicidal[13].

With a view to getting better therapeutic agents, we have synthesized some new nitrile derivatives by the action of 4-acetamido -2-ethoxy benzoyl hydrazine with different cyanohydrin. The new synthesize nitrile being therapeutically active PAS nucleolus in search of agent having better potency.

In presence work we have first prepared 4-acetanido-2-ethoxy benzoyl hydrazine and condensed with different cyanohydrin which is obtain due to the reaction between different aromatic aldehyde with potassium cyanide. To produce higher functionalized d-(4'-acetamide-2'-ethoxy benzoyl hydrazine) aryl aceto nitrile derivatives in good yield for biological interest.

RESULTS AND DISCUSSION

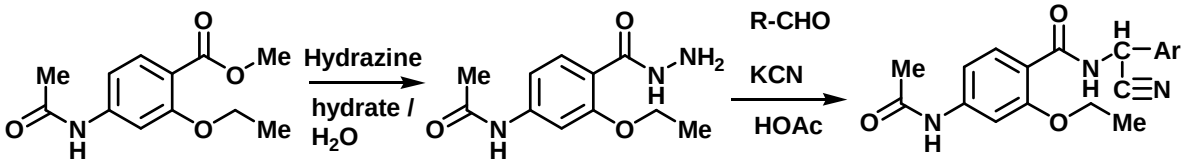
The starting 4-acetamido-2-ethoxy benzoyl hydrazine (2) was prepared by reacting methyl-4-acetamido-2-ethoxy phenyl benzoate (1) with hydrazine hydrate

Full Paper

at ambient temperature. The yield of compound is 80 %. The different cyanohydrins are reactive with phenyl hydrazine. The different cyanohydrin compounds was prepares by reported procedure[14] by reaction of different aromatic aldehyde with potassium cyanide. The different cyanohydrins were not isolated but direct condensed with 4-acetamido-2-ethoxy benzoyl hydrazine (2) in the presence of acetic acid at 0-5°C. Methanol is used as solvent and content was stirred for one hour at 0-5°C. Then kept for 24 hours at room temperature. After work up afforded new α-(4'-acetamido-2'-ethoxybenzoly hydrazino) aryl aceto nitrile 3(a-u) in good-moderate yield.

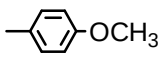
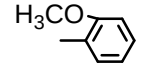
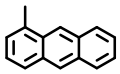
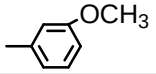
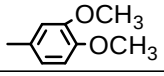
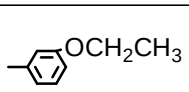
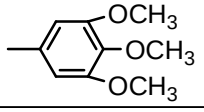
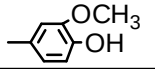
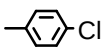
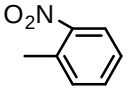
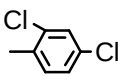
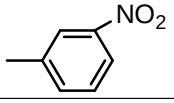
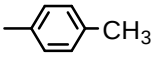
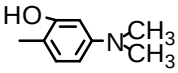
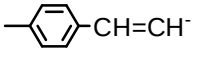
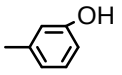
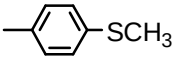
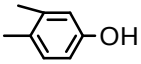
The IR spectra of 3a exhibited an absorption bands at 1649 cm^{-1} due to the >C=O stretching for –CONHNH- and >C=O at 1661 cm^{-1} for –$NHCOCH_3$, -C≡N stretching vibration at 2211 cm^{-1}, C-O-C stretching (asym. and Sym.) at 1251 and 1009 cm^{-1} for Ar-OCH_3, C-N stretching at 1145 cm^{-1}, N-H stretching at 3344 and N-H deformation at 1590 cm^{-1}.

In the ^{1}H NMR spectrum of 3a, singlet at δppm 2.22 for three proton of –$NHCOCH_3$, singlet at δppm 8.77 for –NH-NH- consist two proton, a singlet at δppm 3.93 for –OCH_3 having three proton. Triplet for three protons at δppm 1.42 and quartet for two protons at δppm 4.21 indicate the presence of –OCH_2CH_3 group.



Scheme 1 : Synthesis of α-(4'-acetamido-2'-ethoxy benzoyl hydrazino) aryl aceto nitrile

TABLE 1 : Synthesis of some new α-(4'-acetamido-2'-ethoxy benzoyl hydrazino) aryl aceto nitrile

Entry	R	Product 3	0-5°C	Time	Yield	Entry	R	Product 3	0-5°C	Time	Yield
1		3a	1.0	24	73	12		3l	1.0	12	82
2		3b	2.0	24	87	13		3m	1.5	16	77
3		3c	1.5	12	79	14		3n	2.5	24	82
4		3d	2.0	24	75	15		3o	3.0	24	67
5		3e	1.5	16	69	16		3p	2.0	24	69
6		3f	2.0	24	83	17		3q	2.0	24	72
7		3g	2.5	24	89	18		3r	3.0	16	78
8		3h	3.0	24	79	19		3s	1.5	24	74
9		3i	4.0	24	73	20		3t	1.0	12	81
10		3j	2.0	12	68	21		3u	2.0	24	77
11		3k	1.5	24	71						

The aromatic region also indicates presence of seven aromatic protons. The singlet at δppm 6.94 for –CH consist one proton.

The structure of 3a was further confirmed by mass spectrum analysis. It exhibits a molecular ion peak at M/Z 384 corresponding to its molecular weight.

Similarly, IR, NMR, Mass spectroscopy and elemental analysis, characterized all the compounds.

EVALUATION OF ANTIMICROBIAL ACTIVITY

The newly synthesized α-(4'-acetamido-2'-ethoxy benzoyl hydrazino) aryl aceto nitrile (3a-u) have been screened for antimicrobial activity against staphylococtus aureus. Escherichia coli, Bmega, P. valgaris, using amoxicillin, ampicillin, ciprofloxacin, erythromycin as standard and antifungal activity against aspergillus niger using griseofalvin as standard by the cup-plate method[15,16]. Inhibition was recorded by measuring the diameter of the inhibition zone. Each experiment was repeated twice and the average of the two independent determinations was recorded. The results are cited in TABLE 2.

EXPERIMENTAL

General procedures, Melting points were estimated in open capillaries and may be uncorrected. IR spectra were recorded on KBr discs, using RTIR-8400 spectrometer. ^{1}H NMR spectra were taken on a Bruker AVANCE IT 400 spectrometer in $CDCl_3$ / DMSO. Chemical shift is given in δppm relative to TMS. Mass spectra were determined using direct inlet probe on SCMS-QP 2010 Mass spectrometer (SCHIMADZU). Elemental analyzers were perfumed on a Carlo Erba EA 1108 elemental analyzer SAIF, CDRI Lucknow. Reactions were monitored on Merk aluminium thin layer chromatography (TLC, UV 254 nm) plates. Visualization was accomplished either on UV chamber or in iodine paper.

General procedure for the synthesis of α-(4'-acetamido-2'-ethoxy benzoyl hydrazino) aryl aceto nitriles

Aromatic aldehyde (0.01M) dissolve in ethanol (10 ml) was added in water (5ml) followed by glacial acetic acid (5ml). The contents were then stirred for five minutes at 0-5°C. Now, 4-Acetamido-2-ethoxybenzoyl hydrazine (2.37 gm, 0.01M) dissolve in methanol was added to the reaction mixture at 0-5°C and stirred for 1 to 3 hours. Then kept for 12 hours to 24 hours at room temperature. TLC monitored reaction. The solvent was removed in vacuum and resulting reaction mixture was poured on to crush ice. The separated product was filtered and crystallizes from ethanol to give pure compounds **(3a-u)**. The reaction time and yields are depicted in TABLE 1.

TABLE 2 : Antimicrobial activity of the compounds (3a-u).

Compound	Antimicrobial activity zone of inhibition in mm				Antifungal activity zone of inhibition in mm (A. niger)
	P. Vulgarius	E. Coli	B. Mega	S. aureus	
3a	14	14	19	19	17
3b	19	17	18	15	18
3c	16	21	15	19	20
3d	12	12	17	17	15
3e	17	16	18	17	17
3f	14	16	12	20	14
3g	12	17	18	17	16
3h	20	20	13	19	19
3i	16	16	19	13	15
3j	16	17	15	22	15
3k	15	19	16	20	14
3l	22	20	18	18	23
3m	21	19	18	14	17
3n	14	19	14	18	17
3o	14	15	15	13	16
3p	16	20	17	16	18
3q	22	21	19	14	19
3r	14	19	18	15	22
3s	18	15	18	14	14
3t	21	14	14	17	18
3u	17	12	21	19	16

S_1= amoxicillin, S_2 = Ampicillin, S_3 = Ciprofloxacin, S_4 = Erythromycin, S_5 = griseofulvin among the compounds tested for antibacterial activity, the compounds (3b), (3f), (3l), (3q), exhibit good activity agaist P. valgaris, B. mega. While compounds (3c), (3h), (3e) and (3p) exhibit promising activity agaist E.Coli and S. aureus. Compounds (3c), (3l) and (3s) exhibit good bacterial as well as antifungal activity agaist E. coli, P. valglaris, B. mega respectively.

Full Paper

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino) –p-methoxy phenyl acetonitrile (3a)

White solid, m.p. 270-271°C, IR (KBr) ν_{max} = 3344 cm^{-1} (-N-H), 1649 cm^{-1} (>C=O of –CONHNH), 1661 cm^{-1} (>C=O of –$NHCOCH_3$), 2211 cm^{-1}(-Ca"N str.), 1251 and 1009 cm^{-1}(-C-O str.), 1145 cm^{-1} (-C-N), 2980, 2860, 1460, 1349, 1433, 3075, 1552, 1090, 838 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δppm = 2.22 (S, 3H, -$NHCOCH_3$), 8.77 (S, 2H, -NHNH-), 3.93 (S, 3H, -OCH_3), 1.42 (T, 3H, -OCH_2CH_3), 4.21 (Q, 2H, -OCH_2CH_3), 6.94 (S, 1H, -CH), 6.97-8.17 (M, 7H, Ar-H), MS (EI): 384 M/Z. Anal. Calculated For $C_{20}H_{22}N_4O_4$:C, 62.50; H, 5.72; N, 14.58; Found: C, 62.10; H, 5.75; N, 14.60 %.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino) anthryl acetonitrile (3b)

White solid, m.p. 130°C, IR (KBr) ν_{max} = 3330 cm^{-1} (-N-H str.), 1670 cm^{-1} (>C=O str. of –$NHCOCH_3$), 1650 cm^{-1} (>C=O str. of –CONHNH), 2220 cm^{-1} (-Ca"N str.), 3085 cm^{-1} (-C-H str. of aromatic), 1250, 1009, 840 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δppm = 1.42 (T, 3H, -OCH_2CH_3), 2.28 (S, 3H, -$NHCOCH_3$), 3.98 (Q, 3H, -OCH_2CH_3), 6.97 (S, 1H, -CH), 6.42-8.30 (M, 12H, Ar-H), 8.75 (S, 2H, -NHNH-), MS (EI): 452 M/Z. Anal. Calculated for $C_{27}H_{24}N_4O_3$; C, 71.68; H, 5.3; N, 12.39; Found: C, 72.00; H, 5.4; N, 12.42%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino) phenyl acetonitrile (3c)

White solid, m.p. 230°C, IR (KBr) ν_{max} = 3300 cm^{-1} (-N-H str.), 1666 cm^{-1} (>C=O of –$NHCOCH_3$), 1650 cm^{-1} (>C=O str. of –CONHNH), 2230 cm^{-1}(-Ca"N str.), 3075 cm^{-1}(-C-H str. of aromatic), 1550, 1145, 1251, 1000, 760, 830 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δppm = 1.44 (T, 3H, -OCH_2CH_3), 2.25 (S, 3H, -$NHCOCH_3$), 4.72 (Q, 2H, -OCH_2CH_3), 6.90 (S, 1H, -CH), 6.50-8.15 (M, 8H, Ar-H), 8.80(S, 2H, -NHNH). MS (EI): 352 M/Z. Anal. Calculated for $C_{19}H_{20}N_4O_3$; C, 64.77; H, 5.68; N, 15.91; Found: C, 65.01; H, 5.70; N, 15.90%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino) –m-phenoxy acetonitrile (3d)

Buff white solid, m.p. 170°C, IR (KBr) ν_{max} = 3340 cm^{-1} (-N-H str.), 1675 (>C=O str. of –$NHCOCH_3$), 1655 (>C=O str. of –CONHNH), 2235 (-Ca"N str.), 3085, 2950, 1570, 1251, 1200, 1130, 730, 840, 820 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δppm = 1.20 (T, 3H, -OCH_2CH_3), 3.2 (S, 3H, -$NHCOCH_3$), 4.4 (Q, 2H, -OCH_2CH_3), 6.90 (S, 1H, -CH), 7.2-8.3 (M, 12H, Ar-H), 8.70 (S, 2H, -NHNH-). MS (EI): 444 M/Z. Anal. Calculated for $C_{25}H_{24}N_4O_4$; C, 67.57; H, 5.40; N, 12.61; Found: C, 67.71; H, 5.45; N, 12.64%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino) o-chloro phenyl acetonitrile (3e)

White solid, m.p. 200°C, IR (KBr) ν_{max} = 3310 cm^{-1} (-N-H str.), 1665 cm^{-1} (>C=O of –$NHCOCH_3$), 1660(>C=O str. of –CONHNH), 2220 (-Ca"N str.), 3075, 2980, 1580, 1560, 1200, 1190, 1130, 840 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δppm = 1.8 (T, 3H, -OCH_2CH_3), 2.3 (S, 3H, -$NHCOCH_3$), 4.4 (Q, 2H, -OCH_2CH_3), 6.80 (S, 1H, -CH), 7.0-8.4 (M, 7H, Ar-H). MS (EI): 384 M/Z. Anal. Calculated for $C_{19}H_{19}N_4O_3Cl$; C, 59.06; H, 4.92; N, 15.40; Found: C, 59.10; H, 4.98; N, 14.60%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino) p-chloro phenyl acetonitrile (3f)

White solid, m.p. 235°C, IR (KBr) ν_{max} = 3320 cm^{-1} (-N-H str.), 1675 (>C=O str. of –$NHCOCH_3$), 1660 (>C=O str. of –CONHNH), 2225(-Ca"N str.), 3030, 2940, 2860, 1575, 1225, 1190, 1125, 1009, 820 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δppm = 1.9 (T, 3H, -OCH_2CH_3), 2.4 (S, 3H, -$NHCOCH_3$), 4.5 (Q, 2H, -OCH_2CH_3), 7.0-8.8 (M, 7H, Ar-H), 6.90 (S, 1H, -CH), 8.89 (S, 2H, -NHNH-). MS (EI): 380 M/Z. Anal. Calculated for $C_{19}H_{19}N_4O_3Cl$; C, 59.06; H, 4.92; N, 14.50; Found: C, 59.20; H, 4.96; N, 14.60%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino)-2,4-dichloro phenyl acetonitrile (3g)

White solid, m.p. 190°C, IR (KBr) ν_{max} = 3345 cm^{-1} (-N-H str.), 1660 (>C=O str. of –$NHCOCH_3$), 1640 (>C=O str. of –CONHNH), 2210 (-Ca"N str.), 3070, 2940, 2880, 1575, 1250, 1145, 1010, 730, 840 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δppm = 1.7 (T, 3H, -OCH_2CH_3), 2.3 (S, 3H, -$NHCOCH_3$), 4.3 (Q, 2H, -OCH_2CH_3), 7.0-9.2 (M, 7H, Ar-H). MS (EI): 420 M/Z. Anal. Calculated for $C_{19}H_{18}N_4O_3Cl_2$; C,

54.28; H, 4.28; N, 13.33; Found: C, 54.40; H, 4.20; N, 13.30%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino)-2-fural acetonitrile (3h)

Off white solid, m.p. 185°C, IR (KBr) ν_{max} = 3330 cm^{-1} (-N-H str.), 1675 (>C=O str. of $-NHCOCH_3$), 1650 (>C=O str. of –CONHNH), 2240(-Ca"N str.), 3030 (-C-H str. of aromatic), 2940, 2860, 1575, 1250, 1145, 1025, 840 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δppm = 1.8 (T, 3H, $-OCH_2CH_3$), 2.6 (S, 3H, $-NHCOCH_3$), 4.9 (Q, 2H, $-OCH_2CH_3$), 7.0-9.3 (M, 6H, Ar-H). MS (EI): 418 M/Z. Anal. Calculated for $C_{23}H_{22}N_4O_4$; C, 66.03; H, 5.26; N, 13.40; Found: C, 66.10; H, 5.30; N, 13.42%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino)-2-hydroxy-4-(N,N-dimethyl)phenyl acetonitrile (3i)

White solid, m.p. 220°C, IR (KBr) ν_{max} = 3450 cm^{-1} (-OH str.) 3340 cm^{-1} (-N-H str.), 1665 cm^{-1} (>C=O str. of $-NHCOCH_3$), 1640 cm^{-1} (>C=O str. of –CONHNH), 2240 cm^{-1} (-Ca"N str.), 3030, 2940, 2860, 1570, 1340, 1251, 1210, 1145, 1010, 825 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δppm = 1.8 (T, 3H, $-OCH_2CH_3$), 2.6 (S, 3H, $-NHCOCH_3$), 4.9 (Q, 2H, $-OCH_2CH_3$), 7.0-9.3 (M, 6H, Ar-H). MS (EI): 418 M/Z. Anal. Calculated for $C_{23}H_{22}N_4O_4$; C, 66.03; H, 5.26; N, 13.40; Found: C, 66.10; H, 5.30; N, 13.42%. ^1H NMR (400 MHz, $CDCl_3$) δppm = 1.40 (T, 3H, $-OCH_2CH_3$), 1.7 (S, 6H, $-N(CH_3)_2$), 2.22 (S, 3H, $-NHCOCH_3$), 4.2 (Q, 2H, $-OCH_2CH_3$), 6.95-8.10 (M, 6H, Ar-H). MS (EI): 397 M/Z. Anal. Calculated for $C_{21}H_{25}N_4O_4$; C, 63.48; H, 6.30; N, 14.10; Found: C, 63.55; H, 6.35; N, 14.20%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino)-3-hydroxy phenyl acetonitrile (3j)

White solid, m.p. 230°C, IR (KBr) ν_{max} = 3470 cm^{-1} (-OH str.) 3350 cm^{-1} (-N-H str.), 1660(>C=O str. of $-NHCOCH_3$), 1630 (>C=O str. of –CONHNH), 3070 (-C-H str. of aromatic), 2210(-Ca"N str.), 2960, 2880, 1575, 1245, 1210, 1145, 1005, 810, 870 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δppm = 1.4 (T, 3H, $-OCH_2CH_3$), 2.2 (S, 3H, $-NHCOCH_3$), 4.2 (Q, 2H, $-OCH_2CH_3$), 8.4 (S, 1H, -OH), 6.9-9.4 (M, 7H, Ar-H). MS (EI): 368 M/Z. Anal. Calculated for $C_{19}H_{20}N_4O_4$; C, 61.95; H, 5.43; N, 15.22; Found: C, 62.10; H, 5.45; N, 13.35%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino)-4-hydroxy phenyl acetonitrile (3k)

White solid, m.p. 260°C, IR (KBr) ν_{max} = 3450 cm^{-1} (-OH str.) 3340 cm^{-1} (-N-H str.), 1670 (>C=O str. of $-NHCOCH_3$), 1650 (>C=O str. of –CONHNH), 2210(-Ca"N str.), 3030, 2940, 1575, 1345, 1245, 1145, 1010, 840 cm^{-1}. ^1H NMR (400 MHz, TFA) δppm = 1.4 (T, 3H, $-OCH_2CH_3$), 2.2 (S, 3H, $-NHCOCH_3$), 4.4 (Q, 2H, $-OCH_2CH_3$), 6094 (S, 1H, -OH), 7.2-9.2 (M, 8H, Ar-H). MS (EI): 368 M/Z. Anal. Calculated for $C_{19}H_{20}N_4O_4$; C, 61.95; H, 5.43; N, 15.22; Found: C, 62.05; H, 5.44; N, 13.30%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino)-2-methoxy phenyl acetonitrile (3l)

White solid, m.p. 245°C, IR (KBr) ν_{max} = 3310 cm^{-1} (-N-H str.), 1680(>C=O str. of $-NHCOCH_3$), 1650 (>C=O str. of –CONHNH), 3030 (-C-H str. of aromatic), 2230(-Ca"N str.), 3030, 2960, 2840, 1575, 1430, 1251, 1210, 1145, 1000, 725, 830 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δppm = 1.4 (T, 3H, $-OCH_2CH_3$), 2.30 (S, 3H, $-NHCOCH_3$), 3.85 (S, 3H, $-OCH_3$), 4.20 (Q, 2H, $-OCH_2CH_3$), 6.75 (S, 1H, C-H) 6.95-8.10.(M, 7H, Ar-H), 8.78(S, 2H, -NHNH), MS (EI): 342 M/Z. Anal. Calculated for $C_{20}H_{22}N_4O_4$; C, 62.83; H, 5.76; N, 14.66; Found: C, 62.91; H, 5.80; N, 14.75%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino)-3-methoxy phenyl acetonitrile (3m)

White solid, m.p. 160°C, IR (KBr) ν_{max} = 3300 cm^{-1} (-N-H str.), 1670(>C=O str. of $-NHCOCH_3$), 1660 (>C=O str. of –CONHNH), 3030 (-C-H str. of aromatic), 2200(-Ca"N str.), 2960, 2840, 1570, 1435, 1260, 1200, 1150, 1010, 830 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δppm = 1.42(T, 3H, $-OCH_2CH_3$), 2.32 (S, 3H, $-NHCOCH_3$), 3.84 (S, 3H, $-OCH_3$), 4.20 (Q, 2H, $-OCH_2CH_3$), 6.84 (S, 1H, C-H) 7.2-8.3.(M, 7H, Ar-H), 8.82(S, 2H, -NHNH), MS (EI): 382 M/Z. Anal. Calculated for $C_{20}H_{22}N_4O_4$; C, 62.83; H, 5.76; N, 14.66; Found: C, 62.87; H, 5.80; N, 14.70%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino)3,4-dimethoxy phenyl acetonitrile (3n)

White solid, m.p. 190°C, IR (KBr) ν_{max} = 3320

cm^{-1} (-N-H str.), 1665(>C=O str. of $-NHCOCH_3$), 1640 (>C=O str. of –CONHNH), 3070 (-C-H str. of aromatic), 2230(-Ca"N str.), 2960, 1580, 1560, 1250, 1210, 1145, 1010, 725, 830 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δppm = 1.44 (T, 3H, $-OCH_2CH_3$), 2.20 (S, 3H, $-NHCOCH_3$), 4.01 (S, 6H, $-OCH_3$), 4.25 (Q, 2H, $-OCH_2CH_3$), 6.85 (S, 1H, C-H) 6.95-7.90.(M, 6H, Ar-H), 8.70(S, 2H, -NHNH), MS (EI): 412 M/Z. Anal. Calculated for $C_{21}H_{24}N_4O_5$; C, 61.16; H, 5.80; N, 13.59; Found: C, 61.25; H, 5.90; N, 13.65%.

α-(4'-acetamido-2'-ethoxybenzoylhydrazino)-3,4,5-trimethoxyphenylacetonitrile (3o)

White solid, m.p. 200°C, IR (KBr) ν_{max} = 3305 cm^{-1} (-N-H str.), 1670(>C=O str. of $-NHCOCH_3$), 1645 (>C=O str. of –CONHNH), 3035 (-C-H str. of aromatic), 2225(-Ca N str.), 3030, 2940, 2860, 1575, 1545, 1220, 1200, 1150, 730, 800 cm^{-1}. ^1H NMR (400 MHz, TFA) δppm = 1.42 (T, 3H, $-OCH_2CH_3$), 2.25 (S, 3H, $-NHCOCH_3$), 4.10 (S, 9H, $-OCH_3$), 4.30 (Q, 2H, $-OCH_2CH_3$), 6.80 (S, 1H, C-H) 6.9-7.8.(M, 5H, Ar-H), 8.70(S, 2H, -NHNH), MS (EI): 442 M/Z. Anal. Calculated for $C_{22}H_{26}N_4O_6$; C, 59.73; H, 5.88; N, 12.66; Found: C, 59.80; H, 5.95; N, 12.70%.

α-(4'-acetamido-2'-ethoxybenzoylhydrazino)-3-methoxy-4-hydroxyphenyl acetonitrile (3p)

White solid, m.p. 180°C, IR (KBr) ν_{max} = 3460 (-OH str.), 3320 cm^{-1} (-N-H str.), 1660(>C=O str. of $-NHCOCH_3$), 1640 (>C=O str. of –CONHNH), 2220(-Ca N str.), 3070, 2960, 2840, 1575, 1540, 1220, 1210, 1150, 1030, 710, 830 cm^{-1}. ^1H NMR (400 MHz, DMSO) δppm = 1.7 (T, 3H, $-OCH_2CH_3$), 2.6 (S, 3H, $-NHCOCH_3$), 4.2 (S, 3H, $-OCH_3$), 4.6 (Q, 2H, $-OCH_2CH_3$), 8.2 (S, 1H, -O-H) 6.9-9.5.(M, 6H, Ar-H), 8.77(S, 2H, -NHNH), MS (EI): 398 M/Z. Anal. Calculated for $C_{20}H_{22}N_4O_5$; C, 60.30; H, 5.52; N, 14.07; Found: C, 60.35; H, 5.62; N, 14.15%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino)-2-nitro phenyl acetonitrile (3q)

Pale yellow solid, m.p. 219°C, IR (KBr) ν_{max} = 3315 cm^{-1} (-N-H str.), 1670(>C=O str. of $-NHCOCH_3$), 1650 (>C=O str. of –CONHNH), 3033 (-C-H str. of aromatic), 2220(-Ca N str.), 2960, 1570, 1245, 1210, 1145, 1010, 740, 710 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$), δppm = 1.7 (T, 3H, $-OCH_2CH_3$), 2.4 (S, 3H, $-NHCOCH_3$), 4.5 (Q, 2H, $-OCH_2CH_3$), 6.94 (S, 1H, -C-H) 6.9-9.3(M, 7H, Ar-H), 8.70 (S, 2H, -NHNH), MS (EI): 397 M/Z. Anal. Calculated for $C_{19}H_{19}N_5O_5$; C, 57.43; H, 4.78; N, 17.63; Found: C, 57.50; H, 4.85; N, 17.60%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino)-3-nitro phenyl acetonitrile (3r)

Pale yellow solid, m.p. 150°C, IR (KBr) ν_{max} = 3325 cm^{-1} (-N-H str.), 1660(>C=O str. of $-NHCOCH_3$), 1640 (>C=O str. of –CONHNH), 2230(-Ca N str.), 3070, 2940, 2860, 1570, 1550, 1230, 1210, 1150, 1010, 830 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$), δppm = 1.6 (T, 3H, $-OCH_2CH_3$), 2.4 (S, 3H, $-NHCOCH_3$), 4.5 (Q, 2H, $-OCH_2CH_3$), 6.90 (S, 1H, -C-H) 6.9-9.3(M, 7H, Ar-H), 8.85 (S, 2H, -NHNH), MS (EI): 397 M/Z. Anal. Calculated for $C_{19}H_{19}N_5O_5$; C, 57.43; H, 4.78; N, 17.63; Found: C, 57.55; H, 4.80; N, 17.75%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino)-4-methyl phenyl acetonitrile (3s)

White solid, m.p. 250°C, IR (KBr) ν_{max} = 3340 cm^{-1} (-N-H str.), 1670(>C=O str. of $-NHCOCH_3$), 1647 (>C=O str. of –CONHNH), 2220(-Ca□N str.), 3010, 2940, 1575, 1540, 1230, 1145, 1010, 840, 820 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$), δppm = 1.6 (T, 3H, $-OCH_2CH_3$), 2.6 (S, 3H, $-NHCOCH_3$), 4.4 (Q, 2H, $-OCH_2CH_3$), 2.3 (S, 3H, $-CH_3$), 6.85 (S, 1H, -C-H) 6.9-9.4(M, 7H, Ar-H), 8.77 (S, 2H, -NHNH), MS (EI): 366 M/Z. Anal. Calculated for $C_{20}H_{22}N_4O_3$; C, 65.57; H, 6.01; N, 13.55; Found: C, 65.60; H, 6.05; N, 13.60%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino)-α-vinyl phenyl acetonitrile (3t)

Off white solid, m.p. 240°C, IR (KBr) ν_{max} = 3330 cm^{-1} (-N-H str.), 1675(>C=O str. of $-NHCOCH_3$), 1640 (>C=O str. of –CONHNH), 2220(-Ca"N str.), 3030, 2940, 2860, 1575, 1540, 1245, 1140, 1010, 740, cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$), δppm = 1.6 (T, 3H, $-OCH_2CH_3$), 2.4 (S, 3H, $-NHCOCH_3$), 4.5 (Q, 2H, $-OCH_2CH_3$), 6.84 (S, 1H, -C-H) 6.9-9.5(M, 8H, Ar-H + vinylic -H), 8.80 (S, 2H, -NHNH), MS (EI): 378 M/Z. Anal. Calculated for $C_{21}H_{22}N_4O_3$; C, 66.66; H, 5.8; N, 14.81; Found: C, 66.72; H, 5.85;

N, 14.84%.

α-(4'-acetamido-2'-ethoxy benzoyl hydrazino)-4-thiomethyl phenyl acetonitrile (3u)

White solid, m.p. 255°C, IR (KBr) ν_{max} = 3320 cm^{-1} (-N-H str.), 1665(>C=O str. of $-NHCOCH_3$), 1635 (>C=O str. of –CONHNH), 2205(-Ca"N str.), 3010, 2900, 2840, 1575, 1530, 1250, 1210, 1145, 1000, 810, 840 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$), δppm = 1.6 (T, 3H, $-OCH_2CH_3$), 2.4 (S, 3H, $-NHCOCH_3$), 4.6 (Q, 2H, $-OCH_2CH_3$), 2.7 (S, 3H, $-S-CH_3$), 6.95 (S, 1H, -C-H) 7.1-9.4(M, 7H, Ar-H), 8.74 (S, 2H, -NHNH), MS (EI): 398 M/Z. Anal. Calculated for $C_{20}H_{22}N_3O_3S$; C, 60.30; H, 5.53; N, 14.07; S, 8.04; Found: C, 60.41; H, 5.60; N, 14.10; S, 8.10%.

CONCLUSION

In conclusion, in this article we have been reported some novel highly functionalized α-(4'-acetamido-2'-ethoxy benzoyl hydrazino) aryl acetonitrile in good yield and evaluated for antimicrobial activity. Some of the newly synthesized compounds exhibited good to excellent activity against both gram positive and gram negative bacteria and fungi.

ACKNOWLEDGEMENTS

The authors thankful to department of chemistry, Saurashtra University, Rajkot for providing facilities. We are also thankful to CIL, RSIC, Chandigrah for providing ^1H NMR spectral analysis and SAIF, CDRI Lucknow for elemental analysis of compounds.

REFERENCES

[1] P.Pratesi, E.Srana, L.Villa; Farmaco Ed.Sci., **28(10)**, 753-65 **(1973)**; Chem.Abstr., **80**, 26892u **(1974)**.
[2] Heidenreich Holger, Becker Benedikt; Chem. Abstr., **110**, 78304u **(1989)**.
[3] I.F.Makareuich, M.V.Mokrour, L.Topchif, I.P.Kovalev, V.E.Sokolova, I.Gubin Yu, N.P.Bublik, V.A.Polyakov; Khim.Prir.Soedin., (Russ), **5**, 608-12 **(1983)**; Chem.Abstr., **100**, 156894p **(1984)**.
[4] Vhlondrof Jaochim, Gabbar Hamed Graf Erich, Doppe Fad, Illestephanine; Ger.Offen D.E., **3**, 024836, 28 Jan. **(1982)**; Chem.Abstr., **96**, 142481p **(1982)**.
[5] Bormann Gerhard; Chem.Abstr., **100**, 68184b **(1984)**.
[6] Voigt Hans; Chem.Abstr., **58**, 1412b **(1963)**.
[7] T.V.Stezhko, V.G.Granik, R.G.Glushokov, L.F.Roshehina, A.I.Polezhaeva, M.O.Mashkovskii; Kim.Farm 2h, (Russ), **18(3)**, 290-7 **(1984)**; Chem. Abstr., **101**, 90704p **(1984)**.
[8] M.P.Dave, J.M.Patel, K.A.Thaker; J.Inst., Chem.India, **56(4)**, 169-70 **(1984)**; Eng.Chem. Abstr., **102**, 131660n **(1985)**.
[9] G.Bremanis, I.Kolvins, I.Acena, E.Lukevics, M.Veveris, V.Kauss, P.Trapentsier, E.Liepins; Chem.Abstr., **103**, 5967t **(1985)**.
[10] Uhlendorf Jochim, Leyck Sigurd, A.Nattermann; Chem.Abstr., **100**, 68161s **(1984)**.
[11] M.Bimber Russell; Chem.Abstr., **74**, 87655s **(1971)**.
[12] Tanaka Masato, Sakakura Toshi Yasu; Chem.Abstr., **104**, 88317h **(1986)**.
[13] Sato Hiroshi, Hirose Kenchi; Chem.Abstr., **108**, 556-70 **(1988)**.
[14] G.Bram, A.Loupy, M.Pedouassaaut; Bull.Soc. Chim.Fr., **1**, 124-8 **(1986)**.
[15] A.R.Sundane, K.Rudresh, N.D.Satyanarayan, S.P.Filre Math; Indian J.Pharm.Sci., **60**, 379 **(1989)**.
[16] K.N.Siand, R.N.Dar, B.M.Chopara, R.N.Kaul; Indian J.Pharma.Sci., **27**, 141 **(1965)**.