Journal of Sciences, Islamic Republic of Iran 15(2): 135-138 (2004)
University of Tehran, ISSN 1016-1104

Short Communication

Preparation, Characterisation and Antimicrobial Activities of Some Novel Nitriles and Imidazolines

K.V. Hirpara, S.P. Patel, K.A. Parikh, A.S. Bhimani, and H.H. Parekh*

Department of Chemistry, Saurashtra University, Rajkot - 360 005, Gujarat, India

Abstract

Reaction between 5-methyl-3-aminoisoxazole and ρ-acetamidophenylsulphonylchloride yielded compound **1**. Hydrolysis of compound **1** gave a starting compound 4-methoxybenzal-ρ-5-methyl isoxazol-3-yl-sulphonamido aniline **2**. The compound **2** on condensation with different aldehydes and potassium cyanide yielded the nitriles **3a-l**. Cyclocondensation between oxazolinone and compound **2** yielded imidazolines **4a-l**. All compounds have been characterised using IR, ^{1}H NMR and Mass spectral data and have been evaluated for their antimicrobial activity against different strains of bacteria and fungi.

Keywords: Sulphonamides; Nitriles; Imidazolines; Antimicrobial activity

Introduction

Although a large number of sulphonamide analogs have been synthesized, there still exists much scope for the synthesis of sulphonamide derivatives possessing different pharmacophores [1,2]. Literature survey reveals that various nitriles [3] and 5-oxo-imidazolines [4,5] are potential drugs. This observation prompted us to synthesize some new nitriles and 5-oxo-imidazolines bearing sulphonamide moiety, in order to study their antimicrobial activities.

Condensation between 5-methyl-3-aminoisoxazole and ρ-acetamidophenylsulphonyl chloride yielded compound (**1**) which hydrolysed to give a starting material N-(5-methyl-3-isoxazoyl)-p-aminobenzene-sulfonamide (**2**). Compound (**2**) on treatment with various aldehydes and potassium cyanide afforded N_1-(ρ-cyano-substitutedbenzal)-N4-(5-methyl-3-isoxazolyl) -p-aminobenzenesulfonamides (**3a-l**). Oxazolinones [6] were prepared by the condensation of arylaldehydes with phenyl glycine in presence of sodium acetate and acetic anhydride which when treated with compound (**2**) yielded 4-arylidene-2-phenyl-1-(ρ-5-methylisoxazol-3-yl-aminosulfonylphenyl)-5-oxo-imidazolines (**4a-l**). (Scheme 1, Table 1).

The structure of the synthesized compounds were assigned on the basis of IR, ^{1}H NMR and mass spectral study. The compounds were evaluated for their *in vitro* growth inhibitory activity against Gram positive, Gram negative bacteria and fungal strain *A. niger*.

Antimicrobial Activity

All the compounds reported in Table 2 were tested *in vitro* for their antimicrobial activity against various microbes. Under identical conditions, the standard antibiotics showed zones of inhibition ampicillin 18-22 mm, amoxicillin 17-22 mm, norfloxacin 21-26 mm against bacterial strains and griseofulvin showed zones of inhibition of 26 mm against *A. niger*.

It can be concluded from Table 2 that the compounds (**3j, 3l, 4b**) were highly active against *E. coli.* The

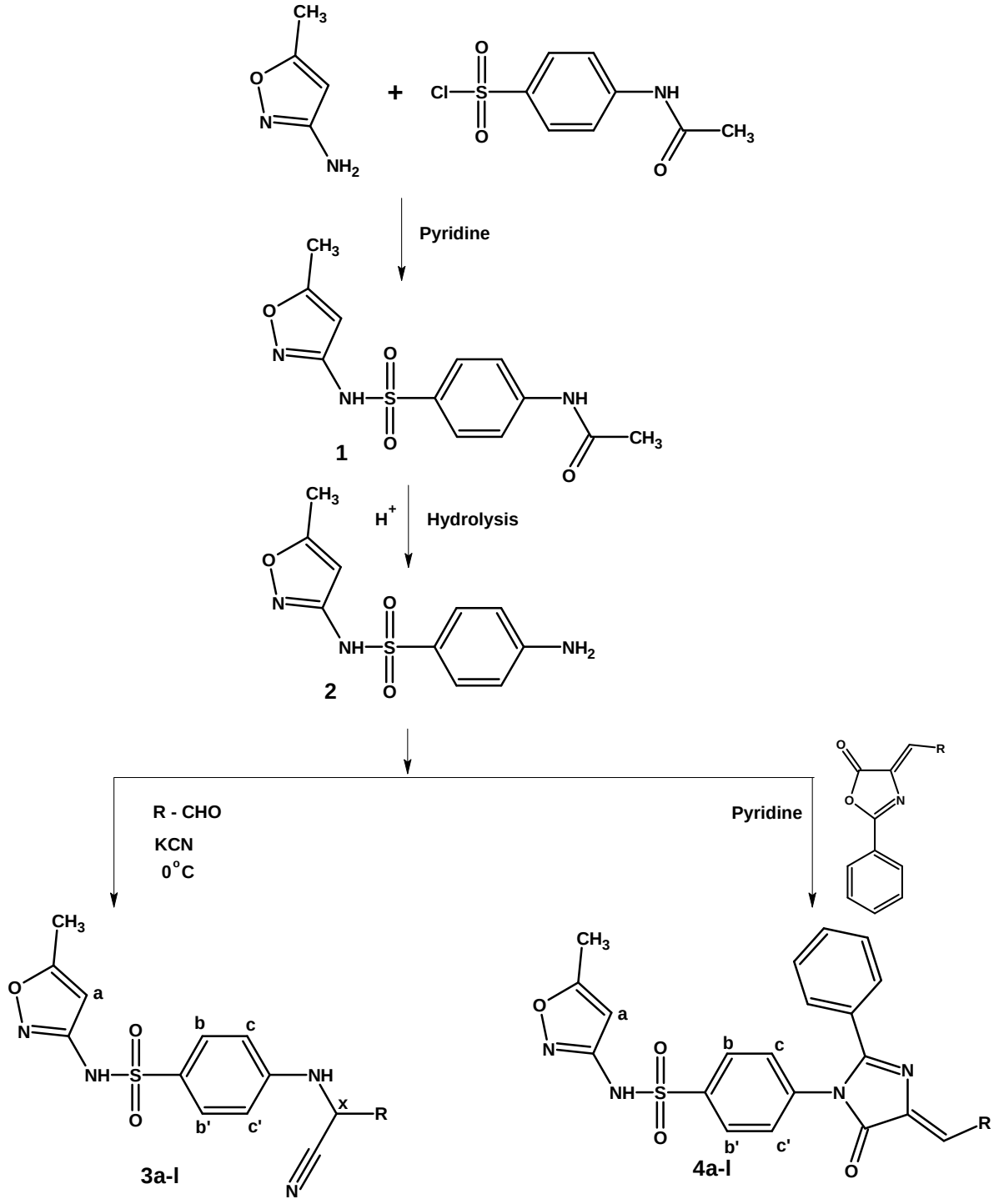
* *E-mail: hhparekh@yahoo.com*

Table 1. Physical and analytical data of compounds **3a-l** and **4a-l**

Compound	R	Molecular Formula	M.P. °C	Yield %	% of N	
					Calculated	Found
3a	C_6H_5-	$C_{18}H_{16}O_3N_4S$	166	70	15.21	15.35
3b	4-OCH_3-C_6H_4-	$C_{19}H_{18}O_4N_4S$	180	59	14.06	13.91
3c	4-Cl- C_6H_4-	$C_{18}H_{15}O_3N_4SCl$	172	72	13.91	13.99
3d	2-Cl-C_6H_4-	$C_{18}H_{15}O_3N_4SCl$	175	68	13.91	14.04
3e	3,4-$(OCH_3)_2$-C_6H_3-	$C_{20}H_{20}O_5N_4S$	175	63	13.08	13.28
3f	2-OH-C_6H_4-	$C_{18}H_{16}O_4N_4S$	183	60	14.57	14.35
3g	4-OH-C_6H_4-	$C_{18}H_{16}O_4N_4S$	190	69	14.57	14.68
3h	4-OH-3-OCH_3-C_6H_3-	$C_{19}H_{18}O_5N_4S$	152	66	13.52	13.31
3i	-CH=CH-C_6H_5-	$C_{20}H_{18}O_3N_4S$	198	58	14.20	14.29
3j	3-NO_2-C_6H_4-	$C_{18}H_{15}O_5N_5S$	138	55	16.94	16.88
3k	α-C_4H_3O-	$C_{16}H_{14}O_4N_4S$	160	64	15.63	15.52
3l	2-NO_2-C_6H_4-	$C_{18}H_{15}O_5N_5S$	178	59	16.94	16.88
4a	C_6H_5-	$C_{26}H_{20}O_4N_4S$	138	60	11.56	11.69
4b	4-OCH_3-C_6H_4-	$C_{27}H_{22}O_5N_4S$	192	60	10.89	10.75
4c	4-Cl-C_6H_4-	$C_{26}H_{19}O_4N_4SCl$	178	68	10.80	10.91
4d	2-Cl-C_6H_4-	$C_{26}H_{19}O_4N_4SCl$	165	61	10.80	10.63
4e	3,4-$(OCH_3)_2$-C_6H_3-	$C_{28}H_{24}O_6N_4S$	168	58	10.29	10.41
4f	2-OH-C_6H_4-	$C_{26}H_{20}O_5N_4S$	168	62	11.19	11.30
4g	4-OH-C_6H_4-	$C_{26}H_{20}O_5N_4S$	163	53	11.19	11.05
4h	4-OH-3-OCH_3-C_6H_3-	$C_{27}H_{22}O_6N_4S$	164	52	10.56	10.68
4i	-CH=CH-C_6H_5-	$C_{26}H_{22}O_4N_4Sl$	172	64	10.97	10.79
4j	3-NO_2-C_6H_4-	$C_{26}H_{19}O_6N_5S$	172	69	13.23	13.29
4k	2-NO_2-C_6H_4-	$C_{26}H_{19}O_6N_5S$	180	56	13.23	13.38
4l	α-C_4H_3O-	$C_{24}H_{18}O_5N_4S$	182	59	11.81	11.68

Table 2. Antimicrobial data of the compounds **3a-l** and **4a-l**

Compound	Antimicrobial activity				Fungal activity
	E. coli	*P. vulgaris*	*B. mega*	*S. aureus*	*A. niger*
3a	13	21	10	18	10
3b	12	12	10	10	11
3c	16	16	11	15	13
3d	12	13	18	13	10
3e	10	18	13	18	12
3f	10	15	12	16	18
3g	18	22	14	12	18
3h	16	16	14	12	13
3i	13	13	13	13	12
3j	19	18	10	18	10
3k	12	19	12	16	11
3l	19	10	11	12	10
4a	18	11	10	10	16
4b	21	12	10	13	19
4c	12	18	13	11	13
4d	16	14	18	12	10
4e	18	17	16	10	10
4f	18	17	16	10	18
4g	13	12	14	16	16
4h	14	13	13	18	12
4i	12	18	11	10	13
4j	16	19	10	21	12
4k	16	12	10	16	11
4l	10	16	13	13	10



Scheme 1

compounds (**3a, 3g, 3k, 4j**) showed significant activity against *P. vulgaris*. In case of *B. mega*, the compounds (**3d** and **4d**) displayed maximum activity. The compounds (**3a, 3e, 3j, 4h, 4j**) exhibited moderate activity against *S. aureus*, while the compounds (**3f, 3g, 4b, 4f**) exhibited significant activity against *A. niger*, respectively.

The antimicrobial activity was assayed by using the

cup-plate agar diffusion method [7] by measuring the inhibition zone in mm. All the compounds were screened *in vitro* for their antimicrobial activity against a variety of bacterial strains such as *Bacillus megaterium, Escherichia coli, Proteus vulgaris, Staphylococcus aureus* and fungal strain *Aspergillus niger* at a 40 µg concentraction.

Experimental

The melting points were determined in open capillary tubes and are uncorrected. Thin layer chromatography was used for follow up of the reaction and purity of the compounds. IR spectra recorded on Shimadzu FTIR-8400 on KBr disc. ^{1}H NMR spectra were recorded on 300 MHz spectrometer using TMS as an internal standard, mass spectra were recorded on Jeol D-300 spectrometer. All the compounds gave satisfactory elemental analysis.

Preparation of p-5-methylisoxazol-3-yl sulphonamido anilines 2

A mixture of 5-methyl-3-amino isoxazole (0.98 gm, 0.01 M), 4-sulphonylchloride acetanilide (2.33 gm, 0.01 M) and pyridine (15 ml) was heated at 125°C in oil bath. The reaction mixture was cooled and poured onto crushed ice. The solid product was separated. The product hydrolised by dl. HCl and filtered. The product was crystallized from ethanol. Yield 62%. M.p. 168°C.

Preparation of N^1-(α-cyano-substitutedbenzal)-N^4-(5-methyl-3-isoxazolyl)-p-aminobenzene sulfonamides (3a-l)

4-Methoxybenzaldehyde (0.01 mol) dissolved in ethanol (10 ml) was added to potassium cyanide (0.01 mol) dissolved in water (2 ml) followed by glacial acetic acid (5 ml). The contents were stirred for 5 minutes to from aldehyde cyanohydrin at 0°C, compound N^1-(α-cyano-substitutedbenzal)-N^4-(5-methyl-3-isoxazolyl)-p-aminobenzenesulfonamides (**3a-l**) **2** dissolved in methanol was added to the reaction mixture, contents were kept at room temperature for 24 h and poured onto ice. The solid product was crystallized from ethanol. **3b**: Yield 59%; m.p. 180°C. Calculated for $C_{19}H_{18}N_4SO_4$: C-57.27, H-4.55, N-14.06%. Found: C-57.19, H-4.41, N-13.91%. IR KBr (cm^{-1}): 3394 (N-H str.), 2233 (C≡N str.), 1326 (S=O str.), 829 (N-O str.), **3c**: ^{1}H NMR (300 MHz $CDCl_3$ + DMSO-d_6) δ ppm: 2.32 (s, 3H, -CH_3), 6.01 (s, 1H -CHa), 6.92 [d, (Jbc = 8.7 Hz), 2H, -Ar-Hb,b'], 7.28 [s, 1H, -CHx], [d, (Jed = 8.9 Hz), 2H, Ar-He,e'], 8.11 [d, (Jcb = 8.7 Hz), 2H, Ar- Hc,c'], 8.21 [d, (Jde= 8.8 Hz), 2H, Ar, Hd,d'] MS = M/z (398, m^+).

Other compounds were prepared similarly. Physical and analytical data of the compounds are recorded in Table 1.

Preparation of 4-arylidene-2-phenyl-1-(ρ-5-methylisoxazol-3-yl-aminosulphonylphenyl)-5-oxoimidazolines 4a-l

A mixture of compound **2** (0.01 mol) and 2-phenyl-4-(benzylidene)-5-oxazolinone (0.01 mol) was refluxed in pyridine for 6-8 h. Resulting mass was poured into crushed ice and neutralised with dil. HCl filtered and the product was recrystallized form methanol **4b**: Yield 60%, m.p. 192°C, calculated for $C_{27}H_{22}N_4O_5S$: C, 63.02; H, 4.31; N, 10.89%; Found: C, 63.15; H, 4.19; N, 10.75%. IR KBr (cm^{-1}): 3310 (N-H str.); 1720 (C=O str.); 1612 (C=N str.); 1380 (S=O str.) ^{1}H NMR (300 MHz) ($CDCl_3$+DMSO-d_6) δ ppm: 2.28 (s, 3H, -CH_3), 3.80 (s, 3H, -OCH_3), 6.08 (s, 1H, -CHa), 6.10 (d, 2H, Ar), 6.57 [d, (J = 8.6 Hz), 2H], 7.00 [d, J = 8.4 Hz, 2H, Ar], 7.45 [d, J = 8.5 Hz, 2H, Ar-]. 7.78-7.79 (m, 5H, Ar-H), 8.12 (s, 1H, -CHx).

Other compounds were prepared similarly. Physical and analytical data of the compounds are recorded in Table 1.

Acknowledgements

The authors are thankful to Dr. A. R. Parikh Prof. and Head, Department of Chemistry, Saurashtra University, Rajkot for needful co-operation. Authors are also thankful to RSIC Chandigarh, CDRI-Lucknow and Alembic Baroda for spectral analytical data.

References

1. Turpin A.J., Song Y.S., and Inman J.K. *J. Med. Chem.*, **42**(1): 69-73 (1999).
2. Trivedi S.D., Kubavat H.T., and Parekh H.H. *Indian J. Pharm. Sci*., **58**(1): 25 (1996).
3. Makarenich I.F., Mokrouz M.V., Topchi F.L., Kovalev I.P., and Sokolova V.E. *Khim. Prir. Soedin* **5**: 608-612 (1983); *Chem. Abstr*., **100**: 156894 p. (1984).
4. Kawasaki K., Kobayashi H., Ehara S., and Sato H. *PCT Int. Appl. WO* **98**: 32, 740 (Cl. C 07D 233/60) (1998); JP Appl. 97/10, 114 (1997); *Chem. Abstr.*, **129**: 148945h (1998).
5. Pilkingten B.L. and Elizabeth R.S. *Brit. U.K. pat-Appl.* G.B., 2, 329, 1802; *Chem. Abstr.*, **131**: 448172 (1999).
6. Vogel A.I. *Practical Organic Chemistry*. ELBS and Longman Ltd. 909 (1971).
7. Barry A.L. The antimicrobial suscptibitity test. Principle and practise, llus lea and Febiger, Philadelphia 180 (1976).