RESEARCH PAPER

Received 3 December 1994.
Indian J.Pharm. Sci., 1996, 58(1) pp. 25-27

Synthesis of Sulphaonamide Derivatives as Antimicrobial Agents

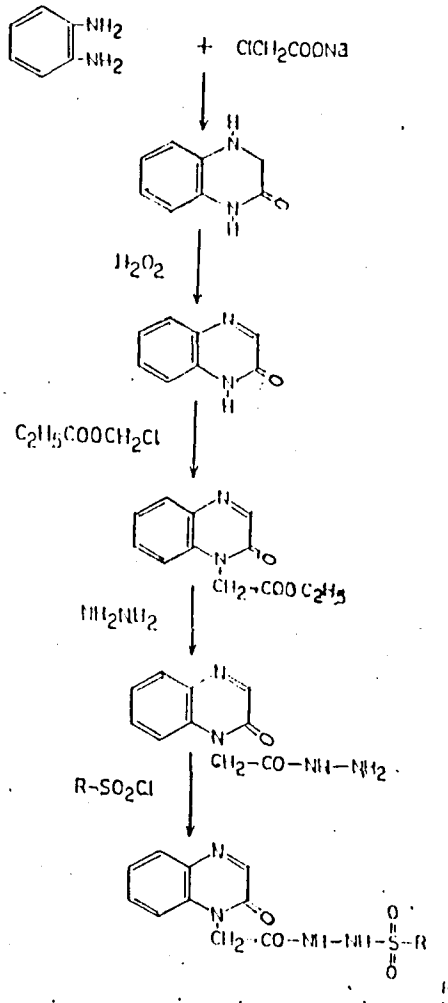
S.D.Trivedi, H.T. Kubavat, H.H. Parekh*
Dept. of Chemistry, Saurashtra University, Rajkot - 360 005.

Several 1-(N-arylsuphonylhydrazine carbonylmethyl)-2(1H)- quinoxalinones were prepared by condensing aryl sulphonylchloride with 2-(1H)-quinoxalinon-1'yl-acetyl hydrazine in presence of pyridine. The constitution of the products was supported by elemental analysis, IR, PMR and mass spectral study. The compounds synthesised were tested in vitro against Salmonella typhosa, Escherichia coli, Bacillus megaterium, and Stephylococcus citrus and a fungal strain, Aspergillus niger. Standard drugs were also tested under identical conditions for comparing the results.

SULPHONAMIDES are associated with a broad spectrum of pharmacological activities[1-4]. The discovery of sulphonamides marked the beginning of chemotherapeutic era by making possible a direct attack on microbial infections[5]. Sulphonamide antibacterials continue to be used because they are effective, inexpensive and free of super infection problems of the broad spectrum antibiotics[6]. In view of above findings, we have synthesised and biolabile sulphonamide derivatives bearing quinoxalinone nucleus[7-8]. The compounds were synthesised by condensing arylsulphonyl chloride with 2-(1H)-quinoxalinon-1'-yl-acetyl hydrazine in presence of pyridine. All the compounds were screened for their antimicrobial activity. The structure of the compounds have been established by analytical data & IR, PMR and mass spectral data.

EXPERIMENTAL

All melting points were determined in open glass capillaries and are uncorrected. IR absorption spectra were determined on a Shimadzu IR-435 spectrophotometer using KBr pellet method and HNMR, spectra on a Hitachi R-1200 60 MHz spectrometer using TMS as internal standard. The mass spectra were recorded on Jeol 300 at 70 e.v. The physical data of the various compound prepared are given in **Table-1**.



2(1H)-Quinoxalinon-l-yl-acyl hydrazine (1)

* For correspondence

Table I : Physical and biological data of the compounds 2a-n

Compound No.	R	M.P. °C	M.F.	% N Found	Antibacterial activity				Antifungal activity
					S.t.	E.c.	S.c.	B.m.	A.n.
2a	Phenyl	180-5	$C_{16}H_{14}O_4N_4S$	15.5	11	11	12	11	12
2b	4-Acetamidophenyl	240	$C_{18}H_{17}O_5N_5S$	16.8	12	11	11	11	12
2c	3-Carboxy-4--acetamidophenyl	300	$C_{19}H_{17}O_7N_5S$	15.1	12	13	13	11	13
2d	3-Carboxy-4--chlorophenyl	253	$C_{17}H_{13}O_6N_4SCl$	15.3	12	11	12	11	15
2e	3-Carboxy-4--hydroxyphenyl	300	$C_{17}H_{14}O_7N_4S$	13.2	12	14	13	11	11
2f	3-Carboxy-4--methoxyphenyl	300	$C_{18}H_{16}O_7N_4S$	13.0	12	14	13	11	11
2g	3-Carboxy-5--methoxyphenyl	300	$C_{18}H_{16}O_7N_4S$	12.9	11	13	11	11	13
2h	3-Carboxy-4--methylphenyl	280	$C_{18}H_{16}O_6N_4S$	12.9	13	13	13	11	11
2i	2-Carboxy-4--methylphenyl	234	$C_{18}H_{16}O_6N_4S$	13.4	12	12	12	12	16
2j	2-Carboxy-5--methylphenyl	300	$C_{18}H_{16}O_6N_4S$	13.2	14	15	12	13	12
2k	4-Carboxphenyl	258	$C_{17}H_{14}O_6N_4S$	14.0	11	12	12	11	12
2l	α-Carboxystyryl	190	$C_{19}H_{16}O_6N_4S$	13.0	14	13	13	11	13
2m	4-Ethanoic acid--phenyl	170	$C_{18}H_{16}O_6N_4S$	13.2	11	13	12	11	13
2n	4-Oxyethanoicacid-phenyl	>300	$C_{18}H_{16}O_7N_4S$	12.9	11	13	13	11	12

* **S.t.** = Salmonell typhosa, **E.c.** = Escherichia coli, **S.c.** = Stephylococus citrus, **B.m.** = Bacillus magaterium, **A.n.** = Aspergillus niger.
Zone of inhibition in mm at a concentration of 50 μg ml
Chloramphenicol (16-28), Norfloxacin (20-33), Griseofulvin (20)

A mixture of ethyl [2(1H)-quinoxalinon-yl] acetate[9] (5 g, 0.024 mol) and excess hydrazine hydrate (2.35 ml, 0.048 mol) in absolute ethanol was refluxed for 3 h. The reaction mixture was then cooled to room temperature and resulting solid was crystallised from water. Yield 66.00 %, m.p. 205° IR (KBr) : 3500-3400 (-NH-NH_2), 1680 (-C=O) 1-[N-(2-Carboxy-4-methylphenyl) sulfonylhydrazine carbonylmethyl-2-(1H)- quinoxalinone (2) :

A mixture of 2-carboxy-4-methylphenylsulphonyl chloride (2.32 g, 0.01 mol) and 2(1H)-quinoxalinon-l-yl-acetylhyrazine (2.18 g, 0.01 mol) was refluxed in dry pyridine (10 ml) for 4-5 hrs. The solvent was distilled off and the product was isolated, recrystallised from dioxane DMF mixture. Yield 49.20 %, m.p. 234°, IR (KBr) : 3400 (-NH), 1650 (>C=O) (NH), 1320 (S=O asym), 1160 (S=O sym.), 828 cm^{-1} (N-SO_2 str.), ^1H NMR (TFA) 2.55 (3H, s, Ar-CH_3),

5.20 (2H., s, -N-CH_2), 7.0-8.5 (8H, m, Ar-H.), 8.95 (2H., s. -NH-NH.. Mass m/z 416(M^+), 121 (100 %), 340, 257, 212, 154, 187, 131.

Similarly other sulphonylchlorides were condensed and physical data are recorded in **Table -1**.

Antimicrobial Screening :

The compounds 2 a-n were screened for their anti-bacterial activity against **Salmonella typhosa, Escherichia coli, Bacillus magaterium** and **Stephylococcus citrus** at a concentration of 50 μg/ml using cup-plate method[10].

RESULTS AND DISCUSSION

It has been observed that most of the compounds were mild to moderately active against Gram positive and Gram negative bacteria. However, maximum activity was observed in compounds bearing R=4-methylphenyl and cinnamyl against **S.typhosa** while R=4 methylphenyl, 2-methoxyphenyl against **E.coli**. In case of **S.citrus** and **B.megaterium**, compounds showed mild activity. The reference antibiotics chloramphenicol and norfloxacin were used under identical condition for comparison.

Antifungal activity was carried out **in vitro** against **Aspergillus niger**. at 50 μg/ml concentration. Petridishes were incubated at 30°C for 48 hr and the zone of inhibition was measured in mm. The reference antibiotic Griseofulvin was used under similar condition for comparison.

The compounds 2 a-n were active against fungal species. Maximum activity was observed in compounds bearing R = 3-carboxy-4- chlorophenyl and 2-carboxy-4-methylphenyl against **A.niger**.

It has been concluded that the activity displayed by the compounds 2 a-n were not comparable with the standard drugs. The biological data was recorded in Table-1.

ACKNOWLEDGEMENT

The authors wish to thank Dr.A.R. Parikh, Professor and Head, Department of Chemistry, Saurashtra University, Rajkot for encouragement and valuable suggessions.

REFERENCES

1. William L., Lucilla A.C., Alan C.S., **J. Med. Chem.**, 1980, 23, 630.
2. Andersen L., Kangasaho M., Nikander H., PCT Int. Appl. WO, 8807, 991 (Cl Co 7D-209/48), 1988, 26; **Chem. Abstr.**, 1989, 110, 135085 s.
3. Pomarnacka, Elzbiet, Brzozowsiki Z., Filczewski M., Szymanska-Kosmala M., Oledzka K., **Acta Pol. Pharma.**, 42(6), 1985, 501; **Chem. Abstr.**, 1987, 106, 138415 c.
4. Henquin J.C., **Diabetologia**, 1992, 32(10), 907; **Chem. Abstr.**, 1993, 118, 87.
5. Shepherd R.G., J. Org. Chem., 1947, 275; **Chem. Abstr.**, 1947, 41, 4465h.
6. Wilson C.O., Gisvold O., Doerge R.F., Textbook of Organic medicinal and pharmaceutical chemistry, Seventh Edition, Toppan Comp. Ltd., Japan, 1977, 203.
7. Alamanni M.C., Pirisino G., Savelli F., Sparatore F., Manco P., Satta M., **Farma co. Ed. Sci.**, 1981, 36(5), 399 (Ital); **Chem. Abstr.**, 1981, 95, 169127 u.
8. Sparatore F., Pirisino G., Alamanni M.C., Manca-Dimich P., Satta M., **Boll. Chim. Farm.**, 1978, 117(11), 638; **Chem. Abstr.**, 1979, 91, 13757.
9. Badr M.Z.A., Mahgoub S.A., Abdel Latif F.F., Fahmy A.M. and Mustafa O.S., **J. Indian Chem. Soc.**, 1990, 67, 216.
10. Barry A.L., The antimicrobial susceptibility test; Principal and practices, 1976, 180; **Chem. Abstr.**, 1977, 64, 25183.