Int. J. Chem. Sci.: 6(2), 2008, 942-948

A SOLID STATE OXIDATION METHOD FOR THE SYNTHESIS OF SULFONES USING OXONE

N. S. MAHAJAN*, R. L. JADHAV, N. V. PIMPODKAR, S. C. DHAVALE[a], H. K. KUNJAWANI[b] and A. M. MANIKRAO[b]

Department of Pharmaceutical Chemistry, Satara College of Pharmacy, SATARA (M. S.) INDIA
[a]Government College of Pharmacy, KARAD (M. S.) INDIA
[b]Department of Pharmaceutical Chemistry, G.S.P.S. Institute of Pharmacy, AKOLA (M. S.) INDIA

ABSTRACT

Various N-substituted-β-(4-phenyl-2-thiazolyol) thio-alkyl/aryl acetamides can be selectively oxidized to the corresponding sulfones in solid-state condition by using oxone. The synthesized compounds were confirmed by using elemental analysis and spectral data. These synthesized compounds were also tested for thesis antibacterial and antifungal activities. None of them were found to possess any promising activity. The advantages of this method are that it is a low cost and safe method with high yield and simple operating conditions.

Key words: 4-Phenyl-2-mercaptothiazoles, Oxone, Antibacterial activity, Antifungal activity

INTRODUCTION

Sulfones find wide applications in the field of medicinal chemistry. 4,4'-Diaminodiphenyl sulfones (DDS), which is a famous antitubercular and antileprotic drug, was first evaluated by Bruttle et al.[1] Eaton and Davis[2] tested a number of chlorosubstituted diphenyl sulphones against summer eggs and adult females of Metatetranyches ulmi and showed them to be antitubercular as well as antithyroid and least toxic. Along with this, sulfones find wide applications in organic synthesis, particularly in carbon-carbon bond forming process[3].

All the above works indicated that sulfones find good applications as an antibacterial agent. These reports made us to think to synthesize sulfones of our newly synthesized compounds.

It has been understood that most of the organic reactions have been studied in

* Author for correspondence; E-mail: nsmahajan17@gmail.com

solution, while only few organic reactions occur quiet effectively in the solid state. Generally these solid-state reactions are carried out by using finely powered reactants and reagents at room temperature. But sometimes grinding of the reaction mixture using pestle and mortar also accelerates these reactions[4].

During our synthetic project, Pyne and Hojipour[5] reported the solid-state oxidation method for the synthesis of sulfones by using oxone (potassium peroxymonosulfate). This data initigated us to synthesize sulfones through solid-state synthesis and evaluate them for their antibacterial and antifungal activities.

The final compounds obtained by above said method were characterized by their elemental analysis and spectral data.

EXPERIMENTAL

Materials and methods

All the melting points and boiling points were determined by open capillary method in liquid paraffin bath and uncorrected. All the solvents were used after distillation. Oxone, aluminum chloride were purchased from S.D. Fine Chemicals, Mumbai. Silica gel G plates (3 x 8 cm) were used for TLC and spots located by iodine vapors in a chamber. Column chromatography was performed on a neutral alumina column (2.5 x 45cm) using appropriate eluent.

The IR spectra (KBr/nujol) were recorded on PERKIN-ELMER FT-IR spectrometer and the values expressed in cm^{-1}. ^1H NMR spectra ($CDCl_3$) were taken on Brooker AC 200 MHz FT using TMS as an internal reference compound.

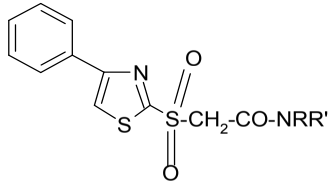
Method of preparation

Preparation of sulfones II: General method

A mixture of the appropriate sulfide (1.72 mmoles), oxone (4.98 g, 7.92 mmoles) and $AlCl_3$ (0.44 g, 3.4 mmoles) was ground with pestle and mortar for 0.5 hr, and the product was taken up in dichloromethane (3 x 10 mL). The solution was washed with aqueous 20% $NaHCO_3$ and water, dried ($MgSO_4$) and the solvent evaporated. The product was > 95% pure as found by TLC and ^1H NMR analyses.

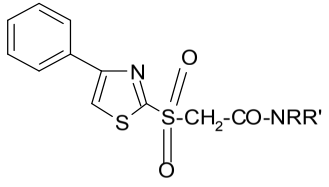
The physicochemical characteristics and spectral data of various compounds **(II a-f)** are given in Table 1 and Table 2, respectively.

Table 1. Physicochemical data of II (a-f)



Comp.	R	R'	M. P. (°C)	Yield (%)	Nature	Mol. formula	Elemental analysis Calc. (%) Found (%)		
							C	H	N
IIa	H	Ph	120-122	95	Pale yellow needles	$C_{17}H_{14}N_2OS_2$	56.98	3.91	7.82
							57.15	4.08	8.01
IIb	H	p- ClPh	118-120	96	Pale yellow shining needles	$C_{17}H_{13}N_2OS_2CL$	51.97	3.13	7.13
							52.10	3.00	7.23
IIc	H	CH_2Ph	112-114	97	Pale yellow shining needles	$C_{18}H_{16}N_2OS_2$	58.06	4.30	7.53
							59.80	3.98	7.65
IId	H	n-C_3H_7	75-77	98	Pale yellow flakes	$C_{14}H_{16}N_2OS_2$	49.13	4.94	8.64
							50.13	5.02	8.65
IIe	RR' = Pyrolidine-1-yl		121-123	98	Light yellow granules	$C_{15}H_{16}N_2OS_2$	53.57	4.76	8.33
							53.52	4.95	8.49
IIf	RR' = Morpholine-1-yl		135-138	97	Pale yellow granules	$C_{15}H_{16}N_2O_2S_2$	51.14	4.55	7.95
							50.85	4.99	7.96

Table 2. Spectral data of II (a-f)



Comp	R	R'	IR (cm^{-1}) KBr					^{1}H NMR (ppm) $CDCl_3$
			vNH	vCO	vC = N	ArH	SO_2	
IIa	H	Ph	3263	1659	1552	689 & 748	1350 & 1160	10.20(s, 1H,NH); 7.90 (d, 1H, 5-H); 7.50-7.19 (m, 10H, $2XC_6H_5$); 4.00 (s, 2H, S-CH_2).
IIb	H	p-ClPh	3268	1660	1550	720 & 830	1345 & 1150	10.20(br s, 1H,NH); 7.90 (d, 1H, 5-H); 7.50-7.10 (m, 9H,Ar-H); 4.00(s, 2H,S-CH_2).
IIc	H	CH_2Ph	3310	1646	1532	705 & 725	1338 & 1128	7.85(br s, 1H,NH); 7.70 (d, 1H, 5-H); 7.43-7.20(m, 10H, $2xC_6$-H_5); 4.50 (d, $2CH_2$,of Benzyl); 4.00 (s, 2H, S-CH_2).
IId	H	n-C_3 H_7	3442 & 3296	1639	1556	690 & 728	1328 & 1120	7.90 (d, 1H, 5-H); 7.51-7.32 (m, 6H,C_6-H_5+ NH); 3.92 (s, 2H, S-CH_2); 3.25 (q, 2H,NH-CH_2); 1.45 (sext, 2H, -CH_2-of n-propyl); 0.81 (t, 3H, -CH_3 of n-propyl)
IIe	RR' = Pyrolidine-1-yl		-	1635	1555	689 & 728	1338 & 1130	-
IIf	RR' = Morpholine-1-yl		-	1639	1557	685 & 730	1345 & 1158	-

Table 3. Antibacterial activity of compounds II (a-f).

Comp.	R	R'	Zone of inhibition (mm)					
			P. aeuroginose		*S. aureus*		*E. coli*	
			100 µg/mL	150 µg/mL	100 µg/mL	150 µg/mL	100 µg/mL	150 µg/mL
IIa	H	C_6H_5	9	9	15	17	5	6
IIb	H	p-ClC_6H_5	9	12	15	16	5	8
IIc	H	$CH_2C_6H_5$	8	9	12	15	2	2
IId	H	n-C_3H_7	5	8	13	15	5	7
IIe	RR' = Pyrolidine-1-yl		10	14	25	27	6	8
IIf	RR' = Morpholine-1-yl		11	15	26	29	9	10
Standard	Norfloxacin		16	22	35	45	10	15

Table 4. Antifungal activity of compounds II (a-f)

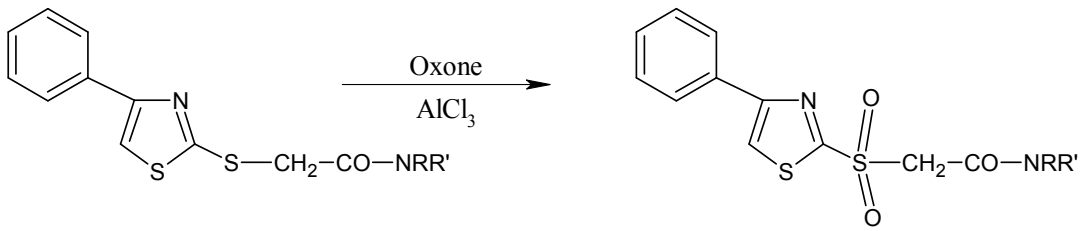
Comp.	R	R'	Zone of inhibition (mm)			
			C. albicans		*A. niger*	
			100 µg/mL	150 g/mL	100 µg/mL	150 g/mL
IIa	H	C_6H_5	8	8	7	8
IIb	H	p-ClC_6H_5	9	9	7	8
IIc	H	$CH_2C_6H_5$	7	8	5	5
IId	H	n-C_3H_7	7	10	5	8
IIe	RR' = Pyrolidine - 1-yl		22	29	25	25
IIf	RR' = Morpholine - 1-yl		25	31	27	28
Standard	Griseofulvin		34	38	32	36

Antibacterial activity

The compounds, **(II a-f)** were screened against *P. aeuroginose*, *E. coli* and *S. aureus* by cup plate method[6]. As compared to the standard drug norfloxacin, these compounds showed moderate activity at concentrations 100 µg/mL and 150 µg/mL (Table 3).

Antifungal activity

The synthesized compounds were screened for antifungal activity using cup plate method[7] against *C. albicans* and *A. niger*. These compounds showed moderate activity at concentrations 100 µg/mL and 150 µg/mL (Table 4).



(I) **(II)**

Where,

(a) R = H; R' = C_6H_5 **(b)** R = H; R' = p-ClC_6H_4

(c) R = H; R' = $CH_2C_6H_5$ **(d)** R = H; R' = n-C_3H_7

(e) RR' = pyrolidine-1-yl **(f)** RR' = morpholine –1-yl.

RESULTS AND DISCUSSION

The synthesized compounds were evaluated for both; antibacterial and antifungal activities. None of the above compounds showed any promising antibacterial and antifungal activities at 100 µg/mL and 150 µg/mL concentrations as compared with norfloxacin and griseofulvin, respectively.

ACKNOWLEDGEMENT

The authors are grateful to KLE's College of Pharmacy, Belgaum for providing all the facilities to carry out the present work. They are also thankful to Prof. M. S. Jagtap, Chairman, Gourishankar Education Society, Satara, and Shri. R. J. Dias, Principal, Satara

College of Pharmacy, Satara for their support.

REFERENCES

1. Buttle et. al., The Lancet, **1**, 1331(1937).
2. Eaton and Davis, Ann. Applied Biol., **37**, 471 (1950).
3. A. R. Hajipour and S. G. Pyne, J. Chem. Research, **5**, 360 (1995).
4. A. R. Hajipour, Synth. Commun., 3627 (1996).
5. S. G. Pyne and A. R. Hajipour, Tetrahedron, **48**, 9385 (1992).
6. S. G. Pyne and B. Dikic, J. Org. Chem., **55,** (1932) (1990).
7. M. Toda, M, Yagi and K. Kiyoshige, J. Chem. Soc. Chem. Commun., 985 (1988).
8. A. R. Hajipour, Indian J. Chem., **36B**, 1069(1997).
9. H. W. Seeley and P. J. Van Denmark., Microbes in Action, A Laboratory Manual of Microbiology, II Edn (1975) p. 55.
10. F. C. Kavangh, Analytical Microbiology, Academic Press, New York (1944) p. 125.

Accepted : 17.03.2008