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NOTE

Synthesis and Antibacterial Activity of Some Chlorosubstituted Isoxazolines

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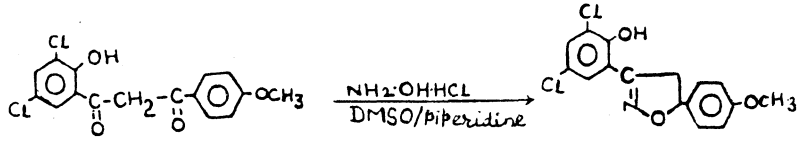
Isoxazolines (2a–d) were prepared from 2'-hydroxychalconedibromides and hydroxylamine hydrochloride in DMSO containing a little piperidine on 2.5 h reflux with 80–85% yield. The compounds (2a–d) were assayed against some gram positive and gram negative bacteria. The results obtained are very interesting.

Literature survey reveals that isoxazolines[1–3] are not only used in textiles and cinematographic films but they also show widely differing antibacterial activity. 3,5-Diarylisoxazolines[4] were reported to have been prepared by the action of $NH_2OH{\cdot}HCl$ on chalcones and flavanones. Isoxazolines have been a subject of considerable interest in the recent years[5–7]. Keeping these facts in view the title compounds were prepared and screened for their antibacterial activity against some gram positive (*S. aureus* and *B. subtilis*) and some gram negative (*E. coli* and *P. aeruginosa*) pathogens.

A mixture of 2'-hydroxychalcone (1d) (0.01 mol) and hydroxylamine hydrochloride (0.02 mol) was refluxed in DMSO (30 mL) containing piperidine (0.5 mL) for 2.5 h. The reaction mixture was poured in cold water and acidified with 1 : 1 HCl. A semisolid thus obtained was triturated and crystallised from ethanol-acetic acid mixture to obtain isoxazoline (2d) with 85% yield.



(1d) (2d)

The compound (2d) gave dark green coloration with ethanolic $FeCl_3$ and was soluble in NaOH, indicating thereby the presence of phenolic —OH group. Its purity was tested by TLC in benzene (R_f 0.56). Its m.p. recorded was uncorrected.

Its IR (Nujol) (cm^{-1}) spectra showed absorption bands at 3400 (very strong H-bonded O—H-stretching), 2922 (strong, O—H stretching in aryl ethers), 1630 (weak, >C=N stretching), 1385 (strong, O—H bending), 1230 (medium, Ar—O—C stretching), 1385 (strong, O—H bending), 1230 (medium, Ar—O—C

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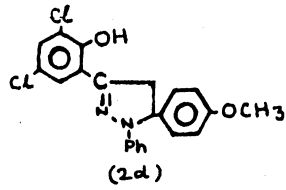
stretching), 722 (strong, C—Cl stretching). Its UV-VIS ($CHCl_3$) spectra showed λ_{max} at 270 and 370 nm whch indicates carbonyl function ($n \rightarrow \pi^*$ transition) and its PMR ($CDCl_3$) showed peaks at 2.5 and 2.8 (dd, 1H, CH_B—CH), 3.4 and 3.5 (dd, 1H —CH_A—CH), 3.85 (s, 3H, Ar—OCH_3), 4.9–5.0 (dd, 1H, —CH—C), 6.8–7.8 (m, 6H, Ar—H), 10.80 (s, 1H, Ar—OH).

On the basis of of elemental analysis chemical properties and spectral results, the compound (2d) was assigned the structure as (2-hydroxy-3,5-dichlorophenyl)-5-phenyl isoxazoline.



(2d)

Similarly the compounds (2a–c) were prepared.

Analytical and physical data of the compounds (2a–d) are given in Table-1.

TABLE-1

Compound	Mol. formula	Yield (%)	m.p. (°C)	R_f	% Nitrogen	
					Found	Calcd.
2a	$C_{15}H_{22}O_2NCl$	80	160	0.36	5.50	5.11
2b	$C_{16}H_{14}O_3NCl$	80	168	0.54	4.90	4.61
2c	$C_{11}H_{11}O_2NCl_2$	85	155	0.41	5.00	4.53
2d	$C_{16}H_{13}O_3NCl_2$	85	234	0.56	4.84	4.14

Antibacterial activity

The compounds 3,5-diarylisoxazolines (2a–d) were assayed against some gram positive[8] (*S. aureus* and *B. subtilis*) and gram negative[9] (*E. coli* and *P. aeruginosa*) *in vitro* by disc diffusion method[10] in dimethyl formamide (DMF) solvent at a concentration of 100 μg/mL.

Most of the compounds showed significant antibacterial activity (Table-2). However their activity was highest against *S. aureus*, *E. coli* and *P. aeruginosa* and moderate against *B. subtilis*.

TABLE-2
ANTIBACTERIAL ACTIVITY OF 3,5-DIARYLISOXAZOLINES

Compound	Substituents	*S. aureus*	*B. subtilis*	*E. coli*	*P. aeruginosa*
2a	—Cl	14	11	13	13
2b	—Cl, —OCH_3	13	10	14	15
2c	2Cl	16	12	15	14
2d	2Cl, —OCH_3	13	10	14	14

It has been interesting to note that antibacterial activity got enhanced with the introduction of —Cl and —OCH_3 groups.

From the results it is obvious that all the compounds have shown strong antibacterial activity against test organisms which are common human pathogens. Therefore they may find application in therapeutic purposes in human diseases, provided they are non-toxic to human body.

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REFERENCES

1. L. Caradonna and M.L. Stein, *Farmaco. Edn. Sci.*, **15**, 674 (1960).
2. N. Stelger, *Chem. Abstr.*, **45**, 10259 (1951).
3. T. Okuda, J. Kitamura and K. A. Azika, *Proc. Gifu. Coll. Pharm.*, **5**, 2083 (1955).
4. A.B. Sammour and Mh.D., Bakasaby, *J. Chem. U.A.R.*, **12**, 1 (1969).
5. C. Eguchi, N. Vasuda, H. Iwagomi, E. Takigawa, M. Okutsu, J. Onuki and T. Nakamiya, *Jpn. Kokai, Tokkyo, Koha*, 7, 984, 592 (1979).
6. Sharma, *Chem. Abstr.*, **112**, 138866z (1990).
7. Uma Den and Ashok K. Rao, *Chem. Abstr.*, **114** (1991).
8. R. Ananthanarayan and C.K. Jayaram Panikar, Text Book of Microbiology, 15th Edn., Orient Longmans (1990).
9. Robert Cruikshank, J.P. Dugud, B.P. Marmicon and R.H.A. Swain, Medicinal Microbiology, 12th Edn., Vol. II, Churchill Livingstone, Edinburgh-London-New York (1982).
10. Derek Brown and Robert Blowers, Laboratory Methods in Anti-microbial Chemotherapy (Disc Method of Sensitivity Testing).

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