Asian Journal of Chemistry Vol. 17, No. 1 (2005), 624–626

NOTE

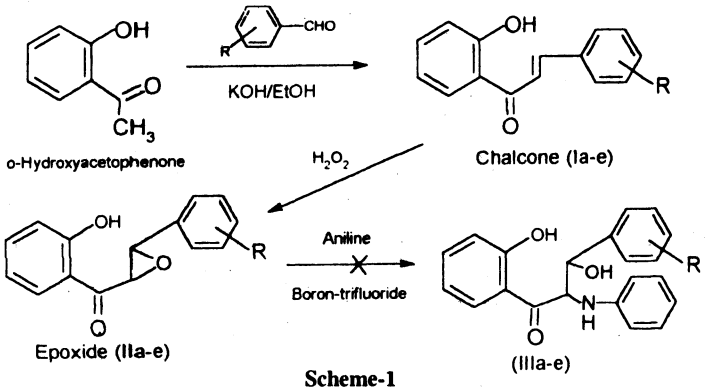
Synthesis and Antibacterial Activity of Epoxides Derived from Chalcones

ASIF HUSAIN* and MOHD. SHAHARYAR
Department of Pharmaceutical Chemistry, Faculty of Pharmacy
Jamia Hamdard (Hamdard University), New Delhi-110 062, India
E-mail: drasifhusain@yahoo.com; Mobile: 9891116086

Epoxides (**IIa–e**) have been synthesized by reacting appropriate chalcones with hydrogen peroxide. These epoxides were reacted with aniline in presence of boron-trifluoride in order to prepare some new dihydroxy compounds (**IIIa–e**); however, these compounds could not be separated in pure form. The epoxides were screened for antibacterial activity.

Key Words: Epoxide, Chalcone, Antibacterial activity.

Chalcones are important intermediate in the synthesis of flavanol[1], dihydroxy flavanol[2], flavanones[3], aurones[4], dihydroxy chalcones[5], etc. Chalcones and its derivatives are reported to have antibacterial, antifungal, antiparasitic, antitubercular and insect repellent properties[6–9]. Keeping in view these observations, it was planned to exploit chalcones to synthesize some new epoxides and dihydroxy compounds. In the present communication, the formation of epoxides by reacting chalcones with hydrogen peroxide has been reported **(Scheme-1).** The structures of the synthesized compounds have been confirmed by IR and ^{1}H NMR spectral analysis. The epoxides were tested for antibacterial activity by agar cup-plate method[10] against the strains of *S. aureus* and *E. coli*.



Scheme-1

Melting points were recorded in liquid paraffin bath using open-end capillaries and are uncorrected. The IR spectra were run on Shimadzu FTIR spectrophotometer in KBr pellets. ^{1}H NMR spectra were recorded on a Bruker 300 MHz NMR spectrometer in $CDCl_6$/DMSO-d_6 using TMS as internal reference. Thin layer chromatography was performed on silica gel (Merck).

Synthesis of chalcone (I)

To a solution of *o*-hydroxyacetophenone (0.01 mol) in oxygen-free distilled ethanol, different aromatic aldehydes, *e.g.*, benzaldehyde, *p*-anisaldehyde, veratraldehyde, 3,4,5-trimethoxybenzaldehyde and *p*-bromobenzaldehyde (0.01 mol) and 5 mL of 2% potassium hydroxide were added. The reaction mixture was refluxed for 4 h. It was cooled to room temperature and poured into ice-cold water. A solid mass so obtained was filtered, washed with sodium bicarbonate solution followed by water and then dried. It was crystallized from acetone to give tlc pure crystals (**I**).

All the chalcones were obtained in moderate to good yields in the range of 60–76% and gave red colour with conc. sulphuric acid. **Ia**: IR (KBr, cm^{-1}); 3100 ν(O—H), 1650 ν(C=O), 1610 ν(CH=CH), 1580 ν(C=C). ^{1}H NMR ($CDCl_3$) δ ppm: 6.88 (s, 1H, H-3 *o*-hydroxy phenyl ring), 7.41 (m, 3H, H-3,4,5 phenyl ring), 7.48 (m, 2H, H-2,6 phenyl ring). The melting points of the products are as follows: R = -H 136–38°, -4-OCH_3 112°, -3,4-$(OCH_3)_2$ 108°, -3,4,5-$(OCH_3)_3$ 102°, -4-Br 138°C.

Synthesis of Epoxide (II)

To a cooled solution of (**I**) (1.0 g) in acetone (20 mL) was added an aqueous solution of sodium hydroxide (1.2 mL, 8%). The reaction mixture was then cooled in an ice bath and hydrogen peroxide (2 mL, 30%) was added. The contents were shaken for 1 h with cooling at 15 min interval and left overnight. The solid mass, which separated out, was filtered and dried to give tlc pure white compound **II**.

The epoxides were obtained in moderate yields in the range of 42–50%. Compound **IIa**: IR (KBr, cm^{-1}): 3120 ν(O—H); 1640 ν(C=O), 1585 ν(C=C, aromatic). ^{1}H NMR (DMSO-d_6) δ ppm: 6.88 (s, 1H, H-3 *o*-Hydroxy phenyl ring), 7.41 (m, 3H, H-3,4,5 phenyl ring), 7.48 (m, 2H, H-2,6 phenyl ring). The melting points of the products are as follows: R = -H 56–58°, -4-OCH_3 54°, -3,4-$(OCH_3)_2$ 48°, -3,4,5-$(OCH_3)_3$ 62–64°, -4-Br 60°C.

Synthesis of compound (III)

To a well-stirred suspension of (**II**) and aniline (1 mL) in dichloromethane (20 mL), borontrifluoride etherte (1 mL) was added dropwise. The reaction mixture was stirred for 30 min. It was then transferred to a separating funnel and washed with water, HCl (10%) and again with water. The organic layer was dried over sodium sulphate and the solvent was evaporated off. The residue so obtained could not be crystallized in spite of several efforts. It was found to be a complex mixture on thin layer chromatography examination.

Antibacterial activity

The newly synthesized epoxides were screened for antibacterial activity against gram-positive bacteria *S. aureus* and gram-negative bacteria *E. coli*. The testing was carried out using 100 μg/mL of sample in DMF. Sensitivity plates were seeded with bacterial inoculum of 1×10^6 CIU/mL and each cup (dia. 10 mm) was loaded with 0.1 mL of test solution. The zones of inhibition were recorded after incubation for 24 h. The activity was compared with standard drug tetracycline. The zone of inhibition was measured in mm and reported in Table-1.

TABLE-1
ANTIBACTERIAL ACTIVITY OF THE EPOXIDES

Compd. (100 μg/mL)	-R	Zone of inhibition (mm)	
		S. aureus	*E. coli*
IIa	H	11	08
IIb	4-OCH_3	10	10
IIc	3,4-$(OCH_3)_2$	08	08
IId	3,4,5-$(OCH_3)_3$	10	11
IIe	4-Br	15	14
Tetracycline (Standard)		20	16

The epoxides were found to be active against test organisms. Compound **IIe** containing bromo group at C-4 of the phenyl ring exhibited significant activity while others showed moderate activity against the two tested microorganisms.

REFERENCES

1. J. Alger and J.P. Flynn, *Proc. R. Irish Acad.*, **42B**, 1 (1934).
2. A.G. Doshi and B.J. Ghiya, *Indian J. Chem.*, **17B**, 509 (1979).
3. T.A. Geissman, Chemistry of Flavanoid Compounds, Pergamon Press, Oxford, p. 159 (1962).
4. T.R. Sheshadri, *Proc. Indian Acad. Sci.*, **30A**, 120 (1948).
5. J.K. Makrandi and S.K. Grover, *Indian J. Chem.*, **21B**, 543 (1982).
6. W.B. Geirger and J.E. Conn, *J. Am. Chem. Soc.*, **67**, 112 (1995).
7. R. Laliberate, J. Manon, Warik and G. Madewar, *Can. J. Chem.*, **46**, 1952 (1968).
8. S.V. Krishna, A. Rajshekar, T.K. Reddy and M.S. Naidu, *Curr. Sci.* (India), **57**, 129 (1988).
9. V.V. Laxmi, P. Shridhar and H. Polasa, *Indian J. Pharm. Sci.*, **47**, 202 (1985).
10. A.L. Barry, in: Illus (Ed.), The Antimicrobial Susceptibility Test: Principles and Practices, Lea & Febiger, Philadelphia, Pa. (USA), p. 180 (1976).

(*Received*: 9 March 2004; *Accepted*: 29 September 2004) AJC-3582