Available online at www.pelagiaresearchlibrary.com

Pelagia Research Library

Der Chemica Sinica, 2014, 5(3):10-14

Pelagia Research Library
ISSN: 0976-8505
CODEN (USA) CSHIA5

Synthesis, characterization and antimicrobial activity of some dibenzo-α-pyrone derivatives

Shalini K. Sawhney[a]*, Birendra Shrivastava[c], Yatendra Kumar[a], Vandana Shrivastava[b] and Ankita Sahai[a]

[a]ITS Paramedical (Pharmacy) College, Muradnagar, Ghaziabad, U.P., India
[b]ITS Dental College, Muradnagar, Ghaziabad, U.P., India
[c]School Of Pharmaceutical Sciences, JNU, Jaipur, Rajasthan, India

---

ABSTRACT

An efficient method has been developed for the synthesis of Dibenzo-α-pyrones derivatives. Firstly, dibenzo-α-pyrones, an active ingredient of Shilajit was prepared using Hurtley synthesis and then the procedure for dibenzo-α-pyrone derivative was carried out through One Pot Mannich reaction using different amines and formaldehyde. The derivatives were characterized by spectroscopic methods(UV, IR, ^{1}H NMR) and analytical methods(mp, TLC, and pKa). Antimicrobial activities of Dibenzo-α-pyrone and its derivatives were tested against some selected bacteria.

Keywords: Dibenzo-α-pyrone, Shilajit, Hurtley synthesis, Mannich reaction, Mannich bases.

INTRODUCTION

Shilajit is a rejuvenator of Ayruvedic origin and is a blackish brown exudation from layers of rocks in many mountain ranges especially Himalayas and Hindukush ranges [1]. Shilajit mainly used for general physical strengthening, urinary tract rejuvenation, enchanced brain functioning potency, kidney rejuvenation and immune system strengthening. It is used for the treatment of arthritis, hypertension, and diabetes as well as for treating many other conditions [2-7].

Dibenzo-α-pyrones (DBαP) have been found to be active constituent of herbal drug Shilajit. DBαP is a 6H-Dibenzo (b,d)-pyran-6-one moeity [8]. Clinical research shows that it increases longevity, improves memory, reduces allergies and respiratory problems, reduces stress and relieves digestive troubles. It has also been reported for analgesic, anti-inflammatory, anti-alzheimer, antiulcerogenic, anxiolytic, nootropic, nutritive tonic, immunomodulator, antioxidant, antiaging, antiallergic, aphrodisiac, rejuvenator, adaptogenic and decreasing blood sugar [10].

In view of the above observation, the isolation of DBαP from crude Shilajit has been a tedious task and the yield produced is less. Therefore, by the application of this rapid and efficient One Pot Synthesis of Mannich deriatives, the products formed in a single step and diversity can be achieved simply by varying the reacting components [8-9]. The structure can be established on the basis of various physical properties and spectral data. The dibenzo-α-pyrone and its derivatives have been subjected to microbes such as *E.coli* for antimicrobial study [11-13].

MATERIALS AND METHODS

Experimental

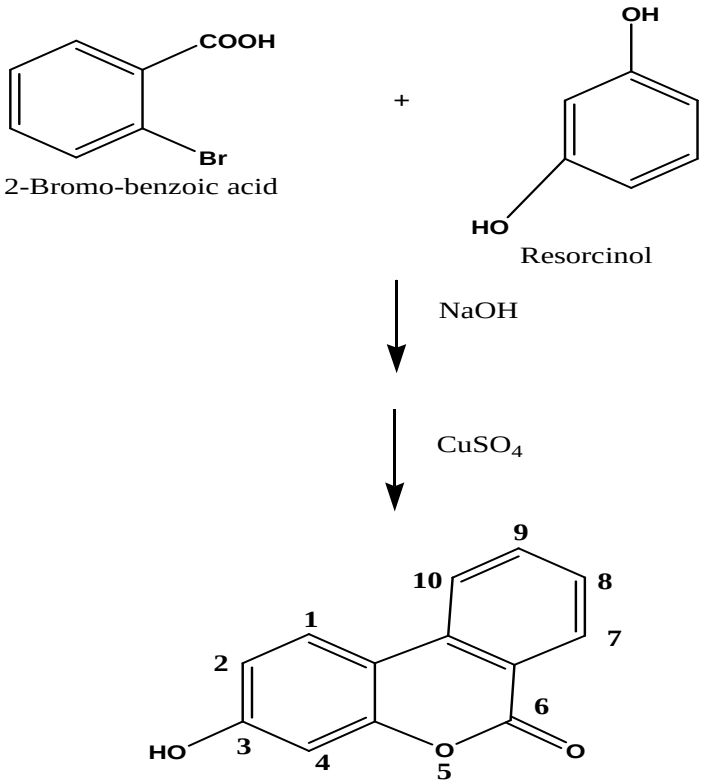
All the materials were of analytical reagent grade. The 2-bromobenzoic acid, resorcinol, formaldehyde and other amines were purified by standard procedures. The purity of them was determined by Thin layer chromatography (TLC). Melting points were recorded using a open capillary method with a physical melting point apparatus (Perfit) and uncorrected. UV spectra were recorded on a Schimadzu model 1800 type. IR spectra were recorded as a KBR pellets on a FT/IR-4100 type A model. ^{1}H NMR spectra were recorded using a Brucker 300 MHz NMR spectrometer using DMSO as a solvent. The purity determination of the substrates and the reactions monitoring by the solvent system were accomplished by TLC on 0.25 mm silica gel plates. Visualization of chromatograms was done under iodine chamber. Mac Konkey agar (Sheep blood agar) was used for the study of antimicrobial activity of the dibenzo-α-pyrone and its derivatives using Disc diffusion method. Ciprofloxacin was used as standard for antimicrobial activities.

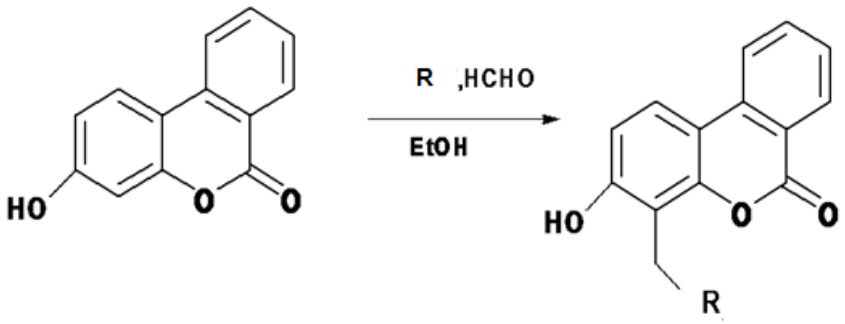
1. Synthesis of Dibenzo-α-pyrone

Dibenzo-α-pyrone was prepared by standard Hurtley reaction using 2-Bromobenzoic acid , resorcinol and NaOH in presence of $CuSO_4$ solution. The resulting dibenzo-α-pyrone was a clay coloured solid which was filtered and recrystallized using ethanol. The purity of the compound was checked through melting point and TLC.

2. Synthesis of Mannich derivatives of Dibenzo-α-pyrone

The resulting clay coloured solid of DBαP was mixed with amines (2a-k) respectively, formaldehyde and ethanol (20 mL). 1 mole each of the reacting substances was taken in a 250 mL round bottomed flask and refluxed for 1.5 hrs as per mannich synthesis. The progress of the reactions were monitored by TLC. After completion of the reaction, the solid precipitates were obtained and filtered which were recrystallized from ethanol to afford pure products. The Mannich derivatives obtained were identified by physical and spectroscopic data.





1 2

R =

(a) CH_3 NH_2

(b) CH_3 CH_2 NH_2

(c) $CH_3CH_2CH_2CH_2$ NH_2

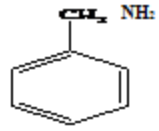
(d) $NHCH_2CHCH_3CH_3$

(e) CH_3NH CH_3

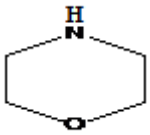
(f) CH_3CH_2NH CH_2CH_3

(g) $CH_3CH_2CH_2CH_2$ NH $CH_2CH_2CH_2CH_3$

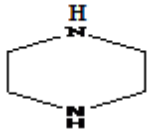
(h)



(i)



(j)



(k)

3. Antimicrobial activity

The biological activity of DBαP and synthesised Mannich derivatives have been studied for their antimicrobial activity using disc diffusion test. The antimicrobial activity was carried out using bacteria (E.coli). The zone of inhibition values were taken at the end of 24 hrs at 37°C for the bacterial stains at three different doses (2, 5, 10 mg). Ciprofloxacin was used as a standard. The values are presented in Table 2.

RESULTS AND DISCUSSION

The DBαP and its Mannich derivatives were characterized by spectral analysis. The analytical data (mp, Mol.wt., R_f, pKa) of DBαP and its derivatives are presented in Table 1.

Infrared spectra

In order to study the binding mode, the IR spectrum of the derivatives was compared with those of the dibenzo-α-pyrones. In IR spectra, the characteristic -OH stretching frequency is found at ν= 3584 – 3700 cm^{-1}. The stretching frequency of aliphatic secondary amines is found at 3350-3310 cm^{-1} and the C-N characteristic stretching vibration is found at 1250-1020 cm^{-1}. The characteristic saturated aliphatic C=O stretching vibration is found at 1715 cm^{-1} and C-O stretch shown at 1224 cm^{-1}. The bands in the region 1200-800 cm^{-1} assigned to C-C stretch. The C-H stretching vibration are shown in the band region 3000-2840 cm^{-1}. The bands at 1497 and 1459 cm^{-1} are assigned to C=C ring stretch.

Table 1: Physico-chemical properties

Compound	Melting Point	Molecular Weight	R_f	Partition Coefficient	Solubility in DMSO
DBP	230°-240°C	211 g	0.33	Lipophilic	Soluble
Methylamine derivative	210°-215°C	253 g	0.54	Hydrophilic	Soluble
Ethylamine derivative	190°-210°C	267 g	0.69	Hydrophilic	Soluble
Butylamine derivative	180°-185°C	295 g	0.56	Lipophilic	Soluble
Isobutylamine derivative	200°-220°C	295 g	0.66	Lipophilic	Soluble
Dimethylamine derivative	200°-210°C	267 g	0.66	Lipophilic	Soluble
Diethylamine derivative	210°-220°C	295 g	0.53	Lipophilic	Soluble
Dibutylamine derivative	210°-215°C	351 g	0.64	Lipophilic	Soluble
Benzylamine derivative	230°-240°C	331 g	0.50	Lipophilic	Soluble
Morpholine derivative	220°-230°C	311 g	0.56	Lipophilic	Soluble
Pyrrolidine derivative	218°-220°C	295 g	0.69	Lipophilic	Soluble
Piperazine derivative	140°-150°C	310 g	0.52	Lipophilic	Soluble

^{1}H NMR

In the ^{1}H NMR spectra, the broad signal around the $\delta = 10.3$ ppm are assigned to the protons of the hydroxy group. The signal around the $\delta = 8.2$-8.1 ppm is assigned to the protons of –NH and the signals around the δ=6.7-7.8 ppm is assigned to the protons of aromatic ring (CH=CH).

Table 2: Antimicrobial activity of Synthesised compounds

Compounds	Zone of inhibition of *E.coli*		
	2 mg	5 mg	10 mg
Ciprofloxacin	19 mm	20 mm	22 mm
DBP	4 mm	5 mm	6 mm
Methylamine derivative	9 mm	3 mm	5 mm
Ethylamine derivative	12 mm	10 mm	8 mm
Butylamine derivative	8 mm	5 mm	9 mm
Isobutylamine derivative	5 mm	10 mm	7 mm
Dimethylamine derivative	8 mm	7 mm	11 mm
Diethylamine derivative	13 mm	17 mm	19 mm
Dibutylamine derivative	8 mm	16 mm	12 mm
Benzylamine derivative	5 mm	12 mm	13 mm
Morpholine derivative	11 mm	5 mm	12 mm
Pyrrolidine derivative	15 mm	8 mm	13 mm
Piperazine derivative	11 mm	11 mm	11 mm

UV spectra

The compounds which were mostly white or off white displays the following UV (MeOH, λmax, nm, log E) 332.5(0.158), 276(1.231), 235(0.707), 208(0.724). But the clay coloured Piperazine derivative showed different UV (MeOH, λmax, nm, log E) 339.5(0.012), 302(0.026), 291.5(0.027), 261.5(0.155), 210(2.463) respectively.

CONCLUSION

The present study concluded that this efficient, simple and new method for the preparation of Mannich derivatives of Dibenzo-α-pyrones showed excellent yields of the reaction product in short reaction time. All the tested compounds with possible structural modification displayed promising antibacterial activity. From the above findings, the target product might be used as a lead compounds in drug discovery for further research.

Acknowledgements

The authors are thankful to the Management, ITS Paramedical (Pharmacy) College, Ghaziabad, U.P., India for providing facilities and technical assistance. Also the authors are grateful to Ms. Meenakshi Bajpai, Principal, ITS Paramedical (Pharmacy), College, U.P., India for their continuous support and encouragement.

REFERENCES

[1] Ghoshal et al. **(2002)** showed the process for preparing purified Shilajit composition from native Shilajit.
[2] Ghosal S., Reddy J.P. and Lal V.K; **1976**; *Journal of Pharmaceutical Sciences*;65(5);pp-772-73
[3] Ghoshal S, Reddy J.P., Lal V.K. **1976**. *J Pharm Sci 65* : 772-773
[4] Mirza A., Alam N., Mahmood D., Bairwa R., Mustafa G., **(2010)**. *Int. J. of Current Pharm. Review and Res*. 1 : 2-11.

[5] Mittal P., Kaushik D., Gupta V., Bansal P., Khokra S. Therapeutic Potentials of "Shilajit Rasayana"- A Review.
[6] Joshi G. C, Tiwari K. C., Pande N. K and Pande G.; **1994;** *B. M. E. B. R*; 15(1-4);pp -106-111
[7] Ghosal S., Mukhopdhyay B, Muruganandam; **1995**; *Indian Journal of Indigenous Medicines* ;17(2); pp-1-12
[8] Hurtley et al. **(1929)** synthesized 3- hydroxyl 8-methoxy benzo chromen-6-one by the replacement of halogen in orthobromo benzoic acid.
[9] Cirigottis K.A.,Ritchie E. and Taylor W.C;**1974**; *Australian Journal of Chemistry*; 27(10);pp-2209-2228
[10] Ashok K. Dolui, Sahana S., and Atul K. et al. **(2011)** ; *Indian Journal of Pharmaceutical Education and Research*; Jan-Mar, 2012/ Vol 46/ Issue 1.
[11] Aslak C. M., Jayalakshmi B., Balasubramaniam A. and Senthilkumar N. et al. **(2011)** ; *Indian Journal of Pharmaceutical Education and Research*; Jul-Sep, 2012/ Vol 46/Issue 3.
[12] Festus A. S. Fabiyi, Oluwafunke Lara Ibironke, Maria Luz Lopez et al. **(2011)**; *International Journal of Chemistry*; doi : 10.5539/ijv.v3n2p3
[13] Jameel Abdul A., Palanisamy M. and Padusha Syed Ali M. et al**. (2012)** *Pelagia Research Library*; Der Chemica Sinica, 2012, 3(4) : 860-863.
[14] Anandarajagopal K., Tiwari Ravi N., Bothara K.G., Sunilson Anbu J., Dineshkumar C. and Promwichit P. et al. **(2010)** *Pelagia Research Library*; 1(2): 132-138.