



SYNTHESIS AND GREEN BROMINATION OF SOME CHALCONES AND THEIR ANTIMICROBIAL SCREENING

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ABSTRACT

Chalcones are the versatile molecules having the structural flexibility which permits structural transformations into flavonoids, flavanones, pyrazoles, oxazoles, pyrimidines etc. Changes in their structure have offered the development of new medicinal agents having improved pharmacological potency. Their derivatives have attracts increasing attention due to numerous pharmacological potential. In the present communication we report the synthesis of chalcones from various acetophenone derivatives with different aromatic aldehydes and green chemistry approach to their bromination with the help of Tetrabutylammonium Tribromide (TBATB). All the synthesized chalcone dibromides were screened for their antimicrobial activity against *Aspergillus flavus*, *Rhizopus sp.*, *Fusarium solani* and *Aspergillus niger*.

KEYWORDS: Chalcone, brominated chalcones, Tetrabutylammonium Tribromide, antimicrobial activity.

INTRODUCTION

Chalcones are well known intermediate for synthesizing various heterocyclic compounds¹. Chalcones are characterized by their possession of a C₆ (A)-CO-CH=CH-C₆ (B) structure, two aromatic ring (A & B) are linked by an aliphatic three-carbon chain which does not participate in forming a hetero ring as is usually found in other types of flavonoids compounds. A few dihydrochalcones C₆ (A)-CO-CH₂-CH₂-C₆ (B) have been found though no evidence concerning the relationship between chalcones and dihydrochalcones or the co-existence of these two compounds is yet known.

Synthetic methods involve the condensation of o-hydroxyacetophenone with substituted benzaldehyde in the presence of acidic or basic condensing agent^{2,3} to give a chalcone, flavanone or a mixture of these. However the suitable methods involve the condensation by means of alkali. Polymethoxy derivative condenses with 50 percent, 60 percent and 70 percent^{4,5} potassium hydroxide in aqueous alcohol to give the chalcones.

Chalcones and flavanones are isomeric and undergo interconversion readily where acids or alkali acts as a catalyst and the change can take place in either direction, usually in acid medium the formation of the flavanone is more favoured in alkaline medium⁶. A considerable variety of methods are available for the preparation of polyhydroxy chalcones. However the methods for the preparation of chalcones show large number of variations. Higher concentration of alkali results self condensation of acetophenone. Whereas the lower concentration of alkali requires longer time for condensation.

Geiger and Conn during their chemical studies on the structure of clavioin found that a structural feature which was responsible for antibacterial activity was α , β -unsaturated keto functional group⁷.

Green Chemistry is defined as invention, design, development and application of chemical products and processes to reduce or to eliminate the use and generation of substances hazardous to human health and environment. Professional developments involved in reinventing the use of materials. Understanding the challenge and prospective

impact of Green Chemistry depends on some familiarity with the context of its adoption and practice. Bromination, especially of aromatic substrates, is usually carried out by elemental bromine⁸, but owing to hazards associated with bromine preferably organic ammonium tribromides (OATB), and pyridine hydrobromide perbromide are used. Because of smoothly with selective bromination of an activated aromatic ring in the presence of an olefinic double bond is possible with such a reagent. Several tribromides have been reported i.e., tetramethylammonium tribromide (TMATB)⁹, phenyltrimethylammonium tribromide (PTATB)¹⁰, tetrabutylammonium tribromide (TBATB)¹¹.

The compounds with the backbone of chalcones have been reported to possess various biological activities such as antimicrobial, antioxidant¹², anti-inflammatory, Analgesic, antiulcerative¹³, antimalarial, anticancer¹⁴, antitubercular, antihyperglycemic¹⁵.

MATERIALS AND METHODS

Melting points reported were determined in a hot paraffin bath and are uncorrected. The IR spectra were recorded on SHIMADZU FTIR Presige-21 spectrophotometer mode 1310. H NMR spectra were recorded on Varian NMR Mercury-300 spectrometer in CDCl₃ solvent with TMS as an internal standard.

General procedure for the preparation of chalcones (3a-e)

To a cooled solution of NaOH and ethanol, acetophenone (0.043 mole) was added followed by the addition of substituted aromatic benzaldehyde (0.043 mole), the reaction mixture was stirred for 2-3 hours till the mixture becomes viscous and then the mixture was kept overnight in a refrigerator. The separated product was filtered under suction and washed well with cold water. Then it was crystallized from rectified spirit.

Synthesis of green reagent tetrabutylammonium tribromide (TBATB)

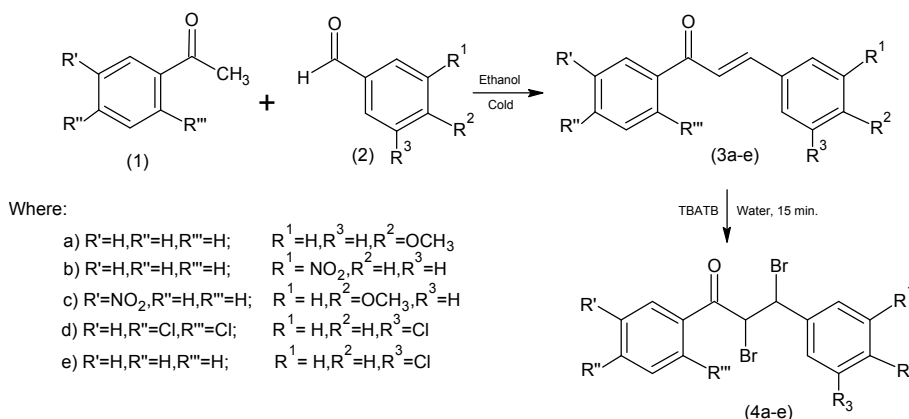
A solution of 2.75 mmol of V₂O₅ in 44.1 mmol of 30% H₂O₂ at 5 °C on reaction with 11 mmol of TBAB in 7 ml of water at ambient temperature produces yellow Bu₄NBr₃ (TBATB)

with 70% yield. The yield can be raised to 97% by the use of a catalytic amount of V_2O_5 and dilute H_2SO_4 and two molar equivalent of KBr. The product on crystallization from acetonitrile affords orange–yellow crystals with a sharp melting point of $75^\circ C$

General procedure for the bromination of chalcones (4a-e)

To TBATB (1mmol) add Chalcone (1mmol) and water 0.5ml, the whole mixture was mixed thoroughly and left at room temperature with occasional grinding for 15 min. Upon completion of the reaction, 20ml of water was added to the reaction mixture and stirred for 10 min. The reaction mixture was filtered, washed with water and air dried to afford the compounds.

SCHEME



The structure of all the synthesized compounds was confirmed on the basis of elemental analysis, molecular weight determination and spectral analysis and are discussed below.

1. 2,3-dibromo-3-(4-methoxyphenyl)-1-phenylpropan-1-one (4a):

Pale Yellow Solid, **M.P.**= $80^\circ C$, **Yield**= 94%, **Elemental analysis for $C_{16}H_{14}O_2Br_2$** : Found **C**= 48.23, **H**= 3.53, **Br**= 40.11, **O**= 8.01, Calculated **C**= 48.27, **H**= 3.54, **Br**= 40.14, **O**= 8.04., **IR (cm⁻¹)**: 3060.17 (Ar-CH), 1672.57 (C=O), 1514.17 (C-C In ring), 689.57 (Ar-H), 685.49 (C-Br); **¹H NMR (δ ppm)**: 8.0 (d, 2H, Ar-H), 7.6 (dd, 2H, Ar-H), 7.4 (d, 2H, Ar-H), 6.9 (d, 2H, CH-C-O), 3.8 (s, 3H, O-CH₃).

2. 2,3-dibromo-3-(3-nitrophenyl)-1-phenylpropan-1-one (4b):

Pale Yellow Solid, **M.P.**= $152^\circ C$, **Yield**= 95%, **Elemental analysis for $C_{15}H_{11}NO_3Br_2$** : Found **C**= 43.59, **H**= 2.64, **Br**= 38.66, **N**= 3.34, **O**= 11.58, Calculated **C**= 43.62, **H**= 2.68, **Br**= 38.69, **N**= 3.39, **O**= 11.62. **IR (cm⁻¹)**: 3076.08 (Ar-CH), 1690.17 (C=O), 1595.25 (C-C In ring), 865.10 (Ar-H), 689.57 (C-Br); **¹H NMR (δ ppm)**: 8.10 (s, 1H, CH-C-NO₂), 7.8 (d, 2H, Ar-H), 7.5 (dd, 1H, Ar-H), 7.3 (d, 2H, Ar-H).

3. 2,3-dibromo-3-(4-methoxyphenyl)-1-(3-nitrophenyl)propan-1-one (4c):

Brownish Yellow Solid, **M.P.**= $105^\circ C$ **Yield**= 89%, **Elemental analysis for $C_{16}H_{13}NO_4Br_2$** : Found **C**= 43.32, **H**= 2.91, **Br**= 36.03, **N**= 3.09, **O**= 14.43, Calculated **C**= 43.37, **H**= 2.96, **Br**= 36.07, **N**= 3.16, **O**= 14.44., **IR (cm⁻¹)**: 3150 (Ar-CH), 1689.39 (C=O), 1570.59 (C-C In ring), 1532.0 (N-O), 823.15 (Ar-H), 563.23 (C-Br); **¹H NMR (δ ppm)**: 8.9 (s, 1H, CH-C-NO₂), 8.4 (d, 1H, Ar-H), 8.2 (d, 1H, Ar-H), 7.9 (d, 2H, Ar-H), 3.9 (s, 3H, O-CH₃).

4. 2,3-dibromo-3-(3-chlorophenyl)-1-(2,4-dichlorophenyl)propan-1-one (4d):

White Solid, **M.P.**= $65^\circ C$, **Yield**= 92%, **Elemental analysis for $C_{15}H_9OCl_3Br_2$** : Found **C**= 38.18, **H**= 1.87, **Br**= 33.86, **Cl**= 22.53, **O**= 3.36, Calculated **C**= 38.22, **H**= 1.92, **Br**= 33.90, **Cl**= 22.56, **O**= 3.39., **IR (cm⁻¹)**: 3067.40 (Ar-CH), 1694.14 (C=O), 1592.07 (C-C In ring), 782.16 (Ar-H), 577.22 (C-Br); **¹H NMR (δ ppm)**: 7.6 (d, 1H, Ar-H), 7.5 (s, 1H, Ar-H), 7.4 (s, 1H, CH-C-Cl), 7.1 (d, 1H, CH-C-Cl).

5. 2,3-dibromo-3-(3-chlorophenyl)-1-phenylpropan-1-one (4e):

Pale Yellow Solid, **M.P.**= $58^\circ C$ **Yield**= 94%, **Elemental analysis for $C_{15}H_{11}OClBr_2$** : Found **C**= 44.72, **H**= 2.73, **Br**= 39.67, **Cl**= 8.78, **O**= 3.74, Calculated **C**= 44.76, **H**= 2.75, **Br**= 39.70, **Cl**= 8.81, **O**= 3.79., **IR (cm⁻¹)**: 3065.47 (Ar-CH), 1690.87 (C=O), 1590.12 (C-C In ring), 675.59 (Ar-H), 580.59 (C-Br). **¹H NMR (δ ppm)**: 7.8 (d, 2H, Ar-H), 7.6 (dd, 1H, Ar-H), 7.5 (d, 2H, Ar-H), 7.3 (d, 1H, CH-C-Cl).

Antimicrobial Screening

Antimicrobial screening was done by using cup plate method at a concentration of 100 μ g/ml. The compounds were evaluated for antimicrobial activity against *Rhizopus sp.*, *Aspergillus flavus*, *Fusarium solani* and *Aspergillus niger*. The results of antimicrobial data are summarized in table 1. All compounds show the moderate to good activity.

Table 1: Antimicrobial activity of test compounds

Compounds	Zone of inhibition in mm.			
	<i>Rhizopus sp.</i>	<i>Aspergillus flavus</i>	<i>Fusarium solani</i>	<i>Aspergillus niger</i>
4a	14	16	08	13
4b	06	11	12	07
4c	09	12	18	15
4d	13	17	17	21
4e	19	16	13	15

RESULTS

The IR spectrum of compounds in KBr shows the characteristic band in the region of $1700 \pm 100 \text{ cm}^{-1}$ which indicate the presence of -C=O group. ^1H NMR spectrum of compounds shows doublet of -CO-CH= at δ 6.9 confirmed the presence of chalcone moiety. Result of IR and ^1H NMR analysis confirmed formation of desired products.

The environmentally benign synthesized compounds show the moderate to good antimicrobial activity against *Rhizopus sp.*, *Aspergillus flavus*, *Fusarium solani* and *Aspergillus niger*.

DISCUSSION

QATBs capable of brominating a wide variety of organic substrates including aromatics in a safer way, either promoted by $\text{V}_2\text{O}_5\text{-H}_2\text{O}_2$ or catalyzed by $\text{MoO}_4^{2-}\text{H}_2\text{O}_2$. The scope of the protocols has been underscored, and the relevance to green chemistry has been highlighted.

Reactions of peroxometal intermediates can as well be exploited to generate an active brominating species (Br^3) *in situ* which can also perform bromination of organic substrates very efficiently without compromising with the environmental acceptability.

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