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Research Article

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Synthesis and Characterization of bromo-nitro Chalcones and Isoxazolines

Suresh D. Dhirbassi* and Surendra R. Dighade

Department of Chemistry, Bar. R.D.I.K. and N.K.D. College, Badnera (M.S.), India

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ABSTRACT

In the present study we have designed a synthesis of different substituted bromo-nitro-Chalcones (I $_{a-d}$) by Claisen-Schmidt condensation of 2-hydroxy-3-bromo-4-nitro-5-methyl acetophenone with substituted aromatic aldehydes in ethanol using 40% KOH. By using these Chalcones, four different 3, 5-diaryl-Δ^2- isoxazolines (II $_{a-d}$) were synthesized with hydroxylamine hydrochloride in pyridine containing few drops of piperidine. The synthesized compounds were characterized by IR and ^{1}H NMR spectral analysis.

Key words: Synthesis Bromo-Nitro-Chalcones, isoxazolines.

INTRODUCTION

The chemistry of Chalcones has generated intensive scientific interest due to their biological and industrial applications. Chalcones are natural bioacids [1-4] and are well known intermediates in the synthesis of heterocyclic compounds exhibiting various biological activities [4-8]. Chalcones and their derivatives possess some interesting biological properties such as antimicrobial [9], antiplatelet [10], antileishmanial [11], antioxidant [12], antihyperglycemic [13], immunomodulatory [14] and inhibition of chemical mediators release [15] activities. 2, 4, 5-trimethoxy chalcones derivatives have been synthesized and reported for antioxidant & antimicrobial agents [16].

Dhanaji Jadhav and Ramma reported the synthesis of 2, 4-difluorinated Chalcones by using Claisen-Schmidt condensation of aromatic aldehydes and substituted acetophenone in alkaline bases and fluorinated Chalcones have been reported to possess anti-inflammatory [17] activities.

Among five membered heterocycles, isoxazolines represent a class of compounds of great biological importance. For instance isoxazolines possess a broad spectrum of biological activity [18-19]. (insecticidal, antibacterial [20], antibiotic, antitumour, antifungal, etc.). Isoxazoline also serves as an important building block for the synthesis of biologically active molecules and serves as a prodrug for an antiarthritic agent [21]. The 3, 5-disubstituted isoxazolines have been reported to possess antimicrobial activity [22].

With this view we reported here the synthesis of novel Chalcones and 3, 5-diaryl-Δ^2- isoxazolines. These compounds were characterized by IR and ^{1}H NMR spectral analysis.

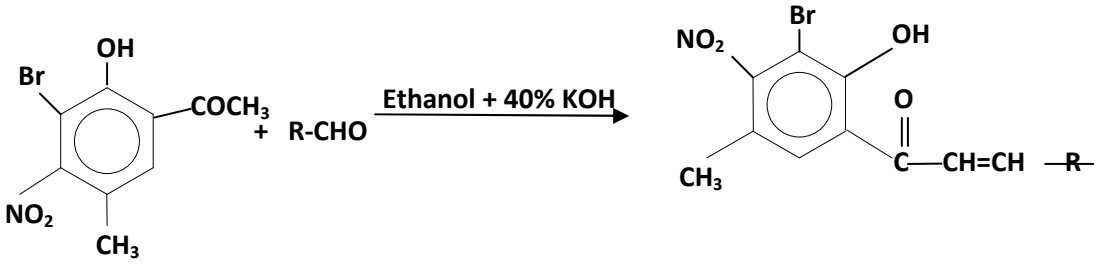
EXPERIMENTAL SECTION

All the products were synthesized & characterized by their spectral analysis. The purity of synthesized compounds were ascertained by thin layer chromatography on silica gel G using iodine vapours as detecting agents. All the Melting points reported were determined in open capillaries M.P. apparatus expressed in ^{0}C and are uncorrected. Chemicals and solvents were of highest purity commercially available. ^{1}H NMR spectra were recorded in the indicated solvent on Bruker AVANCE II 400 NMR spectrometer with TMS as internal standard. I.R. were recorded on Perkin-Elmer-841 spectrometer in KBr disc.

Synthesis of 2-hydroxy-3-bromo-4-nitro-5-methyl acetophenone (I):-
p-cresyl acetate was prepared by known method. Then by fries migration 2-hydroxy-5-methyl acetophenone was obtained. This on bromination gives 2-hydroxy-3-bromo-5-methyl acetophenone. Which further on nitration gives starting compound i.e. 2-hydroxy-3-bromo-4-nitro-5-methyl acetophenone (I).

General method for synthesis of bromo-nitro substituted Chalcones (I_{a-d}):-
The different Bromo-Nitro substituted Chalcones (I_{a-d}) were synthesized by using Claisen-Schmidt condensation of 2-hydroxy-3-bromo-4-nitro-5-methyl acetophenone (I) 0.01 M by reacting it with four different substituted aromatic aldehydes (0.01 M) by reported method in ethanol using 40% KOH. Thus the compounds (I_{a-d}) synthesized & recrystallised. The physical data of compounds (I_{a-d}) are given in table-1.

Scheme I-



(I) (I_{a-d})

The groups **R** are given in table 1.

Table1

Compound No.	R	Mol. Formula	M.P. (^{0}C)	Yield (%)
(I_a)	-CH=CH-Phenyl	$C_{18}H_{14}BrNO_4$	102	63
(I_b)	-2,4-$(Cl)_2$-Phenyl	$C_{16}H_{10}BrCl_2NO_4$	180	70
(I_C)	-2-Cl,6-F-Phenyl	$C_{16}H_{10}BrClFNO_4$	140	65
(I_d)	-2-OH-Phenyl	$C_{16}H_{12}BrNO_5$	96	68

Characterization of compound (I_b)
IR (KBr) cm^{-1}:- 3412 (Ar-OH), 2924 (Ar-C-H), 2853 (Aliphatic C-H), 1640 (-C=O), 1562 &1359 (-NO_2), 1251 (-C-O), 551(C-Br), 697(-C-Cl).

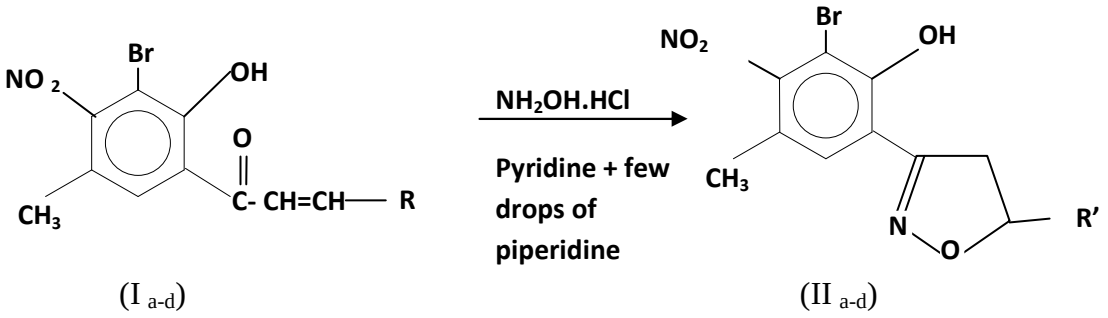
^{1}H NMR ($CDCl_3$) Data: - δ 2.4 (S, 3H, Ar-CH_3), 5.7 (d, 1H, =CH_A), 5.8 (d, 1H, =CH_B), 7.45-8.2 (m, 4H, Ar-H), 13.1 (S, 1H, Ar-OH).

Characterization of compound (I_c)
IR (KBr) cm^{-1}:- 3397 (broad H-bonded Ar –OH), 2916 (C-H of Ar-H stretching), 1634 (-C=O stretching), 1566 & 1330 (-NO_2 stretching), 1260 (-C-O), 1157 (-C-F), 677 (-C-Cl), 557 (-C-Br).

^{1}H NMR ($CDCl_3$) Data: - δ 2.35-2.45 (S, 3H, Ar-CH_3), 7.8 (d, 1H, CH_A), 8.1 (d, 1H, CH_B), 7.1-7.6 (m, 4H, Ar-H), 13.1 (S, 1H, Ar-OH).

Synthesis of 3.5-diaryl isoxazolines (II_{a-d}):-
A mixture of bromo, nitro-substituted Chalcone I_{a-d} (0.01M) and $NH_2OH.HCl$ (0.02M) were refluxed in 20ml pyridine containing few drops of piperidine for 3-4 hours. Cooled & acidified with 1:1 ice cold HCl, Thus compounds (II_{a-d}) were synthesized and recrystallised. Physical data are shown in table 2.

Scheme II:-



(I $_{a-d}$) (II $_{a-d}$)

Table 2: chemical data of the compounds (II $_{a-d}$)

Compound No.	R'	Mol. Formula	M.P. (^{0}C)	Yield (%)
(II_a)	-CH=CH-Phenyl	$C_{18}H_{15}BrN_2O_4$	122	62
(II_b)	-2,4-$(Cl)_2$-Phenyl	$C_{16}H_{11}BrCl_2N_2O_4$	158	66
(II_C)	-2-Cl,6-F-Phenyl	$C_{16}H_{11}BrClFN_2O_4$	120	64
(II_d)	-2-OH-Phenyl	$C_{16}H_{13}BrN_2O_5$	180	67

Characterization of compound (II_b)
IR (KBr) cm^{-1}:- 3419 (Ar-OH), 2918 (Ar-C-H), 2851 (Aliphatic C-H), 1618 (-CH_2 of iso ring), 1560 & 1384(-NO_2), 1184 (-C=N-O), 1255 (-C-O-), 1589 (-C=C-), 574 (-C-Br), 700 (-C-Cl).

^{1}H NMR ($CDCl_3$) Data: - δ 2.3(S, 3H, Ar-CH_3), 3.4 (dd, 1H, CH_A), 3.7 (dd, 1H, CH_B), 5.9 (dd, 1H, CH_X), 6.9-7.9 (m, 4H, Ar-H), 11.8 (S, 1H, Ar-OH).

Characterization of compound (II_c)
IR (KBr) cm^{-1}:- 3392 (Ar-OH stretching), 2918 (Ar-C-H), 2850 (Aliphatic C-H Stret.) 1570&1385 (-NO_2), 1604 (-$CH_2$of iso ring), 1186 (-C=N-O), 1260 (-C-O of phenol), 1186 (-C-F), 572 (C-Br), 690 (-C-Cl).

^{1}H NMR ($CDCl_3$) Data: - δ 2.30 (S, 3H, Ar-CH_3), 3.15 (dd, 1H, CH_A), 3.4 (dd, 1H, CH_B), 5.1 (dd, 1H, CH_X), 6.8-7.8 (m, 4H, Ar-H), 11.5 (S, 1H, Ar-OH).

RESULTS AND DISCUSSION

Thus the bromo-nitro-substituted Chalcones (I_{a-d}) and 3, 5-diaryl-Δ^2- isoxazolines (II $_{a-d}$) were synthesized through the route as shown in reaction schemes. Physical data of compounds are shown in table 1&2. The structure of synthesized compound I_b, I_c , and II_b, II_c were confirmed on the basis of I.R. and NMR spectral analysis.

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