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Design, synthesis, spectral analysis, antibabacterial activity of n-(3-chloro-2-oxo-4-arylazetidin-1-yl)-3 hydroxybenzofuran-2- carboxamide derivatives

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ABSTRACT

3-hydroxybenzofuran-2-carbohydrazide undergoes facile condensation with aromatic aldehydes to afford the corresponding N-arylidene-3-hydroxybenzofuran-2-carbohydrazide in good yields. Cyclo condensation of compounds with chloro acetyl chloride yields N-(3-chloro-2-oxo-4-arylazetidin-1-yl)-3 hydroxybenzofuran-2-carboxamide. The structures of these compounds were established on the basis of analytical and spectral data. The newly synthesized compounds were evaluated for their antibacterial activity.

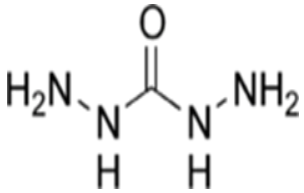
Keywords: Carbohydrazide, Synthesis, ^{1}H NMR, ^{13}C NMR, ESI MASS, Antibacterial activity.

INTRODUCTION

Carbohydrazide is the chemical compound with the formula OC $(N_2H_3)_2$. It is a white, water-soluble solid. It decomposes upon melting. A number of carbazides are known where one or more N-H groups are replaced by other substituents. They occur widely in the drugs, herbicides, plant growth regulators, and dyestuffs [1].

Carbohydrazide and its thioanalog are surprisingly late arrivals on the chemical scene, considering their close relationship with urea, the compound most directly associated with the foundation of organic chemistry [2].

Structure



The molecule is non-planar. All nitrogen centers are at least somewhat pyramidal, indicative of weaker C-N pi-bonding. The C-N and C-O distances are about 1.36 and 1.25 Å, respectively [3].

Uses

Used in industries as:

- oxygen scrubber,
- In photography,
- To stabilize soaps and
- As a reagent.

Uses in analytical chemistry

- For the identification and estimation of both organic and inorganic compounds.[4]

Histochemical Uses

- As an osmiophilic reagent

Pharmacological and related properties

- As an Anti-Convulsant,
- As an Anti-Carcinogen,
- As an Anti-Bacterial agent.
- As a fungicidal agent and
- In formation of polymers.[5]

EXPERIMENTAL SECTION

List of Chemicals and Reagents

Sl.No.	Chemicals or Reagents
1	3-hydroxybenzofuran-2-carbohydrazide
2	aromatic aldehydes
3	Ethanol
4	N-arylidene-3-hydroxybenzofuran-2-carbohydrazide
5	Tri ethyl amine (TEA)
6	1,4-dioxane
7	Chloro acetyl chloride
8	silica gel
9	ethyl acetate
10	Benzene
11	Ether
12	N-hexane

METHODOLOGY

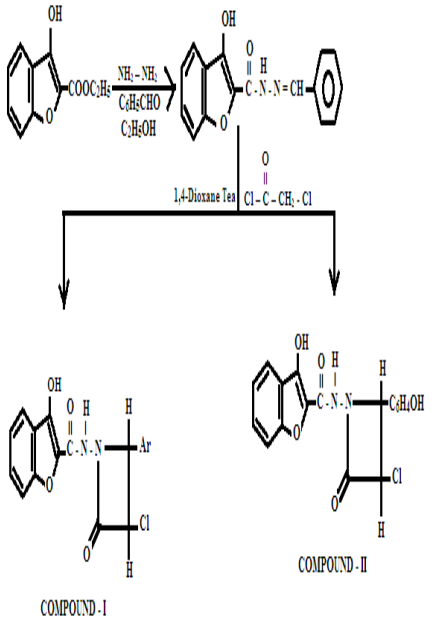
Preparation of N-arylidene-3-hydroxybenzofuran-2-carbohydrazide

A mixture of 3-hydroxybenzofuran-2-carbohydrazide (2) (0.2mole) and the aromatic aldehydes (0.2mole) in ethanol (15ml) was refluxed on a water bath for 1-2 hrs. The solid separated was collected by filtration, dried and recrystallized from Ethanol: H2O (1:1).

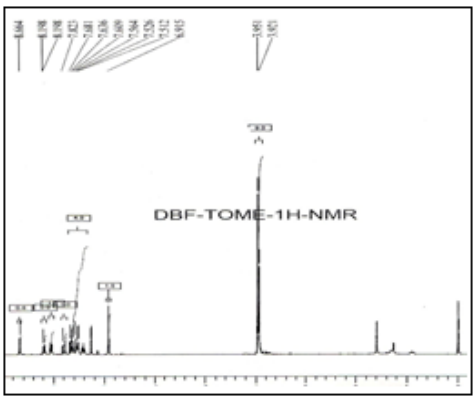
Preparation of N-(3-chloro-2-oxo-4-arylazetidin-1-yl)-3-hydroxybenzofuran-2-carboxamide derivatives

A mixture N-arylidene-3-hydroxybenzofuran-2-carbohydrazide (0.002 mole) and triethyl amine (TEA) (0.004mole) was dissolved in 1,4-dioxane (50 ml), cooled, and stirred. To this well-stirred cooled solution chloro acetyl chloride (0.004 mole) was added drop wise within a period of 30 minutes. The reaction mixture was then stirred for an additional 3 hours and left at room temperature for 48 hours. The resultant mixture was concentrated, cooled, poured into ice-cold water, and then air-dried. The product thus obtained was purified by column chromatographyover silica gel using 35% ethyl acetate: 65% benzene as eluent. Recrystallization from ether/n-hexane gave white powered of N-(3-chloro-2-oxo-4-arylazetidin-1-yl)-3-hydroxybenzofuran-2-carboxamide, which was obtained in 60-78% yield.

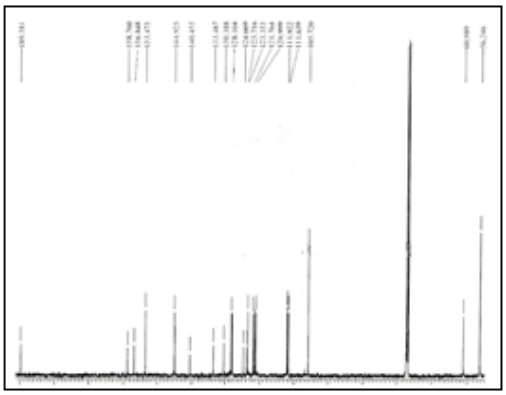
Scheme



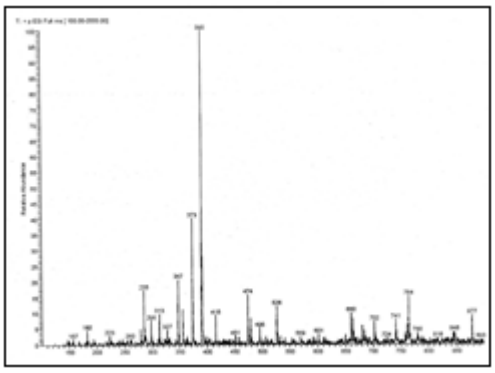
Spectral data



Proton NMR of Compound – I



^{13}C NMR of Compound – I



ESI – MASS of Compound – I

COMPOUND - I

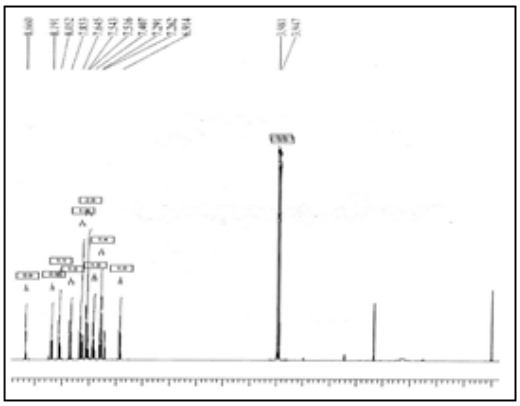
^{1}H NMR [4] 500 Hz (CdCl3) δ

3.92 (s, 3H,-OCH3), 3.95 (s, 6H,-OCH3), 6.91 (s, 2H, ArH),7.51-7.68 (m, 5H, ArH), 7.82 (s, 1H, ArH), 8.19 (s, 1H, Olefinic-H), 8.198 (s, 1H, Olefinic- H), 8.66(s, 1H, ArH).

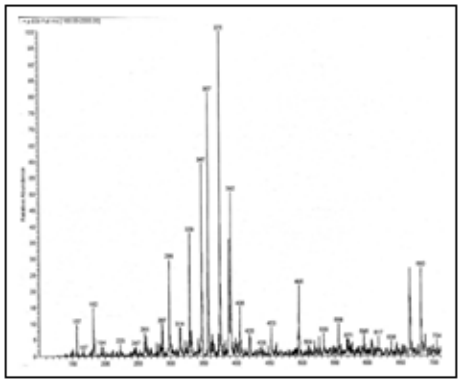
^{13}C NMR [5] 500 Hz (DMSO) δ

56.24 (OCH3),60.98 (OCH3), 105.72 (Ar-C) ,111.63 (Ar- C), 111.92 (Ar-C), 120.99(Ar-C), 121.76(C=C), 123.35 (Ar-C), 123.75 (Ar-C), 124.66 (Ar- C), 128.88 (Ar-C), 130.38 (Ar-C), 133.48 (Ar-C), 140.45 (Ar-C), 144.92 (Ar-C), 153.47 (Ar- C), 156.84 (Ar-C), 158.76 (Ar-C), 189.58 (C=O).

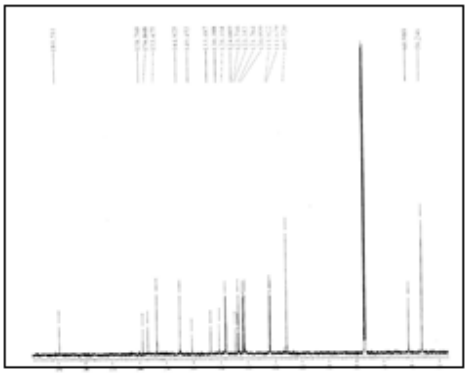
ESI MASS[6]: = (M+1) = 390.



Proton NMR of Compound – II



ESI – Mass of Compound – II



^{13}C NMR of Compound – II

COMPOUND II

^{1}H NMR 500 Hz (CdCl3) δ

3.94 (s, 3H,-OCH3), 3.98 (s, 3H,-OCH3), 6.94 (s, 1H, ArH),7.26 (m, 2H, ArH), 7.40 (s, 1H, ArH), 7.51 (s, 1H, ArH), 7.62 (s, 2H, Ar-H), 7.81 (s, 2H, Ar-H) 8.05 (s, 1H, Ar-H), 8.198 (s, 1H, Olefinic-H), 8.66 (s, 1H, Olefinic-H).

^{13}C NMR 500 Hz (DMSO) δ

56.24 (OCH3),60.98 (OCH3), 105.72 (Ar-C) , 111.63 (Ar- C), 120.99 (Ar-C), 121.76 (C=C), 123.35 (Ar-C), 123.75 (Ar-C), 124.66 (Ar-C), 128.88 (Ar- C), 130.38 (Ar-C), 133.48 (Ar-C), 140.45 (Ar-C), 144.92 (Ar-C), 153.47 (Ar-C), 156.84 (Ar- C), 158.76 (Ar-C), 189.58 (C=O).

ESI MASS: (M+NH4+) = 375.

Pharmacological activity

Observed anti-bacterial activity

Antibacterial activities of all the compounds were studied against gram-positive bacteria (Staphylococcus aureus and Bacillus subtilis) and gram-negative bacteria (E.coli, and klebsiella promioe) at a concentration of 50µg/ml by agar cup plate method. Methanol system was used as control in this method. Under similar condition using tetracycline as a standard for comparison carried out control experiment. The area of inhibition of zone measured in mm. Compounds I and II were found more active against the above microbes.

RESULTS AND DISCUSSION

It was observed that 3-hydroxybenzofuran-2-carbohydrazide on condensation with aromatic aldehydes to yield N-arylidene-3-hydroxybenzofuran-2-carbohydrazide. The cyclocondensation of with chloroacetylchloride resulted in formation of N-(3-chloro-2-oxo-4-arylazetidin-1-yl)-3-hydroxybenzofuran-2-carboxamide. The structures of compound I, II were confirmed ^{1}H NMR data, C^{13} NMR &ESI MASS data of all compounds are presented in under spectral data & Tables 2 & 3. The names of all compounds given in the experimental section were taken from ACD/Name, Version 1.0. The examination of data reveals that the elemental

contents are consistence with the predicted structure shown in scheme.

TABLE 1: Analytical data and elemental analysis of Compounds (I & II)

Compound	Molecular formula	Yield	Melting point	%H found	%C found	%N found
I	$C_{18}H_{14}ClN_2O_4$	65	237	3.66	60.58	7.83
II	$C_{18}H_{15}ClN_2O_5$	66	246	4.06	61.55	7.54

TABLE 2: Antibacterial Activities of Compounds (I & II)

Compounds	Bacillus subtilis	E.coli	Klebsiella promioe	Staphylococcs aureus
parent	49	60	47	51
I	60	71	56	63
II	64	57	63	61
TETRACYCLINES	79	78	86	67

CONCLUSION

We have successfully Design and Synthesised two derivatives of carbohydrazide Conjugates at higher yields (60-78%). All the compounds were purified by Column Chromatography and later recrystallized by Ethyl acetate/ Hexane solvent system. The compounds were characterized by ^{1}H NMR Spectra, ^{13}C NMR Spectra and ESI- Mass Spectra. The number of Protons and Types of protons were confirmed by Proton Nuclear Magnetic resonance (^{1}H NMR Spectra). The number of Carbons and Types of Carbons were confirmed by Carbon Nuclear Magnetic resonance (^{13}C NMR Spectra). The Molecular formulae and Molecular weights of all Compounds were confirmed by Electron-spray Ionisation mass fragmentation. (ESI-MASS). The synthesised analogues were tested for Antibacterial activity and got positive result.

Acknowledgements

First salutation goes to Almighty for giving me the dynamism and sympathetic situations to make this feat. It affords me an immense pleasure to acknowledge with gratitude the help and guidance rendered to me by a host of people, whom, I owe a substantial measure for the completion of this project.

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