International Journal of Engineering and Allied Sciences (IJEAS)
||Volume 2|| ||Issue 2|| ||2016||
ISSN: 2455-2054

Synthesis and Characterization of new series of Benzofuran Amide Derivatives

Anjali Gupta*, Kavita Khatana

Department of Chemistry, School of Basic and Applied Sciences, Galgotias University, Greater Noida, U.P. (India)

*Email: *anjali21in@gmail.com*

----------ABSTRACT----------

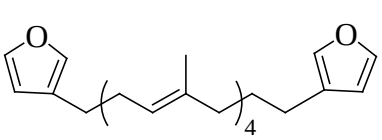
This paper reports the synthesis and characterization of new series of amide derivatives of benzofurans. These benzofuran derivatives have been identified with different spectroscopic techniques, notably infra-red spectroscopy, ^{1}H and ^{13}C nuclear magnetic resonance spectroscopy, supported by mass spectrometry.

Keywords- *Amide, Benzofuran, NMR.*

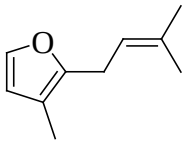
I. INTRODUCTION

Over the last few years, benzofuran moiety has drawn substantial attention due to their natural occurrence as well as their physiological and chemotherapeutic properties. The derivatives of benzofurans are of special interest to researchers for their potential biological activities *viz*., anti-viral [1], anti-cancer [2], anti-inflammatory [3], anti-fungal [4], anti-microbial [5], anti-allergic [6], and antitumor [7] activities. They also find their application as fluorescent sensor [8], antioxidants [9], and in other fields of chemistry and agriculture [10]. Moreover, benzofurans occuring a great number of natural products. Many of the natural benzofurans have physiological, pharmacological and toxic properties. There are well known natural products having related benzofuran ring structures, which are particularly isolated from *Machilus glaucescens*, *Ophryosporus charua*, *Ophryosporus lorentzii*, *Krameria ramosissima*, and *Zanthoxylum ailanthoidol* [11]. Benzofuran containing structureshave been found among naturally occurring furocoumarins, such as psoralen and methoxalen isolated from the seed of *Ammi majus* L. and used for the treatment of psoriasis and other dermal diseases [12,13].
The furan nucleus plays an important role in biological systems e.g.

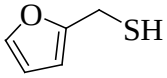
- **a.** Ribose and deoxyribose are both furanose sugars and are chief constituents of the nucleic acids.
- **b.** Several furan derivatives are of great importance in fragrances and flavours.
- **c.** The recent interest in marine natural products has disclosed several series of terpenes in which both ends of the system terminate in furan rings as in difurospinulosin (**1**) [14].
- **d.** The rose owes some of its odour to a terpenoid furan, rosefuran, i.e. 3-methyl-2-(3-methylbut-2-enyl)-furan (**2**), coffee owes some of its characteristics to furylmethanethiol (**3**) and related compounds [15]. Compounds like furaneol (**4**), a natural organic compound is found in strawberries and is responsible for the smell of fresh pineapple. It is also important for the odour of buckwheat and tomato [16-18].



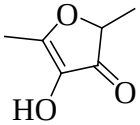
1



2



3



4

In order to explore diverse biological activities, investigating various methods for synthesis and structural modification of benzofuran ring have now become important goal of severalresearch groups. Thus, benzofuran moiety can be taken as leadcompound for the synthesis of novel derivatives with a variety ofbiological activities.

A series of chromone carboxylic acid esters based on *E*-3-(4-oxo-4*H*-1-benzopyran-3-yl)-propenoic acid were evaluated for their ICAM-1 inhibitory activity on human endothelial cells as well as their effect on NADPH catalyzed rat liver microsomal lipid per-oxidation. It was found that these compounds significantly blocks the adhesion of neutrophils to endothelial monolayer [19]. A few compounds significantly inhibited the TNF-α induced expression of VCAM-1 and E-selectin, which play key roles in various inflammatory diseases.

Based on these encouraging results, a new series of benzofuran carboxamides was synthesized to study the variation of size of ring containing hetero atom, replacement of ester linkage by amidic linkage, and effect of substituent group (methoxy) on benzenoid ring.

II. EXPEROMENTAL

2.1.General Procedure

Melting points were determined on a sulphuric acid bath and are uncorrected. The IR spectra were recorded on a Perkin Elmer model 2000 FT-IR spectrophotometer by making KBr discs for solid samples and chloroform film for viscous samples. The ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance 300 spectrometer and Bruker-500 using TMS as internal standard. The chemical shift values are on δ scale and the coupling constant values (*J*) are in Hz. EI mass spectra were recorded on Agilent-6210 ESI-TOF.Analytical TLCs were performed on pre-coated Merck silica gel $60F_{254}$ plates with fluorescence indicator; the spots were detected by viewing under UV light or by iodine chamber. Column chromatography was carried out using silica gel (100-200 mesh).U.V. data was recorded on Shimadzu UV-2501PC UV-VIS spectrophotometer.All other chemicals used were purchased either from S. D. Fine Chemicals, Spectrochem, India or Aldrich Chemical Co., USA and used without further purification**.**

2.2. Synthesis of N-alkyl-7-hydro / methoxybenzofuran-2-carboxamides (7-24)

Differently substituted *N*-alkyl-7-hydro / methoxybenzofuran-2-carboxamides were synthesized starting from substituted salicyaldehydes *via* **Scheme-1**.

Ethyl benzofuran-2-carboxylate (**5**)

The compound **5** was obtained as yellow viscous liquid in 75% yield. **UV (MeOH) λ_{max}**: 261 and 273 nm. **IR ($CHCl_3$) ν_{max}**: 2983.09, 2927.15, 1733.49 (C=O), 1612.63, 1564.63, 1476.48, 1448.19, 1370.78, 1347.17, 1329.87, 1296.97, 1259.34, 1225.35, 1211.89, 1181.83, 1146.27, 1097.24, 1018.51, 946.79, 888.20, 839.76 and 749.73 cm^{-1}. **^{1}H NMR ($CDCl_3$, 300 MHz)**: □□ 1.44 (t, 3H,*J* = 6.9 Hz, -CH_3), 4.45 (q, 2H, *J* = 7.2 Hz, -CH_2), 7.26-7.33 (m, 1H, H-5), 7.43-7.48 (m, 1H, H-6), 7.54 (s, 1H, H-3), 7.60 (d, 1H, *J* = 8.4 Hz, H-7), 7.69 (d, 1H, *J* = 2.0 & 7.8 Hz, H-4).**^{13}C NMR ($CDCl_3$, 100 MHz)**: □□ 14.32 (-CH_3), 61.50 (-CH_2), 112.35, 113.76 (C-6 and C-7), 122.76, 123.73 (C-4 and C-5), 126.94 (C-9), 127.53 (C-3), 145.69 (C-8), 155.67 (C-2), 159.59 (COO).**HRMS**: Calculated for $C_{11}H_{10}O_3$ $[M]^+$190.1953, found 190.5439.

Ethyl 7-methoxybenzofuran-2-carboxylate (**6**)

The compound **6** was obtained as white solid in 70% yield. **Melting point**: 56 ^{o}C.**UV (MeOH) λ_{max}**: 263 nm. **IR (KBr) ν_{max}**: 3127.56, 2956.61, 2932.09, 2844.62, 1714.33 (C=O), 1620.70, 1578.55, 1494.45, 1465.26, 1446.07, 1429.51, 1370.07, 1326.15, 1296.75, 1271.46, 1225.96, 1182.85, 1121.08, 1091.80, 1056.19, 1026.63, 972.82, 941.26, 857.09, 781.29, 732.59 and 623.49 cm^{-1}. **^{1}H NMR (DMSO-d_6, 300 MHz)**: □□ 1.32 (t, 3H, *J* = 7.2 Hz, -CH_3), 3.94 (s, 3H, OCH_3), 4.34 (q, 2H, *J* = 7.2 Hz, -CH_2), 7.10 (d, 1H, *J* = 7.8 Hz, H-6), 7.18-7.25 (m, 2H, H-4 and H-5) and 7.51 (s, 1H, H-3).**^{13}C NMR ($CDCl_3$, 100 MHz)**: □□ 14.30 (-CH_3), 56.00 (OCH_3), 61.38 (-CH_2), 108.86, 114.00, 114.52 (C-4, C-5 and C-6), 124.37 (C-3), 128.57 (C-9), 145.35 (C-8), 145.93 (C-7), 145.95 (C-2), 159.34 (*C*$OOCH_2CH_3$).**HRMS**: Calculated for $C_{12}H_{12}O_4$ $[M+Na]^+$243.0736, found 243.0635.

2.3. General Procedure for the synthesis of N-alkyl benzofuran-2-carboxamides (7-24)

To the solution of **5** / **6** (0.5 g, 2 mmol) in ethanol (3 mL) was added appropriate amine (3 mmol) and the reaction was stirred for 3 days at room temperature. The progress of the reaction was monitored on TLC and after the completion of reaction; the solvent was evaporated and 4 M HCl (4 mL) solution was added to it [20, 21]. The desired compound either got precipitated or extracted with DCM. Compound so obtained was dissolved in DCM and got crystallized by addition of hexane. The desired amide was obtained in 70-80% yield.

***N*-Ethylbenzofuran-2-carboxamide (7)**

The compound **7** was obtained as yellow solid in 74% yield by following the general procedure. **Melting point**: 52 ^{o}C. **UV (MeOH) λ_{max}**: 271 nm. **IR (KBr) ν_{max}**: 3264.66, 3112.74, 3065.42, 2965.40, 2933.12, 2871.39, 1648.18, 1614.63, 1570.37, 1541.92, 1437.98, 1336.19, 1304.86, 1260.06, 1239.54, 1194.21, 1149.10, 1106.73, 1007.46, 947.86, 886.05, 847.63, 829.17, 792.58, 743.77, 734.40 and 670.14cm^{-1}. **^{1}H NMR ($CDCl_3$, 300 MHz)**: □□ 1.28 (t, 3H, *J* = 7.2 Hz, -CH_3), 3.54 (m, 2H, -CH_2), 6.73 (*brs*, 1H, NH), 7.26-7.31 (m, 1H, H-5), 7.37-7.43 (m, 1H, H-6), 7.47-7.50 (m, 2H, H-3 and H-7) and 7.66 (d, 1H, *J*= 7.8 Hz, H-4).**^{13}C NMR ($CDCl_3$, 75 MHz)**: □□ 14.91 (-CH_3), 34.30 (-CH_2), 110.16, 111.68 (C-6 and C-7), 122.71, 123.66 (C-4 and C-5), 126.77 (C-3), 127.66 (C-9), 148.90 (C-8), 154.67 (C-2) and 158.80 (*C*ONH). **HRMS**: Calculated for $C_{11}H_{11}O_2N$ $[M+H]^+$189.0790, found 189.8895.

***N*-propylbenzofuran-2-carboxamide** (**8**)

The compound **8** was obtained as yellow solid in 75% yield by following the general procedure. **Melting point**: 60 ^{o}C.**UV (MeOH) λ_{max}**: 228 and 271 nm.**IR (KBr) ν_{max}**: 3426.35 (N-H str), 3301.59, 3064.46, 2965.05, 2932.53, 2874.88, 1651.66, 1596.83, 1524.21, 1447.89, 1347.30, 1299.51, 1258.49, 1231.32, 1178.57, 1148.97, 1109.70, 1007.76, 946.80, 883.49, 831.94, 747.58 and 613.63 cm^{-1}. **^{1}H NMR ($CDCl_3$, 300 MHz)**: □□ 1.01 (t, 3H, *J* = 7.5 Hz, -CH_3), 1.68 (m, 2H, -C$\underline{H_2}$-CH_3), 3.45 (q, 2H, *J* = 6.9 Hz, NHC$\underline{H_2}$), 6.73 (*brs*, 1H, NH), 7.26-7.31 (m, 1H, H-5), 7.37-7.43 (m, 1H, H-6), 7.46-7.50 (m, 2H, H-3 and H-7) and 7.66 (d, 1H, *J*= 7.8 Hz, H-4).**^{13}C NMR ($CDCl_3$, 75 MHz)**: □□ 11.43 (-CH_3), 22.92 (-$\underline{C}H_2$-CH_3), 41.06 (NH$\underline{C}H_2$), 110.18, 111.68 (C-6 and C-7), 122.70, 123.65 (C-4 and C-5), 126.75 (C-3), 127.67 (C-9), 148.90 (C-8), 154.67 (C-2) and 158.92 (*C*ONH). **HRMS**: Calculated for $C_{12}H_{13}O_2N$ $[M]^+$203.2371, found 203.3093.

***N*-Butylbenzofuran-2-carboxamide** (**9**)

The compound **9** was obtained as yellow solid in 75% yield. **Melting Point**: 46 ^{o}C.**UV (MeOH) λ_{max}**: 271 nm.**IR (KBr) ν_{max}**: 3059.43, 2967.39, 2931.33, 2875.75, 1674.15, 1629.84, 1583.56, 1527.85, 1467.18, 1421.56, 1381.50, 1329.37, 1254.33, 1170.66, 1150.52, 1080.12, 1005.64, 973.57, 918.90, 837.33, 781.00 and 738.11 cm^{-1}. **^{1}H NMR (CDCl$_3$, 400 MHz)**: □□ 0.96 (t, 3H,*J* = 8.0 Hz, -CH$_3$), 1.38-1.48 (m, 2H, -CH$_2$-CH$_3$), 1.59-1.66 (m, 2H, NHCH$_2$CH$_2$), 3.48 (q, 2H, *J* = 6.6 Hz, NHCH$_2$), 6.65 (*brs*, 1H, NH), 7.25-7.29 (m, 1H, H-5), 7.37-7.40 (m, 1H, H-6), 7.45 (s, 1H, H-3), 7.48 (d, 1H, *J* = 8.4 Hz, H-7) and 7.65 (d, 1H, *J*= 7.6 Hz, H-4).**^{13}C NMR (CDCl$_3$, 100 MHz)**: □□ 13.74 (CH$_3$), 20.08 (-CH$_2$-CH$_3$), 31.68 (NHCH$_2$CH$_2$), 39.07 (NHCH$_2$), 110.15, 111.63 (C-6 and C-7), 122.68, 123.62 (C-4 and C-5), 126.71 (C-3), 127.65 (C-9), 148.87 (C-8), 154.64 (C-2) and 158.83 (*C*ONH). **HRMS**: Calculated for $C_{13}H_{15}O_2N$ $[M+H]^+$218.1103, found 218.1194.

***N*-*sec*-Butylbenzofuran-2-carboxamide** (**10**)

The compound **10** was obtained as yellow solid in 75% yield. **Melting point**: 56 ^{o}C.**UV (MeOH) λ_{max}**: 271 nm. **IR (KBr) ν_{max}**: 3265.97, 3056.78, 2970.64, 2931.94, 2877.15, 1643.64, 1598, 1535.64, 1475.00, 1449.45, 1358.07, 1301.23, 1261.10, 1232.97, 1178.30, 1150.18, 1111.54, 1004.09, 953.60, 869.45, 833.70, 743.18 and 614.25 cm^{-1}. **^{1}H NMR (DMSO-*d*$_6$, 400 MHz)**: □□ 0.83 (t, 3H,*J* = 7.2 Hz, -CH$_2$CH$_3$),1.12 (d, 3H, *J* = 6.4 Hz, -CH-CH$_3$), 1.36-1.59 (m, 2H, -CH$_2$CH$_3$), 3.86-3.91 (m, 1H, NHCH), 7.27-7.31 (m, 1H, H-5), 7.39-7.44 (m, 1H, H-6), 7.49 (s, 1H, H-3), 7.61 (d, 1H, *J* = 8.4 Hz, H-7), 7.72 (d, 1H, *J*= 7.6 Hz, H-4) and 8.39 (*brs*, 1H, NH).**^{13}C NMR (DMSO-*d*$_6$, 100 MHz)**: □□ 10.69 (CH$_2$CH$_3$), 20.09 (-CH-CH$_3$), 28.62 (-CH$_2$CH$_3$), 46.11 (NHCH), 109.01, 111.67 (C-6 and C-7), 122.55, 123.52 (C-4 and C-5), 126.53 (C-3), 127.11 (C-9), 149.34 (C-8), 154.05 (C-2) and 157.39 (*C*ONH). **HRMS**: Calculated for $C_{13}H_{15}O_2N$ $[M+Na]^+$240.0995, found 240.1002.

***N*-Pentylbenzofuran-2-carboxamide** (**11**)

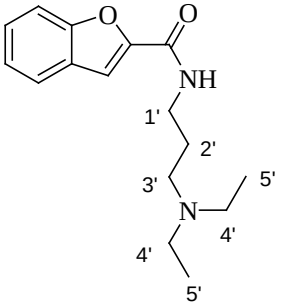
The compound **11** was obtained as yellow solid in 80% yield. **Melting point**: 57 ^{o}C.**UV (MeOH) λ_{max}**: 228 and 271 nm. **IR (KBr) ν_{max}**: 3301.60, 3064.59, 2957.46, 2930.18, 2859.76, 1651.78, 1595.97, 1524.77, 1448.16, 1346.49, 1299.55, 1258.73, 1232.38, 1178.43, 1148.35, 1110.04, 1005.53, 939.75, 832.70 and 747.44 cm^{-1}. **^{1}H NMR (CDCl$_3$, 300 MHz)**: □□ 0.92 (t, 3H,*J* = 6.6 Hz, -CH$_3$), 1.25-1.67 (m, 6H, -CH$_2$CH$_2$CH$_2$-), 3.47 (q, 2H, *J* = 6.9 Hz, -NHCH$_2$), 6.70 (*brs*, 1H, NH), 7.25-7.30 (m, 1H, H-5), 7.37-7.42 (m, 1H, H-6), 7.45-7.50 (m, 2H, H-3 and H-7), and 7.65 (d, 1H, *J*= 7.5 Hz, H-4). **^{13}C NMR (CDCl$_3$, 75 MHz)**: □□ 13.91 (CH$_3$), 22.31, 29.03, 29.29 (-CH$_2$CH$_2$CH$_2$-), 39.34 (-NHCH$_2$), 110.10, 111.62 (C-6 and C-7), 122.64, 123.59 (C-4 and C-5), 126.68 (C-3), 127.64 (C-9), 148.90 (C-8), 154.64 (C-2) and 158.81 (*C*ONH). **HRMS**: Calculated for $C_{14}H_{17}O_2N$ $[M]^+$231.1259, found 231.2895.

***N*-Hexylbenzofuran-2-carboxamide** (**12**)

The compound **12** was obtained as yellow semisolid in 82% yield. **UV (MeOH) λ_{max}**: 272 nm.
IR (KBr) ν_{max}: 3293.27, 3061.04, 2956.45, 2929.84, 2858.82, 1648.11, 1595.26, 1571.50, 1526.18, 1448.34, 1375.80, 1348.48, 1300.56, 1259.19, 1233.78, 1179.48, 1148.28, 1110.48, 1007.27, 947.80, 884.80, 835.62, 748.01 and 614.09 cm^{-1}. **^{1}H NMR (CDCl$_3$, 300 MHz)**: □□ 0.90 (t, 3H,*J* = 6.9 Hz, -CH$_3$), 1.25-1.69 (m, 8H, -CH$_2$CH$_2$CH$_2$CH$_2$-), 3.48 (q, 2H, *J* = 6.9 Hz, -NHCH$_2$), 6.69 (*brs*, 1H, NH), 7.26-7.31 (m, 1H, H-5), 7.38-7.43 (m, 1H, H-6), 7.47 (s, 1H, H-3), 7.49 (d, 1H, *J* = 8.4 Hz, H-7) and

7.67 (d, 1H, *J* = 7.8 Hz, H-4). **^{13}C NMR ($CDCl_3$, 75 MHz)**: □□ 13.99 (-CH_3), 22.51, 26.57, 29.57, 31.44 (-$CH_2CH_2CH_2CH_2$-), 39.37 (-NH$\underline{C}H_2$), 110.13, 111.63 (C-6 and C-7), 122.66, 123.60 (C-4 and C-5), 126.70 (C-3), 127.63 (C-9), 148.86 (C-8), 154.62 (C-2) and 158.81 (*C*ONH). **HRMS**: Calculated for $C_{13}H_{15}O_2N$ $[M]^+$245.3169, found 245.7525.

***N*-(3-(Diethylamino)propyl)benzofuran-2-carboxamide** (**13**)

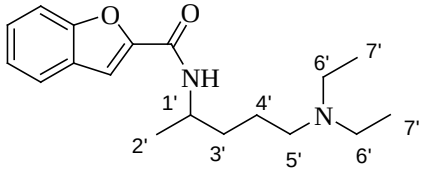


The compound **13** was obtained as yellow semisolid in 75% yield. **UV (MeOH) λ_{max}**: 262 and 272 nm. **IR ($CHCl_3$) ν_{max}**: 3293.51, 3061.43, 2969.76, 2933.69, 2873.32, 2814.33, 1738.90, 1659.29, 1595.78, 1517.95, 1449.28, 1377.04, 1346.39, 1294.70, 1259.03, 1231.51, 1177.00, 1149.72, 1111.41, 1073.90, 954.55, 910.14, 884.03, 833.86, 750.71 and 614.01 cm^{-1}. **^{1}H NMR ($CDCl_3$, 300 MHz)**: □□ 1.12 (t, 6H, *J* = 7.2 Hz, 2 × CH_3), 1.72-1.80 (m, 2H, H-2'), 2.49-2.65 (m, 8H, 2 × H-4', H-3' and H-1'), 6.86 (*brs*, 1H, NH), 7.22-7.32 (m, 2H, H-5 and H-6), 7.35-7.46 (m, 2H, H-3 and H-7), 7.66 (d, 1H, *J*= 7.5 Hz, H-4) and 8.35 (*brs*, 1H, NH). **^{13}C NMR ($CDCl_3$, 75 MHz)**: □□ 11.67 (2 × C 5'), 25.04 (C-2'), 40.33 (C-1'), 46.85 (2 × C-4'), 53.40 (C-3'), 109.45, 111.47 (C-6 and C-7), 122.56, 123.42 (C-4 and C-5), 126.38 (C-3), 127.78 (C-9), 149.66 (C-8), 158.70 (C-2) and 164.82 (*C*ONH). **HRMS**: Calculated for $C_{16}H_{22}O_2N_2$ $[M+H]^+$275.0681, found 274.9719.

***N*-(3-(Dimethylamino)propyl)benzofuran-2-carboxamide** (**14**)

The compound **14** was obtained as yellow semisolid in 75% yield. **UV (MeOH) λ_{max}**: 272 nm.
IR (KBr) ν_{max}: 3412.06, 3059.72, 2953.32, 2860.22, 1725.27, 1654.10, 1595.71, 1569.82, 1525.91, 1472.63, 1448.81, 1372.06, 1298.92, 1259.61, 1229.31, 1181.32, 1148.45, 1097.62, 1007.54, 947.88, 884.63, 839.08, 750.92 and 614.08 cm^{-1}. **^{1}H NMR ($CDCl_3$, 300 MHz)**: □□ 1.79 (m, 2H, -$NCH_2C\underline{H}_2$), 2.31 (s, 6H, 2 × -NCH_3), 2.49 (t, 2H, *J* = 6.3Hz, -NCH_2), 3.57 (q, 2H, *J* = 6.0 Hz, -NHC$\underline{H}_2$), 4.84 (*brs*, 1H, NH), 7.25-7.30 (m, 2H, H-5 and H-6), 7.37-7.49 (m, 2H, H-3 and H-7), and 7.66 (d, 1H, *J*= 7.8 Hz, H-4). **^{13}C NMR ($CDCl_3$, 75 MHz)**: □□ 25.91 (-$NCH_2\underline{C}H_2$), 39.08 (-NH$\underline{C}H_2$), 45.24 (2 × -NCH_3), 58.26 (-NCH_2), 109.65, 111.57 (C-6 and C-7), 122.54, 123.46 (C-4 and C-5), 126.50 (C-3), 127.61 (C-9), 149.20 (C-8), 154.65 (C-2) and 158.86 (*C*ONH). **HRMS**: Calculated for $C_{14}H_{18}O_2N_2$ $[M]^+$246.3049, found246.3866.

***N*-(5-(Diethylamino)pentan-2-yl)benzofuran-2-carboxamide** (**15**)



The compound **15** was obtained as yellow semisolid in 75% yield. **UV (MeOH) λ_{max}**: 261 and 273 nm. **IR ($CHCl_3$) ν_{max}**: 2969, 2933.39, 2870.49, 2802.45, 1731.27, 1631.15, 1576.14, 1498.43, 1461.66, 1372.12, 1328.89, 1296.16, 1258.86, 1211.36, 1181.05, 1146.23, 1096.07, 1018.63, 946.60, 907.55, 887.64, 838.32 and 751.96 cm^{-1}. **^{1}H NMR ($CDCl_3$, 300 MHz)**: □□ 0.99 (t, 6H, *J* = 7.2 Hz, 2 × H-7'), 1.28 (d, 3H, *J* = 6.6 Hz, H-2'), 1.39-1.62 (m, 4H, H-3' and H-4'), 2.33-2.58 (m, 6H, 2 × H-6'and H-5'), 3.32 (m, 1H, H-1'), 4.85 (*brs*, 1H, NH), 7.21-7.43 (m, 2H, H-5 and H-6), 7.45-7.59 (m, 2H, H-3 and H-7) and 7.66 (d, 1H, *J*= 7.8 Hz, H-4). **^{13}C NMR ($CDCl_3$, 75 MHz)**: □□ 11.53 (2 × C-7'), 22.67 (C-2'), 23.93 (C-4'), 35.87 (C-3'), 46.76 (2 × C-6'), 52.68 (C-1'), 61.50 (C-5'), 112.31, 116.94 (C-6 and C-7), 122.79, 123.75 (C-4 and C-5), 127.56 (C-3), 131.11 (C-9), 155.08 (C-8), 161.28 (C-2) and 162.70 (*C*ONH). **HRMS**: Calculated for $C_{18}H_{26}O_2N_2$ $[M]^+$302.1994, found 302.1590.

***N*-Ethyl-7-methoxybenzofuran-2-carboxamide** (**16**)

The compound **16** was obtained as yellow solid in 85% yield. **Melting point**: 76 °C. **UV (MeOH) λ_{max}**: 232 and 273 nm. **IR (KBr) ν_{max}**: 3312.34, 2977.83, 2938.61, 1655.98, 1595.51, 1524.13, 1479.72, 1438.39, 1376.47, 1299.70, 1229.59, 1185.17, 1148.77, 1079.88, 970.06, 844.04, 807.07 and 760.03cm^{-1}. **^{1}H NMR (DMSO-d_6, 300 MHz)**: □□ 1.13 (t, 3H, *J* = 7.2 Hz, -$CH_2C\underline{H}_3$), 3.30 (m, 2H, -$C\underline{H}_2CH_3$), 3.96 (s, 3H, OCH_3), 7.05 (d, 1H, *J*= 7.8 Hz, H-6), 7.21-7.31 (m, 2H, H-4 and H-5), 7.48 (s, 1H, H-3) and 8.67 (*brs*, 1H, NH). **^{13}C NMR (DMSO-d_6, 75 MHz)**: □□ 14.72 (-$CH_2\underline{C}H_3$), 33.57 (-$\underline{C}H_2CH_3$), 55.72 (OCH_3), 108.54, 109.37, 114.31 (C-4, C-5 and C-6), 124.36 (C-3), 128.69 (C-9), 143.51 (C-8), 145.21 (C-7), 149.42 (C-2) and 157.70 (*C*ONH). **HRMS**: Calculated for $C_{12}H_{13}O_3N$ $[M]^+$219.2365, found 219.3226.

7-Methoxy-*N*-propylbenzofuran-2-carboxamide (**17**)

The title compound **17** was obtained as yellow semisolid in 80% yield. **UV (MeOH) λ_{max}**: 273 nm. **IR ($CHCl_3$) ν_{max}**: 3311.10, 2965.02, 2936.66, 2875.16, 1655.27, 1593.56, 1525.32, 1490.43, 1461.38, 1431.14, 1317.95, 1273.62, 1204.63, 1183.52, 1151.59, 1097.18, 1060.27, 975.89, 946.05, 898.72, 854.50, 805.27, 778.48, 730.96 and 701.70cm^{-1}. **^{1}H NMR ($CDCl_3$, 300 MHz)**: □□ 0.98 (t, 3H, *J* = 7.2 Hz, -$CH_2C\underline{H}_3$), 1.65 (m, 2H, -$C\underline{H}_2CH_3$), 3.43 (q, 2H, *J* = 6.9 Hz, -$NHC\underline{H}_2$-), 3.99 (s, 3H, OCH_3), 6.89 (d, 1H, *J*= 6.9 Hz, H-6), 7.16-7.24 (m, 2H, H-4 and H-5) and 7.46 (s, 1H, H-3). **^{13}C NMR ($CDCl_3$, 75 MHz)**: □□ 11.41 (-$CH_2\underline{C}H_3$), 22.89 (-$\underline{C}H_2CH_3$), 41.05 (-$NHCH_2$-), 55.90 (OCH_3), 108.07, 110.59, 114.66 (C-4, C-5 and C-6), 124.10 (C-3), 129.25 (C-9), 144.12 (C-8), 145.46 (C-7), 149.12 (C-2) and 158.77 (*C*ONH). **HRMS**: Calculated for $C_{13}H_{15}O_3N$ $[M+H]^+$234.1053, found 233.9500.

***N*-Butyl-7-methoxybenzofuran-2-carboxamide** (**18**)

The compound **18** was obtained as yellow solid in 75% yield. **Melting point**: 43 °C.**UV (MeOH) λ_{max}**: 233 and 273 nm.**IR (KBr) ν_{max}**: 3313.17, 2956.07, 2934.45, 2872.43, 1657.13, 1596.64,

1525.11, 1479.44, 1438.76, 1376.39, 1289.87, 1229.92, 1079.02, 971.08, 843.81 and 804.43cm^{-1}. **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ = 0.95 (t, 3H, *J* = 7.6 Hz, -$CH_2C\underline{H}_3$), 1.37-1.46 (m, 2H, -$C\underline{H}_2CH_3$), 1.58-1.65 (m, 2H, -$NHCH_2C\underline{H}_2$-), 3.46 (q, 2H, *J* = 6.8 Hz, -$NHC\underline{H}_2$-), 4.00 (s, 3H, OCH_3), 6.89 (d, 1H, *J*= 7.6 Hz, H-6), 7.18-7.25 (m, 2H, H-4 and H-5), 7.45 (s, 1H, H-3). **^{13}C NMR (CDCl$_3$, 100 MHz)**: □□ 13.85 (-$CH_2\underline{C}H_3$), 20.20 (-$\underline{C}H_2CH_3$), 31.81 (-$NHCH_2\underline{C}H_2$-), 39.19 (-$NHCH_2$-), 56.05 (OCH_3), 108.17, 110.74, 114.83 (C-4, C-5 and C-6), 124.46 (C-3), 129.41 (C-9), 144.22 (C-8), 145.56 (C-7), 149.25 (C-2) and 158.79 (*C*ONH). **HRMS**: Calculated for $C_{14}H_{17}O_3N$ $[M]^+$247.1208, found 247.7096.

***N*-Sec-butyl-7-methoxybenzofuran-2-carboxamide** (**19**)

The compound **19** was obtained as yellow semisolid in 75% yield. **UV (MeOH) λ$_{max}$**: 221 and 293 nm. **IR (CHCl$_3$) ν$_{max}$**: 3284.65, 3065.68, 2959.18, 2931.83, 2870.66, 1656.26, 1621.97, 1563.06, 1530.62, 1449.53, 1347.48, 1295.14, 1258.04, 1200.50, 1148.84, 1127.13, 969.51, 948.47, 883.97, 841.94, 807.22, 747.43, 672.22 and 628.90cm^{-1}. **^{1}H NMR (CDCl$_3$, 300 MHz)**: □□ 0.87 (t, 3H, *J* = 7.2 Hz, -$CH_2C\underline{H}_3$), 1.26 (d, 3H, *J* = 6.4 Hz, -$CHC\underline{H}_3$), 1.57-1.65 (m, 2H, -$C\underline{H}_2CH_3$), 3.23-3.32 (m, 1H, -$C\underline{H}CH_3$), 3.88 (s, 3H, OCH_3), 6.77 (d, 1H, *J*= 7.6 Hz, H-6), 6.83-6.89 (m, 2H, H-4 and H-5), 8.28 (s, 1H, H-3). **^{13}C NMR (CDCl$_3$, 75 MHz)**: □□ 10.56 (-$CH_2\underline{C}H_3$), 22.03 (-$CH\underline{C}H_3$), 30.66 (-$\underline{C}H_2CH_3$), 56.02 (OCH_3), 65.59 (-$\underline{C}HCH_3$), 103.32, 113.62, 117.36 (C-4, C-5 and C-6), 122.69 (C-3), 123.51 (C-9), 144.68 (C-8), 148.66 (C-7), 152.86 (C-2) and 162.54 (*C*ONH). **HRMS**: Calculated for $C_{14}H_{17}O_3N$ $[M]^+$247.2897, found 247.5512.

***N*-Pentyl-7-methoxybenzofuran-2-carboxamide** (**20**)

The compound **20** was obtained as brown solid in 80% yield. **Melting point**: 40 ^{o}C.**UV (MeOH) λ$_{max}$**: 232 and 274 nm. **IR (KBr) ν$_{max}$**: 3298.65, 2957.45, 2931.90, 2860.48, 1653.72, 1593.31, 1527.17, 1490.55, 1462.23, 1430.97, 1317.79, 1273.06, 1205.08, 1183.45, 1097.40, 976.09, 939.86, 839.27, 778.55, and 730.46 cm^{-1}. **^{1}H NMR (CDCl$_3$, 300 MHz)**: □□ 0.91 (t, 3H, *J* = 6.9 Hz, -$CH_2C\underline{H}_3$), 1.34-1.70 (m, 6H, -$CH_2CH_2CH_2$-), 3.46 (q, 2H, *J* = 6.9 Hz, -$NHC\underline{H}_2$-), 4.01 (s, 3H, OCH_3), 6.82 (*brs*, 1H, NH), 6.90 (dd, 1H, *J*= 1.5 & 7.5 Hz, H-6), 7.18-7.28 (m, 2H, H-4 and H-5), 7.47 (s, 1H, H-3). **^{13}C NMR (CDCl$_3$, 75 MHz)**: □□ 13.91 (-$CH_2\underline{C}H_3$), 22.23, 28.59, 29.20, (-$CH_2CH_2CH_2$-), 39.41 (-$NHCH_2$-), 55.94 (OCH_3), 108.08, 110.70, 114.74 (C-4, C-5 and C-6), 124.32 (C-3), 129.29 (C-9), 144.13 (C-8), 145.45 (C-7), 149.10 (C-2) and 158.76 (*C*ONH). **HRMS**: Calculated for $C_{15}H_{19}O_3N$ $[M+H]^+$262.1365, found 261.9660.

***N*-Hexyl-7-methoxybenzofuran-2-carboxamide** (**21**)

The compound **21** was obtained as yellow semisolid in 75% yield. **UV (MeOH) λ$_{max}$**: 233 and 273 nm. **IR (CHCl$_3$) ν$_{max}$**: 3314.77, 2932.47, 2859.48, 1655.08, 1596.09, 1523.04, 1479.13, 1407.77, 1376.34, 1291.34, 1230.17, 1080.16, 969.96, 855.18 and 807.18 cm^{-1}. **^{1}H NMR (CDCl$_3$, 400 MHz)**: □□ 0.88 (t, 3H, *J* = 6.8 Hz, -$CH_2C\underline{H}_3$), 1.22-1.65 (m, 8H, -$CH_2CH_2CH_2CH_2$-), 3.45 (q, 2H, *J* = 6.8 Hz, -$NHC\underline{H}_2$-), 4.01 (s, 3H, OCH_3), 6.74 (*brs*, 1H, NH), 6.89 (d, 1H, *J*= 7.6 Hz, H-6), 7.18-7.25 (m, 2H, H-4 and H-5) and 7.45 (s, 1H, H-3). **^{13}C NMR (CDCl$_3$, 100 MHz)**: □□13.99 (-$CH_2\underline{C}H_3$), 22.52, 26.59, 29.59, 31.46 (-$CH_2CH_2CH_2CH_2$-), 39.41 (-$NHCH_2$-), 55.94 (OCH_3), 108.06, 110.64, 114.72 (C-4, C-5 and C-6), 124.27 (C-3), 129.28 (C-9), 144.10 (C-8), 145.44 (C-7), 149.13 (C-2) and 158.66 (*C*ONH). **HRMS**: Calculated for $C_{16}H_{21}O_3N$ $[M+H]^+$276.1521, found 276.1521.

***N*-(3-(Diethylamino)propyl)-7-methoxybenzofuran-2-carboxamide** (**22**)

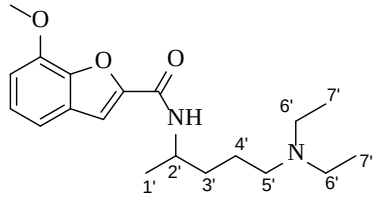
The compound **22** was obtained as yellow semisolid in 65% yield. **UV (MeOH) λ_{max}**: 352 nm. **IR ($CHCl_3$) ν_{max}**: 3397.41, 2926.45, 2854.25, 1721.77, 1659.11, 1591.88, 1463.06, 1398.15, 1270.82, 1218.11, 1091.93, 1028.78 and 794.83 cm^{-1}. **^{1}H NMR ($CDCl_3$, 300 MHz)**: □□ 0.94 (t, 6H, *J* = 6.6 Hz, 2 × -$CH_2C\underline{H}_3$-), 1.67-1.76 (m, 2H, -$NCH_2C\underline{H}_2$-), 2.45-2.49 (m, 8H, 2 × -$C\underline{H}_2CH_3$-, -$NHC\underline{H}_2$- and -NCH_2-), 3.95 (s, 3H, OCH_3), 6.73 (d, 1H, *J*= 7.5 Hz, H-6), 6.78-6.91 (m, 2H, H-4 and H-5), 7.20 (s, 1H, H-3) and 8.26 (*brs*, 1H, NH). **^{13}C NMR ($CDCl_3$, 75 MHz)**: □□ 11.48 (2 ×-$CH_2\underline{C}H_3$-), 29.66 (-$NCH_2\underline{C}H_2$-), 46.83 (-$NHCH_2$), 50.18 (2 × -$\underline{C}H_2CH_3$-), 56.01 (-NCH_2-), 56.87 (OCH_3), 108.06, 113.68, 117.51 (C-4, C-5 and C-6), 122.75 (C-3), 128.33 (C-9), 144.10 (C-8), 148.61 (C-7), 152.67 (C-2) and 164.90 (*C*ONH).

HRMS: Calculated for $C_{17}H_{24}O_3N_2$ $[M]^+$304.1787, found 304.0273.

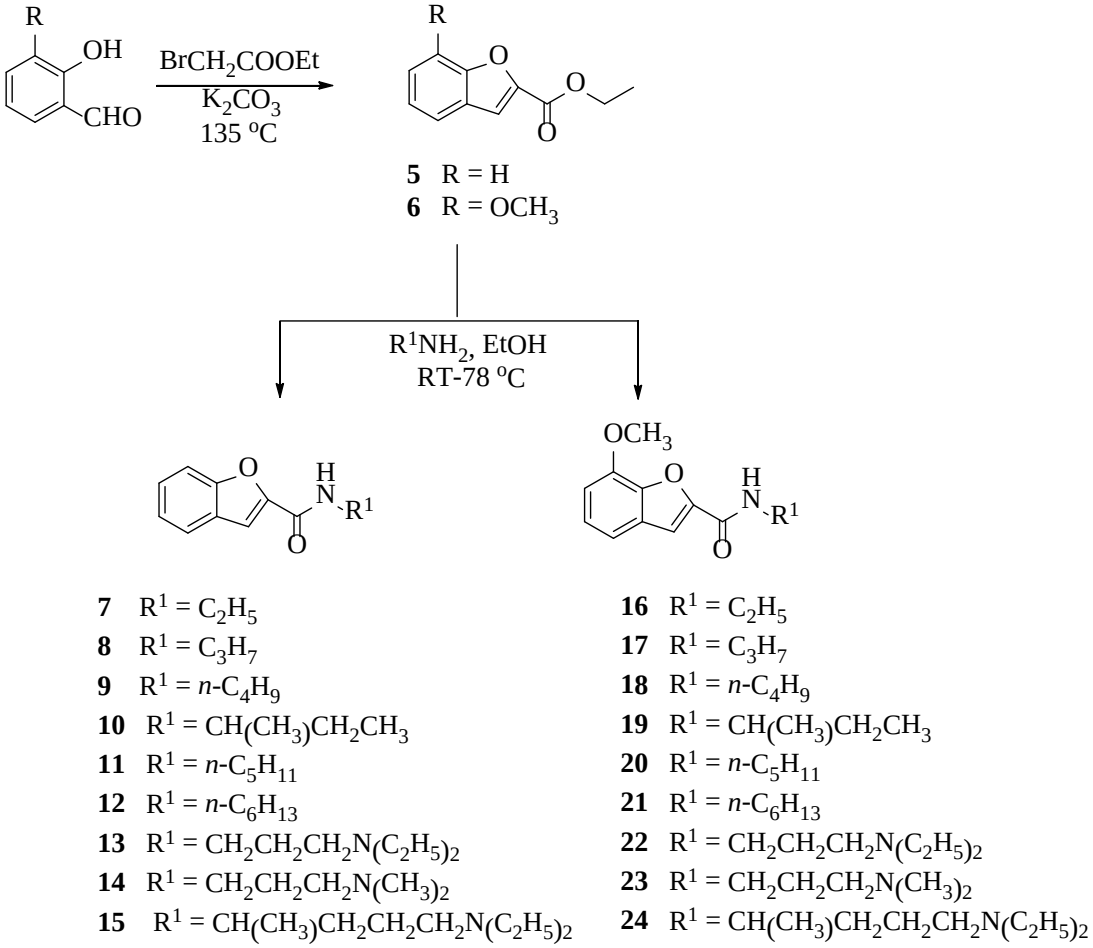
***N*-(3-(Dimethylamino)propyl)-7-methoxybenzofuran-2-carboxamide** (**23**)

The compound **23** was obtained as yellow semisolid in 70% yield. **UV (MeOH) λ_{max}**: 222 and 294 nm. **IR ($CHCl_3$) ν_{max}**: 3371.14, 3059.46, 2941.09, 2857.90, 2818.77, 2769.58, 1745.41, 1632.77, 1467.26, 1381.76, 1343.92, 1254.66, 1169.61, 1081.99, 1040.17, 971.21, 840.69, 780.98 and 737.33 cm^{-1}. **^{1}H NMR ($CDCl_3$, 300 MHz)**: □□ 1.73 (m, 2H, -$NCH_2C\underline{H}_2$-), 2.11 (s, 6H, 2 × -NCH_3), 2.29 (t, 2H, *J* = 5.1 Hz, -NCH_2-), 3.53 (q, 2H, *J* = 6.0 Hz, -$NHC\underline{H}_2$-), 3.77 (s, 3H, OCH_3), 6.67 (d, 1H, *J*= 7.8 Hz, H-6), 6.78-6.81 (m, 2H, H-4 and H-5), 7.31 (s, 1H, H-3) and 8.20 (*brs*, 1H, NH). **^{13}C NMR ($CDCl_3$, 75 MHz)**: □□ 29.23 (-$NCH_2\underline{C}H_2$-), 44.94 (2 × -NCH_3), 55.55 (-$NHCH_2$-), 56.09 (-NCH_2-), 56.51 (OCH_3), 113.39, 117.12, 117.92 (C-4, C-5 and C-6), 122.43 (C-3), 124.09 (C-9), 148.15 (C-8), 151.36 (C-7), 152.22 (C-2) and 164.63 (*C*ONH). **HRMS**: Calculated for $C_{15}H_{20}O_3N_2$ $[M]^+$276.1474, found 276.3516.

***N*-(5-(Diethylamino)pentan-2-yl)-7-methoxybenzofuran-2-carboxamide** (**24**)



The compound **24** was obtained as yellow semisolid in 65% yield. **UV (MeOH) λ_{max}**: 252 nm. **IR ($CHCl_3$) ν_{max}**: 2968.06, 2932.57, 2868.21, 2801.03, 1758.85, 1630.18, 1583.03, 1465.34, 1380.69, 1255.03, 1196.71, 1133.88, 1084.24, 970.11, 839.87, 782.15 and 736.96 cm^{-1}. **^{1}H NMR ($CDCl_3$, 300 MHz)**: □□ 0.91 (t, 6H, *J* = 6.9 Hz, 2 × H-7'), 1.21 (d, 3H, *J* = 6.0 Hz, H-1'), 1.28-1.56 (m, 4H, H-3'-H-4'), 2.30-2.46 (m, 6H, 2 × H-6' and H-5'), 3.29 (m, 1H, H-2'), 3.82 (s, 3H, OCH_3), 5.22 (*brs*, 1H, NH), 6.72 (d, 1H, *J*= 7.8 Hz, H-6), 6.77-6.88 (m, 2H, H-4 and H-5) and 8.23 (s, 1H, H-3). **^{13}C NMR ($CDCl_3$, 75 MHz)**: □□□□□□□□ (2-X'C, 21.57 (C-1'), 22.95 (C-4'), 34.85 (C-3'), 45.78 (2 × C-6'), 54.10 (OCH_3), 63.42 (C-2'), 68.85 (C-5'), 112.68, 116.52, 121.74 (C-4, C-5 and C-6), 123.25 (C-3), 128.97 (C-9), 147.57 (C-8), 154.35 (C-7), 161.68 (C-2) and 168.41 (*C*ONH). **HRMS**: Calculated for $C_{13}H_{15}O_2N$ $[M+H]^+$333.2100, found 332.9387.



Scheme-1. Synthesis of *N*-alkyl-7-hydro / methoxybenzofuran-2-carboxamides.

III. RESULTS AND DISCUSSIONS

Ethyl 7-methoxybenzofuran-2-carboxylate (6)

It was synthesized from *o*-vanillin, potassium carbonate and ethyl bromoacetate in DMF. The compound **6** was obtained in 70% yield as white solid. In its IR spectrum, it showed characteristic absorption band at 1714 cm^{-1} which accounts for the carbonyl stretching of the ester group. In its UV spectrum, it showed absorptions at λ_{max} 220 and 263 nm. In its ^{1}H NMR spectrum (**Figure 1**), a triplet at □ 1.32 for methyl group and a downfield quartet at □□4.34 for methylene protons confirms the presence of ethoxy group of ester. A singlet, integrating for three protons at□ 3.94 and its corresponding peak in ^{13}C NMR at □ 56.00 was identified for methoxy protons. A doublet at □7.10 for H-6 and a multiplet in the range of□ 7.18 -7.25 for H-4 and H-5 were observed. A characteristic downfield singlet at□ 7.51 was observed for H-3, this explains the furan ring formation. In its ^{13}C NMR spectrum (**Figure 2**), peaks at□ 14.30 and □61.38 accounts for the ethyl group of ester linkage. C-2 was observed downfield at□ 145.95 due to attached ester functionality, while carbonyl carbon of ester group was observed at□ 159.34. In HRMS, $[M+Na]^{+\cdot}$ peak was observed at 243.0635 (calculated value: 243.0736).

On the same basis characterization of ethyl benzofuran-2-carboxylate (**5**) was carried out.

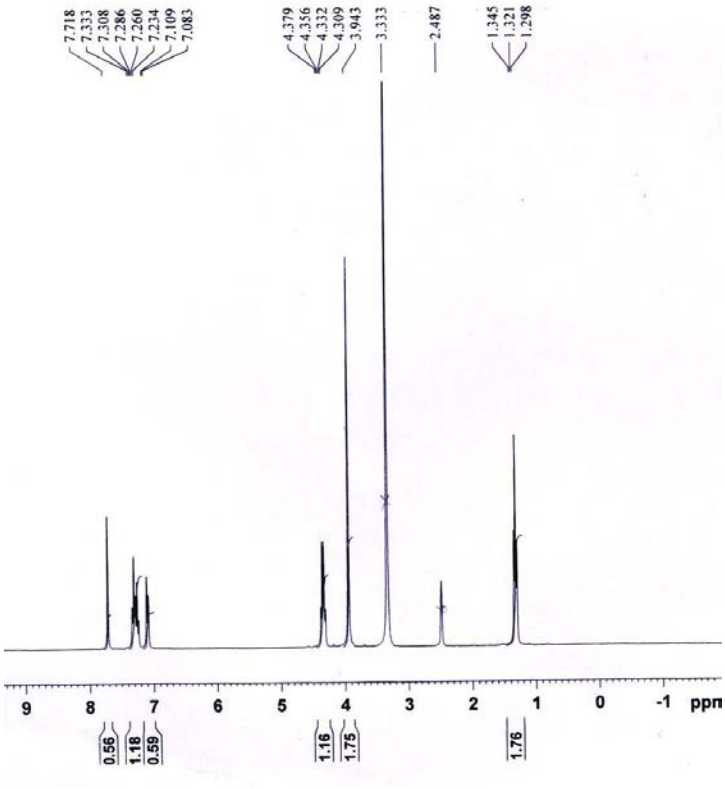


Figure 1. ^{1}H NMR Spectra of Ethyl 7-methoxybenzofuran-2-carboxylate (6).

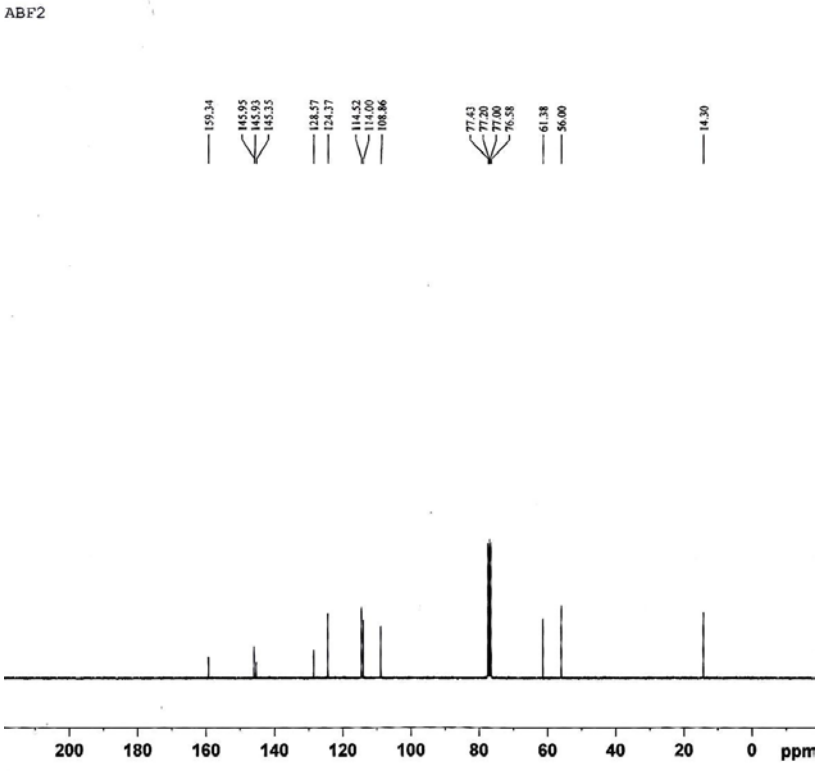


Figure 2. ^{13}C NMR Spectra of Ethyl 7-methoxybenzofuran-2-carboxylate (6).

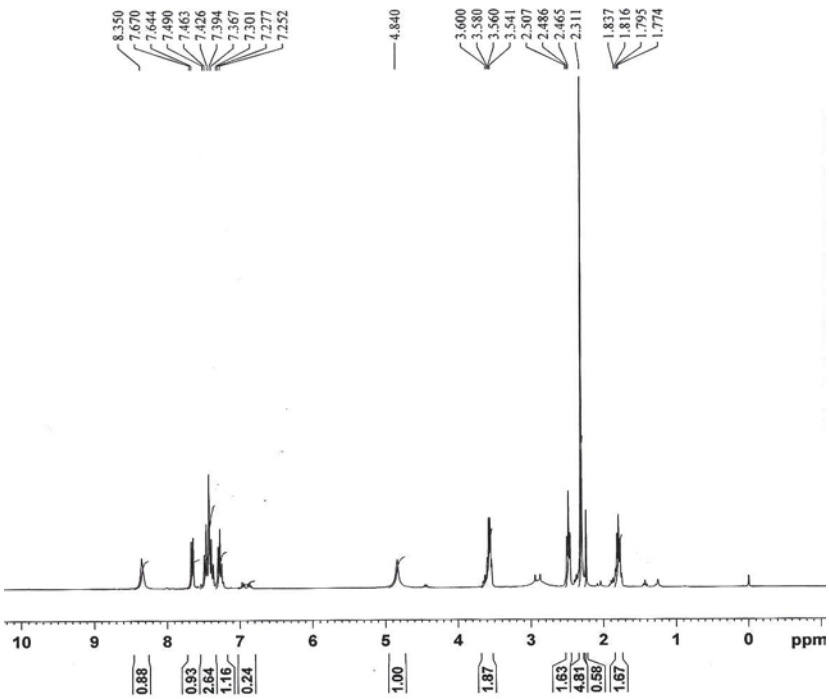


Figure 3. ^{1}H NMR Spectra of *N*-(3-(Dimethylamino)propyl)benzofuran-2-carboxamide (14).

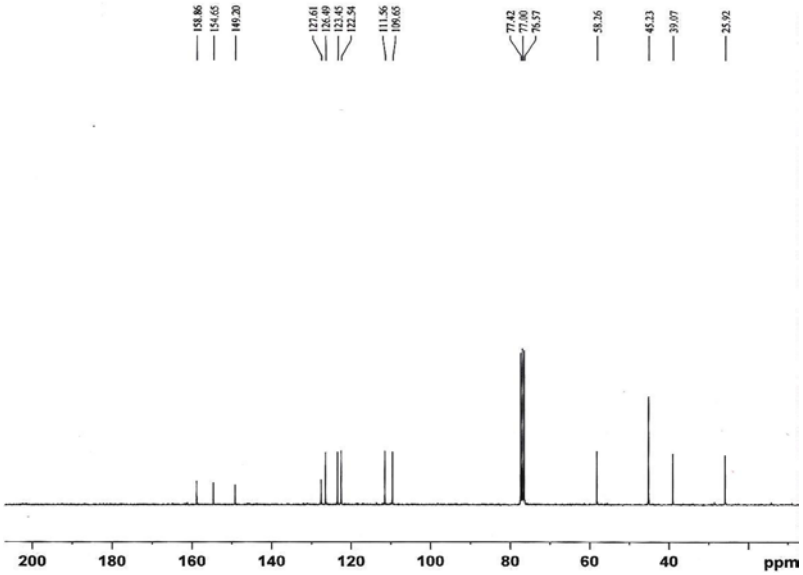
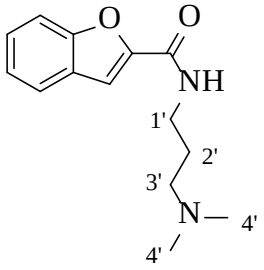


Figure 4. ^{13}C NMR Spectra of *N*-(3-(Dimethylamino)propyl)benzofuran-2-carboxamide (14).

***N*-(3-(Dimethylamino)propyl)benzofuran-2-carboxamide (14)**



It was synthesized from ethyl benzofuran-2-carboxylate (**5**) and 3-*N*,*N*-dimethylpropyl amine in ethanol. The title compound **14** was obtained in 75% yield as yellow semisolid. It showed characteristic absorption band at 1725 cm^{-1} in IR spectrum that accounts for the carbonyl stretching of the amide group. In UV spectrum, it showed absorption at λ_{max} 272 nm. In its ^{1}H NMR spectrum (**Figure 3**), a multiplet at□ 1.79 for methylene group (H -2'), a singlet for two methyl groups attached with tertiary nitrogen (2 × H-4') at □ 2.31, a triplet for methylene group H-3' at □ 2.49 and a quartet at□ 3.57 for H-1' explains the presence of 3-*N*,*N*-dimethylpropyl group. In its ^{13}C NMR spectrum (**Figure 4**), peak at□ 45.24 was observed for the two methyl group attached to nitrogen. Peaks at□ 25.91, □39.08 and □58.26 were identified for the carbons of the propyl group linked with amide bond. C-2 appeared downfield at□ 154.65 due to the attached amide group, while carbonyl carbon of amide group was observed at□ 158.86. In HRMS, $[M]^{+\cdot}$ peak was observed at 246.3866 (calculated value: 246.3049).

On the similar grounds, characterization of *N*-(3-(diethylamino)propyl)-7-hydro / methoxybenzofuran-2-carboxamide **13** and **22**, *N*-(3-(dimethyl)aminopropyl)-7-methoxybenzofuran-2-carboxamide **23**, *N*-(5-(diethylamino)pentan-2-yl)-7-hydro / methoxybenzofuran-2-carboxamide **15** and **24** are done.

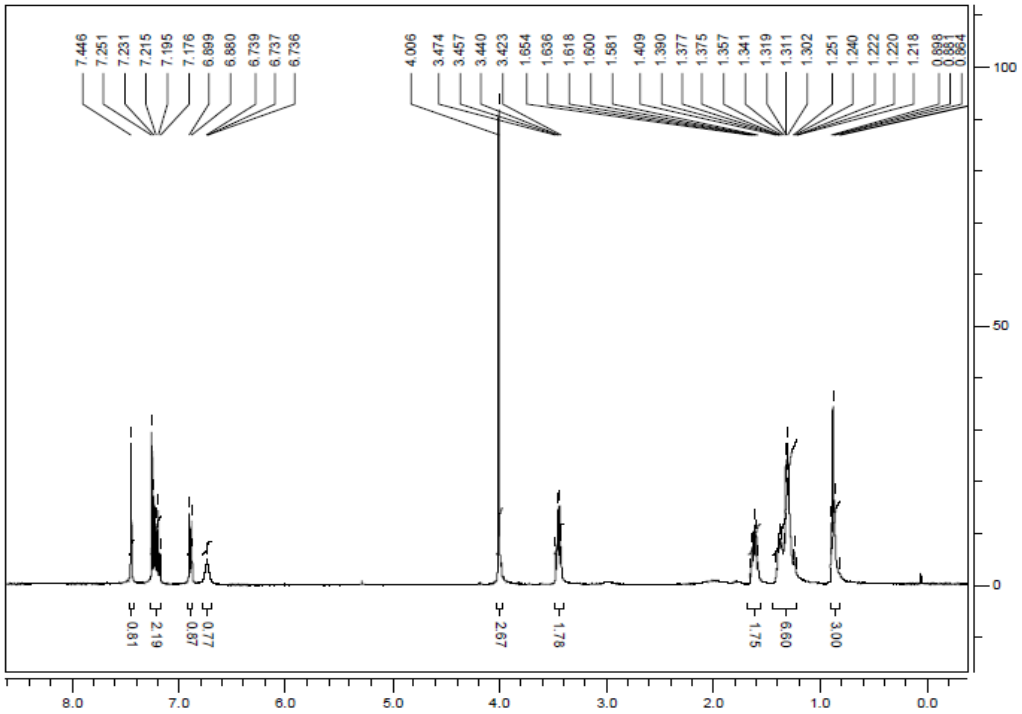


Figure 5. ^{1}H NMR Spectra of *N*-Hexyl-7-methoxybenzofuran-2-carboxamide (21).

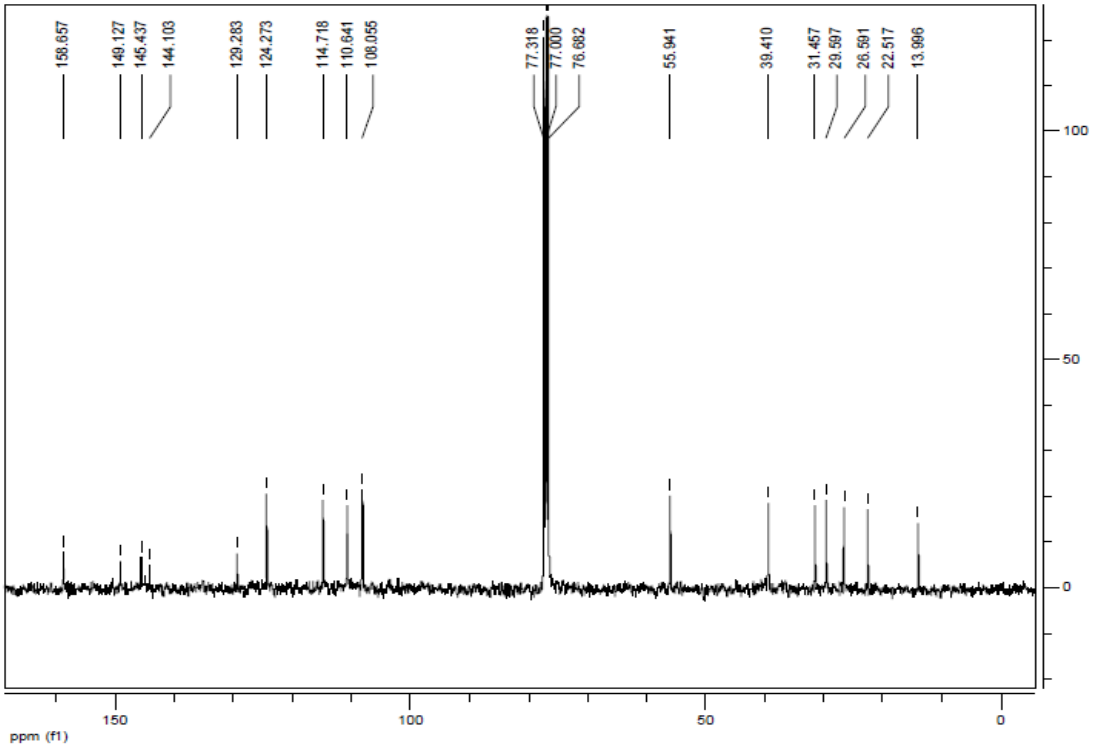
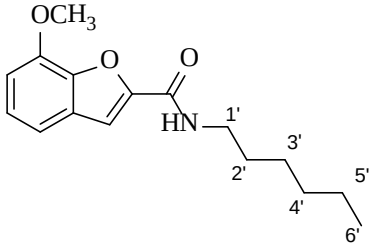


Figure 6. ^{13}C NMR Spectra of *N*-Hexyl-7-methoxybenzofuran-2-carboxamide (21).

***N*-Hexyl-7-methoxybenzofuran-2-carboxamide (21)**



It was synthesized from ethyl-7-methoxybenzofuran-2-carboxylate (**6**) and pentyl amine in ethanol. The compound **21** was obtained in 75% yield as yellow semisolid. In its IR spectrum, it showed characteristic absorption band at 1655 cm^{-1} which accounts for the carbonyl stretching of the amide group. In its UV spectrum, it showed absorptions at λ_{max} 233 and 273 nm. In its ^{1}H NMR spectrum (**Figure 5**), a triplet at □ 0.88 for terminal methyl group, a multiplet for methylene protons in the range of □ 1.22-1.65 and another downfield quartet for methylene protons attached with nitrogen of amide bond at □ 3.45 explains the presence of hexyl group attached *via* amide linkage. A characteristic downfield singlet for H-3 was observed at □ 7.45. In its ^{13}C NMR spectrum (**Figure 6**), the hexyl group carbons appeared at□ 13.99, 22.52, 26.59, 29.59, 31.46 and 39.41. A peak at □ 55.94 was assigned for methoxy group. A downfield peak at□ 145.44 in ^{13}C NMR was identified for C-7 due to the presence of methoxy group at this position. C-2 appeared downfield at □□ 149.13 due to presence of amide group, while carbonyl carbon of amide group was observed at□ 158.66. In HRMS, $[M+H]^{+\cdot}$ peak was observed at 276.1521 (calculated value: 276.1521).

The other amides i.e. *N*-ethyl-7-hydro / methoxybenzofuran-2-carboxamide **7** and **16**, 7-hydro / methoxy-*N*-propylbenzofuran-2-carboxamide **8** and **17**, *N*-butyl-7-hydro / methoxybenzofuran-2-carboxamide **9** and **18**, *N-sec*-butyl-7-hydro / methoxybenzofuran-2-carboxamide **10** and **19**, 7-hydro / methoxy-*N*-pentyl benzofuran-2-carboxamide **11** and **20** and *N*-hexylbenzofuran-2-carboxamide **12** were characterized on similar basis as *N*-hexyl-7-methoxybenzofuran-2-carboxamide **21**.

IV. CONCLUSION

Out of these total twenty compounds synthesized **5-24**, eight compounds (**11**, **15**, **16** and **20**-**24**) are new and synthesized for the first time. All these compounds are well characterized from their physical data (^{1}H, ^{13}C, IR, UV and Mass spectrometery).

REFERENCES

[1] W. J. Wang, L. Wang, Z. Liu, R. W. Jiang, Z. W. Liu, M. M. Li, Q. W. Zhang, Y. Dai, Y. L. Li, X. Q. Zhang, W. C. Ye, *Phytochemistry letters.,* 122 (2016) 238–245.

[2] T. A. Mansoor, P. M .Borralho, X. Luo, S. Mulhovo, C. M. Rodrigues, M. J. Ferreira, *Phytomedicine.,* 20 (2013) 923-9.

[3] D. S. Lee, G. S. Jeong, *European Journal of Pharmacology.,* 728 (2014*)* 1-8.

[4] S. Y. Zhang, A. L. Chen, Q. Li, *Phytochemistry letters.,* 5 (2012) 473–475.

[5] S. N. Richardson, T. K. Nsiama, A. K. Walker, D. R. McMullin, J. D. Miller, *Phytochemistry letters.,* 117 (2015) 436-443.

[6] M. C. Shill, H. Miuguchi, S. Karmakar, T. Kadota, P. K. Mukherjee, Y. Kitamura, Y. Kashiwada, H. Nemoto, N. Takeda, H. Fukui, *Int. Immunopharmacol*., 30 (2016) 18-26.

[7] D. S. Yang, J. G. Wei, W. B. Peng, S. M. Wang, C. Sun, Y. P. Yang, K. C. Liu, X. L. Li, *Fitoterapia.,* 99 (2014) 261–266.

[8] O. Oter, K. Ertekin, C. Kirilmis, M. Koca, M. Ahmedzade, *Sensors and Actuators B: Chemical.,* 122 (2007) 450–456

[9] D. S. Yang, Z. L. Li, Y. P. Yang, W. L. Xiao, X. L. Li, *Chinese Herbal Medicines.,* 7 (2015), 191-194.

[10] P. Pahari, J. Rohr, *J. Org. Chem.,* 74 (2009) 2750.

[11] C. Privat, J. P. Telo, V. Bernardes-Genisson, A. Viera, J. P. Souchard, F. Nepveu, *J. Agric. Food Chem.,* 50 (2002) 1213.

[12] M. W. Khan, M. J. Alam, M. A. Rashid, R. Chowdhury, *Bioorg. Med. Chem.,* 13 (2005) 4796.

[13] L. Alvey, S. Prado, V. Huteau, B. Saint-Joanis, S. Michel, M. Koch, S. T. Cole, F. Tillequin, Y. L. Janin, *Bioorg. Med. Chem.,* 16 (2008) 8264.

[14] A. R. Katrizky, C. W. Ress, *Comprehensive Heterocyclic Compounds, Elseiver Science Ltd.,* 4 (1977

[15] P. Steinhaus, P. Schieberle, *J. Agric. Food Chem.,* 55 (2007) 6262.

[16] Y. Tokitomo, M. Steinhaus, A. Büttner, P. Schieberle, *Biosci. Biotechnol. Biochem.* 269 (2005) 1323.

[17] D. Janes, Kantar, D. Kantar, S. Kreft, H. Prosen, *Food Chem.,* 112 (2008) 120.

[18] R. G. Buttery, G. R. Takeoka, M. Naim, H. D. Rabinowitch, Y. Nam, *J. Agric. Food Chem.,* 49 (2001) 4349.

[19] S. Kumar, B. K. Singh, A. K. Pandey, A. Kumar, S. K. Sharma, H. G. Raj, A. K. Prasad; E. V. Eycken, V. S. Parmar, B. Ghosh, *Bioorg. Med. Chem.*, 42 (2007) 447.
[20] I. V. Ukrainets, N. L. Bereznyakova, I. A. Turaibei, *Chem. Het. Comp.*, 44 (2008) 50.
[21] I. V. Ukrainets, L. V. Sidorenko, O. V. Gorokhova, S. V.Shishkina, A. V. Turov, *Chem.Het. Comp.*, 43 (2007) 617.