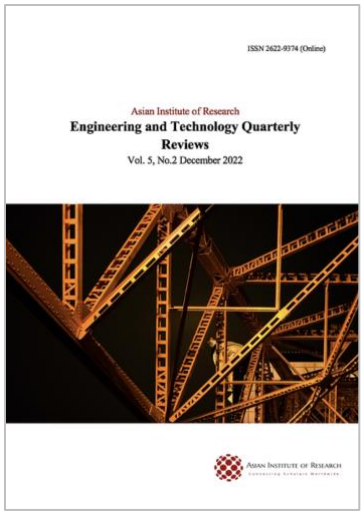

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Synthesis and Characterization of Benzofuranone and its Derivatives

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Abstract
In this experiment a mixture of salicylaldehyde (2 mmol), 4-chlorophenacyl bromide (2 mmol) and potassium tertiary butoxid (T-BuOK) (2mmol) in 10ml of Dichlorometane (DCM), containing molecular sieves was reflexed at 30C^°for 3 hours. Progress of the reaction was monitored by Thin layer chromatography (TLC) using hexane: ethyl acetate (8:2) mixture as mobile phase. After the completion of the reaction, the reaction mixture was washed with 10 % HCl solution followed by water. The organics were dried over anhydrous sodium sulfate. The yellow solid was obtained disolventizing in a rotary evaporator at room temperature affords benzofuran-2-yl (4-chlorophenyl) methanone. Benzofuranone (0.60 ml, 5 mmol) with substituted anilines (5 mmol) in round bottom flasks was refluxed in 15 ml methanol at 40C^° for 3 hours in the presence of 1.5 ml glacial acetic acid. In each case, the precipitated base was filtered off, recrystallized from absolute ethanol and dried in vacuum desiccators. The (Z)-N-(benzofuran-2-yl (4-chlorophenyl) methylene) aniline was obtained.

Keywords: Salicylaldehyde, TLC, DCM, Mobile Phase, Anhydrous Sodium Sulfate and Reflux

1. Introduction

The second half of last century has witnessed an enormous progress in organic synthesis as a consequence of the advent of innovative concepts with high predictable power and the development of new strategies and technologies culminating in the preparation of numerous natural and unnatural products of great complexity.

Formidable goals were achieved owing to the continuous efforts in the search for new reagents and methods, particularly those allowing one to assemble molecular building blocks via chemically efficient and stereo selective carbon-carbon bond-forming reactions (Vertuani, *et al*. 2004). At present, research in this field is even more actively promoted by the interplay of organic chemistry and various disciplines of life science such as biology, pharmacology, and medicine that are posing a pressing demand for natural products and synthetic analogues in meaningful scale and high purity. Although a great deal of new reagents and catalysts have been formulated as the result of profitable studies in organometallic chemistry (Jumbam, 2011).

2. Experimental

2.1. Materials and methods

A brief description of the solvents and reagents used here the analytical procedures followed, different physio-chemical techniques like TLC, melting point, IR, ^{1}HNMR and mass spectroscopic are employed for the characterization of the synthesized compounds those presented here (Collin, 2007).

2.2. Organic solvents

The organic solvents like ethanol, n-hexane, ethyl acetate (E-Merck), were of analytical reagent grade. Distilled water-double distilled water by quartz distillation unit (Harman, 1992).

2.3. Reagents

All the chemical reagents were obtained from the standard commercial sources unless otherwise indicated. DPPH (Sigma Aldrich), anhydrous sodium sulphate (Ranbaxy), salicylaldehyde, phenacyl bromides (E-Merck), sulfonyl chlorides (Mc Murry, 1989).

2.4. Analytical techniques

Thin-layer chromatography (TLC) was the method used to assess the reactions and the purity of the product compound. In this we used the TLC aluminium sheets-silica gel 60 F254 was purchased from Merck. The plates were developed using n-hexane: ethyl acetate (8:2) as mobile solvent. The spot was located by exposing the TLC plates to iodine vapours (Lenoir D, 1989).

Column chromatography was performed by using activated silica gel [60-120 mesh] packed onto the glass column [450 X 40 mm] with methanol as solvent. The crude product was loaded and eluted using mixture of n-hexane: ethyl acetate (8:2). The fractions were collected separately and active fraction was concentrated by using rota evaporator (Chittimalla, et. all. 2008).

2.5. Instrumentation

Melting points of the compounds were determined using SELACO-650 and Veego VMP-III model hot stage melting point apparatus and are uncorrected.

Identification and structure elucidation of newly synthesized compounds under study was carried out by using various spectroscopic techniques such as IR, ^{1}HNMR, mass and elemental analysis (Ledoussal, 1987).

An instrument of FT-IR021 model was used for recording IR spectra of the synthesized compounds. About 2-3 mg of compound was prepared as KBr pellet and the IR spectra were recorded.^{1}HNMR spectra were recorded on Joel GSX 400,400 MHz, spectrophotometer using $CDCl_3$ and DMSO-d_6 as solvents with tetramethylsilane (TMS) as internal standard. Mass spectra of the synthesized compound were obtained using a Q-TOF Waters Ultima instrument (No-Q-Tof GAA 082, Water Corporation, Manchester, UK) fitted with an Electron spray ionization (ESI) source (Dupont, 1999). The data acquisition software used was Version 4.0. Elemental analysis

was carried out on elemental Vario EL instrument. Oxygen was used for combustion and Helium as the mobile phase (Inghaml; Dewick. 1978).

3. General procedure for synthesis of benzofuranone derivatives IV (a-d)

Benzofuranone (0.6 ml, 5mmol) with substituted anilines (5 mmol) in round bottom flasks was refluxed in 15ml methanol at $40C^{\circ}$ for 3 hours in the presence of 1.5 ml glacial acetic acid. Progress of the reaction was monitored by Thin layer chromatography (TLC) using hexane: ethyl acetate (8:2) mixture as mobile phase. After the completion of the reaction, the reaction mixture was washed with 10 % HCl solution followed by water. The organics were dried over anhydrous sodium sulfate. The yellow solid was obtained disolventizing in a rotary evaporator at room temperature affords benzofuran-2-yl (4-chlorophenyl) methanone. In each case, the precipitated base was filtered off, recrystallized from absolute ethanol and dried in vacuum desiccators (Koenigkramer, 1980).

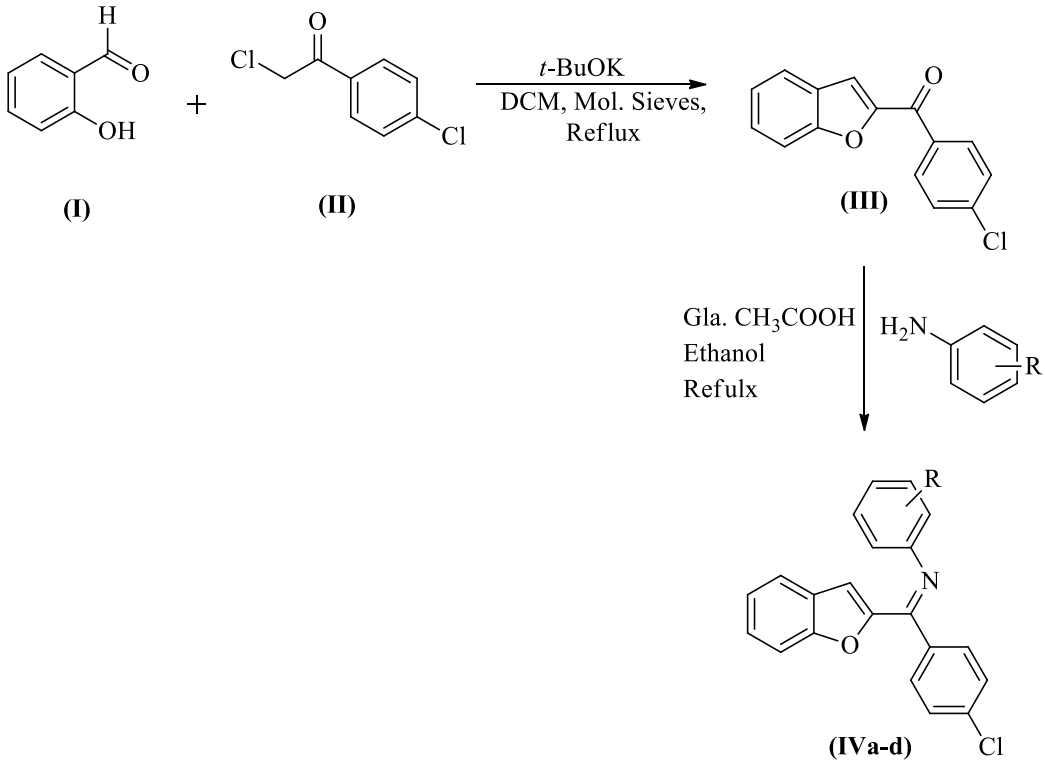
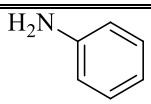
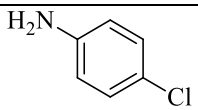
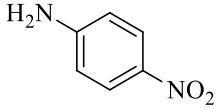
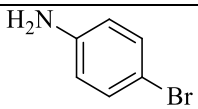


Figure 1: Reaction protocol for the synthesis of benzofuranone derivatives via IV(a-d)

Table 1: Chemical structure, yield and melting point of synthesized derivatives IV(a-d)

Compounds No	R-NH_2	Yield (%)	Melting Point (^{o}C)
Iva		70	107-109
IVb		76.5	210-212
IVc		75	192-198
IVd		72.4	188-189

(Z)-N-(benzofuran-2-yl(4-chlorophenyl) methylene) aniline (IVa).

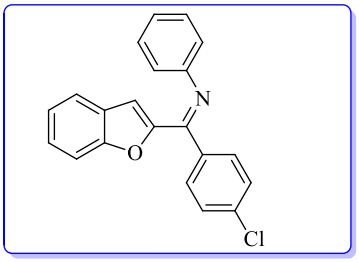


Figure 2: (Z)-N-(benzofuran-2-yl(4-chlorophenyl) methylene) aniline (IVa).

Brown solid, Spectroscopic analysis: IR (KBr)ν_{max}(cm^{-1}): 3132-2966 (Ar-CH), 1628 (C=N); ^{1}H NMR (DMSO-d_6 400 MHz) δ ppm: 6.93-7.90 (m, 14H, Ar-H), MS (ESI) m/z: 331.08 (M^+); Anal.calcd. for $C_{21}H_{14}ClNO$: C, 76.02; H, 4.25; N, 4.22; found: C, 76.09; H, 4.18; N, 4.20 %.

(Z)-N-(benzofuran-2-yl(4-chlorophenyl) methylene)-4-chloroaniline (IVb).

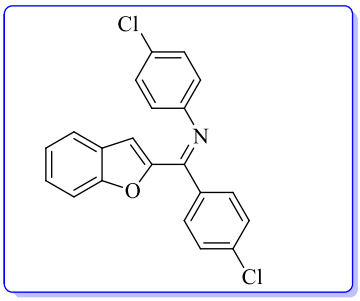


Figure 3: (Z)-N-(benzofuran-2-yl(4-chlorophenyl) methylene)-4-chloroaniline (IVb).

Brown solid, Spectroscopic analysis: IR (KBr)ν_{max}(cm^{-1}): 3130-2960 (Ar-CH), 1625 (C=N); ^{1}H NMR (DMSO-d_6 400 MHz) δ ppm: 6.90-7.92 (m, 13H, Ar-H), MS (ESI) m/z: 365.04 (M^+); Anal.calcd. for $C_{21}H_{13}Cl_2NO$: C, 68.87; H, 3.58; N, 3.82; found: C, 68.87; H, 3.55; N, 3.76 %.

(Z)-N-(benzofuran-2-yl(4-chlorophenyl) methylene)-4-nitroaniline (IVc).

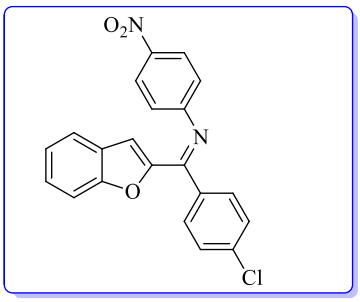


Figure 4: (Z)-N-(benzofuran-2-yl(4-chlorophenyl) methylene)-4-nitroaniline (IVc).

Orange solid, Spectroscopic analysis: IR (KBr)ν_{max}(cm^{-1}): 3135-2968 (Ar-CH), 1620 (C=N); ^{1}H NMR (DMSO-d_6 400 MHz) δ ppm: 6.85-7.90 (m, 13H, Ar-H), MS (ESI) m/z: 376.06 (M^+); Anal.calcd. for $C_{21}H_{13}ClN_2O_3$: C, 66.94; H, 3.48; N, 7.43; found: C, 66.83; H, 3.50; N, 7.46 %.

(Z)-N-(benzofuran-2-yl(4-chlorophenyl) methylene)-4-bromoaniline (IVd).

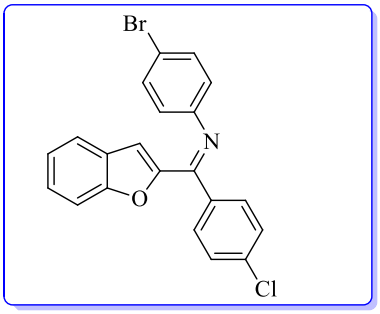


Figure 5: (Z)-N-(benzofuran-2-yl(4-chlorophenyl) methylene)-4-bromoaniline (IVd).

Black solid, Spectroscopic analysis: IR (KBr)ν_{max}(cm^{-1}): 3130-2970 (Ar-CH), 1620 (C=N); ^{1}H NMR (DMSO-d_6 400 MHz) δ ppm: 6.85-7.92 (m, 13H, Ar-H), MS (ESI) m/z: 408.99 (M^+); Anal.calcd. for $C_{21}H_{13}ClBrNO$: C, 61.41; H, 3.19; N, 3.41; found: C, 61.43; H, 3.20; N, 3.46 %.

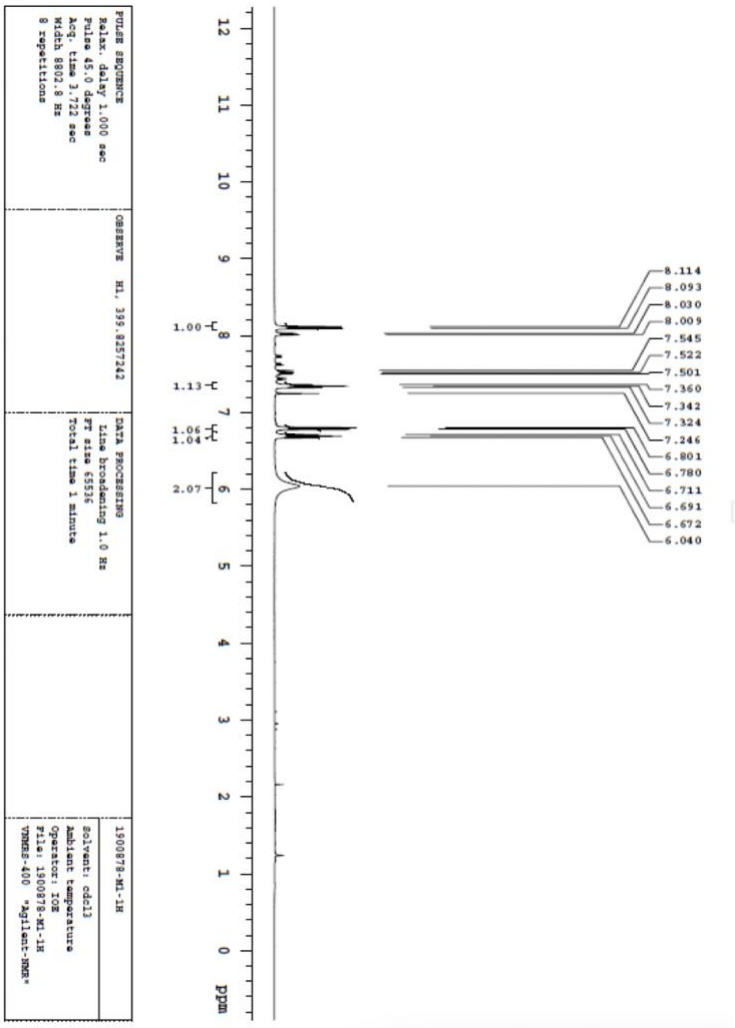


Figure 6: ^{1}H NMR spectra of compound (IVa).

4. Results and discussions

Benzofuranone was first synthesized by **Perkin** from counmarin Ketoesters derived from the acylation of O-hydroxyacetophenone with aliphatic as well as aromatic acid chlorides undergo intramolecular cyclization in the presence of low-valent titanium to afford benzofuranone in good yields. Benzofuranone derivatives are known to possess important biological properties. Substituted benzofuranone find application such as of fluorescent

sensor, antioxidants, brightening agents, a variety of drugs were reported in other field of chemistry and agriculture.

In this present work, a series of four new compounds were synthesized. **Figure 1** illustrates the way used for the preparation of target molecules. As a starting material salicylaldehyde is used to synthesize series of benzofuranone derivatives. The synthetic route involves, initially, o-alkylation of salicylaldehyde with phenacyl chloride in the presence of *t*-BuOK as base furnished o-alkylated aldehyde derivative, which subsequently generates enolate anion undergoing intramolecular cyclocondensation reaction that afforded benzofuranone. Further the compound reacts with different substituted anilines to obtained **(IVa-d)**. The structural synthesized compounds were confirmed by IR, ^{1}H NMR, mass spectra and elemental analysis.

5. Conclusion

Benzofuran is a heterocyclic compound consisting of fused benzene and furan ring. This colourless solid is a component of coal tar. Benzofuran is the "parent" of many related compounds with more complex structures. For example, psoralen is a benzofuran derivative that occurs in several plants. Benzofuran is extracted from coal tar. It is also obtained by dehydrogenation of 2-ethyl phenol.

Benzofuran and its derivatives have attracted much attention in medicinal chemistry for their wide range of various biological activities, including insecticidal, fungicidal, antimicrobial and antioxidant properties. Benzofuran compounds on the promising leads for the design of more efficient antimicrobial agents.

In the present investigation, I have reported the synthesis of benzofuranone derivatives via coupling of substituted anilines by choosing proper experimental conditions. Synthesized compounds were characterized by various analytical and spectral studied.

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