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Original Article

Synthesis and characterization of novel sesamol derivatives having 2-(benzo- [d][1,3] dioxol-5-yloxy)acetohydrazide scaffold

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ABSTRACT

A new series of 2-(benzo- [d],[1,3]dioxol-5-yloxy) acetohydrazide derivatives were synthesized from sesamol and characterized from various spectral methods. All derivatives were synthesized by the given schemes and reaction process was monitored by thin layer chromatography. The structures of synthesized derivatives were confirmed by FT-IR, ^{1}H NMR spectroscopy and elemental analysis methods.

1. INTRODUCTION

Sesame (Sesamum indicum L.) is one of the most important oilseed crops worldwide, and has been cultivated since ancient times for use as a traditional health food [1]. Sesame (Sesamum indicum) is a flowering plant in the genus Sesame. Numerous wild species of sesame were found in Africa, it is generally believed that sesame originated in Africa and a smaller number in India [2]. Sesame oil has a mild odour and a pleasant taste and, as such, is a natural salad oil. It is used as a cooking oil, in shortening and margarine, as a soap fat, in pharmaceuticals and as a synergist for insecticides [3]. Sesame oil is composed of the palmitic, palmitoleic, stearic, oleic, linoleic, linolenic, and eicosenoic fatty acids: Sesame oil is rich in unsaturated fatty acids where the fatty acids composition is 14% saturated 39% mono-unsaturated, and 46% poly-unsaturated fatty acids. Carbohydrates in sesame seed are composed of 3.2% glucose, 2.6% fructose and 0.2% sucrose while the remaining quantity is dietary fibers [4].

Sesame oil have desirable physiological effects including antioxidant activity, blood pressure and serum lipid lowering potential as proven in experimental animals and humans [5]. The major constituent of sesame seeds and oil is sesamol. Chemically sesamol is 2*H*-1,3-Benzodioxol-5-ol. It prevents the spoilage of oils by acting as an antifungal and antioxidant. Sesamol can be used as a chemical intermediate in the industrial synthesis of the pharmaceutical drug paroxetine. 2*H*-1,3-Benzodioxol-5-ol moiety in sesamol is responsible for the CNS activity of drugs having this moiety. For example paroxetine, The present research work focuses on derivatization of 2*H*-1,3-Benzodioxol-5-ol moiety in sesamol so as to obtain potent CNS active drugs [6].

Fig. 1. Sesame seeds and oil

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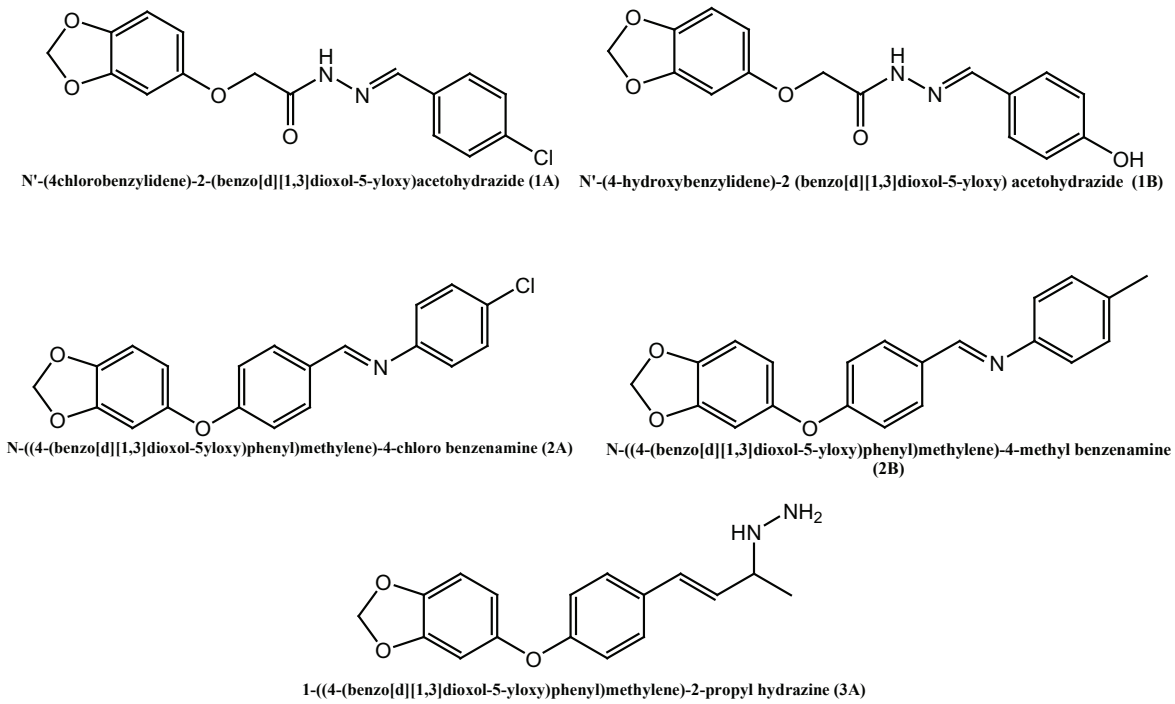

Fig. 2. 2-(benzo- [d],[1,3]dioxol-5-yloxy)acetohydrazide derivatives

2. EXPERIMENTAL

2.1 Materials and methods

All the chemicals and solvents, purchased from Merck (India), Spectrochem (India), Himedia (India) and S. d. Fine were used without further purification. The progress of reaction was monitored by thin layer chromatography, performed on a silica gel 60 F_{254} coated aluminum sheet. The melting points were determined by using Thomas- Hoover melting point apparatus and are uncorrected. The FT-IR spectra were recorded on Perkin-Elmer Spectrum BX-II Spectrophotometer. The ^{1}H-NMR spectra were recorded on Bruker 300 MHz High Resolution NMR spectrometer using TMS as an internal standard. Chemical shifts were reported in ppm (δ) and signals were described as singlet (s), doublet (d), triplet (t) and multiplet (m). All exchangeable protons were confirmed by addition of D_2O.

2.2 Synthesis of N'-(4- substituted benzylidene)-2-(benzo[d][1,3]dioxol-5-yloxy) acetohydrazide (1A, 1B)

A mixture of Sesamol, anhydrous K_2CO_3, chloroethyl acetate and DMF were stirred at room temperature for 8 hours. The reaction mixture was diluted with ice cold water. A solid was separated and synthesis of compound was confirmed by TLC study. A mixture of obtained compound (0.019 M) and hydrazine hydrate (15 ml) was refluxed for 4 h. The excess of hydrazine hydrate was removed *in-vacuo* and the residue was triturated with water, filtered off, dried and recrystallized from 70 % ethanol to give colourless crystals of (Benzo[1,3]dioxol-5-yloxy)-acetic acid hydrazide.

(Benzo[1,3]dioxol-5-yloxy)-acetic acid hydrazide (0.001 M) and p-chloro benzaldehyde or p-hydroxy benzaldehyde (0.001 M) was dissolved in absolute ethanol (40 ml). Add few drops of glacial acetic acid and reflux for 6 hours [7]. Then reaction mixture is poured in ice cold water and filtered (Fig.1). Finally compound was washed with water, dried at room temperature and recrystallized with ethanol. The reaction process is identified by TLC using ethyl acetate: n Hexane (2:3) as mobile phase and iodine as detecting agent.

2.3 Synthesis of N-((4-(benzo[d][1,3]dioxol-5-yloxy) phenyl) methylene) -4-substituted benzenamine (2A, 2 B)

A mixture of Sesamol, anhydrous K_2CO_3, 4-hydoxybenzaldehyde and acetone were refluxed at 60°C for 6 hours. The reaction mixture was diluted with ice cold water. A solid was separated and synthesis of compound was confirmed by TLC study. The solid was washed with water, filtered off and dried at room temperature to obtain 4-(Benzo[1,3]dioxol-5-yloxy)-benzaldehyde.

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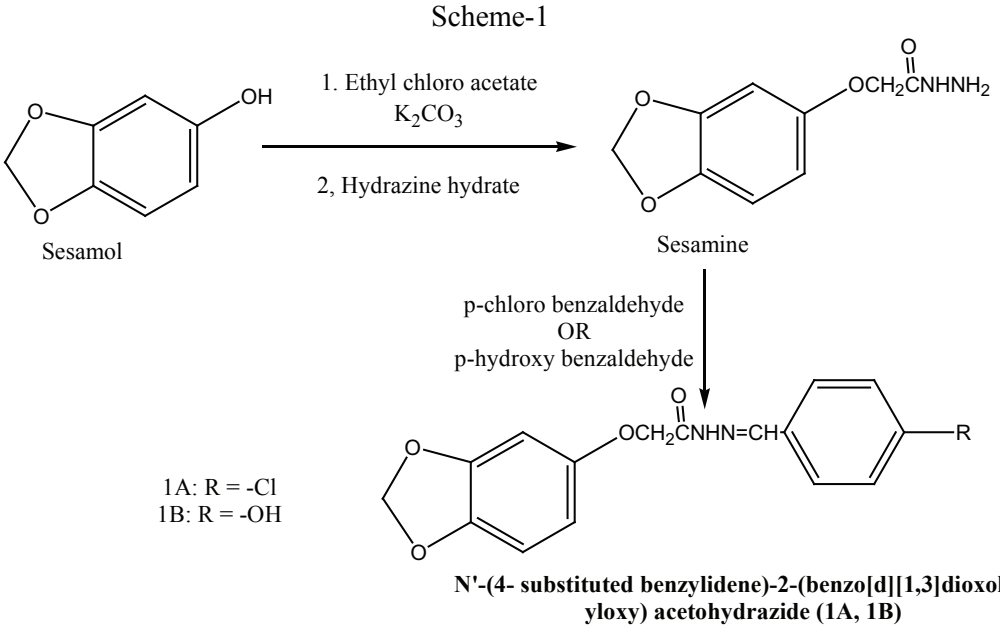

Fig. 3. Synthetic scheme for synthesis of N'-(4- substituted benzylidene)-2-(benzo[d][1,3]dioxol-5-yloxy) acetohydrazide (1A, 1B)

4-(Benzo[1,3]dioxol-5-yloxy)-benzaldehyde (0.001 M) and p-chloro aniline or p-methyl aniline (0.001 M) were dissolved in absolute ethanol (50 ml). Add few drops of glacial acetic acid and reflux for 4 hours. The reaction mixture is poured in ice cold water and filtered the synthesized compound (Fig. 2). Finally compound was washed with water, dried at room temperature and recrystallized with ethanol. The reaction process is identified by TLC using ethyl acetate: n hexane (2:3) as mobile phase and iodine as detecting agent.

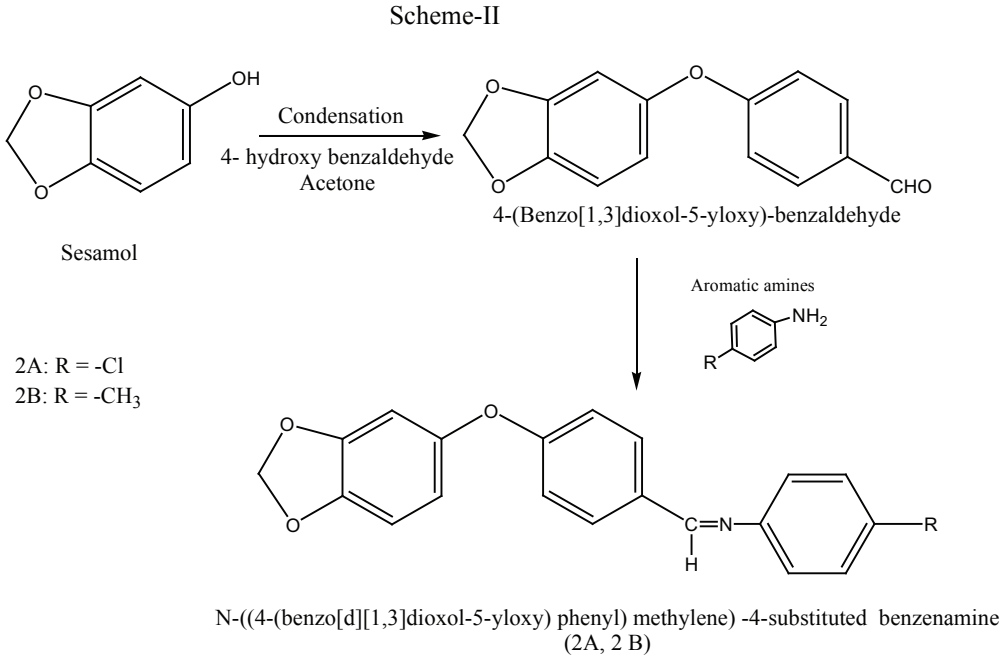

Fig. 4. Synthetic scheme for synthesis of N-((4-(benzo[d][1,3]dioxol-5-yloxy) phenyl) methylene) -4-substituted benzenamine (2A, 2 B)

2.4 Synthesis of 1-((4-(benzo[d][1,3]dioxol-5-yloxy) phenyl)methylene)-2-propyl hydrazine (3A)

A mixture of Sesamol, anhydrous K_2CO_3, 4-hydoxybenzaldehyde and acetone were refluxed at 60°C for 6 hours. The reaction mixture was diluted with ice cold water. A solid was separated and synthesis of compound was confirmed by TLC study. The solid was washed with water, filtered off and dried at room temperature

to obtain 4-(Benzo[1,3]dioxol-5-yloxy)-benzaldehyde.

4-(Benzo[1,3]dioxol-5-yloxy)-benzaldehyde (0.001 M) and propyl hydrazide (0.001 M) were dissolved in absolute ethanol (50 ml). Add few drops of glacial acetic acid and reflux for 4 hours. The reaction mixture is poured in ice cold water and filtered the synthesized compound. Finally compound was washed with water, dried at room temperature and recrystallized with ethanol. The reaction process is identified by TLC using ethyl acetate: n hexane (2:3) as mobile phase and iodine as detecting agent.

Scheme-III

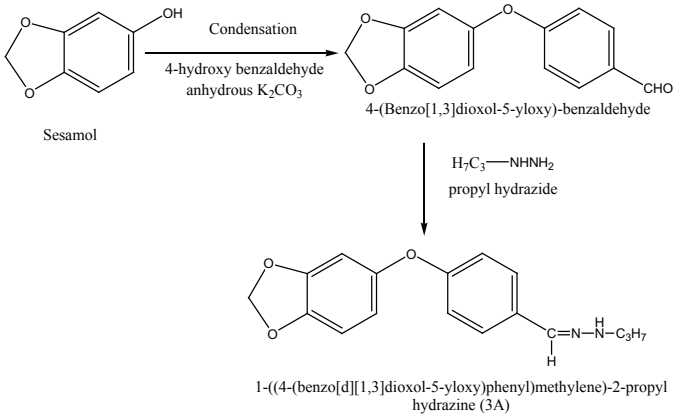

Fig. 5. Synthetic scheme for the synthesis of 1-((4-(benzo[d][1,3] dioxol-5-yloxy)phenyl) methylene) -2-propyl hydrazine (3A)

3. RESULTS AND DISCUSSION

The present study deals with the preparation of sesamol derivatives N'-(4- chloro benzylidene)- 2-(benzo[d][1,3] dioxol-5-yloxy) acetohydrazide (1A), N'-(4-hydroxy benzylidene) -2(benzo[d][1,3]dioxol-5-yloxy) acetohydrazide (1B), N-((4-(benzo[d][1,3]dioxol-5yloxy) phenyl)methylene)-4-chloro benzenamine (2A), N-((4-(benzo[d][1,3]dioxol-5-yloxy)phenyl) methylene)-4-methyl benzenamine (2B), 1-((4-(benzo[d][1,3] dioxol-5-yloxy)phenyl)methylene)-2-propyl hydrazine (3A) and their characterization by element analysis, IR and NMR spectroscopic methods.

3.1 N'-(4- chloro benzylidene)-2-(benzo[d][1,3]dioxol-5-yloxy) acetohydrazide (1A):

Molecular Weight: 332.06; ***Yield:*** 89.5%; ***M.P.:*** 213-215 ^{0}C. The purity of compound was checked by TLC using: Silica gel G, Solvent system; Ethyl acetate: ethanol (2:3) and detecting agent; iodine vapours. Only one sport was obtained (Rf, 0.43). ***Elemental analysis:*** Calculated for $C_{16}H_{13}ClN_2O_4$: C, 57.75; H, 3.94; Cl, 10.0; N 8.42; O, 19.33%. Found: C, 57.78; H, 3.94; Cl, 10. 04; N 8.39; O, 19.29%. ***IR (KBr, cm^{-1}) ν:*** 3261 (N-H), 3050 (Aromatic C-H), 2951 & 2850 (Aliphatic CH), 1646 (C=O), 1626 (Phenyl ring stretch.), 1592 (C=N), 1504 & 1489 (Phenyl C-H out of plane bending), 1469 (CH_2 bending), 1278 (C-O), 1183 (in plane aromatic bending), 1126 (C-O-C, asym), 1039 (C-O-C, sym), 927 (ethylene dioxide characteristic peak), 857 (C-Cl) cm^{-1} (Fig. 4). ***^{1}H NMR (CDCl$_3$, 300 MHz) δ:*** 9.46 (s, 1H, NH, D_2O exchangeable), 8.22 (s, 1H, N=CH), 6.36-7.82 (a set of signals, 11H, Ar-H), 5.96 (s, 2H, O-CH_2-O), 4.55 (s, 2H, O-CH_2-C=O).

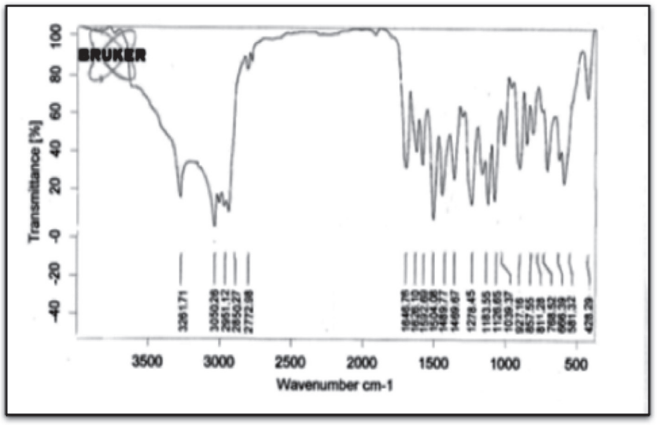

Fig. 6. IR spectra of N'-(4- chloro benzylidene)-2-(benzo[d][1,3] dioxol-5-yloxy) acetohydrazide (1A)

3.2. N'-(4- hydroxy benzylidene)-2-(benzo[d][1,3] dioxol-5-yloxy) acetohydrazide (1B):

Molecular Weight: 314.09; ***Yield:*** 92.4 %; ***M.P.:*** 216-218 ^{0}C. The purity of compound was checked by TLC using: Silica gel G, Solvent system; Ethyl acetate: ethanol (2:3) and detecting agent; iodine vapours. Only one sport was obtained (Rf, 0.92). ***Elemental analysis:*** Calculated for $C_{16}H_{14}N_2O_5$: C, 61.14; H, 4.49; N, 8.91; O, 25.45%. Found: C, 61.18; H, 4.46; N, 8.88; O, 25.47%. ***IR (KBr, cm^{-1}) ν:*** 3472 (O-H), 3265 (N-H), 3048 (Aromatic C-H), 2947 & 2852 (Aliphatic C-H), 1648 (C=O), 1628 (Phenyl ring stretch.), 1599 (C=N), 1504 & 1486 (Phenyl C-H out of plane bending), 1467 (CH_2 bending), 1276 (C-O), 1185 (in plane aromatic bending), 1127 (C-O-C, asym), 1040 (C-O-C, sym), 926 (ethylene dioxide characteristic peak) cm^{-1}. ***^{1}H NMR (CDCl$_3$, 300 MHz) δ:*** 9.42 (s, 1H, NH, D_2O exchangeable), 7.12 (s, 1H, N=CH), 6.38-7.78 (a set of signals, 11H, Ar-H), 5.91 (s, 2H, O-CH_2-O), 4.54 (s, 2H, O-CH_2-C=O).

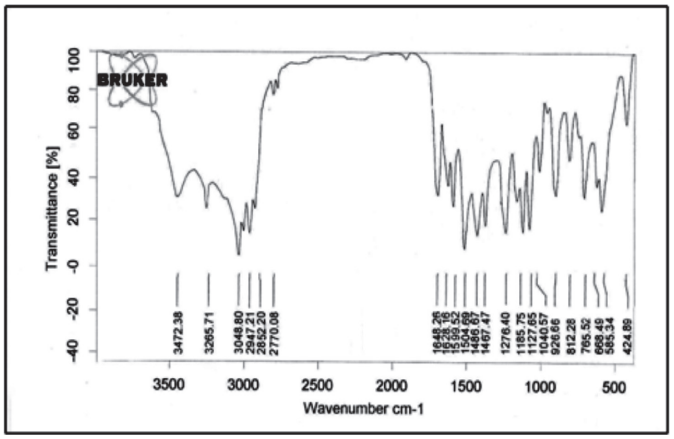

Fig. 7. IR spectra of (4- hydroxy benzylidene)-2-(benzo[d][1,3] dioxol-5-yloxy) acetohydrazide (1B)

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3.3. N-((4-(benzo[d][1,3]dioxol-5-yloxy) phenyl) methylene) -4-chlorobenzenamine (2A)

Molecular Weight: 351.78; ***Yield:*** 83.7 %; ***M.P.:*** 164-166°C. The purity of compound was checked by TLC using: Silica gel G, Solvent system; Ethyl acetate: ethanol (2:3) and detecting agent; iodine vapours. Only one sport was obtained (Rf, 0.61). ***Elemental analysis:*** Calculated for $C_{20}H_{14}ClNO_3$: C, 68.28; H, 4.01; Cl, 10.08; N, 3.98; O, 13.64 %. Found: C, 68.28; H, 3.97; Cl, 10.04; N, 4.03; O, 13.67 %. ***IR (KBr, cm^{-1}) ν:*** 3083 (Aromatic C-H), 2985 & 2877 (Aliphatic CH), 1619 (Phenyl ring stretch.), 1596 (C=N), 1503 & 1483 (Phenyl C-H out of plane bending), 1463 (CH_2 bending), 1276 (C-O), 1181 (in plane aromatic bending), 1129 (C-O-C, asym), 1036 (C-O-C, sym), 926 (ethylene dioxide characteristic peak), 853 (C-Cl) cm^{-1}. ***^{1}H NMR (CDCl$_3$, 300 MHz) δ:*** 9.47 (s, 1H, NH, D_2O exchangeable), 8.16 (s, 1H, N=CH), 6.33-7.85 (a set of signals, 11H, Ar-H).

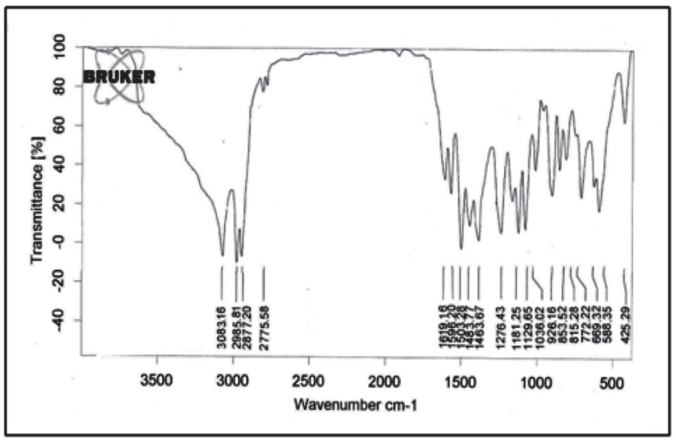

Fig. 8. IR spectra of ((4-(benzo[d][1,3]dioxol-5-yloxy) phenyl) methylene) -4-chlorobenzenamine (2A)

3.4. N-((4-(benzo[d][1,3]dioxol-5-yloxy)phenyl) methylene)-4-methyl benzenamine (2B)

Molecular Weight: 331.36; ***Yield:*** 78.8 %; ***M.P.:*** 165-167°C. The purity of compound was checked by TLC using: Silica gel G, Solvent system; Ethyl acetate: ethanol (2:3) and detecting agent; iodine vapours. Only one sport was obtained. ***Elemental analysis:*** Calculated for $C_{21}H_{21}NO_3$: C, 76.12; H, 5.17; N, 4.23; O, 14.49 %. Found: C, 76.15; H, 5.13; N, 4.25; O, 14.48 %. ***IR (KBr, cm^{-1}) ν:*** 3078 (Aromatic C-H), 2983 & 2878 (Aliphatic CH), 1617 (Phenyl ring stretch.), 1593 (C=N), 1505 & 1484 (Phenyl C-H out of plane bending), 1464 (CH_2 bending), 1453 (CH_2 Bending), 1375 (CH_3 Bending), 1278 (C-O), 1183 (in plane aromatic bending), 1129 (C-O-C, asym), 1033 (C-O-C, sym), 926 (ethylene dioxide characteristic peak) cm^{-1}. ***^{1}H NMR (CDCl$_3$, 300 MHz) δ:*** 9.49 (s, 1H, NH, D_2O exchangeable), 8.12 (s, 1H, N=CH), 6.28 - 7.80 (a set of signals, 11H, Ar-H).

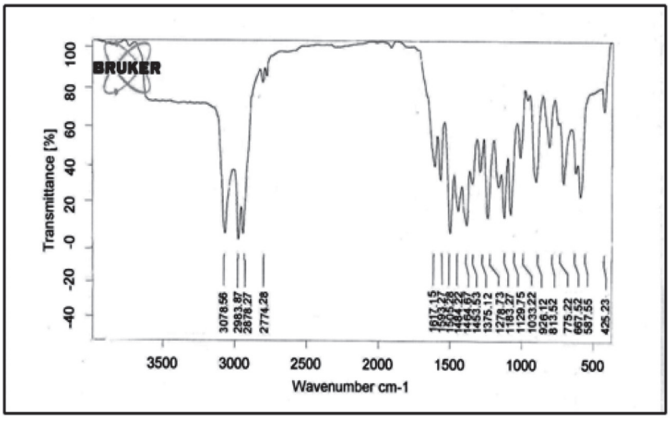

Fig. 9. IR spectra of ((4-(benzo[d][1,3]dioxol-5-yloxy)phenyl) methylene)-4-methyl benzenamine (2B)

3.5. 1-((4-(benzo[d][1,3]dioxol-5-yloxy)phenyl) methylene)-2-propyl hydrazine (3A)

Molecular Weight: 298.13; ***Yield:*** 88.6 %; ***M.P.:*** 182-184°C. The purity of compound was checked by TLC using: Silica gel G, Solvent system; Ethyl acetate: Ethanol (2:3) and detecting agent; iodine vapours. Only one sport was obtained. ***Elemental analysis:*** Calculated for $C_{17}H_{18}N_2O_3$: C, 68.44; H, 6.08; N, 9.39; O, 16.09 %. Found: C, 68.47; H, 6.02; N, 9.41; O, 16.08 %. ***IR (KBr, cm^{-1}) ν:*** 3350 (N-H), 3082 (Aromatic C-H), 2982 & 2876 (Aliphatic CH), 1622 (Phenyl ring stretch.), 1597 (C=N), 1507 & 1484 (Phenyl C-H out of plane bending), 1465(CH_2 bending), 1455 (CH_3 Asym Bending), 1373 (CH_3 Sym Bending), 1282 (C-O), 1185 (in plane aromatic bending), 1127 (C-O-C, asym), 1037 (C-O-C, sym), 928 (ethylene dioxide characteristic peak) cm^{-1}. ***^{1}H NMR (CDCl$_3$, 300 MHz) δ:*** 9.38 (s, 1H, NH, D_2O exchangeable), 8.22 (s, 1H, N=CH).

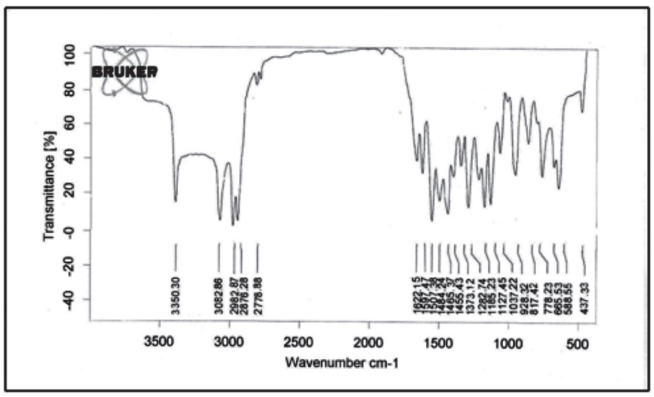

Fig. 10. IR spectra of 1-((4-(benzo[d][1,3]dioxol-5-yloxy)phenyl) methylene)-2-propyl hydrazine

4. CONCLUSION

The sesamol derivatives were prepared successfully by the proposed methods of synthesis and characterized by elemental analysis and spectroscopic methods. Melting point and TLC ascertained the purity of the compounds.

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