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Synthesis of Some Potentially Bioactive Compounds From Visnaginone

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Abstract: The reaction of 5-acetyl-6-hydroxy-4-methoxybenzo[b]furan (visnaginone **Ia**) with 2-diethylaminoethylchloride led to the formation of 5-acetyl-6-diethylamino-ethoxy-4-methoxybenzo[b]furan **(II)**, whereas condensation of compound **II** with some aromatic aldehydes afforded the corresponding chalcones **IIIa-c**. Methylation of visnaginone **(Ia)** gave 5-acetyl-4,6-dimethoxybenzo[b]furan **(Ib)**, which in turn reacted with some aromatic aldehydes to give the corresponding chalcones **IIId,e**. The reaction of chalcones **IIId,e** with hydrazine hydrate in alcohol gave the pyrazoline derivatives **IVa,b,** whereas when the same reaction was carried out in acetic acid it afforded the N-acetylpyrazoline derivatives **Va,b**. Similarly, the reaction of **IIId,e** with phenyl hydrazine in acetic acid led to the formation of phenylpyrazoline derivatives **VIa,b**, whereas condensation of chalcones **IIId,e** with hydroxyl amine hydrochloride gave the isoxazoline derivatives **VIIa,b**. The reaction of compound **II** with phenylhydrazine and 2,4,6-trichlorophenylhydrazine afforded the corresponding phenyl hydrazone derivatives **VIIIa,b**. Mannich bases **IXa,b** were synthesized by the reaction of visnaginone **(Ia)** with piperidine and benzylamine in the presence of formaline.

Keywords: Visnaginone, 6-methoxyvisnaginone, 5-cinnamoylbenzofuran, 5-pyrazoline-benzofuran, 5-isoxazolinebenzofuran, Mannich base.

Introduction

Benzofuran derivatives have been reported to possess biological activities [1-5]. Some derivatives of 6-aminoalkoxy-5-cinnamoyl-4,7-di-methoxybenzofuran have vasodialating and hypotensive effects [6]. Also, 5-acetyl-6-hydroxy-4-methoxy-7-morpholinomethylbenzofuran has hypotensive and arrhythimic activities [7]. The biological activity of Mannich bases as antiamoebic and antiinflammatory agents has also been reported [8]. Some pyrazoline derivatives were used as bacteriostatic, fungicidal and anticancer agents [9]. Also, isoxazoline compounds have been shown to have antituberculosis and antibiotic activities [10-12]. Our plan was to incorporate these active cinnamoyl, pyrazoline and isoxazoline groups and Mannich bases into the structure of the parent compound visnaginone (**Ia**), with the aim of increasing its biological activity.

Results and Discussion

As shown in Scheme 1, visnaginone **(Ia)** was reacted with diethylaminoethyl chloride in acetone to afford 4-methoxy-5-acetyl-6-diethylamino-ethoxybenzofuran **(II)**. The reaction of **II** with some aromatic aldehydes, namely, benzaldehyde, anisaldehyde and 4-chlorobenzaldehyde in dry methanol in the presence of sodium methoxide afforded the cinnamoyl derivatives **IIIa-c.** Methylation of visnaginone **(Ia)** with methyl iodide in dry acetone led to the formation of 6-methoxy visnaginone **(Ib).** The reaction of **(Ib)** with benzaldehyde and anisaldehyde afforded the corresponding chalcones **IIId,e**. The action of hydrazines on chalcones **IIId,e** was studied and it was found that when compounds **IIId,e** were reacted with one equivalent hydrazine hydrate in alcohol, they afforded the pyrazoline derivatives **Iva,b**, and when the same reaction was carried out in acetic acid the N-acetylpyrazolinyl derivatives **Va,b** were obtained. The reaction of **IIId,e** with phenyl hydrazine was carried out in boiling acetic acid to afford the phenyl pyrazolinyl derivatives **VIa,b**. On the other hand, the isoxazolinyl derivatives **VIIa,b** were obtained when chalcones **IIId,e** were reacted with hydroxylamine hydrochloride. Visnaginone **Ia** reacted with phenyl hydrazine and 2,4,6-trichlorophenyl hydrazine to yield the corresponding hydrazones **VIIIa,b**. Also, visnaginone was reacted with piperidine and benzylamine under Mannich conditions to afford the corresponding Mannich bases **IXa,b**.

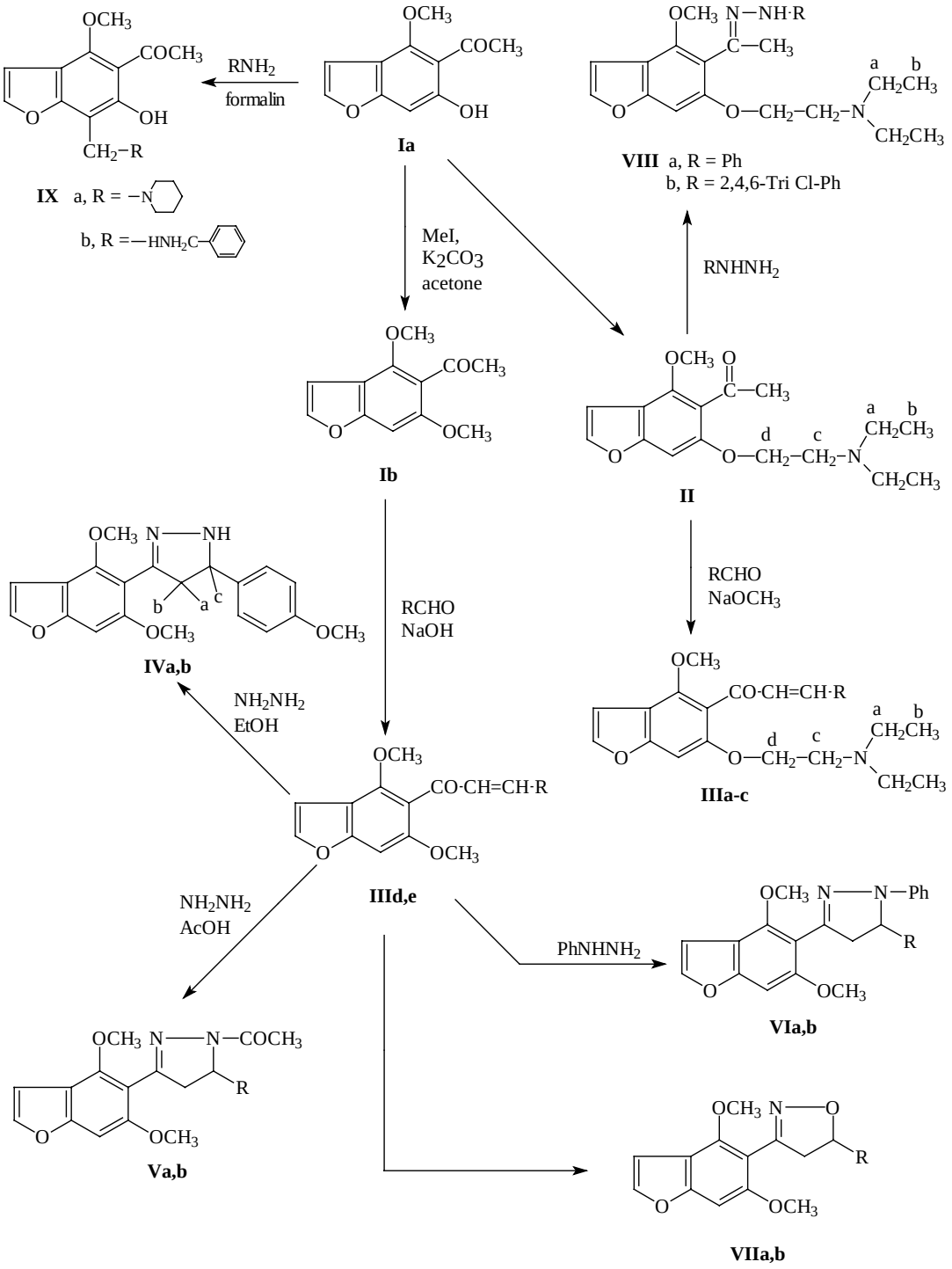
Experimental

General

Melting points are uncorrected. ^{1}H-NMR spectra were run using TMS as internal reference on a Jeol EX-270 NMR spectrometer. IR spectra were recorded on a FT/IR Jasco 300 E instrument. The prepared compounds were analyzed for C, H and N and the microanalytical data is in full agreement with the suggested structures (Table 1). Compound **Ia** was prepared according to Musante [13].

Compound **Ib** was prepared according to Schonberg [14] and compound **IXa** was prepared according to Ragab [7]. The biological activity of the prepared compounds is under investigation and will be published separately in near future.

Scheme 1



III-VII, a,d, R = Ph; b,e, R = C_6H_4-OCH_3 (p); c, R = C_6H_4-Cl (p)

Preparation of 5-acetyl-6-diethylaminoethoxy-4-methoxybenzo[b]furan (II).

A mixture of visnaginone (0.2 mole), potassium carbonate (5.4g) and diethylaminoethyl chloride (0.47 mole) in acetone (340 mL) was refluxed with stirring for 10 hrs. The acetone mixture was filtered off and filtrate was evaporated under reduced pressure, and extracted with chloroform, the chloroform washed with sodium hydroxide solution (5%), then with water, the chloroform extract was dried over anhydrous sodium sulphate and evaporated under reduced pressure to give 5-acetyl-6-diethylamino-ethoxy benzofuran **(II)** as yellowish white oil. IR (KBr) cm^{-1} 2950 (CH-alkyl), 1750 (C=O), 1225 (C-N) and 1150 (C-O-C); ^{1}H-NMR ($CDCl_3$) ppm: δ 1.05 (6H, t, CH_3-b), 2.45 (3H, s, $COCH_3$), 2.55 (4H, q, $2CH_2$-a), 2.8 (2H, t, CH_2-c), 2.95 (2H, t, CH_2-d), 4.00 (3H, s, OCH_3), 6.75 (1H, s, C-7 aromatic), 6.9 (1H, d, H_3-furan) and 7.45 (1H, d, H_2-furan).

General procedure for the preparation of 5-substituted cinnamoyl-6-(2-diethylaminoethoxy)-4-methoxy benzo[b]furans (IIIa-c).

Compound **II** (0.3 mole) was reacted with a mixture of the appropriate aromatic aldehyde (0.3 mole), dry methanol (30 mL) and sodium methoxide (from 3g Na and 30 mL methanol) with stirring at room temperature for 4 hrs., then water (750 mL) was added and the mixture extracted with ethyl acetate. The organic layer washed with water, dried over anhydrous sodium sulphate, concentrated and crystallized from methanol.

5-cinnamoyl-6-(diethylaminoethoxy)-4-methoxybenzo[b]furan (IIIa): Yield 95%, m.p. 110°C. IR: (KBr) cm^{-1}, 3000 (C-H), 1730 (C=O), 1615 (cinnamoyl C=C) and 1135 (C-O-C); ^{1}H-NMR (DMSO-d_6) ppm: δ at 1.0 (6H, t, CH_3-a), 2.45 (4H, q, CH_2-b), 2.7 (2H, t, CH_2-c), 3.57 (2H, t, CH_2-d), 4.0 (3H, s, OCH_3 aromatic), 4.20 (3H, s, OCH_3-C_4), 6.9-7.4 (6H, m, benzene ring), 7.55 (1H, d, H_3 furan) and 7.7 (1H, d, H_2-furan).

5-(4-Methoxycinnamoyl-6-(diethylaminoethoxy)-4-methoxybenzo[b]furan (IIIb): Yield 90%, m.p. 116°C. IR: (KBr) cm^{-1}, 3110 (C-H), 1620 (cinnamoyl C=C), 1635 (C=O) and 1130 (C-O-C); ^{1}H-NMR (DMSO-d_6) ppm: δ 0.9 (6H, t, CH_3-a), 2.4 (4H, q, CH_2-b), 2.6 (2H, t, CH_2-c), 3.5 (2H, t, CH_2-d), 4.00 (3H, s, OCH_3-aromatic), 4.10 (3H, s, OCH_3-C_4), 7.2, 7.9 (1H, dd, 2H-cinnamoyl), 6.95, 7.40 (4H, dd, aromatic protons), 7.45 (1H, s, C-7 aromatic), 7.5 (1H, d, H_3-furan), and 7.7 (1H, d, H_2-furan).

5-(4-Chlorocinnamoyl-6-(diethylaminoethoxy)-4-methoxybenzo[b]furan (IIIc): Yield 85%, m.p. 209°C. IR: (KBr) cm^{-1}, 3050 (C-H), 1600 (cinnamoyl C=C), 1700 (C=O), 1120 (C-O-C), 1220 (C-N) and 730 (C-Cl); ^{1}H-NMR (DMSO-d_6) ppm: δ 0.95 (6H, t, CH_2-a), 2.4 (4H, q, CH_2-b), 2.75 (2H, t, CH_2-c), 3.3 (2H, t, CH_2-d), 4.00 (3H, s, OCH_3), 6.8-7.3 (6H, m, aromatic protons + aliphatic system), 7.5 (1H, s, H-7), 7.8 (1H, d, H-3, furan) and at 7.9 (1H, d, H-2 furan).

General procedure for the preparation of 5-substituted cinnamoyl-4,6-dimethoxybenzo[b]furans (IIId,e).

6-Methoxy visnaginone **Ib** (0.1 mole) was dissolved in ethyl alcohol (15 mL). The appropriate aromatic aldehyde (0.1 mole) was added, followed by the addition of a solution of sodium hydroxide (30%, 12 mL). The mixture was stirred and allowed to stand at room temperature for 24 hrs., then diluted with water (270 mL) and acidified with dilute solution HCl. The precipitate formed was filtered off and crystallized from ethyl alcohol.

5-Cinnamoyl-4,6-dimethoxybenzo[b]furan (IIId): Yield 97%, m.p. 106^{o}C. IR: (KBr) cm^{-1}, 3000 (C-H), 1680 (C=O), 1620 (C=C) and 1165 (C-O-C); ^{1}H-NMR (DMSO-d_6) ppm: δ 3.8 (2H, s, OCH_3-C_4), 3.95 (3H, s, OCH_3-C_4), 6.8 (1H, d, H_3 furan), 6.9, 7.6 (2H, dd, 2H cinnamoyl), 7.1-7.5 (5H, m, aromatic), 7.8 (1H, d, H-3, furan) and at 7.9 (1H, d, H-2 furan).

5-(4-Methoxycinnamoyl-6-(diethylaminoethoxy)-4-methoxybenzo[b]furan (IIIe): Yield 90%, m.p. 108^{o}C. IR: (KBr) cm^{-1}, 3040 (C-H), 1700 (C=O), 1625 (C=C) and 1150 (C-O-C); ^{1}H-NMR (DMSO-d_6) ppm: δ at 0.90 (6H, t, CH_3-a), 2.4 (4H, q, CH_2-b), 2.60 (2H, t, CH_2-c), 3.5 (2H, t, CH_2-d), 4.00 (3H, s, OCH_3 aromatic), 4.10 (3H, s, OCH3-C4), 7.2, 7.7 (1H, dd, 2H cinnamoyl), 6.95-7.4 (5H, m, aromatic protons), 7.45 (1H, s, H-7, aromatic), 7.5 (1H, d, H-3, furan) and at 7.9 (1H, d, H-2 furan).

General procedure for the preparation of 4,6-dimethoxy-5-(aryl-2-pyrazolin-3-yl)benzo[b]furans (IVa,b).

Chalcones **IIId,e** (0.01 mole) were dissolved in ethyl alcohol (10 mL) and refluxed with hydrazine hydrate (0.5 mL) for 10 hrs. The reaction mixture was diluted with water (50 mL) and the solid formed was filtered off and crystallized from ethyl alcohol.

4,6-Dimethoxy-5-(phenyl-3-pyrazolin-3-yl)benzo[b]furan (Iva): Yield 55%; m.p. 131^{o}C. IR: (KBr) cm^{-1}, 3230 (NH), 1620 (C=C), 1590 (C=N) and 1150 (C-O-C); ^{1}H-NMR (DMSO-d_6) ppm: δ 2.8 (1H, dd, Ha, J_{vic} = 8 Hz, J_{gem}=15 Hz), 3.6 (1H, dd, He, J_{vic} = 8 Hz, J_{gem} = 10 Hz), 3.9 (3H, s, OCH_3, C-6), 4.00 (3H, s, OCH_3-C-4), 5.4 (1H, dd, Hc pyrazolinyl, J_{vic} = 10 Hz, J_{gem} = 15 Hz), 6.6 (1H, d, H_3-furan), 6.95-7.40 (4H, m, aromatic), 7.5 (1H, s, C-7), 7.9 (1H, d, H_2-furan), and 9.6 (1H, s, NH, exchangeable with D_2O).

4,6-Dimethoxy-5-(4-methoxyphenyl-2-pyrazolin-3-yl)benzo[b]furan (IVb): Yield 60; m.p. 64^{o}C. IR: (KBr) cm^{-1}, 3210 (NH), 1700 (C=O), 1625 (C=C), 1590 (C=N) and 1155 (C-O-C); ^{1}H-NMR (DMSO-d_6) ppm: δ 2.9 (1H, dd, Ha), 3.6 (1H, dd, He), 3.8 (3H, s, OCH_3, aromatic), 3.9 (3H, s, OCH_3-C-6), 4.0 (3H, s, OCH_3, C-4), 5.4 (1H, dd, He pyrazolinyl), 6.65 (1H, d, H_3-furan), 6.95, 7.65 (4H, dd, aromatic), 7.5 (1H, s, C-7), 7.9 (1H, d, H_2-furan), and 9.6 (1H, s, NH, exchangeable with D_2O).

General procedure for the preparation of 4,6-dimethoxy-5-(1-acetyl-5-aryl-2-pyrazolin-3-yl)benzo[b]furans (Va,b).

Chalcones **IIId,e** (0.01 mole) were dissolved in acetic acid (10 mL) and refluxed with hydrazine hydrate (0.5 mL) for 12 hrs. The reaction mixture was poured onto water. The solid formed was filtered off and crystallized from ethanol.

4,6-Dimethoxy-5-(1-acetylphenyl-2-pyrazolin-3-yl)benzo[b]furan (Va): Yield 90%; m.p. 170^{o}C. IR: (KBr) cm^{-1}, 1670 (keto amide), 1635 (C=N) and observed disappearance of NH band; ^{1}H-NMR (DMSO-d_6) ppm: δ 2.2 (3H, s, $COCH_3$), 2.7 (1H, dd, Ha, J_{vic} = 6 Hz, J_{gem}= 18 Hz), 3.5 (1H, dd, He, J_{vic} = 6 Hz, J_{gem} = 12 Hz), 3.9, 4.00 (3H, s, OCH_3, C-4,6), 6.0 (1H, dd, Hc pyrazolinyl, J_{vic} = 12 Hz, J_{gem} = 18 Hz), 6.9 (1H, d, H_3-furan), 7.1-7.3 (5H, m, aromatic), 7.6 (1H, s, C-7) and 7.95 (1H, d, H_2-furan).

4,6-Dimethoxyacetyl-5-(4-methoxyphenyl-2-pyrazolin-3-yl)benzo[b]furan (Vb): Yield 85%; m.p. 170^{o}C. IR: (KBr) cm^{-1}, 1660 (keto amide), 1635 (C=N); ^{1}H-NMR (DMSO-d_6) ppm: δ 2.1 (3H, s, N-$COCH_3$), 2.8 (1H, dd, Ha), 3.6 (1H, dd, Hc), 3.75 (3H, s, OCH_3-aromatic), 3.9, 4.00 (3H, s, OCH_3, C-4,6), 5.9 (1H, dd, He), 6.9 (1H, d, H_3-furan), 7.1-7.3 (4H, m, aromatic), 7.4 (1H, s, C-7), and 7.95 (1H, d, H_2-furan).

General procedure for the preparation of 4,6-dimethoxy-5-(5-aryl-1-phenyl-2-pyrazolin-3-yl)benzo[b]furans (VIa,b).

Chalcones **IIId,e**, (0.01 mole) were dissolved in glacial acetic acid (10 mL) and refluxed with phenyl hydrazine (1.1 mL) for 8 hrs. The reaction mixture was cooled and poured onto water. The precipitate thus formed was filtered off and crystallized from ethyl alcohol.

4,6-Dimethoxy-5-(5-diphenyl-2-pyrazolin-benzo[b]furan (VIa): Yield 75%; m.p. 120^{o}C; ^{1}H-NMR (DMSO-d_6) ppm: δ 2.8 (1H, dd, Ha, J_{vic} = 8 Hz, J_{gem}= 18 Hz), 3.6 (1H, dd, He, J_{vic} = 12 Hz, J_{gem} = 18 Hz), 3.8 (3H, s, OCH_3, C-6), 400 (3H, s, OCH_3, C-4), 5.85 (1H, dd, Hc, J_{vic} = 8 Hz, J_{gem} = 18 Hz), 6.95 (1H, d, H_3-furan), 7.2-7.5 (10H, m, aromatic), 7.6 (1H, s, C-7) and 7.9 (1H, d, H_2-furan).

4,6-Dimethoxy-1-phenyl-5-(4-methoxyphenyl)pyrazolin-3-yl)-benzo[b]furan (VIb): Yield 75% (ethanol), m.p. 120^{o}C. ^{1}H-NMR (DMSO-d_6) ppm: δ 2.9 (1H, dd, Ha), 3.7 (1H, dd, He), 3.75 (3H, s, OCH_3-aromatic), 3.8 (3H, s, OCH_3-C-6), 4.00 (3H, s, OCH_3-C-4), 5.85 (1H, dd, Hc), 6.9 (1H, d, H_3-furan), 7.1-7.4 (9H, m, aromatic), 7.45 (1H, s, C-7), 7.9 (1H, d, H_2-furan).

General procedure for the preparation of 4,6-dimethoxy-5-(5-aryl-2-isoxazolin-3-yl)benzo[b]furans (VIIa,b).

Chalcones **IIId,e** (0.01 mole) were dissolved in ethanol (10 mL) and a mixture of hydroxylamine hydrochloride (0.8g) in ethanol (8 mL) and water (2 mL) was added, followed by few drops of potassium hydroxide (50%). The reaction mixture was refluxed for 9 hrs. The solid formed was filtered off and crystallized from ethyl alcohol.

4,6-Dimethoxy-5-(phenyl-2-isoxazolin-3-yl)benzo[b]furan (VIIa): Yield 80%; m.p. 138^{o}C; IR: (KBr) cm^{-1}, 1635 (C=N), 1600 (C=C), and 1030 (C-O-C); ^{1}H-NMR (DMSO-d_6) ppm: δ at 2.45 (1H, dd, Ha, J_{vic} = 6 Hz, J_{gem}= 18 Hz), 3.8, 3.9 (3H, s, OCH_3, C-4,6), 4.1 (1H, dd, He, J_{vic} = 6 Hz, J_{gem} = 12 Hz), 5.5 (1H, dd, Hc, J_{vic} = 12 Hz, J_{gem} = 18 Hz), 6.9 (1H, d, H_3-furan), 7.2-7.4 (5H, m, aromatic), 7.5 (1H, s, C-7) and 7.9 (1H, d, H_2-furan).

4,6-Dimethoxy-5-(4-methoxyphenyl)-2-isoxazolin-3-yl)benzo[b]-furan (VIb): Yield 70%; m.p. 70^{o}C. IR: (KBr) cm^{-1}, 1635 (C=N), 1620 (C=C), and 1030 (C-O-C); ^{1}H-NMR (DMSO-d_6) ppm: δ 2.4 (1H, dd, Ha), 3.8 (3H, s, OCH_3, aromatic), 3.9, 4.00 (3H, s, OCH_3-C-4,6), 4.3 (1H, dd, He), 5.5 (1H, dd, Hc), 6.8 (1H, d, H_3-furan), 7.1-7.4 (4H, dd, aromatic, J = 8 Hz), 7.45 (1H, s, C-7), 7.9 (1H, d, H_2-furan).

General procedure for the preparation of 5-(1-arylhydrazono-ethyl)-6-(2-diethylaminoethoxy)-4-methyl benzo[b]furans (VIIIa,b).

Compound **II** (0.01 mole) was dissolved in ethyl alcohol (10 mL), 0.1 mole of a hydrazine was added (phenyl hydrazine in case of VIIIa and 2,4,6-trichlorophenyl hydrazine in case of VIIIb), followed by the addition of few drops of acetic acid and the reaction mixture was refluxed for 5 hrs. and then cooled. The solid material was filtered off and crystallized from ethyl alcohol.

5-(2-Phenyhydrazonethyl)-6-diethylaminoethyl)-4-methoxy-benzo[b]furan (VIIIa): Yield 70%; m.p. 125^{o}C; IR: (KBr) cm^{-1}, 3150 (NH), 1630 (C=C), 1597 (C=N), 1320 (C-N), and 1106 (C-O-C); ^{1}H-NMR (DMSO-d_6) ppm: δ 0.9 (6H, t, $2CH_3$-b), 2.5 (4H, q, $2CH_2$-a), 3.3 (2H, t, $2CH_2$-d), 3.9 (3H, s, OCH_3), 7.1 (1H, d, H_3-furan), 7.4 (5H, m, aromatic), 7.6 (1H, s, C-7), 7.7 (1H, d, H_2-furan), 10.0 (1H, s, NH exchangeable with D_2O).

5-(2,4,6-Trichloro-1-phenyhydrazonoethyl)-6-(diethylamino-ethyl)-4-methoxybenzo[b]furan (VIIIb): Yield 75%; m.p. 130^{o}C; IR: (KBr) cm^{-1}, 3175 (NH), 1630 (C=C), 1597 (C=N), 1320 (C-N), and 1106 (C-O-C); ^{1}H-NMR (DMSO-d_6) ppm: δ 1.00 (6H, t, $2CH_3$-b), 2.6 (4H, q, $2CH_2$-a), 3.2 (2H, t, CH_2-d), 3.9 (3H, s, OCH_3), 7.2 (1H, d, H_3-furan), 7.4 (2H, s, aromatic), 7.6 (1H, s, C-7), 7.7 (1H, d, H_2-furan), 10.0 (1H, s, NH, exchangeable with D_2O).

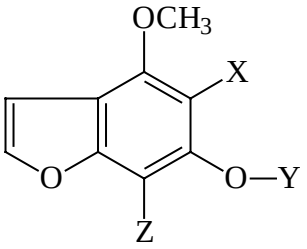
General procedure for the preparation of 5-acetyl-6-hydroxy-4-methoxy-7-substituted methyl benzo[b]furans (IXa,b).

Visnaginone (**Ia**, 0.01 mole) was dissolved in ethyl alcohol (20 mL). Formalin (0.5 mL) and the appropriate amine (0.01 mole) were added. The reaction mixture was refluxed for 3 hrs., and then cooled. The precipitate formed was filtered off and crystallized from ethyl alcohol.

5-Acetyl-6-hydroxy-4-methoxy-7-piperidinomethylbenzo[b]furan (IXa): Yield 80%; m.p. 105°C; IR: (KBr) cm^{-1}, 3400 (broad OH), 3200 (NH), and 1320 (C-N); ^{1}H-NMR (DMSO-d_6) ppm: δ 2.3 (CH_2-N), 3.9 (3H, s, $COCH_3$), 4.0 (3H, s, OCH_3), 4.8-5.2 (10H, m, piperidine), 6.9 (1H, d, H_3-furan), 7.9 (1H, d, H_2-furan), 12.1 (1H, bs, OH).

5-Acetyl-6-hydroxy-4-methoxy-7-benzylaminoethylbenzo[b]furan (IXb): Yield 90%; m.p. 120°C; IR: (KBr) cm^{-1}, 3400 (broad OH), 3150 (NH), 1350 (C-N); ^{1}H-NMR (DMSO-d_6) ppm: δ at 2.4 (2H, s, CH_2-N), 2.6 (2H, s, CH_2-Ph), 3.9 (3H, s, $COCH_3$), 4.00 (3H, s, OCH_3), 6.9 (1H, d, H_3-furan), 7.1-7.3 (5H, m, aromatic), 7.9 (1H, d, H_2-furan), 12.1 (1H, br.s, OH).

Table 1: Physical data for the prepared benzo[b]furan (IIIa-IXb)



No.	X Y Z	M.P. °C (Yield,%)	Mol. Formula Mol. wt.	CHN Analysis % Calc.-Found	
IIIa	Cinnamoyl 2-diethylaminoethyl H	110 95	$C_{24}H_{27}NO_4$ 393	73.28 6.87 3.56	73.45 6.62 3.25
IIIb	p-methoxycinnamoyl 2-diethylaminoethyl H	116 90	$C_{25}H_{29}NO_5$ 423	70.92 6.86 3.31	70.73 6.91 3.16
IIIc	4-chlorocinnamoyl 2-diethylaminoethyl H	190 90	$C_{24}H_{26}NO_4Cl$ 427.5	67.37 6.08 3.27	67.13 6.24 3.43
IIId	cinnamoyl methyl H	106 97	$C_{19}H_{16}O_4$ 308	74.03 5.19	74.35 5.28

IIIe	p-methoxycinnamoyl methyl H	108 90	$C_{20}H_{18}O_5$ 338	71.06 5.33	70.52 5.17
IVa	5-phenyl-2-pyrazolin-3-yl methyl H	131 55	$C_{19}H_{18}N_2O_3$ 322	70.81 5.59 8.69	70.54 5.36 8.35
IVb	4-methoxyphenyl-2-pyrazolin-3-yl methyl H	64 60	$C_{20}H_{20}N_2O_4$ 352	68.18 5.68 7.95	68.39 5.79 8.24
Va	1-acetylphenyl-2-pyrazolin-3-yl methyl	170 90	$C_{21}H_{20}N_2O_4$ 364	69.23 5.49 7.69	69.51 5.61 7.93
Vb	1-acetyl-5-(4-methoxy- phenyl)pyrazolin-3-yl methyl	173 85	$C_{22}H_{22}N_2O_5$ 394	67.00 5.58 7.10	67.26 5.36 7.38
VIa	1,5-diphenyl-2-pyrazolin-3-yl methyl H	121 70	$C_{25}H_{22}N_2O_3$ 398	75.38 5.53 7.04	75.16 5.29 7.32
VIb	1-phenyl-5-(4-methoxy phenyl)-2- pyrazolin-3-yl methyl H	120 75	$C_{26}H_{24}N_2O_4$ 428	72.89 5.61 6.54	72.53 5.89 6.98
VIIa	5-phenyl-2-isoxazoline-3-yl methyl H	138 80	$C_{19}H_{17}NO_4$ 323	70.59 5.26 4.33	70.28 4.83 4.11
VIIb	5-(4-methoxyphenyl)-2- isoxazoline-3-yl methyl H	102 70	$C_{20}H_{19}NO_5$ 353	67.99 5.38 3.97	67.68 5.21 3.71
VIIIa	2-phenylhydrazonoethyl 2-diethylaminoethyl H	125 70	$C_{23}H_{29}N_3O_3$ 395	69.87 7.34 10.63	69.71 7.26 10.41
VIII b	2,4,6-trichloro-1-phenyl- hydrazonoethyl 2-diethylaminoethyl H	130 75	$C_{23}H_{26}N_3O_3$ Cl_3 498.5	55.37 5.22 8.42	55.51 5.35 8.66
IXa	acetyl H piperidinomethyl	105 80	$C_{17}H_{21}NO_4$ 303	67.33 6.93 4.62	67.76 6.84 4.38

IXb	acetyl H benzylaminoethyl	120 90	$C_{19}H_{19}NO_4$ 325	70.15 5.85 4.31	75.38 5.98 4.71

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Sample Availability: Samples of compounds **IIIe**, **IVa**, **IVb**, **Va**, **VIa**, **VIb**, **IXa** and **IXb** are available from MDPI.