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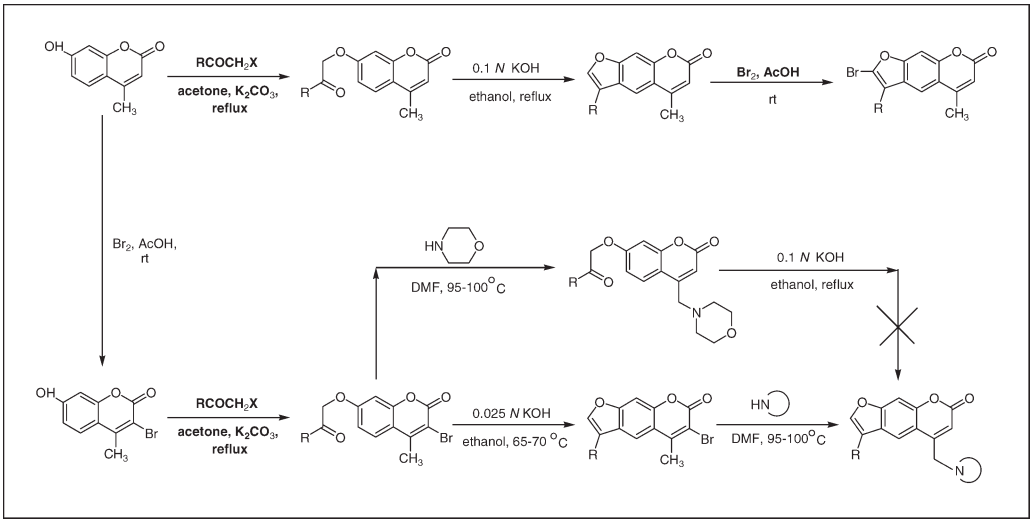

New amino psoralen derivatives have been synthesized *via* bromination. Bromination of 3,5-substituted psoralens has been studied. The second position of the furan ring is more susceptible to bromination than the α-position of the chromen-2-one ring in psoralens. Hence, the target psoralenamines were synthesized starting with 3-bromo-7-hydroxy-4-methyl-chromen-2-one, which was condensed with different α-halo ketones and cyclized in ethanolic potassium hydroxide to get the desired 6-bromo psoralens, which were finally converted into psoralenamines.

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INTRODUCTION

Furocoumarins such as Psoralens (5-methoxy psoralen or bergapton, 8-methoxy psoralen or xanthotoxin, 4,5′,8-trimethyl psoralen) are well known photosensitizing drugs used in Psoralen Ultra Violet-A therapy for the treatment of dermatological disorders, such as psoriasis, vitiligo, mycosis, and atropic eczema [1]; as well as fungal, viral, and bacterial infections [2]. Recently, Psoralen derivatives have also been used in the treatment of cutaneous T-cell lymphoma [3], human immunodeficiency diseases [4], and prevention of rejection of organ transplants [5]. Introduction of aminomethyl group in furocoumarins enhances antibacterial activity [6]. Aminopsoralens are used for nucleic acid probe preparations, preparation of conjugates, inhibition of cell proliferation, inactivation of virus for vaccine preparation, and in particular, for the inactivation of pathogens in blood products [7].

Because of the wide spread and increasing interest in aminopsoralens for their pharmacological action, this study was undertaken to synthesize some new amino psoralen derivatives *via* bromination. Moreover, it was of considerable interest to study the reactivity and orientation of 3,5-substituted psoralens toward bromination. Although it is evident that the third position of furan ring in psoralens is the most reactive towards electrophilic substitution, the behaviour of psoralens in which the third position is blocked has not been reported for bromination. The synthetic pathway followed by MacLeod *et al*. [8] has been employed to prepare the title compounds as outlined in Scheme 1.

RESULTS AND DISCUSSION

β-Methyl umbelliferone (7-hydroxy-4-methyl-chromen-2-one) **1**, [9] was condensed with different α-haloketones, *e.g*., mono chloroacetone and phenacylbromide to give the aryloxyketones **2** which when subjected to cyclization in 0.1*N* ethanolic potassium hydroxide gave the corresponding furocoumarin (psoralen) **3** as shown

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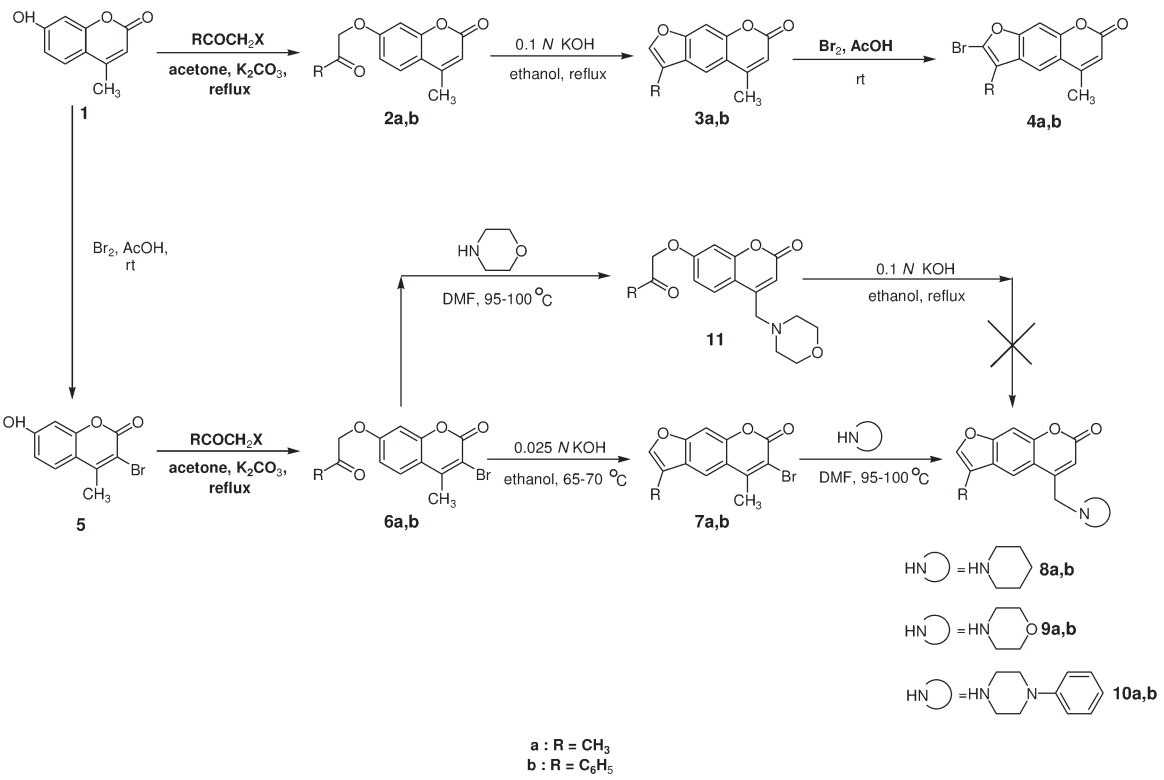
Scheme 1

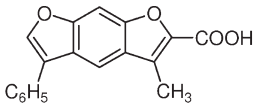


in Scheme 1. Furocoumarin **3** was brominated with bromine in acetic acid to get the desired 6-bromo psoralen, but from the ^{1}H nuclear magnetic resonance (NMR) it was revealed that the product formed was 2-bromo psoralen **4**. This shows that the second position of the furan ring is more reactive towards halogenation compared to the α-position of the chromen-2-one ring in psoralens. In the ^{1}H-NMR of compound 2-bromo-3,5-dimethyl-furo[3,2-*g*]chromen-7-one **4a**, signal at δ 6.27–6.28 ppm corresponding to one proton for C6—H (or α-H of chromen-2-one) and the absence of signal at δ 7.5 ppm for C2—H proton alongwith C3—CH_3 signal at δ 2.24 ppm confirmed the structure. The UV spectrum in dichloromethane showed absorption at 284, 302, 324, 333, 340, and 347 nm. Consequently, the target amino psoralens could not be prepared.

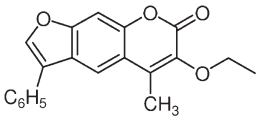
In a slightly modified methodology, β-methyl umbelliferone (7-hydroxy-4-methyl-chromen-2-one) **1** was first brominated using bromine in acetic acid to give 3-bromo-7-hydroxy-4-methyl-chromen-2-one **5** [10] in an addition-elimination reaction, which was then condensed with different α-halo ketones and cyclized to 6-bromo psoralens **7** in a similar fashion as shown in Scheme 1. In the ^{1}H NMR of compound 6-bromo-3,5-dimethyl-furo[3.2-*g*]chromen-7-one **7a**, the absence of signal at δ 6.28 ppm for C6—H proton and singlet for C5—CH_3 signal at δ 2.74 ppm confirmed the substitution of bromine at C—6 position. Further doublets at δ 7.50 ppm (1H, J = 1.6 Hz) for C2—H and δ 2.31–2.32 ppm (3H, J = 1.6 Hz) for C3—CH_3 corroborated the structure **7a**. The mass spectrum (LCMS) was obtained as *m/z* (relative intensity, 100%): 317 (8.88) M+23 (from Na^+), 295.1 (100) M+1, 292.9 (100) M^+ using mobile phase Acetonitrile: Ammonium acetate 1 m*M* (90:10% v/v). The UV spectrum in dichloromethane showed absorption at 282, 302, 323, 331, 342, 355, and 362 nm. Cyclization of 3-bromo aryloxyketones **6** to 6-bromo psoralens **7** was the bottleneck of the process. Cyclization in 0.1*N* ethanolic potassium hydroxide at reflux temperature lowered the over all yield of the reaction drastically due to the formation of mixture of products. One of the product was identified as furocoumarilic acid formed due to alkaline ring contraction [11], which has been confirmed from the ^{1}H NMR and infrared (IR) spectra of 3-methyl-5-phenyl-benzo[1,2-*b*;5,4-*b*′]difuran-2-carboxylic acid **12** obtained during cyclization of 3-bromo-4-methyl-7-(2-oxo-2-phenyl-ethoxy)-chromen-2-one **6b**. The furocoumarilic acid was obtained as white amorphous powder; mp 250°C dec. and whose sodium and potassium salts are hydrophobic. The other product was identified as 6-ethoxy-5-methyl-3-phenyl-furo[3,2-*g*]chromen-7-one **13** formed by nucleophilic attack of ethanol, which also has been confirmed from ^{1}H NMR. The yield of 6-bromo psoralen was lowered due to these

side reactions. Weaker bases like tri ethylamine and potassium carbonate failed to give the expected results. Cyclization in polyphosphoric acid and phosphorus (III) oxychloride failed. Even the idea of first condensing 3-bromo aryloxyketones **6** with amines, followed by cyclization to yield amino psoralens failed, since the cyclization reaction gave several decomposition products. Condensation of 3-bromo-4-methyl-7-(2-oxy-propoxy)-chromen-2-one **6a** with morpholine gave 4-morpholin-4-ylmethyl-7-(2-oxo-propoxy)-chromen-2-one **11** as confirmed from ^{1}H NMR, but could not be cyclized as shown in Scheme 1. Consequently the concentration of ethanolic potassium hydroxide was reduced from 0.1 to 0.025*N* and the cyclization of 3-bromo aryloxyketones **6** to 6-bromo psoralens **7** was carried out at 65–70°C, which gave the desired results. Finally, 6-bromo psoralens were condensed with different amines to give the corresponding amino methyl psoralens **(8, 9, 10)**. ^{1}H NMR of compound 3-methyl-5-piperidin-1-ylmethyl-furo[3,2-*g*]chromen-7-one **8a** showed singlets at δ 6.51 ppm corresponding to one proton for C6—H proton and δ 3.66 ppm corresponding to two protons for C5—CH_2—, which confirmed the formation of 5-amino methyl psoralens. In the ^{13}C NMR, δ values 99.59 ppm for C6 and 59.91 ppm for C5—*C*H_2— further confirmed the structure. The UV spectrum in dichloromethane showed absorption at 281, 301, 305, 329, 337 nm. The mass spectrum (LCMS) for 3-methyl-5-morpholin-4-ylmethyl-furo[3,2-*g*]chromen-7-one **9a**. was obtained as *m/z* (relative intensity, 100%): 338.1 (7.27) M+39 (from K^+), 322.2 (38.18) M+23 (from Na^+), 301.2 (70.90) M+2, 299.9 (100) M+1 using mobile phase acetonitrile:ammonium acetate 1 m*M* (90:10% v/v).

The structures of all compounds have been established on the basis of their elemental analyses and spectral (IR, NMR) data.



3-Methyl-5-phenyl-benzo[1,2-*b*;5,4-*b*']difuran-2-carboxylic acid 12



6-Ethoxy-5-methyl-3-phenyl-furo[3,2-*g*]chromen-7-one 13

EXPERIMENTAL

Melting points (uncorrected) were determined using a scientific capillary melting point apparatus. Purity of the compounds was checked by thin layer chromatography on Acme's silica gel G plates using UV/Iodine vapour as visualizing agent and Acme's silica gel (60–120 mesh) was used for column chromatographic purification. Elemental analyses were carried out on Perkin-Elmer C, H, N, S analyzer (Model-2400). IR spectra were recorded on Perkin-Elmer FTIR spectrometer (spectrum RX1) using potassium bromide optics. UV spectra were recorded on Perkin Elmer Lambda 35 UV/Vis spectrophotometer. The mass spectrum was obtained on Perkin-Elmer Sciex Triple Quadrupole LC/MS/MS Mass Spectrometer (Model-016932) using Ion Spray source. NMR spectra were recorded on Brucker 400 MHz. Spectrophotometer. Chemical shifts are relative to tetramethylsilane on δ-scale. Coupling constants are given in Hz and relative peak areas were in agreement with all assignments.

General procedure for the preparation of 2a, 2b, 6a and 6b. To a stirred solution of 7-hydroxy-4-methyl-chromen-2-one **1** (5 g, 0.028 moles), anhydrous potassium carbonate (4.90 g, 0.035 moles) and catalytic amount(0.05–0.1g) of potassium iodide in (40 mL) of dry acetone was added dropwise a solution of mono chloroacetone (2.62 g, 0.028 moles) in (20 mL) dry acetone at reflux temperature. It was refluxed for 12 h. The reaction mixture was concentrated to dryness and then poured into ice water and the solid collected by filtration. The crude product was crystallized from ethanol to give white crystals (3 g, 46%) of 4-methyl-7-(2-oxo-propoxy)-chromen-2-one **2a**, mp 154–156°C lit. [12] 157°C; IR (KBr): ν_{max}, cm^{-1}: 3061, 1705, 1609, 1591, 1454, 1384, 1360, 1288, 1220, 1166, 958; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.32 (d, 3H, J = 0.8 Hz, C4—CH_3), 2.42 (s, 3H, —$COCH_3$), 4.66 (s, 2H, —OCH_2CO—), 6.18 (d, 1H, J = 0.8 Hz, C3—H), 6.77–6.78 (d, 1H, J = 2.8 Hz, C8—H), 6.89–6.92 (dd, 1H, J = 2.8 Hz and J = 8.8 Hz, C6—H), 7.54–7.56 (d, 1H, J = 8.8 Hz, C5—H). Anal. calcd. for $C_{13}H_{12}O_4$ (232.23): C, 67.23; H, 5.20. Found: C, 67.02; H, 5.11. Potassium iodide is not required for the preparation of compounds **6a** and **6b**.

4-Methyl-7-(2-oxo-2-phenyl-ethoxy)-chromen-2-one (2b). This compound was obtained by column chromatographic purification using petroleum ether (60–80°C): ethyl acetate eluent, as white crystals, 43% yield, mp 169–171°C lit. [13] 173°C; IR (KBr): ν_{max}, cm^{-1}: 3071, 1698, 1612, 1596, 1451, 1391, 1366, 1283, 1230, 1160, 968; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.34 (d, 3H, J = 0.9 Hz, C4—CH_3), 4.58 (s, 2H, —OCH_2CO—), 6.19 (d, 1H, J = 0.9 Hz, C3—H), 6.79–6.80 (d, 1H, J = 2.8 Hz, C8—H), 6.89–6.93 (dd, 1H, J = 2.8 Hz and J = 8.8 Hz, C6—H), 7.52–7.68 (m, 6H, C5—H and C2′-H to C6′-H phenyl protons). Anal. calcd. for $C_{18}H_{14}O_4$ (294.30): C, 73.46; H, 4.79. Found: C, 72.99; H, 4.34.

3-Bromo-4-methyl-7-(2-oxy-propoxy)-chromen-2-one (6a). This compound was obtained as white crystals (DMF/ethanol), 68% yield, mp 204–206°C; IR (KBr): ν_{max}, cm^{-1}: 3062, 2910, 1719, 1698, 1628, 1593, 1392, 1218; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.32 (s, 3H, C4—CH_3), 2.62 (s, 3H, —$COCH_3$), 4.67 (s, 2H, —OCH_2CO—), 6.78–6.79 (d, 1H, J = 2.4 Hz, C8—H), 6.92–6.95 (dd, 1H, J = 2.4 Hz and J = 9.2 Hz, C6—H), 7.60–7.62 (d, 1H, J = 9.2 Hz, C5—H). Anal. calcd. for $C_{13}H_{11}O_4Br$ (311.12): C, 50.18; H, 3.56. Found: C, 50.06; H, 3.23.

3-Bromo-4-methyl-7-(2-oxo-2-phenyl-ethoxy)-chromen-2-one (6b). This compound was obtained as white crystals (toluene), 63% yield, mp 181–182°C; IR (KBr): ν_{max}, cm^{-1}: 3060, 2907, 1717, 1698, 1623, 1598, 1384, 1210; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.36 (s, 3H, C4—CH_3), 4.61 (s, 2H, —OCH_2CO—), 6.79–6.80 (d, 1H, J = 2.4 Hz, C8—H), 6.93–

6.95 (dd, 1H, J = 2.4 Hz and J = 9.2 Hz, C6—H), 7.50–7.66 (m, 6H, C5—H and C2′-H to C6′-H phenyl protons). Anal. calcd. for $C_{18}H_{13}O_4Br$ (373.20): C, 57.93; H, 3.51. Found: C, 57.61; H, 3.31.

General procedure for the preparation of 3a, 3b, 7a and 7b. Compound 4-methyl-7-(2-oxo-propoxy)-chromen-2-one **2a** (1 g, 0.0043 moles) was dissolved in 0.1*N* ethanolic potassium hydroxide (100 mL) and refluxed for 12 h. The excess ethanol was removed by distillation *in vacuo* and the reaction mixture was poured into ice-hydrochloric acid and the solid collected by filtration. The crude product was crystallized from ethanol to give white crystals (0.38 g, 41%) of 3,5-dimethyl-furo[3,2-*g*]chromen-7-one **3a**, mp 224–226°C lit. [12] 220°C; IR (KBr): ν_{max}, cm^{-1}: 3090, 1728, 1639, 1610, 1580, 1388, 1144, 1082; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.21–2.22 (d, 3H, J = 1.5 Hz, C3—CH_3), 2.51–2.52 (d, 3H, J = 1.08 Hz, C5—CH_3), 6.27–6.28 (d, 1H, J = 1.08 Hz, C6—H), 7.36 (s, 1H, C9—H), 7.52 (d, 1H, J = 1.5 Hz, C2—H), 7.58 (s, 1H, C4—H). Anal. calcd. for $C_{13}H_{10}O_3$ (214.21): C, 72.88; H, 4.70. Found: C, 72.62; H, 4.51.

In the preparation of compounds **7a** and **7b** the concentration of ethanolic potassium hydroxide was reduced from 0.1 to 0.025*N* and the reaction was maintained at 65–70°C for 12 h.

5-Methyl-3-phenyl-furo[3,2-g]chromen-7-one (3b). This compound was obtained as white crystals (ethanol), 41% yield, mp 181–182°C lit. [13] 185°C; IR (KBr): ν_{max}, cm^{-1}: 3090, 1720, 1632, 1612, 1575, 1385, 1142, 1075; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.48–2.49 (d, 3H, J = 1.1 Hz, C5—CH_3), 6.29–6.30 (d, 1H, J = 1.1 Hz, C6—H), 7.48–7.49 (m, 1H, C4′-H), 7.54–7.59 (m, 2H, C3′-H and C5′-H), 7.54 (s, 1H, C2—H), 7.65–7.67 (m, 2H, C2′-H and C6′-H), 7.86 (s, 1H, C9—H), 7.90 (s, 1H, C4—H). Anal. calcd. for $C_{18}H_{12}O_3$ (276.28): C, 78.25; H, 4.37. Found: C, 77.85; H, 4.30.

6-Bromo-3,5-dimethyl-furo[3.2-g]chromen-7-one (7a). This compound was obtained as yellow crystals (toluene), 30% yield, mp 224–226°C; IR (KBr): ν_{max}, cm^{-1}: 3088, 2925, 1733, 1693, 1639, 1602, 1556, 1350, 1151, 1074; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.31–2.32 (d, 3H, J = 1.6 Hz, C3—CH_3), 2.74 (s, 3H, C5—CH_3), 7.42 (s, 1H, C9—H), 7.50 (d, 1H, J = 1.6 Hz, C2—H), 7.74 (s, 1H, C4—H); LCMS: *m/z* (relative intensity, 100%): 317 (8.88) M+23 (from Na^+), 295.1 (100) M+1, 292.9 (100) M^+. Anal. calcd. for $C_{13}H_9O_3Br$ (293.11): C, 53.27; H, 3.09. Found: C, 52.98; H, 3.11.

6-Bromo-5-methyl-3-phenyl-furo[3,2-g]chromen-7-one (7b). This compound was obtained as yellow crystals (ethanol), 24% yield, mp 208–210°C; IR (KBr): ν_{max}, cm^{-1}: 3085, 2925, 1734, 1687, 1631, 1605, 1559, 1345, 1154, 1070; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.69 (s, 3H, C5—CH_3), 7.47–7.49 (m, 1H, C4′-H), 7.54–7.58 (m, 2H, C3′-H and C5′-H), 7.56 (s, 1H, C2—H), 7.64–7.66 (m, 2H, C2′-H and C6′-H), 7.87 (s, 1H, C9—H), 8.02 (s, 1H, C4—H). Anal. calcd. for $C_{18}H_{11}O_3Br$ (355.18): C, 60.86; H, 3.12. Found: C, 60.50; H, 3.07.

General procedure for the preparation of 4a and 4b. Compound 3,5-dimethyl-furo[3,2-*g*]chromen-7-one **3a** (1 g, 0.0046 moles) was dissolved in acetic acid (40 mL) by warming and to this stirred solution, a solution of bromine (0.24 mL, 0.0046 moles) in acetic acid (10 mL) was added gradually. It was stirred for 3 h at room temperature and then poured into ice water and the solid collected by filtration. The crude product was crystallized from ethanol to give yellow crystals (0.9 g, 66%) of 2-bromo-3,5-dimethyl-furo[3,2-*g*]chromen-7-one **4a**, mp 230–232°C; IR (KBr): ν_{max}, cm^{-1}: 3085, 1758, 1689, 1640, 1577, 1341, 1121; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.24 (s, 3H, C3—CH_3), 2.52 (d, 3H, J = 1.08 Hz, C5—CH_3), 6.27–6.28 (d, 1H, J = 1.08 Hz, C6—H), 7.36 (s, 1H, C9—H), 7.58 (s, 1H, C4—H). Anal. calcd. for $C_{13}H_9O_3Br$ (293.11): C, 53.27; H, 3.09. Found: C, 52.98; H, 3.11.

2-Bromo-5-methyl-3-phenyl-furo[3,2-g]chromen-7-one (4b). This compound was obtained as yellow crystals (ethanol), 61% yield, mp 238–239°C; IR (KBr): ν_{max}, cm^{-1}: 3084, 1750, 1686, 1636, 1578, 1347, 1110; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.46 (d, 3H, J = 1.05 Hz, C5—CH_3), 6.28 (d, 1H, J = 1.05 Hz, C6—H), 7.47–7.64 (m, 6H, C3—phenyl protons and C9—H), 7.75 (s, 1H, C4—H). Anal. calcd. for $C_{18}H_{11}O_3Br$ (355.18): C, 60.86; H, 3.12. Found: C, 60.82; H, 2.94.

General procedure for the preparation of 8a, 8b, 9a, 9b, 10a and 10b. A solution of 6-bromo-3,5-dimethyl-furo[3.2-*g*]chromen-7-one **7a** (0.5 g, 0.0017 moles) and piperidine (0.35 mL, 0.0035 moles) in dry DMF (10 mL) was heated at 95–100°C for 1 hour. The reaction mixture was poured into ice water and the solid collected by filtration. The crude product was crystallized from ethanol to give light brown crystals (0.28 g, 55%) of 3-methyl-5-piperidin-1-ylmethyl-furo[3,2-*g*]chromen-7-one **8a**, mp 185°C; IR (KBr): ν_{max}, cm^{-1}: 3059, 2971, 1718, 1639, 1616, 1579, 1454, 1337, 1158, 1120, 1096; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.47–1.48 (t, 2H, C4′—CH_2-), 1.59–1.65 (m, 4H, C3′—CH_2- and C5′—CH_2—), 2.27–2.28 (d, 3H, J = 1.2 Hz, C3—CH_3), 2.51 (t, 4H, C2′—CH_2- and C6′—CH_2—), 3.66 (s, 2H, C5—CH_2—), 6.51 (s, 1H, C6—H), 7.35 (s, 1H, C9—H), 7.43–7.44 (d, 1H, J = 1.2 Hz, C2—H), 7.92 (s, 1H, C4—H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 7.84 (C2—*C*H_3), 24.10 (C3′ and C5′), 26.07 (C4′), 55.05 (C2′ and C6′), 59.91 (C5—*C*H_2—), 99.59 (C6), 112.51 (C9), 114.92–115.73 (C4, C4a and C3), 126.23 (C3a), 143 (C2), 151.86 (C8a), 153.04 (C9a), 156.42 (C5), 161.57 (C7). Anal. calcd. for $C_{18}H_{19}O_3N$ (297.35): C, 72.70; H, 6.44; N, 4.71. Found: C, 72.56; H, 6.18; N, 4.44.

3-Phenyl-5-piperidin-1-ylmethyl-furo[3,2-g]chromen-7-one (8b). This compound was obtained by column chromatographic purification using petroleum ether (60–80°C): ethyl acetate eluent, as light brown crystals, 52% yield, mp 158–160°C; IR (KBr): ν_{max}, cm^{-1}: 3051, 2971, 1710, 1633, 1611, 1571, 1450, 1333, 1158, 1122, 1091; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.51 (t, 2H, C4′—CH_2—), 1.64–1.66 (t, 4H, C3′—CH_2— and C5′—CH_2-), 2.52 (t, 4H, C2′—CH_2- and C6′—CH_2—), 3.67 (s, 2H, C5—CH_2—), 6.52 (s, 1H, C6—H), 7.43–7.70 (m, 5H, C3—phenyl protons), 7.55 (s, 1H, C2—H), 7.86 (s, 1H, C9—H), 8.50 (s, 1H, C4—H).

Anal. calcd. for $C_{23}H_{21}O_3N$ (359.42): C, 76.86; H, 5.88; N, 3.89. Found: C, 76.52; H, 5.61; N, 3.67.

3-Methyl-5-morpholin-4-ylmethyl-furo[3,2-g]chromen-7-one (9a). This compound was obtained as light brown crystals (DMF/ethanol), 60% yield, mp 236–238°C; IR (KBr): ν_{max}, cm^{-1}: 3060, 2969, 1719, 1632, 1611, 1577, 1455, 1337, 1153, 1115, 1094; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.30 (d, 3H, J = 1.2 Hz, C3—CH_3), 2.62–2.63 (t, 4H, C3′—CH_2— and C5′—CH_2—), 3.75–3.79 (m, 6H, C2′—CH_2— C6′—CH_2— & C5—CH_2-), 6.56 (s, 1H, C6—H), 7.41 (s, 1H, C9—H), 7.48 (d, 1H, J = 1.2 Hz, C2—H), 7.92 (s, 1H, C4—H); lcms: *m/z* (relative intensity, 100%): 338.1 (7.27) M+39 (from K^+), 322.2 (38.18) M+23 (from Na^+), 301.2 (70.90) M+2, 299.9 (100) M+1.

Anal. calcd. for $C_{17}H_{17}O_4N$ (299.32): C, 68.21; H, 5.72; N, 4.67. Found: C, 67.91; H, 5.56; N, 4.33.

5-Morpholin-4-ylmethyl-3-phenyl-furo[3,2-g]chromen-7-one (9b). This compound was obtained by column chromatographic purification using petroleum ether (60–80°C): ethyl acetate eluent, as light brown crystals, 57%, mp 185–187°C; IR (KBr): ν_{max}, cm^{-1}: 3057, 2966, 1712, 1632, 1606, 1573, 1454, 1330, 1152, 1115, 1091; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.64–2.66 (t, 4H, C3′—CH_2— and C5′—CH_2—), 3.76–3.79 (m, 6H, C2′—CH_2— C6′—CH_2- and C5—CH_2—), 6.59 (s, 1H, C6—H), 7.45–7.76 (m, 6H, C2—H and C3—phenyl protons), 7.80 (s, 1H, C9—H), 8.13 (s, 1H, C4—H).

Anal. calcd. for $C_{22}H_{19}O_4N$ (361.39): C, 73.11; H, 5.29; N, 3.87. Found: C, 72.88; H, 5.10; N, 3.77.

3-Methyl-5-(4-phenyl-piperazin-1-ylmethyl)-furo[3,2-g]chromen-7-one (10a). This compound was obtained as light brown crystals (ethanol), 64% yield, mp 214–216°C; IR (KBr): ν_{max}, cm^{-1}: 3064, 2963, 1720, 1637, 1619, 1579, 1460, 1340, 1158, 1119, 1084; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.31 (d, 3H, J = 1.2 Hz, C3—CH_3), 2.80 (t, 4H, C3′—CH_2- and C5′—CH_2−), 3.27–3.30 (t, 4H, C2′—CH_2- and C6′—CH_2—), 3.83 (s, 2H, C5—CH_2—), 6.60 (s, 1H, C6—H), 6.89–7.32 (m, 5H, N4′-phenyl protons), 7.45 (s, 1H, C9—H), 7.49 (d, 1H, J = 1.2 Hz, C2—H), 7.98 (s, 1H, C4—H).

Anal. calcd. for $C_{23}H_{22}O_3N_2$ (374.43): C, 73.77; H, 5.92; N, 7.48. Found: C, 73.51; H, 5.77; N, 7.09.

3-Phenyl-5-(4-phenyl-piperazin-1-ylmethyl)-furo[3,2-g]chromen-7-one (10b). This compound was obtained as light brown crystals (ethanol/toluene), 62% yield, mp 180°C dec.; IR (KBr): ν_{max}, cm^{-1}: 3061, 2963, 1713, 1631, 1611, 1578, 1450, 1337, 1157, 1108, 1088; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.79 (t, 4H, C3′—CH_2— and C5′—CH_2—), 3.3 (t, 4H, C2′—CH_2— and C6′—CH_2—), 3.80 (s, 2H, C5—CH_2—), 6.57 (s, 1H, C6—H), 6.92–7.68 (m, 10H, C3—phenyl protons and N4′-phenyl protons), 7.55 (s, 1H, C2—H), 7.86 (s, 1H, C9—H), 8.45 (s, 1H, C4—H).

Anal. calcd. for $C_{28}H_{24}O_3N_2$ (436.50): C, 77.04; H, 5.54; N, 6.41. Found: C, 76.72; H, 5.41; N, 6.22.

4-Morpholin-4-ylmethyl-7-(2-oxo-propoxy)-chromen-2-one (11). This product was obtained by column chromatographic purification using petroleum ether (60–80°C): ethyl acetate eluent, as white crystals, 50% yield, mp 138–140°C; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.30 (s, 3H, —$COCH_3$), 2.53–2.55 (t, 4H, C3′—CH_2— and C5′—CH_2—), 3.59 (s, 2H, C4—CH_2—), 3.72–3.74 (t, 4H, C2′—CH_2— and C6′—CH_2—), 4.64 (s, 2H, C7—OCH_2CO—), 6.40 (s, 1H, C3—H), 6.75–6.76 (d, 1H, J = 2.56 Hz, C8—H), 6.86–6.89 (dd, 1H, J = 2.6 Hz and J = 8.88 Hz, C6—H), 7.78–7.80 (d, 1H, J = 8.88 Hz, C5—H).

Anal. calcd. for $C_{17}H_{11}O_5N$ (309.27): C, 66.02; H, 3.58; N, 4.52. Found: C, 66.01; H, 3.33; N, 4.41.

3-Methyl-5-phenyl-benzo[1,2-b;5,4-b′]difuran-2-carboxylic acid (12). This compound was obtained as white amorphous powder (ethanol), 52% yield, mp 250°C dec.; IR (KBr): ν_{max}, cm^{-1}: 3433, 3107, 3030, 2922, 1682, 1627, 1598, 1440, 1366, 1332, 1318, 1165, 1119; ^1H NMR ($(CD_3)_2SO$, 400 MHz): δ 2.58 (s, 3H, C3—CH_3), 7.32–7.36 (m, 1H, C4′-H), 7.44–7.47 (m, 2H, C2′-H and C6′-H), 7.63–7.66 (m, 3H, C6—H, C3′-H and C5′-H), 7.93 (s, 1H, C4—H), 7.96 (s, 1H, C8—H).

Anal. calcd. for $C_{18}H_{12}O_4$ (292.28): C, 73. 96; H, 4.13. Found: C, 73.84; H, 4.03.

6-Ethoxy-5-methyl-3-phenyl-furo[3,2-g]chromen-7-one (13). This compound was obtained by column chromatographic purification using petroleum ether (60–80°C): ethyl acetate eluent, as white crystals, 55% yield, mp 169–171°C; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.46–1.50 (t, 3H, C6—OCH_2CH_3), 2.66 (s, 3H, C5—CH_3), 4.46–4.51 (q, 2H, C6—OCH_2CH_3), 7.42–7.46 (m, 1H, C4′-H), 7.52–7.56 (m, 2H, C2′-H and C6′-H), 7.68–7.70 (m, 3H, C2—H, C3′-H and C5′-H), 7.81 (s, 1H, C4—H), 7.94 (s, 1H, C9—H).

Anal. calcd. for $C_{20}H_{16}O_4$ (320.34): C, 74.98; H, 5.03. Found: C, 74.73; H, 4.98.

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