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Facile synthesis of various 4-carboxylic acid derivatives and their amide analogues of benzopyrans

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A series of 4-carboxyalkyl amide derivatives of benzopyrans **6a-d** and **7a-d** have been prepared in 40-64% overall yields. In the proposed synthetic strategy, the key intermediate 4-methyl substituted chroman **3** is obtained by condensing substituted phenol and mesityl oxide in presence of PPA. The required carboxylic acid function has been introduced at C-4 in benzopyran ring through a novel route.

Keywords: Benzopyran, chromakalim, selenium dioxide, carboxylalkyl amide.

Chromans, chromones and chromanones representing common benzopyran frame work abundantly found in a number of natural products like flavanoids, iso-flavanoids, coumarins, homo-, iso- and neo-flavo-noids[1,2] exhibiting interesting biological activities such as anti-allergic, tyrosine kinase inhibitory, estrogen receptor agonist or antagonist activity or inhibitor activity of steroidegenic enzymes[3,4]. Chromones/chromanones or in simple terms benzopyranones can be potential intermediates for the synthesis of heterocyclic analogs of steroids and or important building blocks for the preparation of pterocarpans and isoflavones with strong fungicidal activity[5]. Another important activity associated with chromans having substitutions at 2- and 4-positions have been that of its smooth muscle relaxant activity and these compounds have been used for the treatment of disorders such as asthma and hypertension with chromakalim being the best representative example of these anti-hypertensives[6].

In the previous paper[7] we described in detail the novel synthetic methodology to prepare substituted 4-pyridyl benzopyrans with variation in the substitution in aromatic as well as in the pyran ring. In an extension to these studies we now propose to synthesize substituted 4-carboxylic acid derivatives of benzopyrans and thereafter their amide analogues.

Most obvious synthetic strategy for the insertion of carboxylic group at 4 position of benzpyran moiety is to treat[8] 4-bromo-6-nitro-benzopyran with copper(I) cyanide in DMF to afford 4-cyanobenzopyran which could easily be hydrolysed in presence of strong acid to afford 4-carboxylic acid analogues[9] **(Scheme I)**. However, more direct environment friendly approach is required for thorough screening of these biologically important congeners.

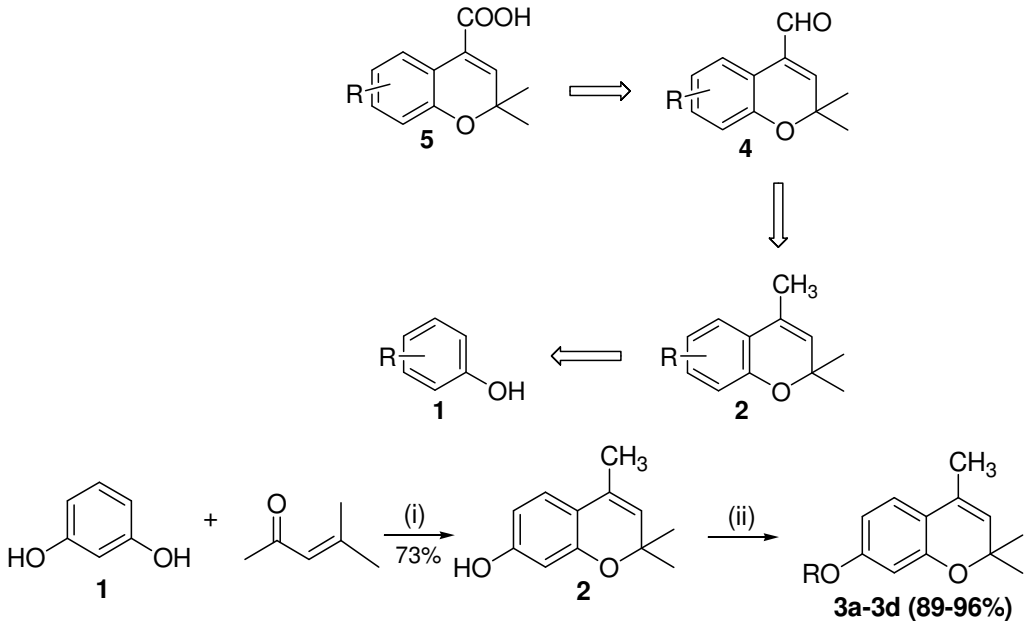
Therefore, in the present work, a novel and practical approach for the generation of focused library consisting novel benzopyran-4-carboxylic acid derivatives has been taken up. Retro-synthetic route for the preparation of these novel analogues has been discussed in the results and discussion part.

Results and Discussion

In order to achieve 4-carboxylic acid substituted benzopyran derivatives, a novel route where the use of toxic reagent like CuCN could be obviated was chosen. The retro synthetic route for this is outlined below. The key intermediate **2** was synthesized by condensing readily available resorcinol **1** and mesityl oxide in presence of PPA following the procedure reported by our group[10].

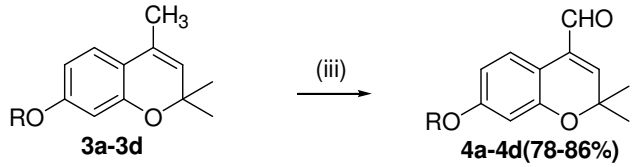
Vinylic methyl group of chromene **3** thus obtained, was subjected to SeO_2 oxidation resulting in 2,2-dimethyl-4-formyl-7-methoxy-2*H*-1-benzopyran **4** in moderate yield **(Scheme II)**. Formation of **4a-d** was confirmed by its spectral data. Presence of peak at δ 9.66 in ^{1}H NMR and stretching of carbonyl at 1690 cm^{-1} in IR confirmed the presence of formyl group.

Target derivatives benzopyran 4-carboxylic acids, **5a-d** were achieved by oxidation with Tollens reagent (58-63% yield). Finally, the amides were obtained



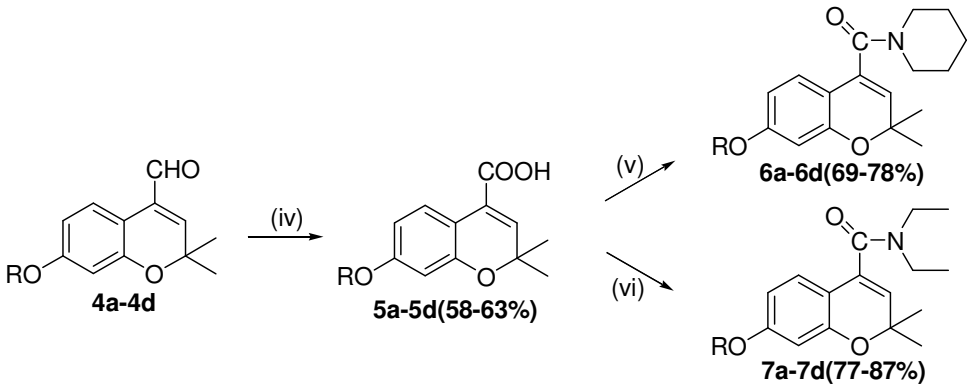
Reagents and conditions: (i) PPA, stir mechanically at RT; (ii) Methyl iodide, acetone, K_2CO_3, reflux.

Scheme I — Synthesis of 2,2-dimethyl-4-formyl-7-alkoxy-2*H*-1-benzopyran



Reagents and conditions: (iii) Dioxan, SeO_2, reflux on heating mentle.

Scheme II — Novel bezopyran-4-formyl analogues



Reagents and conditions: (iv) NaOH, $AgNO_3$; (v) a) $SOCl_2$, Pyridine, Benzene; b) Piperidine, benzene, stirred at RT; (vi) a) $SOCl_2$, Pyridine, Benzene; b) N,N-diethyl amine, benzene, stirred at RT.

Scheme III — Novel bezopyran-4-carboxylic acid alkyl amides analogues

from carboxylic acids through acid chloride formation and condensation with appropriate amines (**Scheme III**).

The cyclic amide product **6a** was identified by the presence of a four proton multiplet at δ 3.30-3.64 corresponding to two methylenes attached to the nitrogen and rest of methylenes were located at δ 1.02 to 1.67 as multiplet while H-3 proton located at δ 6.46 as a singlet in proton-NMR. Mass spectral analysis was in accord with the structure.

The 4-carboxylic acid acyclic amides of benzopyran analogues were identified by NMR spectroscopy, *e.g*. the formation of the amide **7a** was confirmed by its ^{1}H NMR spectral data, wherein H-3 olefinic proton appeared at δ 6.63 as a singlet and N(CH_2) protons were located at δ 3.33-3.63 as a quartet and the protons corresponding to two -CH_3 groups appeared at δ 1.33 (t). The formation of **7a** was further confirmed by MS data wherein M^+ at *m/z* 289 corresponded to its molecular formula.

Summary

A series of 2,2-dimethyl-4-carboxyalkyl amide derivatives of benzopyrans **14a-h** have been prepared by the novel synthetic strategy, introduction of carboxylic acid function at C-4 in benzopyran ring has been achieved through a novel route *via* 2,2,4-trimethyl -2*H*-1-benzopyran which is the key intermediate. The structures of all new products have been confirmed by the elemental analysis and *m/z* value of all the compounds gave satisfactory results.

Experimental Section

Solvents and other chemicals were of reagent grade and were used without further purification. Laboratory grade solvents were purified and dried by reported methods. All melting points were determined in capillary tubes on a Buchi technical apparatus (BUCHI-510) and are uncorrected. NMR spectra were obtained on Bruker Supercon 200 MHz and 500 MHz instruments and are expressed in δ values downfield from tetramethylsilane (TMS) as the internal standard. Mass spectra were recorded with a Jeol MS-D 300 mass spectrometer. IR spectra (KBr pellet or neat sample) were recorded on Perkin Elmer-377 and Shimadzu IR-435 spectrophotometers. Column chromatography was performed on silica gel (100-200 mesh) and TLC on silica gel 60 F_{254} (Merck). For the visualization of spots either UV or iodine vapour or 10% aqueous sulfuric acid containing 2% ceric ammonium sulfate or 5% ethanolic solution of 2,4-dinitrophenylhydrazine was used.

Preparation of 2,2,4-trimethyl-7-hydroxy-2*H*-1-benzopyran

Resorcinol (5.5 g, 0.05 mol) and mesityl oxide (4.9 g, 0.0 5mol) were dissolved in polyphosphoric acid (30 mL). The mixture was stirred for three days at RT, and was worked up by adding water (250 mL). It was extracted with ethyl acetate (3 × 50 mL), and the extracts were combined, dried, evaporated, and chromatographed over silica gel column using pet. ether:ethyl acetate (85:15) to afford pure 2,2,4-trimethyl-7-hydroxy-2*H*-1-benzopyran as a semi solid (3.42 g, 60% yield). ^{1}H NMR($CDCl_3$): δ 1.44 (6H, s, 2 × CH_3), 2.01(3H, s, CH_3), 5.35 (1H, s, 3-H), 6.43 (1H, d, *J* = 2.5 Hz, 8-H), 6.50 (1H, dd, *J* = 8.5 Hz and 2.5 Hz, 6-H), 7.06 (1H, d, *J* = 8.5 Hz, 5-H); IR: 3300, 2950, 1650, 1580, 1500, 1370, 1330, 1280, 1250, 1150, 1130, 1060, 990, 940, 900, 850, 820, 760 cm^{-1}; MS: *m/z* 190(1), 178 (21), 176(100), 92(11), 78(18), 53(14).

Preparation of 2,2,4-trimethyl-7-methoxy-2*H*-1-benzopyran, 3a

To a solution of **2** (3.8 g, 0.02 mol) in dry acetone (80 mL) were added potassium carbonate 0.5 g and methyl iodide 2.84 g (0.02 mol). The mixture was refluxed for 4 hr, on a water bath. After cooling the reaction mixture, it was filtered and filtrate concentrated. The residue obtained was purified by column chromatography over silica gel (pet. ether:ethyl acetate, 97:3) to afford the product **3a** (3.66 g) yield 90% as semi solid. ^{1}H NMR($CDCl_3$): δ 1.61 (6H, s, 2 × CH_3), 2.00 (3H, s, CH_3), 3.77 (3H, s, OCH_3), 6.33 (1H, d *J* = 2.5Hz, 8-H), 6.45 (1H, dd, *J* = 8.5 and `2.5Hz, 6-H) , 5.43 (1H, s, 3-H), 7.10 (1H, d, *J* = 8.5Hz, 5-H); IR: 3300, 2940, 2360, 2220, 1640, 1580, 1520, 1370, 1330, 1270, 1250, 1140, 1130, 1065, 990, 940, 910, 850, 825, 760 cm^{-1}; MS: *m/z* 204(18), 192(100), 190(7), 106(33), 92(81), 67(29).

Similarly compounds **3b-d** were prepared. Their spectral data are as under.

3b: ^{1}H NMR ($CDCl_3$): δ 1.10 (3H, t, *J* = 6.5 Hz, CH_3), 1.40 (6H, s, 2 × CH_3), 1.98 (3H, s, CH_3), 3.98 (2H, q, *J* = 6.5 Hz, OCH_2), 5.18 (1H, s, 3-H), 6.19 (1H, d, *J* = 2.5 Hz, 8-H), 6.30 (1H, dd, *J* = 8.5 and 2.5 Hz, 6-H), 7.18 (1H , d, *J* = 8.5 Hz, 5-H); IR: 3320, 2950, 1650, 1570, 1520, 1350, 1310, 1250, 1130, 1120, 1070,

980, 940, 920, 850, 820, 760 cm^{-1}; MS: *m/z* 218(22), 206(100), 204(7), 120(18), 106(13), 81(2).

3c: ^{1}H NMR ($CDCl_3$): δ 0.95 (3H, t, *J* = 6 Hz, CH_3), 1.06-1.36 (4H, 2 × CH_2), 1.50 (6H, s, 2 × CH_3), 1.91 (3H, s, CH_3), 3.86 (2H, t, *J* = 6 Hz, OCH_2), 5.21 (1H, s, 3-H), 6.36 (1H, d, *J* = 2.5 Hz, 8-H), 6.48 (1H, dd, *J* = 8.5 and 2.5 Hz, 6-H), 7.03 (1H, d, *J* = 8.5 Hz, 5-H); IR: 2850, 1610, 1480, 1380, 1360, 1280, 1170, 1140, 1060, 1020, 900, 840, 800, 760 cm^{-1}; MS: *m/z* 246(19), 231(63), 175(100), 147(13), 117(27), 84(65), 71(16), 58(37).

3d: ^{1}H NMR ($CDCl_3$): δ 1.23 (6H, d, *J* = 6 Hz, 2 × CH_3), 1.35 (6H, s, 2 × CH_3), 1.90 (3H, s, 1 × CH_3), 4.46 (1H, h, *J* = 6 Hz, OCH), 5.21 (1H, s, 3-H), 6.33 (1H, d, *J* = 2 Hz, 8-H), 6.43 (1H, dd, *J* = 8.5 Hz and 2.5 Hz, 6-H), 7.33 (1H, d , *J* = 8.5 Hz, 5-H); IR: 3750, 2900, 2850, 1620, 1500, 1380, 1280, 1150, 1060, 1000, 950, 900, 860, 800 cm^{-1}; MS: *m/z* 232(11), 217(43), 175(100), 146(8), 115(5), 91(7), 79(3), 65(4), 43(31).

Preparation 2,2-dimethyl-4-formyl-7-methoxy-2*H*-1-benzopyran, 4a

A solution of SeO_2 (2.22 g, 0.02 mol), dioxan (15 mL) and water (0.5 mL) was heated to 50-55°C and stirred until the solid SeO_2 dissolved. **3a** (4.1 g, 0.02 mol) was added to the reaction mixture and refluxed with stirring for 4 hr. After cooling to RT, the reaction mixture was diluted with water and extracted with ethyl acetate (3 × 30 mL). Combined extracts was washed with water, dried over sodium sulphate and evaporated *in vacuo* to yield a residue. The crude product was subjected to silica gel column chromatography using pet. ether:ethyl acetate (4:1) to afford pure formyl derivative **4a** 2,2-dimethyl-4-formyl-7-methoxy-2*H*-1-benzopyran **4a** as a gummy mass (3.2 g, yield 72%). ^{1}H NMR ($CDCl_3$): δ 1.50 (6H, s, 2 × CH_3), 3.78 (3H, s, OCH_3), 6.30 (1H, s, 3-H), 6.46 (1H, d, *J* = 2.5 Hz, 8-H), 6.56 (1H, dd, *J* = 8.5 and 2.5 Hz, 6-H), 8.18 (1H, d, *J* = 8.5 Hz, 5-H), 9.68 (1H, s, CHO); IR: 3180, 2940, 1645, 1570, 1530, 1380, 1340, 1280, 1250, 1150, 1130, 1080, 995, 950, 920, 850, 830, 760 cm^{-1}; MS: *m/z* 218(38), 206(100), 204(6), 178(41), 120(17), 106(14), 81(3).

Similarly compounds **4b-d** were prepared. Their spectral data are as follows

4b: ^{1}H NMR($CDCl_3$): δ 1.21 (3H, t, *J* = 6.5 Hz, CH_3), 1.45 (6H, s, 2 × CH_3), 4.05 (2H, q, *J* = 6.5 Hz, OCH_2), 6.26 (1H, d, *J* = 2 Hz, 8-H), 6.36 (1H, dd, *J* = 8.5, 2.5 Hz, 6-H), 6.40 (1H, s, 3-H), 8.15 (1H, d, *J* = 8.5 Hz, 5-H), 9.65 (1H, s, CHO); IR: 3750, 2950, 2900, 1685, 1600, 1490, 1385, 1295, 1175, 1140, 1040, 890, 840, 760 cm^{-1}; MS: *m/z* 232(26), 217(100), 189(41), 161(32), 77(10), 69(7), 63(7).

4c: ^{1}H NMR($CDCl_3$): δ 1.06 (3H, t, *J* = 6Hz, CH_3), 1.26-1.86 (4H, m, 2 × CH_2), 1.55 (6H, s, 2 × CH_3), 4.00 (2H, t, *J* = 6Hz, OCH_2), 6.33 (1H, d, *J* = 2Hz, 8-H), 6.50 (1H, dd, *J* = 8.5 and 2.5Hz, 6-H), 6.66 (1H, s, 3-H), 8.20 (1H, d, *J* = 8.5Hz, 5-H), 9.73 (1H, s, CHO); IR: 3320, 1590, 1420, 1260, 1120, 800, 620 cm^{-1}; MS: *m/z* 260(23), 245(100), 189(92), 161(39), 43(6).

4d: ^{1}H NMR ($CDCl_3$): δ 1.33 (6H, d, *J* = 6 Hz, 2 × CH_3), 1.56 (6H, s, 2 × CH_3), 4.60 (1H, h, *J* = 6 Hz, OCH), 6.55 (2H, m, 6 and 8-H), 6.38 (1H, s ,3-H), 8.20 (1H, d , *J* = 8.5 Hz, 5-H), 9.73 (1H, s ,CHO); IR: 2900**,** 1980, 1685, 1500, 1460, 1360, 1280, 1140, 1060, 1000, 940, 900, 860, 750 cm^{-1}; MS: *m/z* M^+(+1) 247(38), 232(100), 190(23), 175(18), 161(10), 115(9), 91(13), 77(6), 43(2).

Preparation of 2,2-dimethyl-7-methoxy-2H-1-benzopyran-4-carboxylic acid, 5a

To an aqueous NaOH solution (0.2 g NaOH, 0.1 mol in 1.5 mL water) were added silver nitrate (0.25 g) and **4a** (1.09 g, 0.005 mol) in portions at 0°C. The mixture was allowed to stir at 5°C. The reaction was monitored by TLC using BCG. After 6 hr, the reaction mixture was neutralized with 6N HCl and extracted with ethyl acetate (3 × 10 mL). The combined extract was washed, dried and concentrated to give yellow oil which was subjected to column chromatography, using pet. ether:ethyl acetate (70:30) as eluent to give pure crystalline product 2,2-dimethyl-7-methoxy-2*H*-1-benzopyran-4-carboxylic

5a: (0.38g, yield 33%), m.p. 156-58°C. ^{1}H NMR ($CDCl_3$): δ 1.61 (6H, s, 2 × CH_3), 3.91 (3H, s, OCH_3), 6.55 (1H, d, *J* = 2.5 Hz, 8-H), 6.70 (1H, dd, *J* = 8.5 and 2.5 Hz, 6-H), 6.80 (1H, s, 3-H), 8.05 (1H, d, *J* = 8.5 Hz, 5-H); IR: 3450, 2900, 1680, 1620, 1575, 1500, 1430, 1370, 1300, 1250, 1200, 1160, 1045, 1010, 930, 950, 920, 880, 810, 760, 730 cm^{-1}; MS: *m/z* M^+(-1)233(7), 232(42), 217(100), 190(18), 175(17), 115(11), 76(14), 52(11).

Similarly compounds **5b-d** were prepared. Their spectral data are as under.

5b: ^{1}H NMR ($CDCl_3$+DMSO-d_6): δ 1.40 (3H, t, *J* = 6.5Hz, CH_3), 1.70 (6H, s, 2 × CH_3), 4.13 (2H, q, *J* = 6.5 Hz, OCH_2), 6.50 (1H, d, *J* = 2 Hz, 8-H), 6.61 (1H, dd, *J* = 8.5 and 2.5 Hz 6-H), 6.66 (1H, s, 3-H), 8.10

(1H, d, *J* = 8.5 Hz, 5-H); IR: 3150, 1680, 1615, 1260, 1185, 1145, 1050, 710 cm^{-1}; MS: *m/z* 248(17), 233(100), 205(60), 177(11), 115(4), 91(6), 77(10), 65(5), 43(29).

5c: ^{1}H NMR($CDCl_3$): δ 1.03 (3H, t, *J* = 6 Hz, CH_3), 1.40-1.83 (4H, 2 × CH_2), 1.50 (6H, s, 2 × CH_3), 4.08 (2H, t, *J* = 6.5 Hz, OCH_2), 6.57 (1H, d, *J* = 2.5 Hz, 8-H), 6.65 (1H, dd, *J* = 8.5, 2.5 Hz, 6-H), 6.70 (1H, s, 3-H), 8.21 (1H, d, *J* = 8.5 Hz, 5-H); IR: 3250, 1780, 1655, 1250, 1180, 1160, 1120, 730, 710 cm^{-1}; MS: *m/z* 276(16), 262(88), 206(100), 177(10), 131(3), 115(4), 103(3), 91(5), 77(6).

5d: ^{1}H NMR ($CDCl_3$): δ 1.40 (6H, d, *J* = 6Hz, 2 × CH_3), 1.50 (6H, s, 2 × CH_3), 4.58 (1H, h, *J* = 6 Hz, OCH), 6.53 (2H, m, 6 and 8-H), 6.65 (1H, s, 3-H), 7.83 (1H, d, *J* = 8.5 Hz, 5-H); IR: 2850, 1680, 1540, 1410, 1360, 1240, 1140, 1060, 1020, 910, 860, 755 cm^{-1}; MS: *m/z* 262(12), 247(26), 205(100), 177(7), 77(4), 43(21).

Preparation of 2,2-dimethyl-7-methoxy-2H-1-benzopyran-4-carboxylic acid-N,N-diethyl amide, 6a

A solution of 7-methoxy-2,2-dimethyl-2*H*-1-benzopyran-4-carboxylic acid **5a** (0.23 g, 0.001 mol), thionyl chloride (0.18 g, 0.0015 mol) and pyridine (4 drops) in dry benzene (15 mL) was heated to reflux on water bath for 2 hr. The reaction mixture was concentrated to remove excess of thionyl chloride and redissolved in dry benzene. Diethyl amine (0.07 g, 0.001 mol) was added, the reaction mixture was stirred at room temperature for 2 hr. After the completion of reaction it was washed with dilute hydrochloric acid solution (5%) followed by water and finally the solvent evaporated. It was chromatographed over silica gel column and elution with pet ether:ethyl acetate (90:10) furnished the product as a semi solid (0.090 g, yield 38%). It was analysed for $C_{17}H_{23}NO_3$ (Found: C, 69.98; H, 7.88; N, 4.82 (Requires: C, 70.55; H, 8.02; N, 4.84%). ^{1}H NMR ($CDCl_3$): δ 1.30 (6H, t, *J* = 6 Hz, 2 × CH_3), 1.50 (6H, s, 2 × CH_3), 3.33-3.63 (4H, q, *J* = 6 Hz, 2 × NCH_2), 3.83 (3H, s, OCH_3), 6.52 (1H, d, *J* = 2.5 Hz, 8-H), 6.57 (1H, dd, *J* = 8.5 Hz and 2.5 Hz, 6-H), 6.63 (1H, s, 3-H), 6.96 (1H, d, *J* = 8.5Hz, 5-H); IR: 2950, 1680, 1620, 1585, 1440, 1390, 1360, 1300, 1210, 1150, 1040, 810 cm^{-1}; MS: *m/z* 289(11), 274(100), 189(5), 188(2), 175(32), 159(6), 72(6). Anal: Calcd for $C_{17}H_{23}NO_3$: C, 70.56; H, 8.01; N, 4.84%. Found: C, 69.809; H, 8.10; N, 4.79%.

Similarly compounds **6b-d** were prepared. Their spectral data are as under.

6b: ^{1}H NMR($CDCl_3$): δ 1.23-1.60 (9H, m, 3×CH_3), 1.68 (6H, s, 2 × CH_3), 3.33-3.63 (4H, m, 2 × NCH_2), 4.06 (2H, q, *J* = 6 Hz, OCH_2), 6.40 (1H, d, *J* = 2 Hz, 8-H), 6.50 (1H, dd, *J* = 8.5 and 2.5Hz, 6-H), 6.63 (1H, s, 3-H), 7.11 (1H, d, *J* = 8.5 Hz, 5-H); IR: 2970, 2230, 1640, 1620, 1580, 1440, 1370, 1360, 1300, 1210, 1140, 1010, 810 cm^{-1}; MS: *m/z* M^+(+1) 304(11), 289(100), 204(4), 189(11),175(3), 91(4), 72(10), 69(5).

6c: ^{1}H NMR ($CDCl_3$): δ 0.98 (3H, t, *J* = 6 Hz, CH_3), 1.33 (8H, m, 2 × CH_3 and CH_2), 1.33 (6H, t, *J* = 6 Hz, 2 × CH_3), 1.50 (6H, s, 2 × CH_3); 3.35-3.66 (4H, bs, 2 × NCH_2), 4.12 (2H, t, *J* = 6 Hz, OCH_2), 6.44 (1H, d, *J* = 2.5 Hz, 8-H), 6.64 (1H, dd, *J* = 8.5 and 2.5 Hz, 6-H), 6.87 (1H, s, 3-H), 8.10 (1H, d, *J* = 8.5 Hz, 5-H); IR: 2980, 1630, 1590, 1430, 1380, 1360, 1310, 1240, 1160, 1040, 810, 760 cm^{-1}; MS: *m/z* 260(12), 245(24), 202(100), 173(7), 74(5), 41(20).

6d: ^{1}H NMR($CDCl_3$): δ 1.30 (6H, bs, 2×CH_3), 1.34 (6H, d, *J* = 6 Hz, 2 × CH_3), 1.50 (6H, s, 2 × CH_3), 3.44-3.78 (6H, m, 2 × NCH_2), 4.58 (1H, h, *J* = 6 Hz, OCH), 6.54 (2H, m, 6 and 8-H), 6.65 (1H, s, 3-H), 7.83 (1H, d , *J* = 8.5 Hz, 5-H); IR: 2850, 1640, 1540, 1410, 1360, 1240, 1140, 1060, 1020, 910, 860, 755 cm^{-1}; MS: *m/z* 317(23), 302(100), 260(18), 222(9), 132(11), 98(7).

Preparation of 2,2-dimethyl-7-methoxy-2*H*-1-benzopyran-4-carboxylic acid piperidine amide, 7a

A solution of 7-methoxy-2,2-dimethyl-2*H*-1-benzopyran-4-carboxylic acid **5a** (0.23 g, 0.001 mol), thionyl chloride (0.189 g, 0.0015 mol) and pyridine (3 drops) in dry benzene was heated to reflux on water bath for 2 hr and the resulting acid chloride treated with piperidine as described for **6a** to give **7a**. The reaction mixture was worked up. Finally the solvent was evaporated and residue chromatographed over silica gel, eluted with the solvents pet ether : ethyl acetate (90:10) to give the product as semi solid (0.120 g, yield 40%). It was analysed for $C_{18}H_{23}NO_3$ as Found: C, 70.31; H, 7.60, N, 4.76. Requires C, 71.72; H, 7.70; N, 4.65.

^{1}H NMR ($CDCl_3$): δ 1.02-1.67 (6H, bm, 3 × CH_2), 1.48 (6H, s, 2 × CH_3), 3.30-3.64 (4H, m, 2 × NCH_2), 3.81 (3H, s, OCH_3), 6.28 (1H, d, *J* = 2.5 Hz, 8-H), 6.33 (1H, dd, *J* = 8.5 Hz and 2.5 Hz, 6-H), 6.46 (1H, s, 3-H), 7.13 (1H, d, *J* = 8.5 Hz, 5-H); IR: 2960, 1680, 1580, 1420, 1380, 1360, 1320, 1210, 1150, 1060, 810,

760 cm^{-1}; MS: *m/z* 301(22), 286(100), 202(17), 201(32), 187(13), 171(9), 84(5). Anal: Calcd for $C_{18}H_{23}NO_3$: C, 71.73; H, 7.68; N, 4.66. Found: C, 70.93; H, 7.88; N, 4.70%.

Similarly compounds **7b-d** were prepared. Their spectral data are as under.

7b: ^{1}H NMR ($CDCl_3$): δ 1.03-1.66 (9H, m, 3 × CH_2 and CH_3), 1.63 (3H, s, 2×CH_3), 3.41-3.58 (4H, m, 2 × NCH_2), 4.06 (2H, q, *J* = 6 Hz, OCH_2), 6.42 (2H, m, 6 and 8-H), 6.61 (1H, s, 3-H), 8.13 (1H, d, *J* = 8.5 Hz, 5-H); IR: 2960, 2210, 1650, 1630, 1560, 1410, 1320, 1310, 1300, 1180, 1140, 1010, 820 cm^{-1}; MS: *m/z* M^+(+1) 316(12), 302(22), 301(100), 190(13), 161(19), 85(7), 69(9).

7c: ^{1}H NMR ($CDCl_3$): δ 0.93 (3H, d, *J* = 6 Hz, CH_3), 1.06-1.83 (6H, bm, 3×CH_2), 1.43 (6H, s, 2 × CH_3), 3.33-3.63 (4H, m, 2 × NCH_2), 3.93 (2H, t, *J* = 6Hz, OCH_2), 6.50 (2H, m, 6 and 8-H), 6.58 (1H, s, 3-H), 6.96 (1H, d, *J* = 8.5 Hz, 5-H); IR: 2960, 1650, 1610, 1580, 1440, 1390, 1340, 1310, 1220, 1160, 1040, 820, 750 cm^{-1}; MS: *m/z* 343(27), 315(100), 230(15), 228(11), 226(8), 199(38), 113(6), 87(2).

7d: ^{1}H NMR ($CDCl_3$): δ 1.06-1.68 (6H, bm, 3 × CH_2), 1.33 (6H, d, *J* = 6 Hz, 2 × CH_3), 1.48 (6H, bs, 2 × CH_3), 3.41-3.73 (4H, bs, 2 × NCH_2), 4.43 (1H, h, *J* = 6 Hz, OCH), 6.42 (2H, m, 6 and 8-H), 6.58 (1H, s, 3-H), 6.86 (1H, d, *J* = 8.5 Hz, 5-H); IR: 2850**,** 1640, 1540, 1410, 1360, 1240, 1140, 1060, 1020, 910, 860, 755 cm^{-1}; MS: *m/z* 329(2), 314(47), 272(100), 234(14), 144(4), 110(6), 98(3).

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