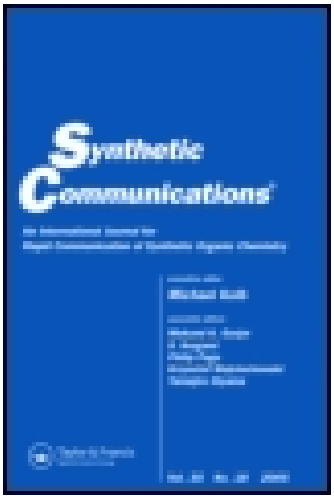

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Facile Synthesis of 7-Methoxy-2-aryl-3-phenyl/or-H-8-[2-(4,6-dimethyl-3,5-dicarbethoxy-pyridy

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Facile Synthesis of 7-Methoxy-2-aryl-3-phenyl/or-H-8-[2-(4,6-dimethyl-3,5-dicarbethoxy-pyridyl)]-4H-1-benzopyran-4-ones

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Abstract: Condensation of 8-formyl-7-methoxy-2-phenyl-4H-1-benzopyran-4-ones **(5a–f)** with ethyl-3-aminocrotonate **(6)** in glacial acetic acid under Hantzsch conditions afforded 7-methoxy-2-aryl-3-phenyl/or-H-8-[2-(4,6-dimethyl-3,5-dicarbethoxy-pyridyl)]-4H-1-benzopyran-4-ones **(7a–f)** in good yields.

Keywords: 4H-1-benzopyran-4-ones, pyridylfarones

INTRODUCTION

Substituted flavones, chromones, chalcones, and flavonones have been recognized as important classes of bioactive heterocyclics. 4-Aryl-1,4-dihydropyridines obtained by the Hantzsch synthesis[1] were found to be highly effective calcium antagonists.[2] For example, nifedipine and its analogs nicordipine[3] and nimodipine[4] are powerful calcium antagonists, which lower the frequency of attack of angina pectoris and reduces blood pressure.[3] Its activity is due to its coronary vasodilatory effect. The recent interest in dihydropyridines is due to the co-enzyme NADH, reduced nicotinamide adenine dinucleotide, which has unique activity to

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reduce stereoselectively unsaturated functional groups such as carbonyl and conjugated olefins.[5]

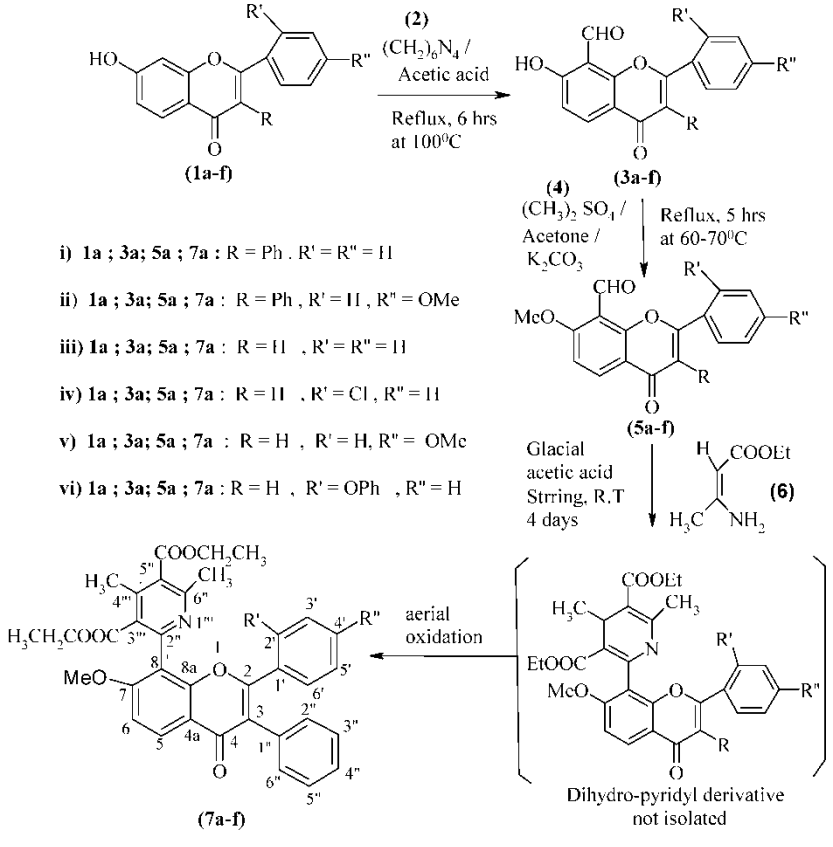
In view of the diverse biological activity shown by 1,4-dihydropyridines, we planned a simple route to synthesize 8-pyridyl-substituted flavones **(7a–f)**. Synthesis of some of the target molecules by other routes were reported earlier. Reaction of substituted salicyaldehydes with ethyl-3-aminocrotonate in acetic acid medium gave coumarin fused to pyridines.[6] Reaction of chromone-3-carboxaldehyde with methyl acetoacetate and ammonia in methanol gave 1,4-dihydropyridyl chromones.[7] The synthesis of chromones fused to pyrano-pyridines fused at 7 : 8 by the reaction of 7-hydroxy-8-formyl-2,3-dimethyl chromones with ethyl-3-aminocrotonate in acetic acid under Hantzsch conditions.[8] Irradiation of 4-aryl/alkyl-1,4-dihydropyridine derivatives results in the formation of a pyridine product by dehydrogenation.[9] Oxygen plays an important role in oxidation. Ceric ammonium nitrate (CAN) can also oxidize the dihydropyridines to pyridine derivatives with stirring at room temperature.

In this article, we report the synthesis of 7-methoxy-2-aryl-3-phenyl/or-H-8-[2-(4,6-dimethyl-3,5-dicarbethoxy-pyridyl)]-4H-1-benzopyran-4-ones **(7a–f)** and 8-formyl-7-methoxy-2-phenyl-4H-1-benzopyran-4-ones **(5a–f)**. 7-Hydroxy-2-phenyl-4H-1-benzo- pyran-4-ones **(1a–f)** on reaction with hexamine **(2)** in glacial acetic acid (Duff reaction)[10] gave 8-formyl-7-hydroxy-2-phenyl-4H-1-benzopyran-4-ones **(3a–f)**.

Compounds **3a–f** and dimethylsulphate **(4)** in acetone–K_2CO_3 medium refluxed in a steam bath for 6–8 h gave 8-formyl-7-methoxy-2-phenyl-4H-1-benzopyran-4-ones **(5a–f)**. Compound **5a** is characterized from its spectral data. In MS, it showed a quasi-molecular ion peak at m/z-357. Its IR spectrum showed peaks due to the aldehyde carbonyl group (C═O) at 1693 cm^{-1} and at 1609 cm^{-1} due to flavone carbonyl group (C═O). Its UV spectrum showed absorption maxima at 315 nm (log ε 4.26), 256 nm (log ε 4.36), and 229 nm (log ε 4.22). In its ^{1}H NMR spectrum, recorded in $CDCl_3$ (200 MHz), the H-5 proton resonated at δ 8.40 (d, $J = 10$ Hz) whereas the H-6 proton resonated at δ 7.00 (d, $J = 10$ Hz). The C-7 methoxy group protons (7-OCH_3) appeared at δ 4.10 as singlet, and the C-8 carboxaldehyde proton (8-CHO) appeared at δ 10.60 as singlet. Aromatic protons appeared at δ 7.10–7.50 (10H) as multiplet. Its ^{13}C NMR spectrum, recorded in $CDCl_3$ (50.3 M Hz), showed a chemical shift at δ 186.05 due to carbonyl carbon of carboxaldehyde. The peak at δ 178.10 is due to flavone carbonyl carbon. The oxymethine carbons C-2, C-7, and C-8a resonated at δ 168.50, 163.20, and 161.05, respectively, and the methoxyl carbon resonated at δ 56.30. Other carbons resonated at δ 106.75 (C-3), 128.05 (C-5), 107.05 (C-6), 110.05 (C-8), 117.50 (C-4a), C-1′ (129.50), 126.50 (C-2′ & C-6′), 128.40 (C-3′ & C-5′), 132.02 (C-4′), 131.50 (C-1″), 130.75 (C-2″ & C-6″), 128.05 (C-3″ & C-5″), and 127.50 (C-4″) respectively.

8-Formyl-7-methoxy-2-phenyl-4H-1-benzopyran-4-ones **(5a–f)** were condensed with 2 equivalent moles of ethyl-3-aminocrotonate **(6)** in glacial

acetic acid under Hantzsch conditions to afford 7-methoxy-2-aryl-3-phenyl/or-H-8-[2-(4,6-dimethyl-3,5-dicarbethoxy-pyridyl)]-4H-1-benzopyran-4-ones **(7a–f)** (Scheme 1). Compound **7a** is characterized from its spectral data. In MS, it showed a quasi-molecular ion peak at m/z-578. Its IR spectrum showed two peaks at 1731 cm^{-1} due to the ester carbonyl group (C═O) and 1644 cm^{-1} due to the carbonyl group (C═O) of flavone. Its UV spectrum showed absorption maxima at 312 nm (log ε 4.69) and 242 nm (log ε 4.93). Its ^1H NMR spectrum, recorded in $CDCl_3$ (200 MHz), showed the characteristic peaks of the heterocyclic substituted pyridyl ring attached to the eighth position of the flavone ring. It showed two singlets at δ 2.40 and δ 2.65 due to the C-4‴-methyl and C-6‴-methyl of the pyridine ring. The protons of 3‴-O-$\underline{CH_2}$-CH_3 and 5‴-O-$\underline{CH_2}$-CH_3 resonate at δ 4.45 and δ 4.00 as quartets ($J = 7.0$ Hz). The protons of 3‴-O-CH_2-$\underline{CH_3}$ and 5‴-O-CH_2-$\underline{CH_3}$ resonate at δ 1.48 and δ 0.90 as triplets. The C-7 methoxy group protons (7-OCH_3) appeared at δ 3.85 as a singlet. The H-5 proton



Scheme 1.

resonated at δ 8.35 as a doublet ($J = 10$ Hz). Aromatic protons appeared at δ 7.05–7.40 (11H) as a multiplet (side phenyl protons and C_6-H). Its ^{13}C NMR spectrum, recorded in $CDCl_3$ (50.3 MHz), showed characteristic peaks of the newly formed pyridyl ring. The two methyl carbons of the pyridyl ring appeared at 17.05 (C-4‴) and at 23.75 (C-6‴). It showed a chemical shift at δ 176.50 due to carbonyl carbon of flavone and carbonyl of carbethoxy ester carbons at δ 168.05 (C-5‴-COOEt) and 166.50 (C-3‴-COOEt). Sp^3 carbons of 7**a** -COO-$\underline{CH_2}$-CH_3 appeared at 62.05 (C-5‴) and at 61.50 (C-3‴), and -COO-CH_2-$\underline{CH_3}$ carbons appeared at 14.05 (C-5‴) and at 13.10 (C-3‴). The pyridyl ring carbons resonated at δ 129.05 (C-1‴), 161.05 (C-6‴), 155.75 (C-4‴), 122.02 (C-3‴), and 122.02 (C-5‴). The oxymethine carbons C-2, C-7, and C-8a resonated at δ 154.50, 149.50, and 143.75, respectively, and the methoxyl carbon resonated at δ 56.05. Other Sp^2 carbons resonated at δ 109.02 (C-3), 109.02 (C-6), 129.15 (C-5), 116.50 (C-8), 117.50 (C-4a), C-1′ (129.50), 127.20 (C-2′ & C-6′), 128.10 (C-3′ & C-5′), 131.02 (C-4′), 132.75 (C-1″), 129.75 (C-2″ & C-6″), 131.05 (C-3″ & C-5″), and 131.02 (C-4″).

EXPERIMENTAL

Melting points were determined on a Polmon instrument (model no. MP 96). IR spectra were recorded on FT-IR Perkin-Elmer 1605 spectrometer, and ^1H NMR (200 MHz) and ^{13}C NMR (50.3 MHz) were recorded on a Varian Gemini 200 spectrometer using TMS as internal standard (chemical shifts in δ ppm). UV spectra were obtained on a Shimadzu UV-visible spectrophotometer (model UV-1601). Mass spectra were recorded on a VG micromass 70-70H instrument.

General Procedure

7-Hydroxy-2-phenyl-4H-1-benzopyran-4-ones (**1a**–**f**) by Modified Baker–Venkataraman Transformation

A mixture of resacetophenone (1.52 g, 10 mmol), benzoylchloride (2.80 g, 20 mmol), anhydrous potassium carbonate (10 g), and acetone (200 ml) was refluxed for 8–10 h by a modified Baker–Venkataraman transformation to give the intermediate diketone, which on treatment with aqueous potassium carbonate underwent cyclisation to give 7-benzoyloxy-2-phenyl-4H-1-benzopyran-4-one (not isolated). The 7-benzoyloxy group was further hydrolyzed by alkali to give 7-hydroxy-2-phenyl-4H-1-benzopyran-4-ones **(1a–f)** in 70% yield. Compounds **1a**–**c** and **1e** are known and were reported in literature, and **1d** and **1f** are new. Their analytical and spectral data are presented here.

Data

2-(2-Chlorophenyl)-7-hydroxy-4H-1-benzopyran-4-one (1d): Recrystallized from methanol as pale yellow crystals, mp 210°C (70%); IR (KBr) 3422 (OH) cm^{-1}, 1638 (C═O) cm^{-1}; UV (MeOH) 242 nm (log ε 3.98), 254 nm (log ε 3.94), and 304 nm (log ε 3.99). MS (EI) M^+ m/z at 272 (50%). ^{1}H NMR (200 MHz) ($CDCl_3$): δ 6.55 (s, H-3), 7.00 (dd, $J = 10$, 2.0, H-6), 7.10 (s, H-8), 8.00 (d, $J = 10.0$ Hz, H-5), 7.40–7.60 (m, 4H, aromatic protons), 10.25 (s, OH). Anal. calcd. for $C_{15}H_9O_3Cl$: C, 66.07; H, 3.33; found C, 66.08; H, 3.34%.

7-Hydroxy-2-(2-phenoxyphenyl)-4H-1-benzopyran-4-one (1f): Recrystallised from methanol as pale yellow coloured crystals, mp 224°C (70%); IR (KBr) 3406 (OH) cm^{-1}, 1632 (C═O) cm^{-1}; UV (MeOH) 256 nm (log ε 4.04), 270 nm (log ε 3.99), and 308 nm (log ε 4.22). MS (EI) M^+ m/z at 330 (45%). ^{1}H NMR (200 MHz) ($CDCl_3$): δ 6.70 (s, H-3), 7.00 (dd, $J = 10$ 2.0, H-6), 6.95 (s, H-8), 7.95 (d, $J = 10.0$ Hz, H-5), 7.05–7.65 (m, 8H, aromatic protons), 10.30 (s, OH). Anal. calcd. for $C_{21}H_{14}O_4$: C, 76.36; H, 4.27; found C, 76.30; H, 4.29%.

General Procedure

8-Formyl-7-hydroxy-2-phenyl-4H-benzopyran-4-ones (**3a–f**)

A solution of 7-hydroxy-2-phenyl-4H-1-benzopyran-4-ones (10 mmol) **(1a–f)** dissolved in glacial acetic acid (50 ml) was treated with hexamethylene tetrammine (40 mmol) (HMT) and heated in a water bath for 6–8 h. The solution is treated with hot dil. HCl (1 : 1) followed by further heating for 30 min. It was diluted to 500 ml with water and left overnight in a refrigerator. The reaction mixture was then extracted with ether, and the ethereal solution was washed with sodiumbicarbonate solution and water. Concentration of the dried ether extract furnished crude 8-formyl-7-hydroxy-2-phenyl-4H-1-benzopyran-4-one **(3a–f)** in 72% yields. These were recrystallized from benzene as pale yellow crystals. Compounds **3a–c** and **3e** are known and were reported in literature, and **3d** and **3f** are new. Their analytical and spectral data are presented here.

Data

2-(2-Chlorophenyl)-8-formyl-7-hydroxy–4H-1-benzopyran-4-one (3d): Recrystallized from methanol as pale yellow crystals, mp 144°C (66%); IR (KBr) 1675 (aldehyde > C═O) cm^{-1}, 1625 (flavone > C═O) cm^{-1}; UV (MeOH) 306 nm (log ε 4.27), 262 nm (log ε 4.41), and 238 nm (log ε

4.50). MS (EI) M^+ m/z at 300 (45%). ^{1}H NMR (200 MHz) ($CDCl_3$): δ 6.60 (s, H-3), 7.00 (d, $J = 10.0$ Hz, H-6), 8.35 (d, $J = 10.0$ Hz, H-5), 7.20–7.60 (m, 4H, aromatic protons), 10.50 (s, CHO), 12.45 (s, OH). Anal. calcd. for $C_{16}H_9O_4Cl$: C, 63.91; H, 3.02; found C, 63.93; H, 3.04%.

8-Formyl-7-hydroxy-2-(2-phenoxyphenyl)-4H-1-benzopyran-4-one (3f): Recrystallized from methanol as pale yellow crystals, mp 192°C (65%); IR (KBr) 1682 (aldehyde > C═O) cm^{-1}, 1633 (flavone > C═O) cm^{-1}; UV (MeOH) 305 nm (log ε 4.50), 257 nm (log ε 4.55), and 233 nm (log ε 4.79). MS (EI) M^+ m/z at 356 (55%). ^{1}H NMR (200 MHz) ($CDCl_3$): δ 6.75 (s, H-3), 7.00 (d, $J = 10.0$ Hz, H-6), 8.35 (d, $J = 10.0$ Hz, H-5), 7.05–7.50 (m, 9H, aromatic protons), 10.50 (s, CHO), 12.40 (s, OH). Anal. calcd. for $C_{22}H_{14}O_5$: C, 73.74; H, 3.94; found C, 73.76; H, 3.96%.

General Procedure

8-Formyl-7-methoxy-2-phenyl-4H-1-benzopyran-4-ones (**5a–f**)

A mixture of 8-formyl-7-hydroxy-2-phenyl-4H-1-benzopyran-4-one (10 mmol) **(3a–f)** and dimethylsulphate (10 mmol) dissolved in dry acetone (100 ml) containing anhydrous potassium carbonate was refluxed in a water bath for 6–8 h. Acetone solution is evaporated and the residual solid poured over crushed ice in a beaker. On filtration, the crude solid separates and was recrystallized from benzene to afford 8-formyl-7-methoxy-2-phenyl-4H-1-benzopyran-4-ones **(5a–f)** as colorless crystals in 85% yields. Compounds **5a–f** were characterized by analytical and spectral data.

Data

2,3-Diphenyl-8-formyl-7-methoxy-4H-1-benzopyran-4-one (5a): Recrystallized from methanol as pale yellow crystals, mp 14°C (85%); IR (KBr) 1693 (aldehyde > C═O) cm^{-1}, 1609 (flavone > C═O) cm^{-1}; UV (MeOH) 315 nm (log ε 4.26), 256 nm (log ε 4.36), and 229 nm (log ε 4.49). MS (EI) M^+ m/z at 356 (35%). ^{1}H NMR (200 MHz) ($CDCl_3$): δ 7.00 (d, $J = 10.0$ Hz, H-6), 8.40 (d, $J = 10.0$ Hz, H-5), 7.10–7.50 (m, 10H, aromatic protons), 10.60 (s, CHO), 4.10 (s, 3H, OMe). Anal. calcd. for $C_{23}H_{16}O_4$: C, 77.52; H, 4.53; found C, 77.53; H, 4.54%.

8-Formyl-7-methoxy-2-(4-methoxyphenyl)-3-phenyl-4H-1-benzopyran-4-one (5b): Recrystallized from methanol as pale yellow crystals, mp 195°C (82%); IR (KBr) 1670 (aldehyde > C═O) cm^{-1}, 1630 (flavone > C═O) cm^{-1}; UV (MeOH) 315 nm (log ε 4.70), 254 nm (log ε 4.86), and 230 nm

(log ε 4.59). MS (EI) M^+ m/z at 386 (45%). ^{1}H NMR (200 MHz) ($CDCl_3$): δ 6.80 (d, $J = 10.0$ Hz, H-6), 8.45 (d, $J = 10.0$ Hz, H-5), 7.20–7.40 (m, 5H, aromatic protons), 7.50 (d, 2H, $J = 9$ Hz, H-2′, 6′), 7.10 (d, 2H, $J = 9$ Hz, H-3′, 5′), 10.65 (s, CHO), 4.10 (s, 3H, OMe), 3.95 (s, 3H, OMe). Anal. calcd. for $C_{24}H_{18}O_5$: C, 74.80; H, 4.70; found C, 74.82; H, 4.72%.

8-Formyl-7-methoxy-2-phenyl-4H-1-benzopyran-4-one (5c): Recrystallized from methanol as pale yellow crystals, mp 210°C (84%); IR (KBr) 1693 (aldehyde > C═O) cm^{-1}, 1633 (flavone > C═O) cm^{-1}; UV (MeOH) 316 nm (log ε 4.30), 248 nm (log ε 4.55), and 220 nm (log ε 4.59). MS (EI) M^+ m/z at 280 (60%). ^{1}H NMR (200 MHz) ($CDCl_3$): δ 6.75 (s, 1H), 7.05 (d, $J = 10.0$ Hz, H-6), 8.35 (d, $J = 10.0$ Hz, H-5), 7.50–7.90 (m, 5H, aromatic protons), 10.70 (s, CHO), 4.05 (s, 3H, OMe), 3.95 (s, 3H, 4″-OMe). Anal. calcd. for $C_{17}H_{12}O_4$: C, 72.65; H, 4.32; found C, 72.67; H, 4.34%.

2-(2-Chlorophenyl)-8-formyl-7-methoxy-4H-1-benzopyran-4-one (5d): Recrystallized from methanol as pale yellow crystals, mp 195°C (78%); IR (KBr) 1683 (aldehyde > C═O) cm^{-1}, 1636 (flavone > C═O) cm^{-1}; UV (MeOH) 304 nm (log ε 4.30), 253 nm (log ε 4.54), and 222 nm (log ε 4.58). MS (EI) M^+ m/z at 314 (50%). ^{1}H NMR (200 MHz) ($CDCl_3$): δ 6.85 (s, 1H), 7.05 (d, $J = 10.0$ Hz, H-6), 8.40 (d, $J = 10.0$ Hz, H-5), 7.30–7.70 (m, 4H, aromatic protons), 10.50 (s, CHO), 4.10 (s, 3H, OMe). Anal. calcd. for $C_{17}H_{11}O_4Cl$: C, 64.86; H, 3.52; found C, 64.90; H, 3.54%.

8-Formyl-7-methoxy-2-(4-methoxyphenyl)-4H-1-benzopyran-4-one (5e): Recrystallized from methanol as pale yellow crystals, mp 168°C (80%); IR (KBr) 1685 (aldehyde > C═O) cm^{-1}, 1643 (flavone > C═O) cm^{-1}; UV (MeOH) 308 nm (log ε 4.26), 254 nm (log ε 4.40) and 218 nm (log ε 4.46). MS (EI) M^+ m/z at 310 (48%). ^{1}H NMR (200 MHz) ($CDCl_3$): δ 6.65 (s, 1H, H-3), 7.05 (d, $J = 10.0$ Hz, H-6), 8.40 (d, $J = 10.0$ Hz, H-5), 8.05 (d, 2H, $J = 9$ Hz, H-2′, 6′), 7.05 (d, 2H, $J = 9$ Hz, H-3′, 5′), 10.65 (s, CHO), 4.10 (s, 3H, 7-OMe), 3.90 (s, 3H, 4″-OMe). Anal. calcd. for $C_{18}H_{14}O_5$: C, 69.67; H, 4.55; found C, 69.69; H, 4.57%.

8-Formyl-7-methoxy-2-(2-phenoxyphenyl)-4H-1-benzopyran-4-one (5f): Recrystallized from methanol as pale yellow crystals, mp 159°C (75%); IR (KBr) 1688 (aldehyde > C═O) cm^{-1}, 1632 (flavone > C═O) cm^{-1}; UV (MeOH) 310 nm (log ε 3.93), 261 nm (log ε 3.98), and 225 nm (log ε 4.08). MS (EI) M^+ m/z at 372 (45%). ^{1}H NMR (200 MHz) ($CDCl_3$): δ 6.75 (s, 1H), 7.05 (d, $J = 10.0$ Hz, H-6), 8.45 (d, $J = 10.0$ Hz, H-5), 7.50–7.90 (m, 9H, aromatic protons), 10.50 (s, CHO), 4.05 (s, 3H, OMe). Anal. calcd. for $C_{23}H_{16}O_5$: C, 74.19; H, 4.33; found C, 74.21; H, 4.35%.

General Procedure

7-Methoxy-2-aryl-3-phenyl/or-H-8-[2-(4,6-dimethyl-3,5-dicarbethoxy-pyridyl)]-4H-1-benzopyran-4-ones (**7a**–**f**)

A mixture of 8-formyl-7-methoxy-2-phenyl-4H-1-benzopyran-4-one **(5a**–**f)** (10 mmol) and ethyl-3-aminocrotonate **(6)** (20 mmol) in acetic acid (20 ml) is kept at room temperature for 4 days with constant stirring. It was diluted to 100 ml with ice-cold water and left overnight at room temperature. The reaction mixture was then extracted with ethyl acetate to give a crude product. Crude product on column chromatography over silica gel by eluting with petroleum ether–ethyl acetate (v/v, 7 : 3) gave **7a**–**f** in 75% yields. Compounds **7a**–**f** were characterized by analytical and spectral data.

Data

2,3-Diphenyl-7-methoxy-8-[2-(4,6-dimethyl-3,5-dicarbethoxy-pyridyl)]-4H-1-benzopyran-4-one (7a): Recrystallized from methanol as pale yellow coloured crystals, mp 140°C (75%); IR (KBr) 1731 (ester > C═O) cm^{-1}, 1644 (flavone > C═O) cm^{-1}; UV (MeOH) 312 nm (log ε 4.69), 242 nm (log ε 4.93). MS (EI) M^+ m/z at 577 (35%). ^{1}H NMR (200 MHz) ($CDCl_3$): δ 8.35 (d, $J = 10.0$ Hz, H-5), 7.05–7.40 (m, 11H, H-6 merged, aromatic protons), 3.85 (s, 3H, 7-OMe), 4.45 (q, 2H, $J = 7$ Hz, 3‴-O$\underline{CH_2}$-CH_3), 4.00 (q, 2H, $J = 7$ Hz, 5‴-O$\underline{CH_2}$-CH_3), 2.65 (s, 3H, 6‴-CH_3), 2.40 (s, 3H, 4‴-CH_3), 1.48 (t, 3H, 3‴-OCH_2-$\underline{CH_3}$), 0.90 (q, 2H, 5‴-OCH_2-$\underline{CH_3}$). Anal. calcd. for $C_{35}H_{31}NO_7$: C, 72.78; H, 5.41; N, 2.42; found C, 72.80; H, 5.43; N, 2.44%.

7-Methoxy-2-(4-methoxyphenyl)-3-phenyl-8-[2-(4,6-dimethyl-3,5-dicarbethoxy-pyridyl)]-4H-1-benzopyran-4-one (7b): Recrystallized from methanol as pale yellow crystals, mp 182°C (74%); IR (KBr) 1725 (ester > C═O) cm^{-1}, 1603 (flavone > C═O) cm^{-1}; UV (MeOH) 315 nm (log ε 4.30), 249 nm (log ε 4.50). MS (EI) M^+ m/z at 507 (25%). ^{1}H NMR (200 MHz) ($CDCl_3$): δ 8.25 (d, $J = 10.0$ Hz, H-5), 7.85 (d, 2H, $J = 9$ Hz, H-2′, 6′), 7.10–7.40 (m, 5H, aromatic protons), 6.95 (d, 2H, $J = 9$ Hz, H-3′, 5′), 6.75 (d, $J = 10$ Hz, H-6), 3.95 (s, 3H, 4′-OMe), 3.75 (s, 3H, 7-OMe), 4.35 (q, 2H, $J = 7$ Hz, 3‴-O$\underline{CH_2}$-CH_3), 3.95 (q, 2H, $J = 7$ Hz, 5‴-O$\underline{CH_2}$-CH_3), 2.75 (s, 3H, 6‴-CH_3), 2.25 (s, 3H, 4‴-CH_3), 1.45 (t, 3H, 3‴-OCH_2-$\underline{CH_3}$), 1.05 (q, 2H, 5‴-OCH_2-$\underline{CH_3}$). Anal. calcd. for $C_{36}H_{31}NO_8$: C, 71.16; H, 5.47; N, 2.31; found C, 71.18; H, 5.49; N, 2.33%.

7-Methoxy-2-phenyl-8-[2-(4,6-dimethyl-3,5-dicarbethoxy-pyridyl)]-4H-1-benzopyran-4-one (7c): Recrystallized from methanol as pale yellow crystals, mp 175°C (78%); IR (KBr) 1718 (ester > C═O) cm^{-1}, 1644

(flavone > C═O) cm^{-1}; UV (MeOH) 310 nm (log ε 4.06), 243 nm (log ε 4.38). MS (EI) M^+ m/z at 501 (20%). ^1H NMR (200 MHz) ($CDCl_3$): δ 8.30 (d, $J = 10.0$ Hz, H-5), 7.05 (d, $J = 10$ Hz, H-6), 6.75 (s, 1H, H-3), 7.60–8.05 (m, 5H, aromatic protons), 4.05 (s, 3H, 7-OMe), 4.50 (q, 2H, $J = 7$ Hz, 3‴-O$\underline{CH_2}$-CH_3), 4.05 (q, 2H, $J = 7$ Hz, 5‴-O$\underline{CH_2}$-CH_3), 2.55 (s, 3H, 6‴-CH_3), 2.45 (s, 3H, 4‴-CH_3), 1.50 (t, 3H, 3‴-OCH_2-$\underline{CH_3}$), 1.05 (q, 2H, 5‴-OCH_2-$\underline{CH_3}$). Anal. calcd. for $C_{29}H_{27}NO_7$: C, 69.45; H, 5.43; N, 2.79; found C, 69.47; H, 5.45; N, 2.81%.

2-(2-Chlorophenyl)-7-methoxy-8-[2-(4,6-dimethyl-3,5-dicarbethoxypyridyl)]-4H-1-benzopyran-4-one (7d): Recrystallized from methanol as pale yellow crystals, mp 172°C (72%); IR (KBr) 1725 (ester > C═O) cm^{-1}, 1610 (flavone > C═O) cm^{-1}; UV (MeOH) 312 nm (log ε 4.50), 237 nm (log ε 4.68). MS (EI) M^+ m/z at 535 (30%). ^1H NMR (200 MHz) ($CDCl_3$): δ 8.25 (d, $J = 10.0$ Hz, H-5), 7.10 (d, $J = 10$ Hz, H-6), 6.65 (s, 1H, H-3), 7.30–7.60 (m, 4H, aromatic protons), 3.95 (s, 3H, 7-OMe), 4.45 (q, 2H, $J = 7$ Hz, 3‴-O$\underline{CH_2}$-CH_3), 3.95 (q, 2H, $J = 7$ Hz, 5‴-O$\underline{CH_2}$-CH_3), 2.60 (s, 3H, 6‴-CH_3), 2.40 (s, 3H, 4‴-CH_3), 1.45 (t, 3H, 3‴-OCH_2-$\underline{CH_3}$), 0.90 (q, 2H, 5‴-OCH_2-$\underline{CH_3}$). Anal. calcd. for $C_{29}H_{26}ClNO_7$: C, 64.99; H, 4.89; N, 2.61; found C, 65.01; H, 4.91; N, 2.63%.

7-Methoxy-2-(4-methoxyphenyl)-8-[2-(4,6-dimethyl-3,5-dicarbethoxypyridyl)]-4H-1-benzopyran-4-one (7e): Recrystallized from methanol as pale yellow crystals, mp 168°C (75%); IR (KBr) 1724 (ester > C═O) cm^{-1}, 1625 (flavone > C═O) cm^{-1}; UV (MeOH) 313 nm (log ε 4.88), 232 nm (log ε 4.99). MS (EI) M^+ m/z at 531 (50%). ^1H NMR (200 MHz) ($CDCl_3$): δ 8.25 (d, $J = 10.0$ Hz, H-5), 7.05 (d, $J = 10$ Hz, H-6), 6.75 (s, 1H, H-3), 7.40–7.95 (m, 4H, aromatic protons), 4.05 (s, 3H, 4′-OMe), 3.95 (s, 3H, 7-OMe), 4.40 (q, 2H, $J = 7$ Hz, 3‴-O$\underline{CH_2}$-CH_3), 3.95 (q, 2H, $J = 7$ Hz, 5‴-O$\underline{CH_2}$-CH_3), 2.55 (s, 3H, 6‴-CH_3), 2.40 (s, 3H, 4‴-CH_3), 1.45 (t, 3H, 3‴-OCH_2-$\underline{CH_3}$), 1.00 (q, 2H, 5‴-OCH_2-$\underline{CH_3}$). Anal. calcd. for $C_{30}H_{29}NO_8$: C, 67.79; H, 5.50; N, 2.64; found C, 67.81; H, 5.52; N, 2.66%.

7-Methoxy-2-(2-phenoxyphenyl)-8-[2-(4,6-dimethyl-3,5-dicarbethoxypyridyl)]-4H-1-benzopyran-4-one (7f): Recrystallized from methanol as pale yellow crystals, mp 165°C (70%); IR (KBr) 1725 (ester > C═O) cm^{-1}, 1610 (flavone > C═O) cm^{-1}; UV (MeOH) 316 nm (log ε 4.88), 228 nm (log ε 4.99). MS (EI) M^+ m/z at 593 (45%). ^1H NMR (200 MHz) ($CDCl_3$): δ 8.25 (d, $J = 10.0$ Hz, H-5), 7.05 (d, $J = 10$ Hz, H-6), 6.75 (s, 1H, H-3), 7.10–7.60 (m, 9H, aromatic protons), 3.95 (s, 3H, 7-OMe), 4.45 (q, 2H, $J = 7$ Hz, 3‴-O$\underline{CH_2}$-CH_3), 4.00 (q, 2H, $J = 7$ Hz, 5‴-O$\underline{CH_2}$-CH_3), 2.55 (s, 3H, 6‴-CH_3), 2.45 (s, 3H, 4‴-CH_3), 1.42 (t, 3H, 3‴-OCH_2-$\underline{CH_3}$), 1.05 (q, 2H, 5‴-OCH_2-$\underline{CH_3}$). Anal. calcd. for $C_{35}H_{31}NO_8$: C, 70.82; H, 5.26; N, 2.36; found C, 70.84; H, 5.28; N, 2.38%.

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