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CAN MEDIATED MULTICOMPONENT SYNTHESIS OF BENZOXANTHENE AND BENZOCHROMENE LIBRARIES

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Abstract: Libraries of benzoxanthenes as well as benzochromenes were efficiently synthesized via one-pot, three-component reactions of 2-naphthol, aldehydes, and cyclic 1,3-diketones/malononitrile/ethyl cyanoacetate in the presence of catalytic amount of ceric ammonium nitrate (CAN) under solvent free conditions. The protocol offers rapid synthesis of structurally diverse benzoxanthenes and benzochromenes for biologically screening. All the synthesized compounds were evaluated for their anti-proliferative activity and several compounds were exhibiting promising anti-proliferative activity.

Keywords: Benzoxanthene; Benzochromene; CAN; Multi-component reactions; Anticancer

Introduction

Design of highly efficient chemical reaction sequences that provide maximum structural complexity and diversity with a minimum number of synthetic steps to assemble compounds with interesting properties is a major challenge of modern drug discovery [I]. Recently multi-component reactions have emerged as a highly valuable synthetic tool in the context of modern drug discovery. The atom economy and convergent character, the simplicity of a one-pot procedure, the possible structural variations, the accessible complexity of the molecules, and the very large number of accessible compounds are among the described advantages of multi-component reactions [II]. Thus, they are perfectly amenable to automation for combinatorial synthesis [III-VI].

Benzoxanthenes and benzochromenes are important classes of biologically active heterocycles [VII]. These compounds are being utilized as in photodynamic therapy as well as benzoxanthenes find application in laser technology [VIII]. Benzoxanthenes have also been employed as dyes [IX], pH sensitive fluorescent materials for visualization of biomolecules [X-XI]. Many benzoxanthene derivatives are potent nonpeptidic inhibitors of recombinant human calpain I [XII], and novel CCR1 receptor antagonists [XIII]. Benzochromenes are

widely employed as pigments, cosmetics, potential agrochemicals, and also as components of many natural products [XIV-XVI].

Due to enormous biological and industrial importance associated with benzo(xanthenes)chromenes, various methods of their preparation has been reported [XVII-XXVI]. In our continuing efforts towards the developments of improved synthetic routes for biologically important heterocycles [XXVII-XXX] we report here a rapid and efficient synthesis of structurally diverse libraries of benzo(xanthenes)chromenes.

General Information: Unless otherwise specified all the reagents and catalysts were purchased from Sigma-Aldrich and were used without further any purification. The common organic solvents were purchased from Ranbaxy. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Chromatographic purification of products was accomplished using flash chromatography on 230-400 mesh silica gel. Reactions were monitored by thin-layer chromatography (TLC) on 0.25mm silica gel plates visualized under UV light, iodine or $KMnO_4$ staining. ^1H and ^{13}C NMR spectra were recorded on a Brucker DRX -200 & 300 Mhz Spectrometer. Chemical shifts (δ) are given in ppm relative to TMS and coupling constants (*J*) in Hz. IR spectra were recorded on a FT IR spectrophotometer Shimadzu 8201 PC and are reported in terms of frequency of absorption (cm^{-1}). Mass spectra (ESI MS) were obtained by Micromass Quattro II instrument.

General procedure for the synthesis of 12-substituted-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-ones (4a-o): In a 25 ml round bottom flask, 2-naphthol (1 mmol), cyclic 1,3-diketone (1 mmol), aldehyde (1 mmol) and CAN (5 mol %) were taken. The reaction mixture was heated at 120 ^{0}C for 30 minutes under solvent free conditions. The reaction was followed by TLC monitoring. After completion, ethyl acetate was added to the reaction mixture and was shaken well to dissolve all organic compounds. Then it was filtered to remove CAN. The filtrate was concentrated and the crude obtained was purified by silica-gel column chromatography to yield pure compounds.

General procedure for the synthesis of 14-substituted-14H-dibenzo[a, j]xanthenes (5a-n): In a 25 ml round bottom flask, aldehyde (1 mmol), 2-naphthol (2 mmol), and CAN (5 mol %) were taken. The reaction mixture was stirred at 120 ^{0}C under solvent-free conditions for 30 minutes. After completion, the reaction mixture was cooled to room temperature and ethyl acetate was added and shaken well to dissolve all organic components then filtered to remove CAN. The filtrate was concentrated to yield crude which was purified by silica gel column chromatography.

General procedure for the synthesis of 3-amino-1-substituted-1H-benzo[f]chromenes (7a-k): In a 25 ml round bottom flask, aldehyde (1 mmol), 2-naphthol (1 mmol), malononitrile/ethyl cynoacetate (1 mmol), and CAN (5 mol %) were taken. The reaction mixture was stirred at 120 ^{0}C under solvent-free conditions for 30 minutes. After completion, the reaction mixture was cooled to room temperature and ethyl acetate was added and shaken well to dissolve all organic components then filtered to remove CAN. The filtrate was concentrated to yield crude which was purified by silica gel column chromatography.

Characterization data for synthesized compounds:

9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4a). Mp 154-155 ^{0}C; ESI MS (m/z) = 355 [M+H]. IR (KBr, cm^{-1}): 3125, 2954, 1651, 1595, 1398, 1375, 1228, 1176, 1025, 808, 743, 699, 510. ^1H NMR ($CDCl_3$, 300 MHz) δ = 0.96 (s, 3H), 1.11 (s, 3H), 2.27 (dd, *J* = 7.0 & 16.0 Hz, 2H), 2.57 (s, 2H), 5.71 (s, 1H), 7.03-7.06 (m, 1H), 7.15-7.18 (m, 2H), 7.31-7.44 (m, 5H), 7.75-7.78 (m, 2H), 7.99 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 27.2, 29.3, 32.3, 34.7, 41.4, 50.9, 114.3, 117.0, 117.7, 123.7147.8, 124.9, 126.3, 127.0, 128.3, 128.4, 128.5, 128.9, 131.4, 131.5, 144.7, 163.9, 196.9. Elemental Analysis Calculated for $C_{25}H_{22}O_2$: C, 84.72; H; 6.26. Found: C, 84.75; H; 6.28.

12-(4-methoxyphenyl)-9,9-dimethyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4b). Mp 205-206 ^{0}C; ESI MS (m/z) = 385 [M+H]. IR (KBr, cm^{-1}): 3121, 2958, 1652, 1607, 1507, 1462, 1382, 1218, 1143, 1028, 834, 747, 661, 539. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 0.97 (s, 3H), 1.11 (s, 3H), 2.27 (dd, *J* = 6.0 & 16.0 Hz, 2H), 2.56 (s, 2H), 3.68 (s, 3H), 5.65 (s, 1H), 6.69-6.71 (m, 2H), 7.24-7.45 (m, 5H), 7.74-7.78 (m, 2H), 7.98 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 27.2, 29.3, 32.3, 33.9, 41.4, 50.9, 55.1, 113.6, 114.4, 117.1, 117.9, 123.7, 124.9, 127.0, 128.4, 128.7, 129.4, 131.4, 131.5, 137.2, 147.7, 157.8, 163.7, 197.0. Elemental Analysis Calculated for $C_{26}H_{24}O_3$: C, 81.22; H; 6.29. Found: C, 81.15; H; 6.20.

12-(4-chlorophenyl)-9,9-dimethyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4c). Mp 181-182 ^{0}C; ESI MS (m/z) = 389 [M+H]. IR (KBr, cm^{-1}): 3133, 2958, 1648, 1596, 1483, 1400, 1375, 1224, 1139, 1009, 841, 747, 535. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 0.96 (s, 3H), 1.12 (s, 3H), 2.28 (dd, *J* = 8.5 & 16.0 Hz, 2H), 2.56 (s, 2H), 5.68 (s, 1H), 7.12-7.14 (m, 2H), 7.25-7.45 (m, 5H), 7.76-7.79 (m, 2H), 7.90 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 27.1, 29.3, 32.3, 34.2, 41.4, 50.9, 113.9, 117.1, 123.5, 125.0, 127.2, 128.4, 128.5, 129.1, 129.8, 131.2, 131.5, 131.9, 143.3, 147.7, 164.1, 196.9. Elemental Analysis Calculated for $C_{25}H_{21}ClO_2$: C, 77.21; H; 5.44. Found: C, 77.12; H; 5.33.

12-(3,4-dimethylphenyl)-9,9-dimethyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4d). Mp 181-182 ^{0}C; ESI MS (m/z) = 383 [M+H]. IR (KBr, cm^{-1}): 3125, 2958, 1650, 1593, 1398, 1371, 1237, 1226, 1172, 819, 747, 478. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 0.99 (s, 3H), 1.11 (s, 3H), 2.09 (s, 3H), 2.13 (s, 3H), 2.27 (dd, *J* = 4.0 & 16.0 Hz, 2H), 2.56 (dd, *J* = 2.5 & 17.5 Hz, 2H), 5.63 (s, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 7.03-7.10 (m, 2H), 7.25-7.43 (m, 3H), 7.72-7.77 (m, 2H), 8.04 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 19.4, 20.0, 27.4, 29.2, 32.4, 34.3, 41.4, 51.0, 114.5, 117.1, 118.1, 123.8, 124.9, 125.9, 127.0, 128.4, 128.7, 129.5, 129.7, 131.5, 134.4, 136.2, 142.3, 147.7, 163.8, 196.2. Elemental Analysis Calculated for $C_{27}H_{26}O_2$: C, 84.78; H; 6.85. Found: C, 84.71; H; 6.80.

9,9-dimethyl-12-(3-nitrophenyl)-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4e). Mp 169-170 ^{0}C; ESI MS (m/z) = 400 [M+H]. IR (KBr cm^{-1}): 3125, 2954, 2864, 1649, 1596, 1529, 1375, 1344, 1225, 1025, 812, 748, 683, 510. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 0.95 (s, 3H), 1.13 (s, 3H), 2.29 (dd, J_1 = 13.0 & 16.0 Hz, 2H), 2.61 (s, 2H), 5.82 (s, 1H), 7.35-7.47 (m, 4H), 7.79-8.12 (m, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 27.1, 29.3, 32.3, 34.8, 41.4, 50.8, 113.1, 116.0, 117.3, 121.6, 123.1, 123.3, 125.2, 127.4, 128.7, 129.1, 129.7, 131.0, 131.6, 134.9, 146.8, 147.8, 148.4, 164.6, 196.8. Elemental Analysis Calculated for $C_{25}H_{21}NO_4$: C, 75.17; H; 5.30; N, 3.51. Found: C, 75.08; H; 5.20; N, 3.38.

9,9-dimethyl-12-(thiophen-2-yl)-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4f). Mp 180-181 ^{0}C; ESI MS (m/z) = 361 [M+H]. IR (KBr, cm^{-1}): 3105, 2958, 1651, 1593, 1376, 1224, 1177, 1147, 1009, 813, 746, 700, 661, 507. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 1.05 (s, 3H), 1.14 (s, 3H), 2.35 (s, 2H), 2.57 (s, 2H), 6.04 (s, 1H), 6.74-6.77 (m, 2H), 7.00-7.01 (m, 1H), 7.30-7.51 (m, 3H), 7.78-7.82 (m, 2H), 8.04 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 27.2, 29.3, 29.4, 32.3, 41.4, 50.9, 113.8, 117.1, 117.2, 123.5, 124.0, 125.0, 125.1, 126.3, 127.2, 128.4, 129.1, 131.4, 147.8, 148.6, 164.6, 196.8. Elemental Analysis Calculated for $C_{23}H_{20}O_2S$: C, 76.64; H; 5.59. Found: C, 76.55; H; 5.50.

12-tert-butyl-9,9-dimethyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4g). Mp 110-111 ^{0}C; ESI MS (m/z) = 335 [M+H]. IR (KBr, cm^{-1}): 3125, 2962, 1642, 1592, 1394, 1220, 1176, 1005, 812, 750, 616, 490. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 0.78 (s, 9H), 1.14 (s, 3H), 1.27 (s, 3H), 2.28 (d, *J* = 16.5 Hz, 1H), 2.42 (d, *J* = 16.5 Hz, 1H), 2.52 (d, *J* = 18.0 Hz, 1H), 2.65 (d, *J* = 18.0 Hz, 1H), 4.62 (s, 1H), 7.28 (d, *J* = 9.0 Hz, 1H), 7.40-7.43 (m, 1H), 7.49-7.52 (m, 1H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 8.21 (d, *J* = 9.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 27.4, 27.8, 30.1, 31.7, 35.9, 40.0, 41.6, 51.0, 113.9, 116.8, 118.4, 124.6,

126.0, 127.8, 128.2, 131.3, 132.7, 150.6, 167.6, 197.2. Elemental Analysis Calculated for $C_{23}H_{26}O_2$: C, 82.60; H; 7.84. Found: C, 82.51; H; 7.71.

12-ethyl-9,9-dimethyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4h). Yellow oil; ESI MS (m/z) = 307 [M+H]. IR (Neat, cm^{-1}): 3130, 2960, 1651, 1595, 1394, 1225, 1177, 1145, 813, 748, 649, 480. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 0.61 (t, *J* = 7.5 Hz, 3H), 1.16 (s, 3H), 1.20 (s, 3H), 1.83-1.86 (m, 2H), 2.37 (d, *J* = 4.5 Hz, 2H), 2.55 (d, *J* = 3.5 Hz, 2H), 4.74 (t, *J* = 4.0 Hz, 1H), 7.20 (d, *J* = 8.5 Hz, 1H), 7.42-7.45 (m, 1H), 7.56-7.53 (m, 1H), 7.70 (d, *J* = 9.0 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 9.0, 27.3, 27.4, 28.7, 29.7, 32.2, 41.4, 51.1, 112.1, 116.8, 117.7, 123.3, 124.8, 126.7, 128.0, 128.6, 131.2, 131.5, 148.7, 166.3, 197.6. Elemental Analysis Calculated for $C_{21}H_{22}O_2$: C, 82.32; H; 7.24. Found: C, 82.22; H; 7.30.

12-(4-hydroxyphenyl)-9,9-dimethyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4i) Mp 210 ^{0}C. ESI MS (*m/z*) = 371 (M+H). IR (KBr, cm^{-1}): 3223, 3071, 2957, 2870, 1631, 1590, 1511, 1449, 1380. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 0.97 (s, 3H), 1.11 (s, 3H), 2.18-2.36 (m, 2H), 2.57 (s, 2H), 5.65 (s, 1H), 6.61 (d, *J* = 8.5 Hz, 2H), 6.98 (s, 1H), 7.17 (d, *J* = 9.0 Hz, 2H), 7.31-7.44 (m, 3H), 7.75-7.80 (m, 2H), 7.99 (d, *J* = 8.3 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 27.1, 29.2, 32.3, 33.9, 41.4, 50.8, 114.5, 115.4, 116.9, 117.9, 123.8, 124.9, 126.9, 128.3, 128.7, 129.5, 131.4, 131.5, 136.4, 147.5, 154.5, 164.5, 198.2. Elemental Analysis calculated for $C_{25}H_{22}O_3$: C, 81.06; H, 5.99. Found C, 80.96; H, 5.90.

12-phenyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4j). Mp 202-203 ^{0}C; ESI MS (*m/z*) = 327 (M+H). IR (KBr, cm^{-1}): 3129, 3052, 2954, 1645, 1594, 1453, 1373, 1229, 1189, 999, 955, 816, 758, 701, 531. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 1.96-2.06 (m, 2H), 2.34-2.47 (m, 2H), 2.66-2.75 (m, 2H), 5.74 (s, 1H), 7.04-7.08 (m, 1H), 7.15-7.18 (m, 2H), 7.32-7.43 (m, 5H), 7.75-7.78 (m, 2H), 7.96 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 20.3, 27.8, 34.7, 37.1, 115.6, 117.0, 117.7, 123.7, 124.9, 126.3, 127.0, 128.3, 128.4, 128.5, 128.9, 131.4, 131.5, 145.1, 147.8, 165.6, 197.1. Elemental Analysis Calculated for $C_{23}H_{18}O_2$: C, 84.64; H; 5.56. Found: C, 84.50; H, 5.48.

12-(4-chlorophenyl)-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4k). Mp 208-209 ^{0}C; ESI MS (*m/z*) = 313 (M+H). IR (KBr, cm^{-1}): 3130, 3052, 2962, 1647, 1593, 1488, 1368, 1228, 1189, 1139, 1089, 1000, 954, 818, 753, 530. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 1.93-2.08 (m, 2H), 2.35-2.48 (m, 2H), 2.63-2.76 (m, 2H), 5.72 (s, 1H), 7.12-7.16 (m, 2H), 7.25-7.44 (m, 5H), 7.76-7.79 (m, 2H), 7.88 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 20.3, 27.8, 34.2, 37.0, 115.1, 117.0, 117.1, 123.5, 125.1, 127.1, 128.5, 129.1, 129.9, 131.2, 131.5, 132.0, 143.6, 147.8, 165.8, 197.1. Elemental Analysis Calculated for $C_{23}H_{17}ClO_2$: C, 76.56; H; 4.75. Found: C, 76.42; H, 4.68.

12-(3,4-dimethylphenyl)-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4l). Mp 174-175 ^{0}C; ESI MS (m/z) = 355 [M+H]. IR (KBr, cm^{-1}): 3121, 2962, 2933, 1651, 1594, 1373, 1225, 1190, 1140, 997, 955, 821, 747, 617, 495, 459. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 1.97-2.07 (m, 2H), 2.11 (s, 3H), 2.14 (s, 3H), 2.34-2.48 (m, 2H), 2.62-2.77 (m, 2H), 5.67 (s, 1H), 6.92 (d, *J* = 7.5 Hz, 1H), 7.03-7.09 (m, 2H), 7.32-7.44 (m, 3H), 7.74-7.78 (m, 2H), 7.99 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 19.3, 19.9, 20.3, 27.8, 34.2, 37.1, 115.9, 117.0, 118.1, 123.8, 124.8, 125.9, 127.0, 128.3, 128.6, 129.5, 129.7, 131.4, 131.5, 134.4, 136.3, 142.6, 147.8, 165.5, 197.0. Elemental Analysis Calculated for $C_{25}H_{22}O_2$: C, 84.72; H; 6.26. Found: C, 84.60; H; 6.15.

11-phenyl-8,9-dihydrobenzo[f]cyclopenta[b]chromen-10(11H)-one (4m). Mp 237-238 ^{0}C; ESI MS (*m/z*) = 313 (M+H). IR (KBr, cm^{-1}): 3391, 3125, 1705, 1667, 1596, 1377, 1232, 1101, 1011, 942, 811, 747, 696, 528, 509. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 2.45-2.55 (m, 2H), 2.73-2.84 (m, 2H), 5.58 (s, 1H), 7.09-7.12 (m, 1H), 7.18-7.21 (m, 2H), 7.26-7.28 (m, 2H), 7.38-7.40 (m, 3H), 7.77-7.84 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 25.4, 33.8, 36.0, 116.1, 117.4,

118.9, 124.2, 125.2, 126.6, 127.2, 128.2, 128.4, 128.5, 129.6, 131.7, 131.8, 143.6, 149.2, 177.1, 202.5. Elemental Analysis Calculated for $C_{22}H_{16}O_2$: C, 84.59; H; 5.16. Found: C, 84.48; H; 5.09.

11-(4-chlorophenyl)-8,9-dihydrobenzo[f]cyclopenta[b]chromen-10(11H)-one (4n). Mp 233-234 ^{0}C; ESI MS (*m/z*) = 347 (M+H). IR (KBr, cm^{-1}): 3426, 3131, 1699, 1658, 1396, 1233, 1088, 1013, 9445, 819, 744, 527. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 2.45-2.56 (m, 2H), 2.75-2.84 (m, 2H), 5.55 (s7.82-7.85 (m, 2H),, 1H), 7.15-7.21 (m, 4H), 7.38-7.41 (m, 3H), 7.69-7.71 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 25.4, 33.8, 35.5, 115.5, 117.4, 118.3, 124.0, 125.3, 127.3, 128.6, 128.7, 129.5, 129.9, 131.6, 131.8, 132.4, 142.0, 149.2, 177.2, 202.4. Elemental Analysis Calculated for $C_{22}H_{15}ClO_2$: C, 76.19; H; 4.36. Found: C, 76.07; H; 4.28.

11-(3,4-dimethylphenyl)-8,9-dihydrobenzo[f]cyclopenta[b]chromen-10(11H)-one (4o). Mp 223-224 ^{0}C; ESI MS (*m/z*) = 313 (M+H). IR (KBr, cm^{-1}): 3407, 3131, 1709, 1670, 1591, 1396, 1237, 943, 825, 746, 498. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 2.12 (s, 3H), 2.13 (s, 3H), 2.47-2.50 (m, 2H), 2.75-2.79 (m, 2H), 5.50 (s, 1H), 6.93-7.03 (m, 3H), 7.36-7.40 (m, 3H), 7.79-7.83 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 19.4, 19.9, 25.3, 33.8, 35.5, 116.5, 117.4, 119.2, 124.2, 125.1, 125.5, 127.1, 128.4, 129.3, 129.4, 129.7, 131.8, 131.9, 134.8, 136.6, 141.2, 149.2, 177.1, 202.5. Elemental Analysis Calculated for $C_{24}H_{20}O_2$: C, 84.68; H; 5.92. Found: C, 84.56; H; 5.85.

14-phenyl-14H-dibenzo[a,j]xanthene (5a). Mp 181 ^{0}C; ESI MS (*m/z*) = 359 (M+H). IR (KBr, cm^{-1}): 3024, 1590, 1410, 1245. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 6.49 (s, 1H), 6.98 (t, *J* = 7.6 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.48 (d, *J* = 8.8 Hz, 2H), 7.52 (d, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 2H), 7.77 (d, *J* = 8.8 Hz, 2H), 7.83 (d, *J* = 8.0 Hz, 2H), 8.40 (d, *J* = 8.4 Hz, 2H). Elemental Analysis Calculated for $C_{27}H_{18}O$: C, 90.47; H; 5.06. Found: C, 90.35; H; 4.94.

14-(3-Hydroxyphenyl)-14H-dibenzo[a.j]xanthene (5b). Mp 261-263 ^{0}C; ESI MS (*m/z*) = 375 (M+H). IR (KBr, cm^{-1}): 3446, 1620, 1588, 1247, 961, 816, 745, 694. ^{1}H NMR (DMSO-d_6, 200 MHz) δ = 6.41 (s, 1H), 6.79-7.11 (m, 3H), 7.35-7.86 (m, 12H), 8.44 (d, *J* = 9.6 Hz, 2H), 8.84 (bs, 1H). ^{13}C NMR (DMSO-d_6, 75 MHz) δ = 36.40, 113.32, 114.89, 117.53, 117.60, 118.90, 123.36, 124.36, 126.73, 128.43, 128.77, 129.00, 130.86, 131.12, 146.70, 147.88, 157.31. Elemental Analysis Calculated for $C_{27}H_{18}O_2$: C, 86.61; H; 4.85. Found: C, 86.55; H; 4.88.

14-(4-Methoxyphenyl)-14H-dibenzo[a.j]xanthene (5c). Mp 213-215 ^{0}C; ESI MS (*m/z*) = 389 (M+H). IR (KBr, cm^{-1}): 2999, 2833, 1734, 1591, 1508, 1457, 1430, 1399, 1247, 1027, 958, 829, 807, 740. ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 3.58 (s, 3H), 6.40 (s, 1H), 6.65 (d, *J* = 9.7 Hz, 2H), 7.32-7.85 (m, 12H), 8.35 (d, *J* = 9.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 36.9, 53.2, 114.3, 117.2, 118.3, 123.5, 124.1, 127.4, , 129.1, 129.4, 131.4, 133.7, 137.2, 149.3, 158.2. Elemental Analysis Calculated for $C_{28}H_{20}O_2$: C, 86.57; H; 5.19. Found: C, 86.41; H; 5.20.

14-(4-Methylphenyl)-14H-dibenzo[a.j]xanthene (5d). Mp 238-240 ^{0}C; ESI MS (*m/z*) = 373 (M+H). IR (KBr, cm^{-1}): 3020, 2908, 1620, 1591, 1509, 1457, 1430, 1247, 959, 837, 810, 739. ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 2.18 (s, 3H), 6.39 (s, 1H), 6.90 (d, *J* = 9.6 Hz, 2H), 7.32-7.80 (m, 12H), 8.36 (d, *J* = 9.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 19.1, 35.4, 115.7, 116.2, 121.3, 122.7, 125.2, 126.4, 127.4, 129.2, 129.5, 134.0, 140.8, 146.6. Elemental Analysis Calculated for $C_{28}H_{20}O$: C, 90.29; H; 5.41. Found: C, 90.32; H; 5.44.

14-(2-chlorophenyl)-14H-dibenzo[a,j]xanthene (5e). Mp 213–215 ^{0}C; ESI MS (*m/z*) = 393 (M+H). IR (KBr, cm^{-1}): 3059, 1625, 1594, 1516, 1462, 1404, 1248. ^{1}H NMR ($CDCl_3$, 300 MHz): d 6.82 (s, 1H), 6.92 (m, 2H), 7.25-7.27 (m, 1H), 7.37–7.65 (m, 8H), 7.79-7.84 (m, 4H), 8.75 (d, *J* = 8.5 Hz, 1H). Elemental Analysis Calculated for $C_{27}H_{17}ClO$: C, 82.54; H; 4.36. Found: C, 82.44; H; 4.25.

14-(4-(3-chloropropoxy)phenyl)-14H-dibenzo[a,j]xanthene (5f). Mp 158 ^{0}C; ESI MS (*m/z*) = 451 (M+H). IR (KBr, cm^{-1}): 3065, 2912, 2846, 1590, 1509, 1399, 1378, 1250, 1182. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 1.98-2.17 (m, 2H), 3.42 (t, *J* = 6.4 Hz, 1H), 3.57 (t, *J* = 6.4Hz, 1H), 3.79-3.87 (m, 2H), 6.46 (s, 1H), 6.64 (d, *J* = 8.7 Hz, 2H), 7.41-7.59 (m, 8H), 7.62-7.83 (m, 4H), 8.39 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 32.6, 37.5, 41.9, 64.4, 114.8, 117.9, 118.4, 123.1, 124.6, 127.2, 129.2, 129.2, 129.6, 131.5, 131.8, 138.0, 149.1, 157.4. Elemental Analysis Calculated for $C_{30}H_{23}ClO_2$: C, 79.90; H, 5.14. Found: C, 79.82; H, 5.05.

14-(4-chlorophenyl)-14H-dibenzo[a,j]xanthene (5g). Mp 286-288 ^{0}C; ESI MS (*m/z*) = 393 (M+H). IR (KBr, cm^{-1}): 3026, 2914, 1621, 1590, 1241. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 6.42 (s, 1H), 7.10 (d, *J* = 9.6 Hz, 2H), 7.62–7.30 (m, 12H), 8.30 (d, *J* = 9.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 35.4, 116.5, 117.2, 122.8, 124.1, 126.6, 127.9, 128.2, 128.8, 129.2, 130.2, 147.5. Elemental Analysis Calculated for $C_{27}H_{17}ClO$: C, 82.54; H; 4.36. Found: C, 82.44; H; 4.25.

14-(2,4-dichlorophenyl)-14H-dibenzo[a,j]xanthene (5h). Mp 252 ^{0}C; ESI MS (*m/z*) = 427 (M+H). IR (KBr, cm^{-1}): 3066, 2933, 1619, 1592, 1248. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 6.71 (s, 1H), 6.90 (d, *J* = 9.5 Hz, 1H), 7.23-7.82 (m, 12H), 8.60 (d, *J* = 9.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 42.8, 125.8, 126.8, 131.6, 132.9, 133.3, 135.4, 135.8, 137.0, 137.6, 138.9, 139.6, 140.1, 141.4, 150, 157.5. Elemental Analysis Calculated for $C_{27}H_{16}Cl_2O$: C, 75.89; H; 3.77. Found: C, 75.78; H; 3.68.

14-(3-Fluorophenyl)-14H-dibenzo[a.j]xanthene (5i). Mp 259 ^{0}C; ESI MS (*m/z*) = 377 (M+H). IR (KBr, cm^{-1}): 3154, 1594, 1403, 1240, 1207, 1069, 817, 747; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 6.51 (s, 1H) 6.72–8.38 (m, 16H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 38.1, 113.8 and 114.0($J_{C–F}$ 21.5 Hz), 115.6 and 115.9 ($_{JC–F}$ 21.5 Hz), 117.1, 118.2, 122.9, 124.31 and 124.34 ($J_{C–F}$ 2.8 Hz), 124.8, 127.4, 129.3, 129.5, 130.1 and 130.2 ($J_{C–F}$ 8.3 Hz), 131.5, 131.7 ($J_{C–F}$ 19.4 Hz), 147.8, 147.9 ($J_{C–F}$ 6.2 Hz), 149.2, 161.7, 165.0; Elemental Analysis Calculated for $C_{27}H_{17}FO$: C, 86.15; H, 4.55; F, 5.05. Found: C, 86.11; H, 4.54, F, 5.07.

14-(2-Nitrophenyl)-14H-dibenzo[a.j]xanthene (5j). Mp 293 ^{0}C; ESI MS (*m/z*) = 404 (M+H). IR (KBr, cm^{-1}): 3400, 3058, 1593, 1523, 1350, 1240, 1142, 810, 748; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 7.52 (s, 1H) 7.10-8.56 (m, 16H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 32.9, 118.0, 118.4, 123.0, 124.6, 125.0, 125.3, 127.8, 128.0, 129.4, 129.5, 129.9, 130.8, 132.1, 132.6, 134.5, 141.3, 147.5, 149.8; Elemental Analysis Calculated for $C_{27}H_{17}NO_3$: C, 80.38; H, 4.25; N, 3.47. Found: C, 80.25; H, 4.24, N, 3.57.

14-(3-trifluoromethylphenyl)-14-*H*-3,11-dibromodibenzo[*a,j*]xanthene (5k). Mp 202-204 ^{0}C; ESI MS (*m/z*) = 582 (M+H). ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 6.41 (s, 1H), 7.25-7.30 (m, 2H), 7.50 (d, *J* = 8.8 Hz, 2H), 7.61-7.73 (m, 6H), 7.99 (d, 2H, *J* = 1.8 Hz), 8.14 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75MHz) δ = 37.9, 116.4, 118.5, 119.2, 123.8, 123.9, 124.4, 124.5, 125.2, 128.6, 129.3, 129.7, 130.3, 130.8, 131.0, 131.1, 131.4, 132.3, 145.3, 148.8. Elemental Analysis Calculated for $C_{28}H_{15}Br_2F_3O$: C, 57.56; H; 2.59. Found: C, 57.47; H; 2.65.

14-isopropyl-14H-dibenzo[a,j]xanthene (5l). Mp 155 ^{0}C; ESI MS (*m/z*) = 325 (M+H). IR (KBr, cm^{-1}): 1622, 1591, 1515, 1457, 1240. ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 8.26 (d, *J* = 8.0 Hz, 2H), 7.90-7.72 (m, 4H), 7.61-7.49 (m, 2H), 7.43-7.32 (m, 4H), 5.42 (d, *J* = 7.0 Hz, 1H), 2.28 (m, 1H), 0.81 (d, *J* = 7.0 Hz, 6H). Elemental Analysis Calculated for $C_{24}H_{20}O$: C, 88.85; H 6.21. Found: C, 88.78; H, 6.15.

14-benzyl-14H-dibenzo[a,j]xanthene (5m). Mp 178 ^{0}C; ESI MS (*m/z*) = 373 (M+H). IR (KBr, cm^{-1}): 3061, 3019, 1617, 1587, 1511, 1488, 1451, 1397, 1241. ^{1}H NMR ($CDCl_3$, 300 MHz) *δ* = 3.27 (d, *J* = 4.7 Hz, 2H), 5.80 (t, *J* = 4.7 Hz, 1H), 6.12 (d, *J* = 9.0 Hz, 2H), 6.84-7.20 (m, 5H), 7.45-7.91 (m, 8H), 8.25 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ* = 33.0, 41.33, 115.27, 117.39, 122.18, 124.10, 126.10, 126.68, 127.18, 128.35, 128.88, 129.76, 130.84,

131.30, 137.55, 150.11; Elemental Analysis Calculated for $C_{28}H_{20}O$: C, 90.33; H, 5.37; found: C, 90.27; H, 5.37

14-propyl-14H-dibenzo[a,j]xanthene (5n). Mp 152 ^{0}C; ESI MS (*m/z*) = 325 (M+H). IR (KBr): 3066, 2961, 2874, 1623, 1591, 1518, 1488, 1461, 1434, 1400, 1245 cm−1; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 0.62 (t, *J* = 7.2 Hz, 3H), 1.04 (m, 2H), 2.03 (m, 2H), 5.58 (t, *J* = 4.6 Hz, 1H), 7.40 (d, *J* = 8.8 Hz, 2H), 7.45-7.66 (m, 4H), 7.79 (d, *J* = 8.8 Hz, 2H), 7.89 (d, *J* = 7.7 Hz, 2H), 8.27 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 14.8, 20.20, 42.0, 43.10, 115.40, 118.60, 122.48, 123.40, 126.24, 128.3, 128.48, 128.80, 133.60, 150.3; Elemental Analysis Calculated for $C_{24}H_{20}O$: C, 88.85; H, 6.21; found: C, 88.90; H, 6.12.

.**3-amino-1-(4-nitrophenyl)-1H-benzo[f]chromene-2-carbonitrile (7a).** Mp 190 ^{0}C; ESI MS (m/z) = 344 (M+H). IR (KBr, cm^{-1}): 3429, 3331, 2190. ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 5.56 (s, 1H), 7.16 (bs, 2H), 7.37 (d, *J* = 9.0 Hz, 1H), 7.40-7.50 (m, 2H), 7.47 (d, *J* = 8.5 Hz, 2H), 7.71-8.00 (m, 2H), 7.98 (d, *J* = 9.0 Hz, 1H), 8.15 (d, *J* = 8.5 Hz, 2H); Elemental Analysis Calculated for $C_{28}H_{20}O$: C, 69.96; H, 3.82; N, 12.24. Found: C, 69.89; H, 3.71; N, 12.10.

3-amino-1-(1H-indol-3-yl)-1H-benzo[f]chromene-2-carbonitrile (7b). Mp 220 ^{0}C; ESI MS (*m/z*) = 336 (M+H). IR (KBr, cm^{-1}): 3420, 3215, 2155, 1648, 1538. ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 3.82 (s, 1H), 7.01 (bs, 2H), 7.40-7.81 (m, 11H), 10.30 (s, 1H). Elemental Analysis Calculated for $C_{27}H_{17}NO_3$: C, 78.32; H, 4.48; N, 12.46. Found: C, 78.25; H, 4.34, N, 12.59.

3-Amino-1-(4-fluorophenyl)-9-methoxy-1H-benzo[f]-chromene-2-carbonitrile (7c). Mp 238–239 ^{0}C; ESI MS (m/z) = 347 (M+H). IR (KBr, cm^{-1}): 3465, 3359, 2183, 1662, 1654, 1592, 1509, 1408, 1239, 1218, 827. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 3.69 (s, 3H), 4.52 (s, 2H), 5.12 (s, 1H), 6.85 (s, 1H), 6.96 (t, *J* = 8.2 Hz, 2H), 7.02-7.19 (m, 4H), 7.70 (t, *J* = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 37.8, 55.5, 58.3, 103.6, 114.5, 115.1, 115.7, 116.0, 117.3, 121.0, 126.5, 129.5, 129.6, 130.5, 132.1, 142.5, 147.7, 158.5, 159.6, 160.1, 162.9. Elemental Analysis Calculated for $C_{21}H_{15}FN_2O_2$: C, 72.82; H, 4.37; N, 8.09. Found: C, 72.70; H, 4.40; N, 8.10;

3-Amino-1-(4-fluorophenyl)-1H-benzo[f]chromene-2- carbonitrile (7d). Mp 237–238 ^{0}C; ESI MS (m/z) = 317 (M+H). ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 4.62 (s, 2H), 5.24 (s, 1H), 6.94 (t, J = 8.6 Hz, 2H), 7.12-7.17 (m, 2H), 7.25 (d, *J* = 6.8 Hz, 1H), 7.40 (dd, *J* = 2.8 Hz, 2H), 7.63-7.65 (m, 1H), 7.80-7.83 (m, 2H). Elemental Analysis Calculated for $C_{20}H_{13}FN_2O$: C, 75.94; H, 4.14; N, 8.86. Found: C, 76.00; H, 4.02; N, 8.72.

3-Amino-1-(furan-2-yl)-1H-benzo[f]chromene-2-carbonitrile (7e). Mp 225–226 ^{0}C; ESI MS (m/z) = 289 (M+H). ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 5.48 (s, 1H), 6.22-6.30 (m, 2H), 7.08 (s, 2H), 7.27 (d, *J* = 9.2 Hz, 1H), 7.42-7.54 (m, 3H), 7.91 (d, *J* = 8.9 Hz, 2H), 8.03 (d, *J* = 8.5 Hz, 1H). Elemental Analysis Calculated for $C_{18}H_{12}N_2O_2$: C, 74.99; H, 4.20; N, 9.72. Found: C, 75.05; H, 4.12; N, 9.60.

3-Amino-1-pentyl-1H-benzo[f]chromene-2-carbonitrile (7f). Colourless oil. ESI MS (m/z) = 293 (M+H). ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 0.79-0.83 (t, *J* = 6.1 Hz, 3H), 1.21-1.46 (m, 6H), 7.44-7.59 (m, 2H), 1.79-1.82 (m, 2H), 4.25 (t, *J* = 8.7 Hz, 1H), 4.68 (s, 2H), 7.14 (d, *J* = 9.2 Hz, 1H), 7.71 (d, *J* = 8.6 Hz, 1H), 7.81-7.91 (m, 2H). Elemental Analysis Calculated for $C_{19}H_{20}N_2O$: C, 78.05; H, 6.89; N, 9.58. Found: C, 77.92; H, 6.82; N, 9.45.

3-Amino-1-phenyl-1H-benzo[f]chromene-2-carbonitrile (7g). Mp 278–279 ^{0}C; ESI MS (m/z) = 299 (M+H). IR (KBr, cm^{-1}): 3435, 3208, 2185, 1669, 1560. ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 5.30 (s, 1H), 7.00 (s, 1H), 7.13-7.47 (m, 8H), 7.85 (d, *J* = 4.5 Hz, 1H), 7.90-7.96 (m, 2H). Elemental Analysis Calculated for $C_{20}H_{14}N_2O$: C, 80.52; H, 4.73; N, 9.39. Found: C, 80.40; H, 4.60; N, 9.25.

3-Amino-1-(2-chlorophenyl)-1H-benzo[f]chromene-2-carbonitrile (7h). Mp 265-267 ^{0}C; ESI MS (m/z) = 333 (M+H). ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 4.54 (s, 2H), 5.89 (s, 1H), 6.91 (d, *J* = 8.8 Hz, 1H), 7.02-7.12 (m, 2H), 7.24-7.26 (m, 1H), 7.37-7.45 (m, 3H), 7.67 (d, *J* = 7.7

Hz, 1H); 7.78-7.82 (m, 2H). Elemental Analysis Calculated for $C_{20}H_{13}ClN_2O$: C, 72.18; H, 3.94; N, 8.42. Found: C, 72.10; H, 4.00; N, 8.30.

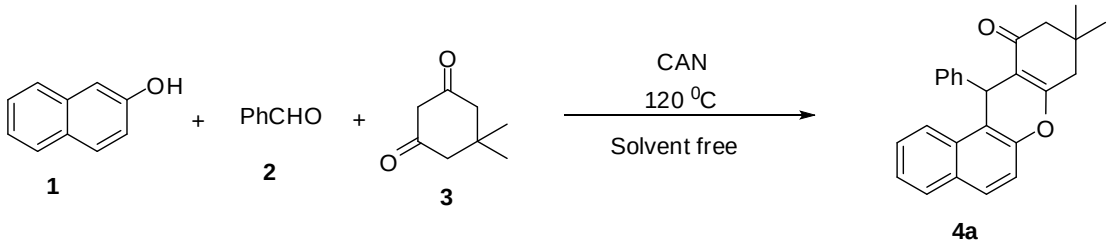
3-Amino-1-(4-methoxyphenyl)-1H-benzo[f]chromene-2-carbonitrile (7i). Mp 194 ^{0}C; ESI MS (m/z) = 329 (M+H). ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 3.72 (s, 3H), 4.60 (s, 2H), 5.19 (s, 1H), 6.78 (d, *J* = 7.5 Hz, 2H), 7.09 (d, *J* = 7.6 Hz, 2H), 7.22 (d, *J* = 10 Hz, 1H), 7.39-7.36 (m, 2H), 7.69-7.66 (m, 1H), 7.78 (d, *J* = 8.6 Hz, 2H). Elemental Analysis Calculated for $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.91; N, 8.53. Found: C, 76.86; H, 4.98; N, 8.65.

3-Amino-1-p-tolyl-1H-benzo[f]chromene-2-carbonitrile (7j). Mp 253-254 ^{0}C; ESI MS (m/z) = 313 (M+H).^{1}H NMR ($CDCl_3$, 300 MHz) δ = 4.57 (s, 2H), 5.21 (s, 1H), 7.02-7.12 (m, 4H), 7.25 (d, *J* = 8.6 Hz, 1H), 7.37-7.40 (m, 2H), 7.68-7.71 (m, 1H), 7.78-7.81 (m, 2H). Elemental Analysis Calculated for $C_{21}H_{16}N_2O$: C, 80.75; H, 5.16; N, 8.97. Found: C, 80.84; H, 5.05; N, 9.15.

Ethyl 3-amino-1-(4-chlorophenyl)-1H-benzo[f]chromene-2-carboxylate (7k). Mp 190–191 ^{0}C; ESI MS (m/z) = 380 (M+H). ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 1.36 (t, *J* = 5.9 Hz, 3H), 4.21(q, *J* = 5.1 Hz, 2H), 6.31 (s, 2H), 5.56 (s, 1H), 7.13 (d, *J* = 7.1 Hz, 2H), 7.25-7.27 (m, 3H), 7.35-7.47 (m, 2H), 7.76 (t, *J* = 8.4 Hz, 2H), 7.94 (d, *J* = 8.7 Hz, 1H). Elemental Analysis Calculated for $C_{22}H_{18}ClNO_3$: C, 69.57; H, 4.78; N, 3.69. Found: C, 69.45; H, 4.80; N, 3.58.

Results and discussion

Our initial experiments were focused on one-pot, three-component reaction of 2-naphthol, benzaldehyde, and dimedone using different catalysts under solvent free conditions, and the results are listed in Table 1 (Scheme 1).



Scheme 1.

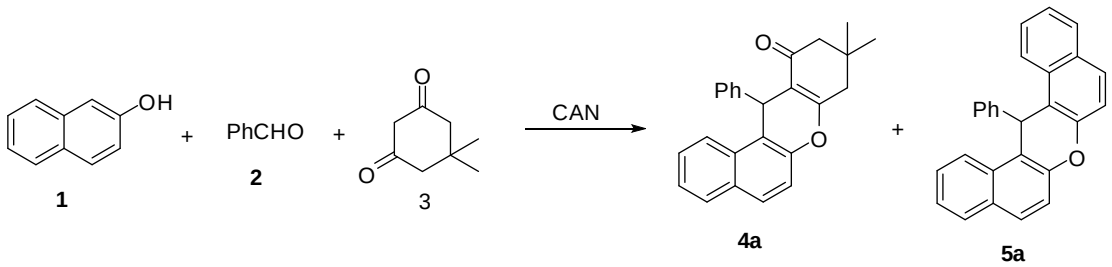
It was found that ceric ammonium nitrate (CAN) showed better catalytic activity among other catalysts such as $FeCl_3$, $SnCl_4$, $ZnCl_2$, and $AlCl_3$. Although Ce(IV) derivatives are normally employed as single-electron oxidants, the use of the commercially available, inexpensive, and easily handled CAN in carbon-carbon and carbon-heteroatom bond forming reactions has recently attracted much attention [31-34], although these studies are still in their early stages. The main current goal in this area is the development of reactions that allow the use of catalytic amounts of CAN [35-41]. When 5 mol % CAN was used, the reaction proceeded smoothly and gave the product **4a** in 94% yield (Table 1, entry 6). Moreover, we found that the yields were obviously affected by the amount of CAN loaded. When 0.5 mol %, 2 mol % and 10 mol % of CAN were used, the yields were 39%, 70%, and 93% respectively (Table 1, entries 7-9). Therefore, 5 mol % of CAN was sufficient to push the reaction forward and further increasing the amount of CAN did not increase the yields. The catalytic activity of the recycled CAN was also examined. CAN was reused five times for the reaction without noticeable loss of activity (Table 1, entry 10). In addition, no product was detected in the absence of the catalyst (Table 1, entry 1). The above results showed that CAN was essential in the reaction, and the best results were obtained when the reaction was carried out with 5 mol % of CAN under solvent free conditions at 120 ^{0}C.

Table 1. Screening of catalysts for one-pot condensation of 2-naphthol, benzaldehyde, and dimedone [a]

Entry	Catalyst	Catalyst (mol %)	Time (min)	Yield (%)[b]
1	None	-	120	<5
2	$FeCl_3$	5	30	25
3	$SnCl_4$	5	30	37
4	$ZnCl_2$	5	30	32
5	$AlCl_3$.	5	30	35
6	CAN	5	30	94
7	CAN	0.5	30	39
8	CAN	2	30	70
9	CAN	10	30	93
10[c]	CAN	5	30	94, 93, 94, 93, 92

[a]Reaction conditions: 2-naphthol (1.0 mmol), benzaldehyde (1.0 mmol), and 5,5-dimethylcyclohexane-1,3-dione (1.0 mmol), solvent free, 120 ^{0}C. [b] Isolated yield. [c] Catalyst was reused five times.

Then, we examined the effect solvents over the above reaction. The results of table 2 indicate that solvents affected the efficiency of the reaction. Yields were poor in acetonitrile, dichloromethane and tetrahydrofuran (Table 2, entries 1-3). Better yields were obtained in more polar solvents like methanol and ethanol (Table 2, entry 4 & 5). However the best results were obtained under solvent free conditions (Table 2, entry 6). In addition, 14-phenyl-14H-dibenzo[a,j]xanthene **5a** was obtained as a side product in all solution phase reactions (Scheme 2). On the other hand **5a** were not isolated under solvent free conditions.



Scheme 2.

Table 2. Solvent effect on the reaction of 2-naphthol, benzaldehyde, and dimedone catalyzed by CAN

Entry	Solvent	Temp (^{0}C)	Time (min)	Yield (%)	
				4a	**5a**
1	Acetonitrile	Reflux	120	38	10
2	Dichloromethane	Reflux	120	32	5
3	Tetrahydrofuran	Reflux	120	25	13
4	Methanol	Reflux	120	46	12
5	Ethanol	Reflux	120	50	10
6	None	120	30	94	Not isolated

In order to study the generality of this protocol, a library of 12-substituted-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-ones was built using 2-naphthol, aldehydes and cyclic 1,3-dicarbonyl compounds (Figure 1). The diversity in benzoxanthene library was generated using aliphatic, electron rich as well as electron deficient aromatic aldehydes, cyclohexane-1,3-dione, 5,5-dimethylcyclohexane-1,3-dione and cyclopentane-1,3-dione.

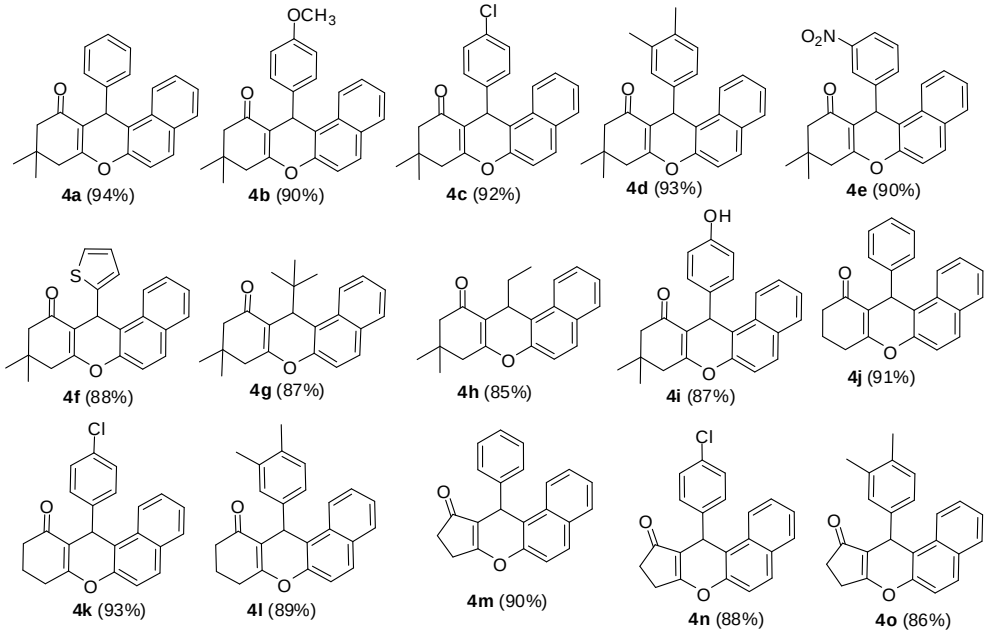
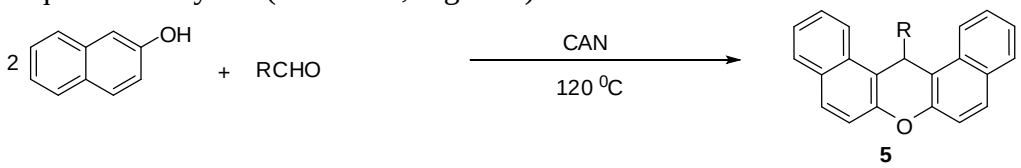


Figure 1.

It was observed that in the absence of cyclic 1,3-diketone, the CAN catalyzed reaction of 2-naphthol and aldehyde under solvent free conditions resulted to the formation of compound **5** in almost quantitative yield (Scheme 3, Figure 2).



Scheme 3.

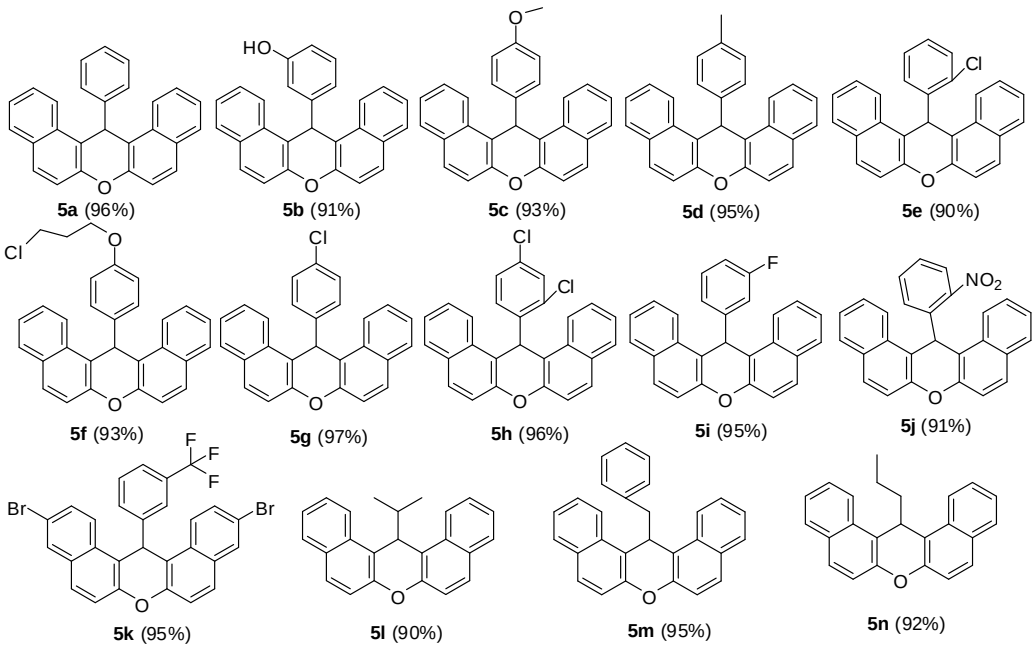


Figure 2. 14-substituted-14H-dibenzo[a, j]xanthenes

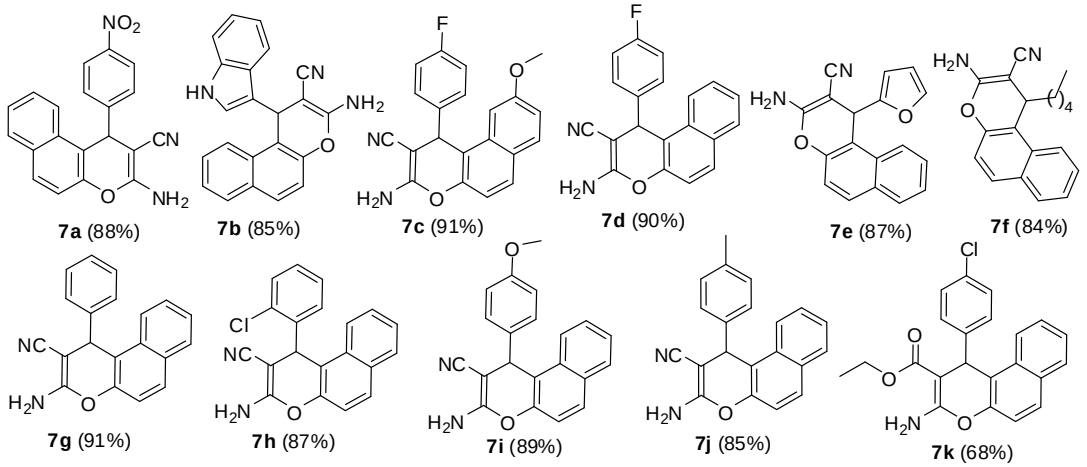
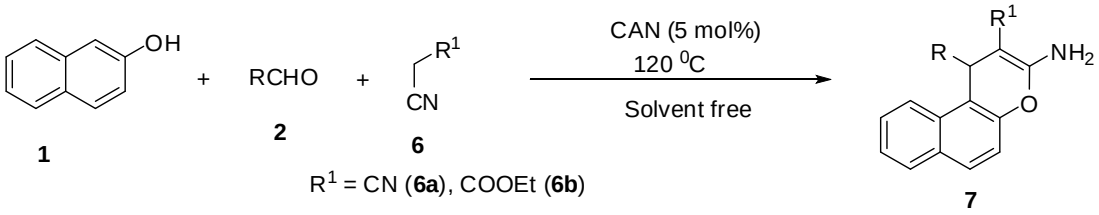


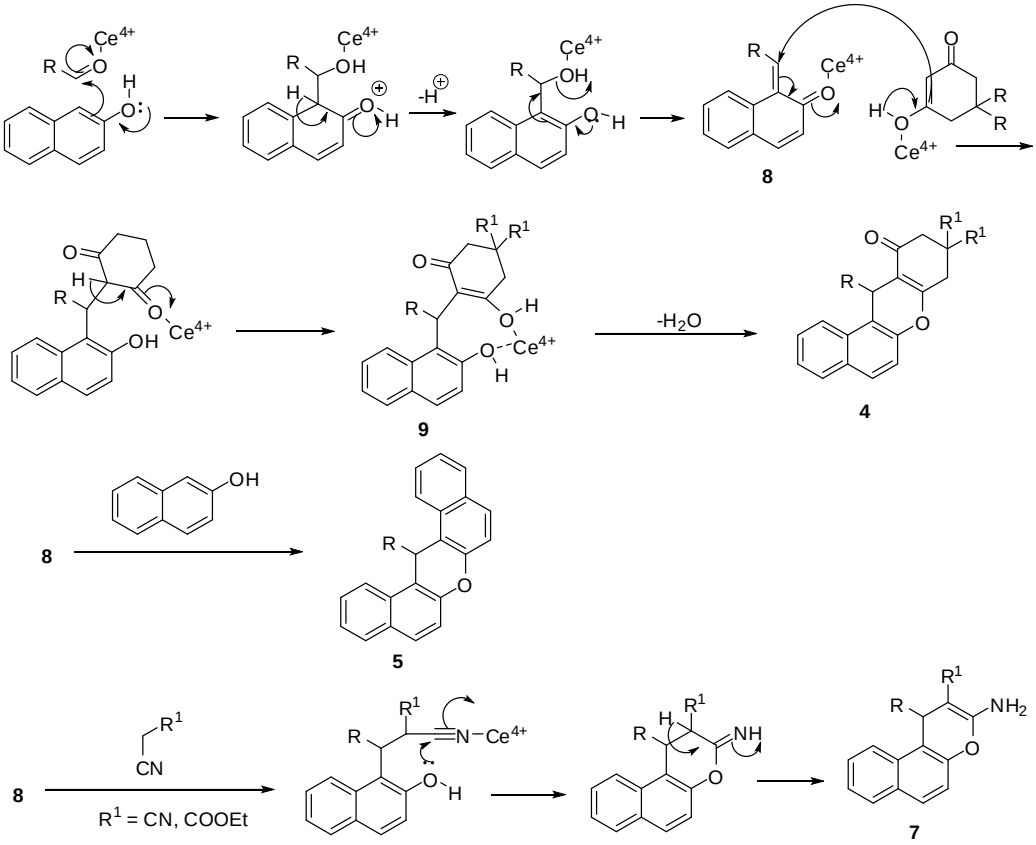
Figure 3. 3-amino-1-substituted-1H-benzo[f]chromenes

Using malononitrile or ethyl cynoacetate as third component in the CAN mediated multi-component reaction of 2-naphthol and aldehydes, we synthesized a library of benzochromes (Scheme 4, Figure 3).



Scheme 4.

The formation of benzoxanthenes and benzochromenes could be explained by a proposed tentative mechanism (Scheme 5). It was supposed that the reaction occurred via the ortho-quinone methides intermediate **8**, which was formed by the nucleophilic addition of β-naphthol to aldehyde catalyzed with CAN. Subsequent attack of cyclic 1,3-dicarbonyl compounds to the intermediate **8**, afforded **9**. Then compounds **9** eliminated one molecule of H_2O and afforded compound **4.**



Scheme 5.

In the absence of cyclic 1,3-dicarbonyls the second molecules of β-naphthol attacks to intermediate **8** leading to the formation compound **5**. Reaction of malononitrile (**6a**) or ethyl cyanoacetates (**6b**) with intermediate **8** yields benzochromenes **7**.

All the synthesized compounds were screened for their anti-proliferative activity in human prostate cancer (DU-145), breast cancer (MCF-7), cervical carcinoma (C-33A), lung carcinoma (A 549), oral squamous cell carcinoma (KB), control for general cytotoxicity (Vero) cancer cell lines. The compounds which were showing activity below 50 μg/ml were summarised in table 3. Benzochromenes (**4b**, **4c**, **4f**, **4i**, **4n**, **7a, 7b, 7c, 7e, 7i and 7k**) were found more active then comparison to benzoxanthenes (**5b**, **5f** and **5j**). Compounds **4i** (6.7 μg/ml) and **7a** (8.9 μg/ml) was most potent in MCF-7, showed more activity than anti breast cancer drug tamoxifen (10 μg/ml).

Table 3. Inhibition of proliferation of the compounds

Compounds	IC_{50} (μg/ml)					
	DU 145	MCF-7	C-33A	A 549	KB	Vero
4b	12.5	18.1	8.2	13.7	4.0	8.9
4c	14.3	19.8	14.7	12.6	17.6	5.2
4f	8.0	11.7	9.9	6.1	6.7	18.2
4i	11.3	6.7	17.7	27.7	21.8	5.7
4n	26.7	23.3	19.2	32.8	16.9	13.3
5b	19.0	21.1	36.6	16.3	18.5	38.6
5f	21.7	37.8	38.6	36.8	11.7	41.9
5j	25.6	21.9	28.6	23.2	16.3	29.7
7a	13.3	8.9	14.6	8.3	7.6	12.5
7b	10.0	12.2	10.5	5.4	15.2	8.1
7c	16.7	22.1	19.7	18.9	21.6	14.0

7e	18.6	15.7	15.0	22.5	14.2	11.7
7i	12.4	14.2	27.1	10.2	19.6	18.9
7k	17.4	16.7	11.9	12.9	12.9	19.6

Conclusion

In conclusion, we have efficiently synthesized structurally diverse libraries of benzoxanthenes, and benzochromenes via CAN catalyzed three-component reactions under solvent free conditions. The advantages of this method include the use of recyclable catalyst, high yields, simple workup procedure, and easy isolation. Anti-proliferative activities were evaluated for all the synthesized compounds, some of the synthesized compounds exhibited significant activity in various cell lines.

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