Donor-acceptor Pyran-2-ones: Absorption and Fluorescence Spectra of 4-Substituted 2*H*-1-Benzo/napthopyran-2-ones

Rajesh S. Kenny and Uday C. Mashelkar*

Organic Research Laboratory, Patkar-Varde College of Science, Goregaon (W), Mumbai 400062, India

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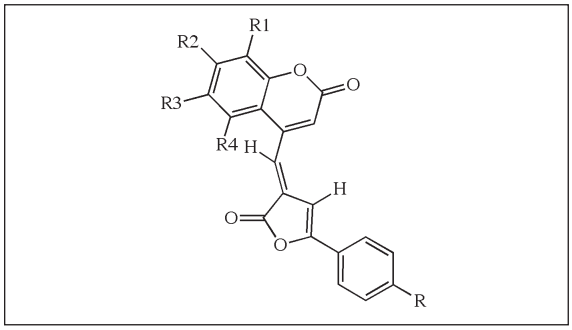

The absorption spectra and emission spectra of 4-substituted 2*H*-1-benzo/napthopyran-2-ones **3a-l** have been determined in THF and DMSO. The substituent at the 4-position of the 2*H*-benzo/napthopyran-2-one, establishes a compact conjugation pathway in which the pyran-2-one nucleus can act as an acceptor ring.

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The synthesis and development of fluorescence sensors for biological application has been an important field of chemistry and pharmaceutics. Recently many novel series of fluorescent probes have been designed and synthesized [1-8]. Fluorescence Microscopy is at the present time, probably the most widely used microscopy technique as it enables the molecular composition of the structures being observed to be identified through the use of fluorescently-labeled probes of high chemical specificity such as antibodies. Benzopyran-2-one exhibit fluorescence that is dependent on the nature of their substituents [9-12].

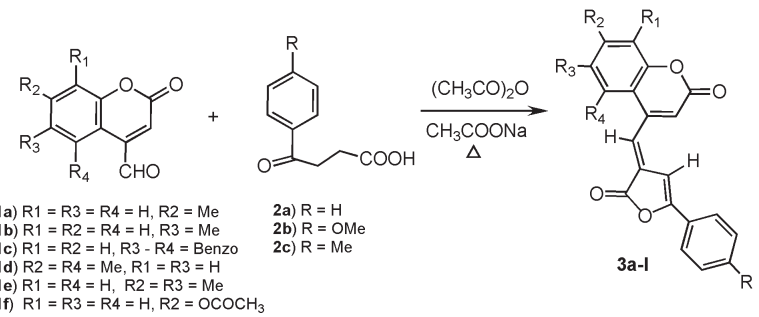
A common requirement to be fulfill while designing an ideal fluorophore is that the fluorogenic moiety should have a fluorescence emission maximum (F1 max) at longer wavelengths than 480 nm, in order to bypass the background fluorescence of many biological materials, which is "blue" (430-470 nm) in appearance [13]. Although the presently used fluorophore, *i.e*. an isothiocyanate derivative of fluorescein (FITC), meet this criterion, since the Fl max of its conjugate with gamma globulin is 525 nm [14]. This fluorophore has serious drawbacks like concentration quenching as it has a small Stokes shift [15,16], its fluorescence is sensitive to pH [17] and it is photo chemically reactive, decomposes rapidly, and its fluorescence fades and/or changes from green to blue, forcing rapid and error-prone judgments on the appearance of slide preparations.

By making the use of the simple synthetic methodology, we in this paper have discussed the synthesis of 5-phenyl furanone substituted 2*H*-1-benzo/napthopyran-2-ones and also evaluated its UV-Vis and fluorescence spectra. As the furanone ring is substituted at the 4-position of the 2*H*-benzo/napthopyran-2-one moiety, it forms a compact conjugation pathway in which the pyran-2-one nuclei can act as an acceptor ring. Introduced a donor group like methoxy at the opposite end of the acceptor, over the conjugation pathway *i.e*. 4-position of the phenyl ring, results in a Donor-acceptor system. The resultant effect on the shift in the absorption band has been studied. The synthesized 2*H*-benzo/napthopyran-2-one derivatives are orange to red in color and show intense green fluorescence when dissolved in some solvents. The UV-Vis spectra are recorded in a medium polar solvent like THF and a highly polar solvent like DMSO where as the fluorescence spectra are recorded in DMSO.

Results and Discussion.

Scheme 1

1. Synthesis and Conformational Assignment.



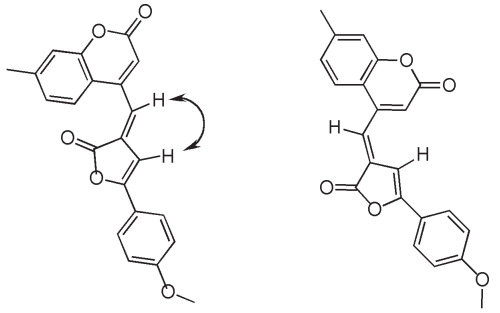
1a) R1 = R3 = R4 = H, R2 = Me
1b) R1 = R2 = R4 = H, R3 = Me
1c) R1 = R2 = H, R3 - R4 = Benzo
1d) R2 = R4 = Me, R1 = R3 = H
1e) R1 = R4 = H, R2 = R3 = Me
1f) R1 = R3 = R4 = H, R2 = $OCOCH_3$

2a) R = H
2b) R = OMe
2c) R = Me

Not even a single example from this class of compound has been described in the literature. The parent molecules 2*H*-benzo/napthopyran-2-ones **3a-l** has been synthesized as described in Scheme 1. The starting materials *i.e.* 4-formyl benzo/napthopyran-2-ones **1a-f** [18a-d] are synthesized following the literature procedure, few of them are developed by us. The aldehydes **1a-f** were condensed with (un)substituted benzoyl propionic acids **2a-c** [19a-b] in acetic anhydride and sodium acetate to give the desired compounds **3a-l**.

Based on the incremental parameters of the δ values for exocyclic double bond in its NMR spectra, Khan *et al.* has suggested (*E*)-configuration for these molecules [19b]. One NMR phenomenon known as the *nuclear Overhauser effect* (nOe) provides exactly the missing information about the *proximity* in space of protons. The stereochemistry of the single-isomer **3b** was examined in a ^{1}H NOE experiment. Irradiation of the furanone ring proton at δ 6.60 do not result in enhancement of the exocyclic proton appearing at δ 7.42 and *vice-versa*, which is in agreement with the *E* conformation assigned to the above molecule. The enhancement is expected in the *Z* isomer as shown in the figure below. One of the interesting nOe effect observed is by the irradiation of the exocyclic ring proton at δ 7.42 to show the enhancement of the C5 proton of coumarin ring which appears as doublet at δ 7.6. Thus the literature survey and the nOe NMR studies allowed us to assign the *E* conformation for all the furanone substituted 2*H*-1-benzo/napthopyran-2-ones **3a-l**.

Scheme 2



Conformers of **3b**

2. Spectroscopic Properties.

All 2*H*-1-benzo/napthopyran-2-one derivatives **3a-l** reported in this paper have fluorescent properties, however the fluorescent intensities are largely different among the molecules. In order to evaluate the structural property studies, the absorption spectra of these compounds are recorded in THF and DMSO, where the emission spectra are recorded in DMSO only. The data is summarized in Table 1 below. To obtain the longer absorption wavelengths, the presence of a donor group at the *para* position of the phenyl ring is necessary. The introduction of a methoxy group resulted in a shift in the λ max value towards the red region of the absorption by approximately 20 to 25 nm with respect to their phenyl or *p*-toluyl analogs. There was found a bathochromic shift in the λ max values of the compounds in polar solvent *i.e*. DMSO by 5 to 12 nm than the same recorded in medium polar solvent *i.e.* THF, except the examples **3e, 3f, 3g** and **3h**. This can be explained on the basis that the highly polar resonance form is stabilized in a polar solvent where as the less polar resonance form is stabilized in the medium polar solvent resulting in a solvatochromic effect. The compounds **3e**, **3g** and **3h** do not showed much change with changing solvent polarity, whereas the compound **3f** showed negative solvatochromic effect. The synthesized molecules showed fluorescence emission maximum (F1 max) between 440 to 530 nm. Table 1, which lists the photophysical characteristics of the compounds studied, clearly demonstrates that by increasing the donating property of the compounds a bathochromic shift in the absorption spectra is observed, whereas no such trend was observed in the emission spectra of the compounds. All the twelve compounds **3a-l**, displays an intense fluorescence emission and some of them show large stokes' shift of more then 90 nm. Based on the results we have obtained we suggest that some of the compounds synthesized by us can have application as novel fluorescence probes.

EXPERIMENTAL

Melting points are taken in open capillary and are uncorrected. ^{1}H NMR spectra were run on a Brucker AM 300 instrument using TMS as an internal standard. IR spectra were recorded in KBr, on a Shimadzu FTIR-4200 spectrophotometer. Elemental analysis was carried out on Carlo Enra instrument EA-1108 Elemental analyser. UV spectra were recorded on Shimadzu UV-visible Spectrophotometer UV-2100 with concentration of approximately 10^{-4} moles/lit and Fluorescence spectra were recorded on Shimadzu-50001 spectrofluorophotometer with concentration of approximately 10^{-6} moles/lit.

General Procedure.

4-[(7-Methyl-2*H*-1-benzopyran-2-one-4-yl)methylene]-2-phenyl-5-(4*H*)furanone (**3a**).

7-Methyl benzopyran-2-one-4-carboxaldehyde **1a** (0.94 g, 0.005 moles), fused sodium acetate (2.0 gm) and benzoyl propionic acid **2a** (0.98 g, 0.0055 moles) were intimately mixed by grinding in a mortar. The mixture was mixed with Ac_2O (3 ml), heated on a boiling water bath for 20 min. with shaking and stirring, diluted with water and the product that separated was filtered, dried and crystallized twice from ethanol solvent afforded yellow-orange needles, 0.94 g (yield = 57%, M. P. = 242-44 °C). EI MS: M^+ = 330. IR (KBr): 3111, 2925, 2349, 1787, 1725, 1622, 1495, 1349, 1188, 996, 813 and 750. ^{1}H NMR ($CDCl_3$): δ = 2.5

Table 1

Substituents and photophysical properties of 2*H*-1-benzo/napthopyran-2-ones **3a-l** at 25 °C.

Compd	Subsrituents [c] R, R1, R2, R3, R4	l max [a] (nm) THF	DMSO	l em [b] (nm) DMSO	Stokes Shift (nm)
3a	R2 = Me	392	402	488	86
3b	R =OMe, R2 = Me	421	427	504	77
3c	R3 = Me	392	401	492	91
3d	R =OMe, R3 = Me	424	429	493	64
3e	R3-R4 = Benzo	379	378	476	98
3f	R =OMe, R3-R4 = Benzo	397	391	444	53
3g	R = R2 = R4 = Me	378	378	448	70
3h	R = OMe, R2 = R4 = Me	391	391	450	59
3i	R = R2 = R3 = Me	398	409	467	58
3j	R = OMe, R2 = R3 = Me	417	428	491, 528	63, 100
3k	R = Me, R2 = $OCOCH_3$	401	410	520	110
3l	R = OMe, R2 = $OCOCH_3$	423	430	494	64

[a] Maximum absorption wavelength in solvents, THF or DMSO; [b] Maximum emission wavelength excited at the maximum absorption wavelength in DMSO; [c] Substituents where R, R1, R2, R3 and R4 are not indicated represents H atom.

(s, 3H), 6.6 (s, 1H), 6.8 (s, 1H), 7.16 (d, *J* = 7.9, 1H), 7.22 (s, 1H), 7.47-7.55 (m, 4H), 7.6 (d, *J* = 7.9, 1H), 7.76-7.81 (m, 2H).

Anal. Calcd. for $C_{21}H_{14}O_4$: C, 76.36; H, 4.27. Found: C, 76.48; H, 4.16.

4-[(7-Methyl-2*H*-1-benzopyran-2-one-4-yl)methylene]-2-(4-methoxy) phenyl-5-(4*H*)furanone (**3b**).

The compound was obtained as red needles, from ethanol (Yield = 59%, M. P. = 225 °C char). IR (KBr): 2922, 2855, 1784, 1726, 1622, 1582, 1507, 1348, 1246, 1181, 1026, 820 and 751. 1H NMR (CDCl3): δ = 2.5 (s, 3H), 3.9 (s, 3H), 6.60 (s, 1H), 6.68 (s, 1H), 7.05 (d, *J* = 8.63, 2H), 7.14 (d, *J* = 8.08, 1H), 7.2 (s, 1H), 7.42 (s, 1H), 7.62 (d, *J* = 8.1, 1H), 7.73 (d, *J* = 8.62, 2H).

Anal. Calcd. for $C_{22}H_{16}O_5$: C, 73.33; H, 4.48. Found: C, 73.15; H, 4.29.

4-[(6-Methyl-2*H*-1-benzopyran-2-one-4-yl)methylene]-2-phenyl-5-(4*H*)furanone (**3c**).

The compound was obtained as yellow-orange needles, from ethanol (Yield = 64%, M. P. = 262-63 °C). IR (KBr): 3147, 3052, 1786, 1714, 1614, 1566, 1548, 1349, 1276, 1194, 922, 877, 821 and 754. ^{1}H NMR ($CDCl_3$): δ = 2.45 (s, 3H), 6.63 (s, 1H), δ6.8 (s, 1H), 7.32 (t, *J* = 8.6 & *J* = 8.88, 1H), 7.42 (d, *J* = 8.1, 1H), 7.45-7.55 (m, 5H), 7.78-7.79 (m, 2H).

Anal. Calcd. for $C_{21}H_{14}O_4$: C, 76.36; H, 4.27. Found: C, 76.27; H, 4.20.

4-[(6-Methyl-2*H*-1-benzopyran-2-one-4-yl)methylene]-2-(4-methoxy) phenyl-5-(4*H*)furanone (**3d**).

The compound was obtained as orange-red needles, from ethanol (Yield = 55%, M. P. = 230 °C char). IR (KBr): 3122, 2925, 1785, 1731, 1603, 1585, 1507, 1347, 1270, 1246, 1179, 944, 812 and 747. ^{1}H NMR (CDCl3): δ = 2.45 (s, 3H), 3.9 (s, 3H), 6.63 (s, 1H), 6.70 (s, 1H), 7.00 (d, *J* = 8.68, 2H), 7.28 (d, *J* = 8.44, 1H), 7.41 (d, *J* = 8.37, 1H), 7.42 (s, 1H), 7.53 (s, 1H), 7.73 (d, *J* = 8.67, 2H).

Anal. Calcd. for $C_{22}H_{16}O_5$: C, 73.33; H, 4.48. Found: C, 73.20; H, 4.35.

4-[(2*H*-1-Naphtho[3,4-*b*]pyran-2-one-4-yl)methylene]-2-phenyl-5-(4*H*)furanone (**3e**).

The compound was obtained as orange-red prisms, from ethylacetate/cyclo hexane (Yield = 72%, M. P. = 242 °C char). IR (KBr): 3120, 1785, 1735, 1581, 1541, 1491, 1310, 1275, 1212, 989, 881 and 740. ^{1}H NMR ($CDCl_3$): δ = 6.7 (s, 1H), 6.9 (s, 1H), 7.53-7.57 (m, 3H), 7.6 (d, *J* = 8.1, 1H), 7.65 (t, *J* = 8.7 & *J* = 8.68, 1H), 7.7 (t, *J* = 8.63 & *J* = 8.86, 1H), 7.82-7.87 (m, 3H), 8.0 (d, *J* = 8.89, 1H), 8.12 (d, *J* = 8.88, 1H), 8.4 (d, *J* = 8.88, 1H).

Anal. Calcd. for $C_{24}H_{14}O_4$: C, 78.68; H, 3.85. Found: C, 78.52; H, 3.99.

4-[(2*H*-1-Naphtho[3,4-*b*]pyran-2-one-4-yl)methylene]-2-(4-methoxy) phenyl-5-(4H)furanone (**3f**).

The compound was obtained as red prisms, ethylacetate/cyclo hexane (Yield = 65%, M. P. = 235 °C). IR (KBr): 3117, 1772, 1735, 1593, 1569, 1508, 1417, 1311, 1249, 1035, 993, 824 and 739. ^{1}H NMR ($CDCl_3$): δ = 3.95 (s, 3H), 6.7 (s, 1H), 6.75 (s, 1H), 7.05 (d, *J* = 8.89, 2H), 7.59 (d, *J* = 8.8, 1H), 7.65 (t, *J* = 8.68 & *J* = 8.65, 1H), 7.7 (t, *J* = 8.66 & *J* = 8.66, 1H), 7.75 (s, 1H), 7.8 (d, *J* = 8.89, 2H), 8.0 (d, *J* = 8.65, 1H), 8.12 (d, *J* = 8.62, 1H), 8.45 (d, *J* = 8.62, 1H).

Anal. Calcd. for $C_{25}H_{16}O_5$: C, 75.75; H, 4.07. Found: C, 75.50; H, 4.25.

4-[(5,7-Dimethyl-2*H*-1-benzopyran-2-one-4-yl)methylene]-2-(4-methyl)phenyl-5-(4*H*)furanone (**3g**).

The compound was obtained as yellow-orange needles, from ethanol (Yield = 81%, M. P. = 245 °C deco). IR (KBr): 2918, 1782, 1733, 1618, 1583, 1450, 1334, 1247, 1178, 999, 883 and 746. ^{1}H NMR (CDCl3): δ = 2.42 (d, 6H, 2(Me)), 2.61(s, 3H), 6.39 (s, 1H), 6.61 (s, 1H), 6.94 (s, 1H), 7.07 (s, 1H), 7.27(d, *J* = 8.61, 2H), 7.54 (s, 1H), 7.64 (d, *J* = 8.21, 2H).

Anal. Calcd. for $C_{23}H_{18}O_4$: C, 77.08; H, 5.06. Found: C, 76.94; H, 4.89.

4-[(5,7-Dimethyl-2*H*-1-benzopyran-2-one-4-yl)methylene]-2-(4-methoxy)phenyl-5-(4*H*)furanone (**3h**).

The compound was obtained as orange-red needles, from ethanol (Yield = 52%, M. P. = 255 °C char). IR (KBr): 3110, 1778, 1730, 1602, 1593, 1577, 1510, 1452, 1313, 1244, 1026, 995, 825 and 750. ^{1}H NMR ($CDCl_3$): δ = 2.40 (s, 3H), 2.61(s, 3H), 3.87(s, 3H), 6.40 (s, 1H), 6.54 (s, 1H), 6.93 (s, 1H), 6.97 (d,

J = 9.00, 2H), 7.06 (s, 1H), 7.50 (s, 1H), 7.70 (d, *J* = 9.00, 2H).

Anal. Calcd. for $C_{23}H_{18}O_5$: C, 73.79; H, 4.85. Found: C, 73.63; H, 4.58.

4-[(6,7-Dimethyl-2*H*-1-benzopyran-2-one-4-yl)methylene]-2-(4-methyl)phenyl-5-(4*H*)furanone (**3i**).

The compound was obtained as yellow-orange needles, from ethanol (Yield = 75%, M. P. = 260 °C char). IR (KBr): 3161, 1780, 1705, 1624, 1562, 1452, 1344, 1220, 1186, 983, 881 and 756. ^{1}H NMR ($CDCl_3$): δ = 2.34 (s, 3H), 2.37(s, 3H), 2.42(s, 3H), 6.57 (s, 1H), 6.75 (s, 1H), 7.18 (s, 1H), 7.29 (d, *J* = 7.82, 2H), 7.45 (s, 1H), 7.49 (s, 1H), 7.67 (d, *J* = 8.22, 2H).

Anal. Calcd. for $C_{23}H_{18}O_4$: C, 77.08; H, 5.06. Found: C, 76.97; H, 5.17.

4-[(6,7-Dimethyl-2*H*-1-benzopyran-2-one-4-yl)methylene]-2-(4-methoxy)phenyl-5-(4*H*)furanone (**3j**).

The compound was obtained as orange-red needles, chloroform/cyclohexane (Yield = 63%, M. P. = 235 °C char). IR (KBr): 3161, 1780, 1706, 1622, 1562, 1506, 1390, 1331, 1176, 1024, 981, 831 and 756. ^{1}H NMR ($CDCl_3$): δ = 2.35 (s, 3H), 2.39(s, 3H), 3.87(s, 3H), 6.57 (s, 1H), 6.68 (s, 1H), 6.99 (d, *J* = 9.00, 2H), 6.18 (s, 1H), 7.44 (s, 1H), 7.46 (s, 1H), 7.73 (d, *J* = 8.61, 2H).

Anal. Calcd. for $C_{23}H_{18}O_5$: C, 73.79; H, 4.85. Found: C, 73.92; H, 4.67.

4-[(7-Acetoxy-2*H*-1-benzopyran-2-one-4-yl)methylene]-2-(4-methyl) phenyl-5-(4*H*)furanone (**3k**).

The compound was obtained as orange needles, from ethanol (Yield = 60%, M. P. = 247 °C char). IR (KBr): 1778, 1712, 1616, 1569, 1539, 1417, 1346, 1272, 1134, 993, 891 and 752. ^{1}H NMR (DMSO-d6): δ = 2.30 (s, 3H, $COCH_3$), 2.38(s, 3H, CH_3), 6.76 (s, 1H), 7.20 (d, *J* = 6.65, 1H), 7.32-7.38 (m, 3H), 7.43 (s, 1H), 7.54 (s, 1H), 7.81 (d, *J* = 8.21, 2H), 7.95 (d, *J* = 9.00, 1H).

Anal. Calcd. for $C_{23}H_{16}O_6$: C, 71.13; H, 4.15. Found: C, 71.34; H, 4.02.

4-[(7-Acetoxy-2*H*-1-benzopyran-2-one-4-yl)methylene]-2-(4-methoxy)phenyl-5-(4*H*)furanone (**3l**).

The compound was obtained as red prisms, from ethanol (Yield = 73%, M. P. = 253 °C char). IR (KBr): 3149, 1784, 1755, 1714, 1620, 1571, 1541, 1348, 1228, 1176, 1026, 993, 891 and 754. ^{1}H NMR (DMSO-d6): δ = 2.30 (s, 3H, $COCH_3$), 3.86(s, 3H, CH_3), 6.76 (s, 1H), 7.09 (d, *J* = 9.00, 2H), 7.20 (d, *J* = 9.00, 1H), 7.33 (s, 1H), 7.37 (s, 1H), 7.47 (s, 1H), 7.88 (d, *J* = 8.61, 2H), 7.96 (d, *J* = 8.21, 1H).

Anal. Calcd. for $C_{23}H_{16}O_7$: C, 68.32; H, 3.99. Found: C, 68.20; H, 4.15.

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