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On the Spectral Properties of Some Fused 4-Methylcoumarins

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Preparations of the ring-fused 4-methylcoumarins **2**—**10** were reexamined, and the nuclear magnetic resonance (NMR), ultraviolet (UV) and fluorescence spectral characteristics were determined. Fluorescence properties were found to be sensitive to the type and the position of the ring fused to the parent 4-methylcoumarin **1**. The angularly benzo-fused **3** was highly fluorescent, whereas the linearly benzo-fused **4** and the pyrono-fused **7** and **9** were only weakly fluorescent.

Keywords——benzocoumarin; pyronocoumarin; ^{1}H-NMR; UV; fluorescence spectrum; fluorescence quantum yield

During our studies on stable diazomethylcoumarins as potential fluorogenic reagents,[1] a need arose to compare availability as well as the fluorescence intensities among a series of fused 4-methylcoumarins **2**—**9** together with the homologous compound **10** shown in Chart 1, in which benzene, pyrane, pyrone or a hydrogenated ring is fused at the 5—6, 6—7, or 7—8 positions of the parent 4-methylcoumarin (**1**). While the effect of ring substituents on the fluorescence properties of coumarin is well recognized,[2] little is known about the spectral properties, especially the fluorescence characteristics, of fused coumarin ring systems such as **2**—**10**.

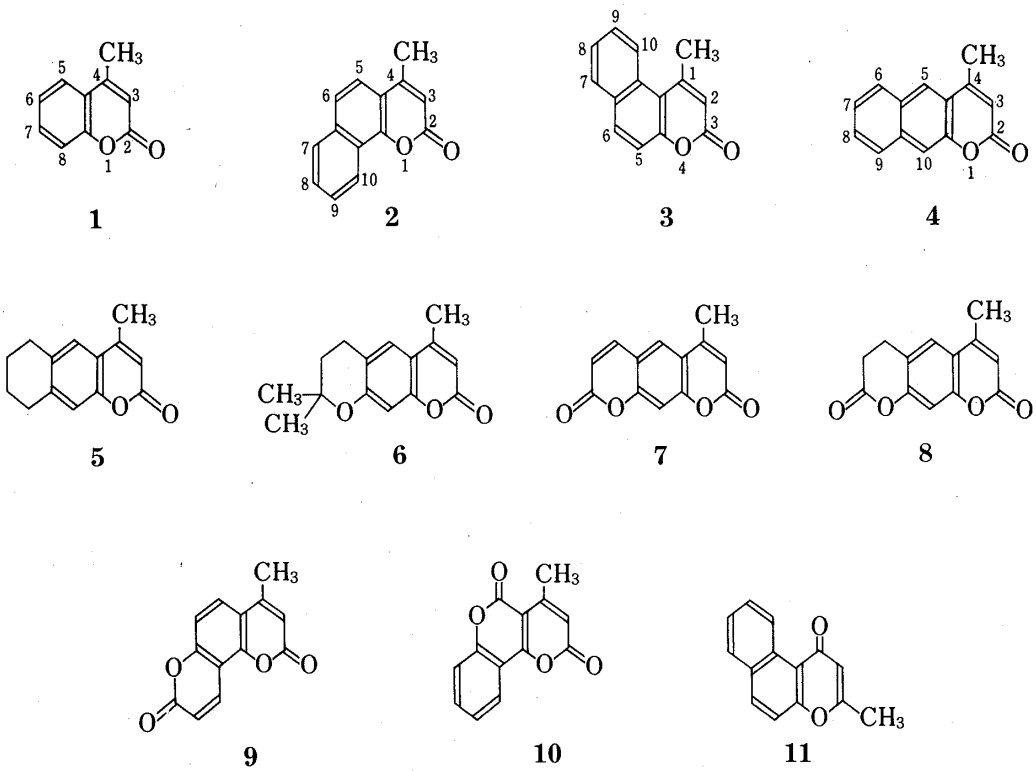

Chart 1

The reported procedures for the preparations of **2**—**10** were reexamined, since little information is given in the literature. Compounds **3**, **4**, **7** and **9** were not necessarily readily available *via* the reported methods on a preparative scale. In contrast to the easy preparation of **2** from 1-naphthol,[3] and in spite of the reported preparation[4] of **3** in 30% yield, Pechmann condensation of 2-naphthol with ethyl acetoacetate under the reported conditions[4] was shown to give a mixture of **3** and its isomeric and non-fluorescent 3-methyl-1*H*-naphtho[2,1-*b*]pyran-1-one (**11**) in only very low yield (below 8% in total). Several attempts to raise the yield were unsuccessful under various reaction conditions. Further, the repeated examination of the described procedure[5] for the dehydrogenation of **5** using *N*-bromosuccinimide revealed the formation of the reported **4** contaminated by its monobromo derivative (**12**) as the unknown non-fluorescent side-product, which could only be chromatographically separated from **4** with difficulty. Bromine substitution at the naphthalene ring of **4**, probably at the C^6- or C^9-position, but not at the C^4-methyl[4] or the active C^3-position[6] of the coumarin ring, can be assumed from the ultraviolet (UV), infrared (IR) and nuclear magnetic resonance (NMR) spectral data, although further studies were not undertaken to determine the exact position of attachment. The obtained yields of **7** and **9** were again unsatisfactory for preparative purposes.

All the structures of **2**—**10** were reconfirmed from the elemental analyses and NMR

TABLE I. Physical and ^{1}H-NMR Data

Compd. No.	Appearance (Recryst. solvt.)	mp (°C) (lit., mp)	Lit.	^{1}H-NMR ($CDCl_3$)[a] δ (ppm)		
				C^4–Me (3H, s)	C^3–H (1H, s)	Others
2	Needles (EtOH)	173 (170)	3)	2.41	6.26	7.28—7.83 (5H, m, C^{5-9}–H), 8.39—8.48 (1H, m, C^{10}–H)
3	Prisms (Acetone)	182—183 (182—183)	4)	2.90[b]	6.35[c]	7.26—7.99 (5H, m, C^{5-9}–H), 8.52—8.60 (1H, m, C^{10}–H)
4	Prisms (Acetone)	225—226 (216—218)	5)	2.54	6.33	7.46—8.06 (6H, m, Ar–H)
5	Prisms (EtOH)	155—156 (155—156)	9)	2.38	6.17	1.76—1.92 (4H, m, $C^{7,8}$–H), 2.83 (4H, br, $C^{6,9}$–H) 6.97 (1H, s, C^{10}–H), 7.24 (1H, s, C^5–H)
6	Needles (EtOH)	175—176 (172—173)	10)	2.36	6.05	1.37 (6H, s, C^8–Me), 1.85 (2H, t, J=6.6 Hz, C^7–H), 2.85 (2H, t, J=6.6 Hz, C^6–H), 6.69 (1H, s, C^{10}–H), 7.28 (1H, s, C^5–H)
7	Prisms (AcOH)	261—262 (243—244)	11)	2.49	6.33	6.45 (1H, d, J=9.8 Hz, C^7–H), 7.24 (1H, s, C^{10}–H), 7.71 (1H, s, C^5–H), 7.76 (1H, d, J=9.8 Hz, C^6–H)
8	Prisms (AcOEt)	231—232 (225—226)	11)	2.44	6.24	2.77—2.93 (2H, m, C^7–H), 3.05—3.18 (2H, m, C^6–H), 7.00 (1H, s, C^{10}–H), 7.44 (1H, s, C^5–H)
9	Needles (THF)[d]	269—272 (304—305)	12)	2.49	6.33	6.54 (1H, d, J=9.8 Hz, C^9–H), 7.27 (1H, d, J=8.8 Hz, C^6–H), 7.75 (1H, d, J=8.8 Hz, C^5–H), 8.33 (1H, d, J=9.8 Hz, C^{10}–H)
10	Needles (DMF)[d]	243—245 (242—245)	13)	2.65	6.23	7.25—7.76 (3H, m, C^{7-9}–H), 8.05—8.15 (1H, m, C^{10}–H)

a) Numbering systems follow the representative listings shown in Chart 1. Abbreviations: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad.
b) C^1–Me. *c*) C^2–H.
d) THF, tetrahydrofuran; DMF, dimethylformamide.

TABLE II. UV and Fluorescence Data

Compd. No	UV (EtOH) λ_{max} nm ($\varepsilon \times 10^{-4}$)	F (EtOH)[a]			
		λ^{ex}_{max} nm	λ^{em}_{max} nm	Quantum yield	Relative intensity
1	270 (1.10), 311 (0.61)	334	380	1.9×10^{-3}	1.0
2	264.5 (2.98), 274.5 (3.87), 2.92 (0.64) 304 (0.80), 317 (0.79), 351.5 (0.55)	274	425	7.8×10^{-2}	41
3	230.5 (4.81), 248 (1.77), 316.5 (1.05) 347 (1.14), 362.5 (0.83)	262, 318 348	415	1.6×10^{-1}	84
4	225.5 (3.86), 263 (2.54), 273 (2.70) 320.5 (1.55)	265, 271 322	459	9.2×10^{-3}	4.8
5	280 (0.71), 324 (0.53)	268, 303 339	393	8.8×10^{-3}	4.6
6	220 (1.60), 246 (0.32), 256.5 (0.25) 329.5 (2.46)	332	387	1.2×10^{-1}	63
7	260 (3.21), 325.5 (1.71), 341 (1.63)	313, 360	396	4.8×10^{-2}	25
8	276.5 (1.01), 284 (1.03), 318.5 (1.14)	331	389	5.2×10^{-1}	274
9	291 (2.44)	328	444	3.0×10^{-3}	1.6
10	237 (0.78), 256.5 (1.12), 266.5 (1.07) 334.5 (1.17), 346.5 (1.26)	253, 331 384	396	2.8×10^{-2}	15

a) Fluorescence: ex, excitation; em, emission.

spectra, although some of the observed melting points were different from those reported, as shown in Table I. The angular compounds can be distinguished from the linear ones by the presence of NMR proton signal(s) at lower field ($\delta > ca.$ 8.0 ppm).

UV and fluorescence data for **1**—**10** in ethanol are summarized in Table II, which also shows the fluorescence quantum yields relative to quinine sulfate. The relatively simple UV spectrum of the linearly benzo-fused **4** is supposed to be correlated to that of naphthalene,[5] just as is that of coumarin to benzene,[7] whereas more complicated spectra were observed for the angular compounds, **2**, **3** and **10**. Pyrono-fused **7** and **9** showed rather simple UV spectra. Data in Table II indicate that the fluorescence properties of **2**—**10** are sensitive to the type of ring fused and the position of its attachment. Although they are all more or less fluorescent as compared to **1**, the benzo-fused compounds (**2**, **3**, **4**) generally show a higher fluorescence intensity than the pyrono-fused ones (**7**, **9**, **10**). In accordance with the reported[8] benzo-annellation effect in the case of coumarin itself, marked differences in the fluorescence quantum yields as well as in the emission maxima can be seen among the present methyl-substituted benzocoumarin series, *i.e.*, the 5,6-fused angular compound **3** shows fluorescence of high intensity, but not as high as in the case of the parent 5,6-benzocoumarin,[8] whereas the linearly-fused **4** fluoresces very weakly with the emission maximum much more shifted to the red (79 nm) relative to that of **1**. The difference in intensity between angular and linear geometry is reversed with the pyronocoumarins, **7** and **9**. Fluorescence properties of **5**, **6** and **8** can be inferred from the analogy with those of the corresponding 7-substituted derivatives of **1**, and the effect of appropriate ring substitution on fluorescence intensity seems to be larger than that of ring condensation. The fluorescence data shown above appear to provide a useful basis for the development of fluorogenic reagents containing coumarin ring systems.

Experimental

General Methods——All the melting points were determined on a Yanaco micro melting point apparatus and are uncorrected. IR spectra were determined using a Hitachi 215 grating spectrophotometer. Proton NMR spectra were

recorded at 100 MHz in $CDCl_3$ on a JEOL JNM-FX-100 spectrometer using Me_4Si as an internal standard. Mass spectrum (MS) was taken on a Shimadzu LKB-900B spectrometer (direct inlet, at 70 eV). UV spectra were obtained in EtOH with a Hitachi 200-10 spectrophotometer. Fluorescence spectra were measured in non-fluorescent EtOH on a Shimadzu RF-503 difference spectrofluorometer. Relative fluorescence quantum yields were calculated from the UV and fluorescence emission spectra (excitation at 340 nm) according to the method reported in the literature,[14] based on quinine sulfate in 0.1 N H_2SO_4 (quantum yield = 0.55).

Materials——Seven fused 4-methylcoumarins **2** and **5**—**10** were prepared according to the procedures reported in the literature cited in Table I. All the products were recrystallized at least twice before spectral measurement, and their purities were checked by thin-layer chromatography (TLC). Satisfactory microanalysis data were obtained for all products.

1-Methyl-3*H*-naphtho[2,1-*b*]pyran-3-one (3)[4]——Conc. H_2SO_4 (450 ml) was added dropwise to a stirred mixture of 2-naphthol (72 g, 0.5 mol) and ethyl acetoacetate (74.8 g, 0.58 mol) at 0 °C, and the whole mixture was stirred at room temperature for 15 h. The brown-colored mixture was poured onto ice (5 l), and the resulting oil was extracted with $CHCl_3$ (1.2 l in total). Drying of the solution over anhyd. $MgSO_4$ and evaporation of the solvent followed by treatment of the residue with a small amount of Et_2O gave a powder (8.8 g), which showed two separate spots on TLC. NMR measurement showed that this material is composed of **3** and 3-methyl-1*H*-naphtho[2,1-*b*]pyran-1-one (**11**), the proportion of which was determined to be 1.2 : 1 by measuring the peak ratio of the appropriate CH_3 proton signals. The mixture was recrystallized from acetone to give 4.5 g (4%) of **3**, mp 182—183 °C. IR (KBr): 1698, 1210 cm^{-1}. *Anal.* Calcd for $C_{14}H_{10}O_2$: C, 79.98; H, 4.79. Found: C, 79.99; H, 4.82. NMR and UV data, see Tables I and II.

Compound **11** was isolated from the mother liquor of the above recrystallization, and recrystallized. Prisms from benzene, mp 166—167 °C (lit.,[15] mp 168 °C). IR (KBr): 1659, 1614, 1242 cm^{-1}. UV λ_{max}^{EtOH} nm (ε): 229 (21900), 259 (18200), 302 (10000), 334 (4630). NMR ($CDCl_3$) δ: 2.33 (3H, s, CH_3), 6.25 (1H, s, C^2–H), 7.31—8.00 (5H, m, C^{5-9}–H), 10.00 (1H, d, J = 8.1 Hz, C^{10}–H). *Anal.* Calcd for $C_{14}H_{10}O_2$: C, 79.98; H, 4.79. Found: C, 80.01; H, 4.82.

4-Methyl-2*H*-naphtho[2,3-*b*]pyran-2-one (4)[7]——A mixture of 6,7,8,9-tetrahydro-4-methyl-2*H*-naphtho[2,3-*b*]pyran-2-one (**5**)[9] (4.3 g, 20 mmol), *N*-bromosuccinimide (NBS) (7.5 g, 42 mmol) and benzoyl peroxide (1.5 g) in CCl_4 (180 ml) was refluxed with stirring. After 2.5 h, AcOK (30 g) and AcOH (10 ml) were added to the reaction mixture under cooling, and the whole was again refluxed for 1 h with vigorous stirring. The resulting mixture was poured into ice-water, and the separated CCl_4 layer was collected, washed with 5% Na_2CO_3 and H_2O, then dried over anhyd. $MgSO_4$. Evaporation of the solvent gave an oily residue, which was treated with a small amount of CH_3CN to give a powder (2.7 g) showing two adjacent spots on TLC. The crude product was subjected to chromatography over silica gel (Wakogel C-200) using a mixture of benzene and CCl_4 for gradient eluent. The monobromo compound **12** was obtained from the first fraction eluted with benzene–CCl_4 (3 : 1 v/v), weighing 340 mg (6%). Prisms from acetone, mp 116—118 °C. IR (KBr): 1715, 1625, 1216 cm^{-1}. UV λ_{max}^{EtOH} nm (ε): 228 (37900), 265.5 (25400), 276.5 (30800), 326.5 (16600). MS *m/e* (rel intensity): 290 (99, $M^+ + 2$), 288 (100, M^+), 261 (30), 259 (29), 181 (26), 152 (54). NMR ($CDCl_3$) δ: 2.61 (3H, s, CH_3), 6.41 (1H, s, C^3–H), 7.24—7.88 (4H, m, Ar-H), 8.48 (1H, s, Ar-H). *Anal.* Calcd for $C_{14}H_9BrO_2$: C, 58.16; H, 3.14; Br, 27.64. Found: C, 57.87; H, 3.09; Br, 27.58.

The second fraction, eluted with benzene–CCl_4 (4 : 1 v/v), provided **4**, 1254 mg (30%), mp 225—226 °C. IR (KBr): 1716, 1646, 1216 cm^{-1}. *Anal.* Calcd for $C_{14}H_{10}O_2$: C, 79.98; H, 4.79. Found: C, 79.59; H, 4.91. NMR and UV data, see Tables I and II.

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