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Synthesis of Novel Fluorophores Derived from Pyranylidenemalonitrile†

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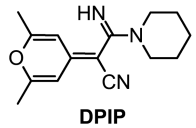
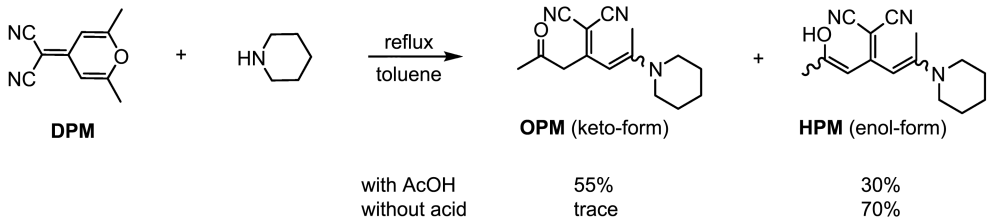
The synthesis and characterization of new fluorophores is receiving increasing attention because of the potential applications of fluorophores as light emitting materials in LED[1-3] and fluorometric probes for biomolecules.[4,5] For this purpose 2-(2,6-dimethyl-pyran-4-ylidene)-malononitrile (**DPM**) is used as a key intermediate for synthesis of the red emission dyes *viz.* 4-(dicyanomethylene)-2-methyl-6-(*p*-dimethylaminostyryl)-4*H*-pyran(DCM),[6] 4-(dimethylene-2-methyl-6-[2-(2,3,6,7-tetrahydro-1*H*,5*H*-benzo[ij]quinolizin-8-yl)vinyl]-4*H*-pyran as well as in the synthesis of the symmetrical DCM derivative, 4-(dicyanomethylene)-2,6-bis(4-dimethylaminostyryl)-4*H*-pyran.[7] Now a days, these materials have become attractive because of their tunable electronic properties, representing low excitation gap and are suitable for electron or hole transferring in various electronic devices. In an effort to develop a novel fluorescent chromophores useful in light-involved electronic devices also applicable in fluorometric diagnosis, we synthesized and identified novel fluorophores **OPM**, **HPM** and **DDP** showing the emissions (λ_{max}) in a range of 410-425 nm. The new chromophores were derived from **DPM** by the reactions with primary or secondary amines with the selectivity in their formations under the different reaction conditions.

Reaction of **DPM** with piperidine (4.5 eq) and CH_3COOH (1 eq) in toluene afforded a mixture of products *viz* **OPM** and **HPM**. However, the same reaction without any acid under the same reaction conditions resulted in exclusive formation of **HPM** in 70% yield with trace amount of **OPM**. This surprising selectivity was considered to be attributed to amine based conversion of **OPM** to **HPM** by keto-enol tautomerization or direct generation of enol-form adduct (**HPM**). For the mechanistic study of keto-enol tautomerization, **OPM** in $CDCl_3$ was treated with AcOH or amine base and C(O)C<u>H</u>$_2$ peak was monitored by NMR spectroscopy. Also, **HPM** was treated with AcOH in $CDCl_3$ and **HPM**'s

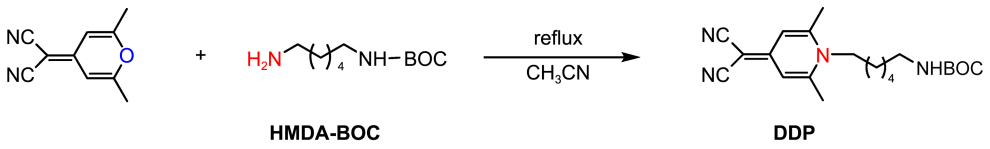


DPIP

NMR peak [(C(OH)=C<u>H</u>] was monitored. When **OPM** in $CDCl_3$ was treated with 1.5 eq of piperidine, it was converted to **HPM** (ca 25% conversion) in 3 days. In acidic condition, however, the conversion of **OPM** to **HPM** was not observed. Interestingly, **HPM** in acidic solution was converted to **OPM** affording a mixture of **OPM** and **HPM** after 5 days. These results suggested that while **OPM** was considered quite inert in acidic solution, **HPM** was in equilibrium with **OPM**.



Scheme 1. Reactions of **DPM** with a secondary amine, piperidine.



Scheme 2. Reaction of **DPM** with a primary amine under catalyst-free condition.

†This paper is dedicated to Professor Eun Lee on the occasion of his honourable retirement.

It was not easy to distinguish enol-form (**HPM)** from the 1,2-addition adduct **DPIP** possessing same chemical formula. Based on the NMR spectroscopic methods including DEPT, COSY and g-HSQC, **HPM**'s structure was confirmed and allowed to rule out the formation of **DPIP**. In addition, the same reactions of **DPM** with pyrrolidine under acid free condition gave the similar results giving keto/enol isomers of 1:4 ratio.

After getting the unexpected results by catalyst-free reaction of **DPM** with piperidine, we have diverted our attention towards the primary amine and carried out reaction of **DPM** with 6-amino-hexyl-carbamic acid *tert*-butyl ester (**HMDA-BOC**) in CH_3CN under catalyst-free conditions at reflux temperature. In contrast of our expectation, it also underwent 1,6-addition affording dehydrative cyclization product (**DDP**) as major (Scheme 2). It is worthy of note that 1,2-additions of amines to nitrile group of **DPM** were not observed under acidic as well as acid-free conditions. The formation of **DDP** is considered to be initiated by 1,6-addition of HMDA-BOC to **DPM** then followed by ring closure *via* intra molecular nucleophilic attack of secondary amine and subsequent dehydration.

The absorption and emission spectra for **OPM**, **HPM** and **DDP** are shown in Figure 1 and Figure 2 respectively. The absorption spectrum of **OPM** (Fig. 1) showed two major bands; one in the range of 250-300 nm (λ_{max} = 273 nm) and other broad band in the range of 300-375 nm. **HPM** in its absorption spectra showed slight red-shift from those in **OPM**, showing λ_{max} values at 286 nm. In the absorption spectrum of **DDP**, significant change has been observed in comparison with those of **OPM** and **HPM**. Instead of two major absorption bands, only one absorption band (λ_{max}) appeared at 359 nm. The λ_{max} absorption of **DPP** appears in the range of the wavelength where the second highest absorption bands of **OPM** and **HPM** are shown. This result suggested that the chromophores contributing the emissions of **OPM** and **HPM** appeared near 350 nm might be similar to that of **DPP**. All the emissions of **OPM**, **HPM** and **DDP** showed λ_{max} values in the range of 410-430 nm. In addition, **HPM** and **DDP** represented weak emission bands near at 480 nm.

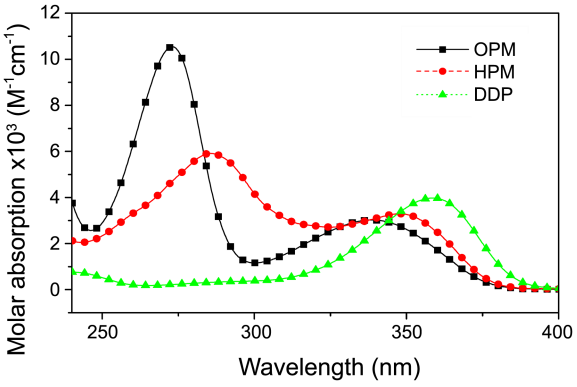


Figure 1. Absorption spectra for **OPM**, **HPM** and **DDP** in ethanol.

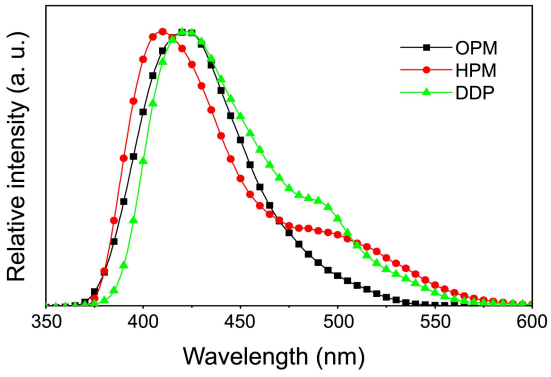


Figure 2. Emission spectra for **OPM**, **HPM** and **DDP** in ethanol; excitation wavelengths are 273, 286 and 345 nm, respectively.

In a summary, we have synthesized a new fluorophores *viz* **OPM**, **HPM** and **DDP** from **DPM** under different experimental conditions. These novel compounds exhibited the characteristic fluorescent emissions in the blue region in ethanol solution.

Experimental Section

DPM (2-(2,6-Dimethyl-pyran-4-ylidene)-malononitrile) and **HMDA-BOC** were prepared by the literature procedures.[8,9] The UV-visible, photoluminescence spectra were recorded on Shimadzu UV-2101PC spectrophotometer and Varian Cary Eclipse Fluorescence spectrometer, respectively. ^1H and ^{13}C NMR spectra were recorded on Bruker 500 MHz or Varian 300 MHz spectrometer. The National Center for Inter-university Facilities at Seoul National University performed all elemental and FAB mass analysis.

Synthesis of OPM and HPM. To a solution of **DPM** (3.0 g, 16.1mmol), piperidine (6.2 g, 72.8 mmol) in toluene (50 mL) was added 1.0 mL of glacial acetic acid at room temperature, then refluxed for 48 hrs. After being cooled to room temperature, the reaction mixture was evaporated and dried under vacuum. Column chromatography on silica gel (hexane: ethyl acetate = 7:3) gave successively 2-(6-oxo-2-(piperidin-1-yl)hept-2-en-4-ylidene)malononitrile (**OPM**) and 2-(2-hydroxy-6-(piperidin-1-yl)hepta-2,5-dien-4-ylidene) malononitrile (**HPM**) in 55 and 30% yield, respectively.

OPM(keto-form): UV-vis λ_{max}(molar absorption, $M^{-1}cm^{-1}$) in ethanol 273 nm (1.1×10^4), 339 nm (3.0×10^3). Fluorescence λ_{max}= 422 nm(in ethanol); ^1H-NMR in $CDCl_3$(500 MHz): δ 6.43(s, 1H), 3.83(s, 2H), 3.63/3.61(m, 4H), 2.40(s, 3H), 2.29(s, 3H), 1.68(br s, 6H). ^{13}C-NMR in $CDCl_3$(125 MHz), δ 201.5, 160.3, 159.7, 148.2, 116.1, 113.6, 90.8, 48.2, 47.1, 28.8, 24.4, 23.4, 23.0 ppm ; MS(70 eV), m/e = 257(M^+, 85), 242(96), 228(85) 214(100), 201(57), 186(82), 174(75), 159(79), 147(60) 132(83), 117(23), 104(60), 91(25), 84(85), 77(51), 65(30), 55(56); IR(KBr): 3022(w), 2940(m), 2839 (m), 2200(s), 1720(s), 1583, 1557, 1441, 1357, 1164, 1090, 536, 500 cm^{-1} ; Anal. for $C_{15}H_{19}N_3O$: found C 69.99, H 7.38, N 16.41, calcd. C 70.01, H 7.44, N 16.33.

HPM(enol-form): UV-vis λ_{max}(molar absorption, $M^{-1}cm^{-1}$) in ethanol 286 nm (5.9×10^3), 348 nm (3.3×10^3). Fluorescence λ_{max}= 409 nm, 485 nm(sh) in ethanol; ^1H-NMR in

$CDCl_3$(500MHz): δ 11.30(br s, 1H), 6.51(s, 1H), 6.03(s, 1H), 3.43/3.40(m, 4H), 2.41(s, 3H), 2.35(s, 3H), 1.77/1.71(m, 6H); ^{13}C-NMR in $CDCl_3$ (125 MHz): δ 161.8, 159.9, 156.2, 147.5, 140.6, 108.4, 104.4, 101.7, 50.2, 24.7, 23.3, 23.1, 17.0; MS(70 eV), *m*/*e*(%) = 257(M^+, 46), 240 (7.5), 228(35) 214(59), 201(44), 189(100), 175(44), 159 (13), 146(21) 128(7), 114(9), 101(14), 84(50), 77(10), 56(7); HRMS for M^+ 257.1528(calcd), 257.1514(obs); IR(KBr): 3399(vw), 3163(w), 2939(m), 2858(w), 2255(m), 1645(s), 1583(s), 1493(w), 909(vs), 763(vs), cm^{-1}; Anal. for $C_{15}H_{19}N_3O$: found C 70.11, H 7.40, N 16.35, calcd. C 70.01, H 7.44, N 16.33.

Synthesis of *tert*-Butyl 6-(4-(dicyanomethylene)-2,6-dimethylpyridin-1(4*H*)-yl)hexylcarbamate (DDP). To a round bottom flask containing acetonitrile (50 mL), **DPM** (3.0 g, 16.1 mmol) and **HMDA-BOC**, (6-amino-hexyl)-carbamic acid tert-butyl ester (6.9 g, 32.2 mmol) were added at room temperature. The reaction mixture was refluxed for 4 hrs and then cooled to room temperature, evaporated and dried under vacuum. Flash column chromatography (methylene chloride/MeOH = 8:2) gave DDP in 80% yield. DDP: UV-vis λ_{max}(molar absorption, $M^{-1}cm^{-1}$) in ethanol 240 nm (7.6×10^2), 359 nm (4.0×10^3). Fluorescence λ_{max} in ethanol: 422 nm, 490 nm(sh). ^{1}H-NMR in $CDCl_3$ (300 MHz): δ 6.68(s, 2H), 4.54(br s, 1H), 3.88(t, 2H), 3.08-3.14(m, 2H), 2.44(s, 6H), 1.70-2.21(m, 17H); ^{13}C-NMR in $CDCl_3$ (75MHz): δ 154.5, 154.2, 146.0, 117.3, 112.3, 77.6, 47.5, 43.0, 38.5, 28.3, 28.0, 26.8, 24.7, 24.5, 19.1; IR(KBr): 2933(m), 2816(m), 2191(s), 2165(s)1645(s), 1685, 1647, 1174, 847, cm^{-1}; Anal. for $C_{21}H_{30}N_4O_2$: found C 68.21, H 8.21, N 14.99, calcd. C 68.08, H 8.16, N 15.12.

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