HETEROCYCLES, Vol. 95, No. 2, 2017, pp. 972-979. © 2017 The Japan Institute of Heterocyclic Chemistry
Received, 2nd September, 2016, Accepted, 25th November, 2016, Published online, 17th February, 2017
DOI: 10.3987/COM-16-S(S)62

ABSORPTION AND FLUORESCENCE PROPERTIES OF CHALCONES HAVING PYRROLE OR INDOLE MOIETY

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Abstract – 2'-Hydroxychalcone derivatives having pyrrole ring have been synthesized and their absorption and fluorescence properties have been examined in connection to intramolecular hydrogen bonding.

INTRODUCTION

The chalcone derivatives with pyrrole ring have been studied from the view points of having a wide of biological activities such as antioxidant and anticarcinogenic activities.[1-3] We have been studying the photochemical and photophysical properties of various kinds of chalcone derivatives.[4-14] Although some of the compounds having chalcone skeleton and pyrrole or indole substituent have been synthesized, spectroscopic properties of these compounds have not been reported so far.[15-22] Furthermore, for some compound, singlet oxygen production on excitation of chalcone derivatives have been reported.[1] In some compounds, the excited state deactivates quite rapidly by way of intramolecular hydrogen atom transfer reaction in the excited singlet state.[5,6] Therefore, it seems important to study the deactivation processes from the excited state by studying spectroscopic properties to explore the importance of chalcone derivatives having pyrrole or indole moiety for biological activities. We also aimed to find a way to increase the quantum yield of fluorescence emission of 2'-hydroxychalcone derivatives by introducing proper substituents and/or changing molecular structure. In this respect, we have studied the spectroscopic properties of chalcone derivatives **1**-**3** having pyrrole or indole instead of benzene ring.

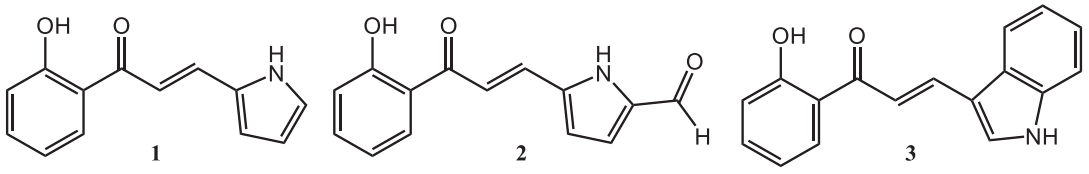


Figure 1. Structures of 2'-hydroxychalcone derivatives examined in this work

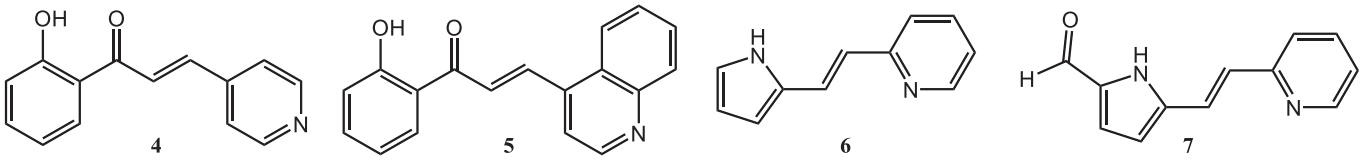


Figure 2. Structures of 2'-hydroxychalcone derivatives examined in previous work

RESULTS AND DISCUSSION

Chalcone derivatives **1-3** were synthesized by condensation of corresponding aldehyde and ketones as described in Experimental section. Compounds **1-3** form O-H:O intramolecular hydrogen bonding as revealed by observation of OH proton at considerably low field in ^{1}H-NMR spectroscopy at 13.2, 12.7 and 15.2 ppm for compound **1**, **2**, and **3**, respectively. The absorption spectra of **1-3** in benzene are shown in Figure 3. The absorption maxima at longer wavelength region together with extinction coefficient are summarized in Table 1. The observation of absorption maximum at 390-400 nm should be ascribable to the existence of intramolecular hydrogen bonding to extend the conjugation of the whole molecules. The maximum wavelength of **3** appeared at slightly shorter wavelength compared to that of **1** probably due to the change of conjugation by indole group instead of pyrrole group.

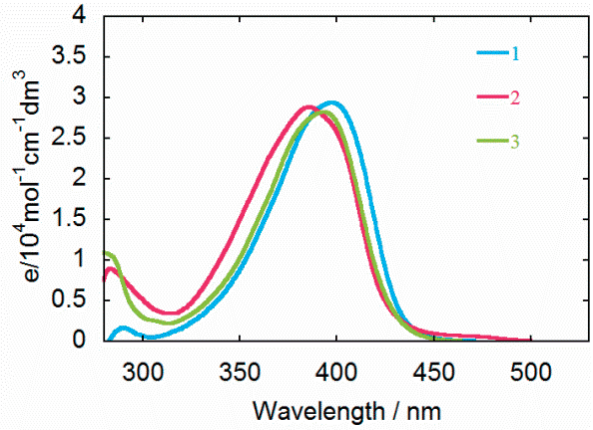


Figure 3. Absorption spectra of **1-3** in benzene

Fluorescence spectra of **1-3** were studied in various solvents. Typical examples observed in benzene are shown in Figure 4. Compounds **1** and **3** exhibited considerably weak fluorescence at longer wavelength region peaking at ca. 640 nm with the quantum yield (Φ_f) of ca. 10^{-5} for **1** and 3.8×10^{-5} for **3** at 298 K (Table 1). These values are comparable to those of related chalcones having pyridine **4** or quinoline **5**.[15] We could not observe the fluorescence from **2** by our instrument of fluorescence spectroscopy and therefore the quantum yield of fluorescence emission from **2** is beyond our detection limit and much lower than 10^{-5}. In the case of hydrogen bonded compounds such as **6** having pyrrole and pyridine at

both end of C=C double bond, hydrogen atom transfer took place to produce the tautomer in the excited singlet state. The fluorescence quantum yield of the tautomer of **6** is as low as 10^{-3}, but is increased to 0.1 by introduction of CHO group at pyrrole ring such as **7**.[16] The reason why we synthesized and studied the compound **2** is that we may increase the quantum yield of fluorescence emission from the tautomer of **2**. But in these chalcone derivatives CHO group did not increase the fluorescence emission from the tautomer. Together with the previous reports for chalcone derivatives,[10,14] substitution of electron donating group or electron accepting group in benzene ring somewhat changed the quantum yield of fluorescence emission of the tautomer produced by intramolecular hydrogen atom transfer, but the effect is small and the quantum yield is at most in the range of 10^{-4}. Among the compounds studied, heteroaromatic ring such as pyrrole, indole, pyridine and quinoline are ineffective to increase the fluorescence emission and the non-radiative deactivation seems to be dominant in these chalcones. Therefore, 2'-hydroxychalcone derivatives are rather stable on photoirradiation and only undergo intramolecular hydrogen atom transfer reaction in the excited state and finally go back to the stating material by reverse hydrogen atom transfer in the ground state. The observed fluorescence at ca. 640 nm can be assigned to the tautomer produced by intramolecular hydrogen atom transfer in the excited singlet state as shown in Figure 4. As to the photostability of the compounds **1**-**3**, the absorption spectra of **1**-**3** did not change on irradiation with 395 nm light and is highly stable on photoirradiation.

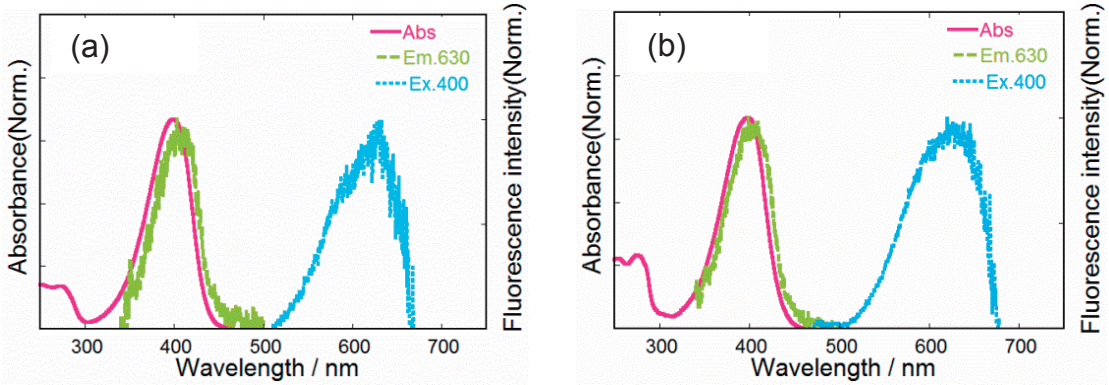


Figure 4. Fluorescence and fluorescence excitation spectra of **1** (a) and **3** (b) in benzene

Table 1. Parameters of absorption and fluorescence spectra of **1**-**3** in benzene

Compound	λ_{abs}/nm	$\varepsilon(\lambda_{Abs})/10^4$ mol^{-1} cm^{-1} dm^3	λ_{FL}/nm	ΔE_{ss}/cm	Φ_{FL}
1	397	2.94	642	9500	$\leqq 10^{-5}$
2	385,399	2.88	-	-	-
3	393	2.82	636	9400	3.8×10^{-5}

As described in the part of introduction, chalcones, especially pyrrole or indole derivatives have been studied as biologically important compounds and are sometimes discussed to produce singlet oxygen by energy transfer from the excited triplet state chalcone or to produce superoxide anion radical by electron transfer reaction. We have tried to directly observe the important step of energy transfer to observe the triplet state of chalcones **1**-**3**, but we could not observe the triplet state of the corresponding chalcones by laser flash photolysis. Although we could not exclude the small contribution of the involvement of triplet state chalcones, one could comment that the direct observation of the precursor species should be essential in discussing the photochemical and photophysical properties of molecules.

From the experimental results, we will propose the potential energy surfaces of deactivation from the excited singlet state after photoexcitation of **1**-**3** including the possibility of deactivation through intramolecular hydrogen bonding and the intersystem crossing to the triplet state (Figure 5). In conclusion, the compounds studied here did not enhance the quantum yield of fluorescence emission from neither normal form nor tautomer form and the main deactivation process should be non-radiative deactivation through intramolecular hydrogen bonding.

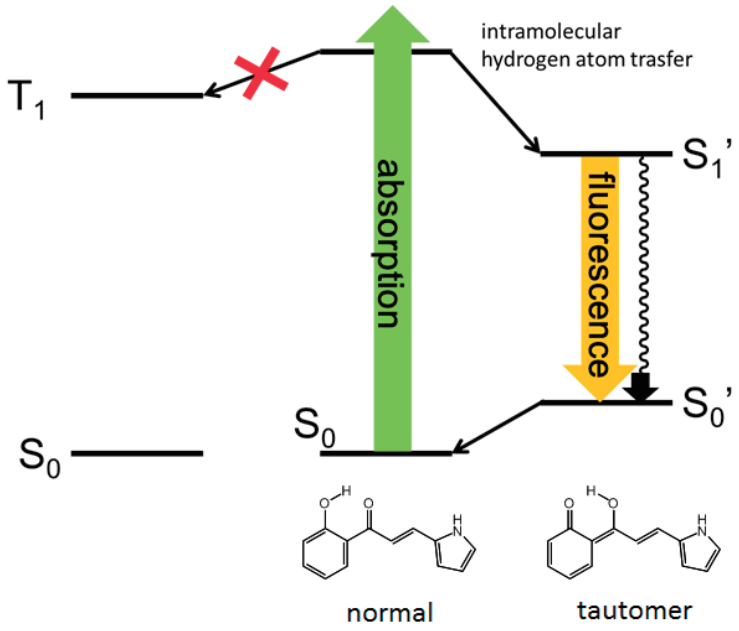
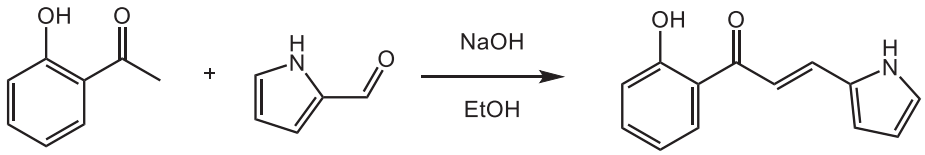


Figure 5. Potential energy surfaces of photoinduced hydrogen atom transfer and subsequent processes

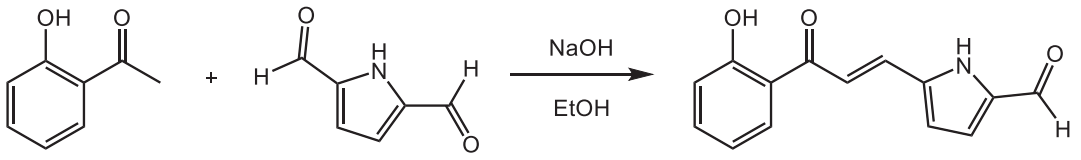
EXPERIMENTAL

(2*E*)-1-(2-Hydroxyphenyl)-3-(1*H*-pyrrol-2-yl)-2-propen-1-one (**1**)[22]



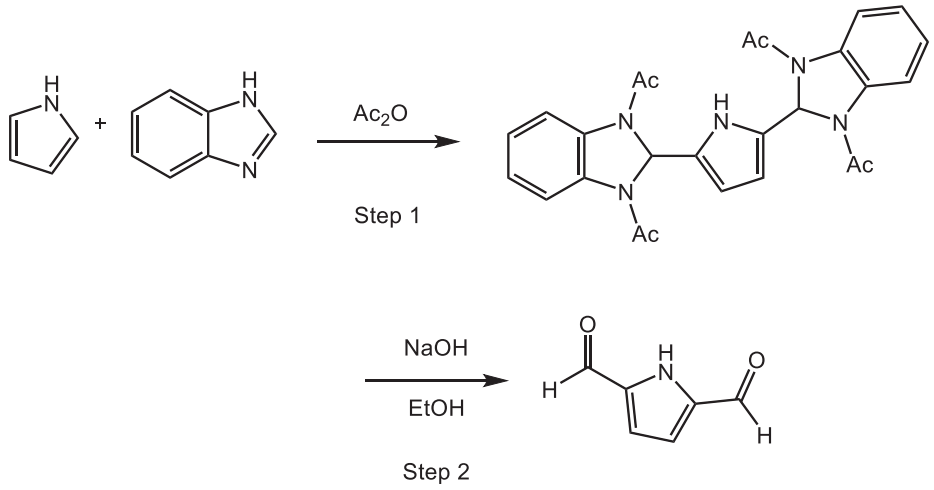
To a mixture of pyrrole-2-carboxaldehyde (0.40 g, 4.2 mmol) and 2'-hydroxyacetophenone (0.58 mL, 4.2 mmol) in Et_2O (5.0 mL) was added a solution of 1 M NaOH (7.5 mL). The solution was stirred for 7 h at 50 °C and then a solution of 1M HCl was added to make neutralized. The resulting mixture was extracted with EtOAc. The combined organic phases were washed with brine, and then dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The orange solid was collected by filtration followed by purification by silica gel column chromatography [eluent: EtOAc / hexane (1:3)]. The solid was recrystallized from EtOH for two times to give the compound **1** (102 mg, 11%) as a yellow needle crystal; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 13.20 (s, 1H, OH), 11.20 (br, 1H), 8.07 (d, *J* = 7.0 Hz, 1H), 7.85 (d, *J* = 15.2 Hz, 1H), 7.68 (d, *J* = 15.2 Hz, 1H), 7.51 (t, *J* = 7.0 Hz, 1H), 7.17 (s, 1H), 6.92-6.97 (m, 2H), 6.83 (s, 1H), 6.29 (s, 1H).

5-[3-(2-Hydroxyphenyl)-3-oxo-1-propen-1-yl]-1*H*-pyrrole-2-carboxaldehyde (**2**)



To a mixture of 2,5-diformylpyrrole (0.49 g, 4.0 mmol) and 2'-hydroxyacetophenone (4.8 mL, 4.0 mmol) in THF (4.7 mL) was added a solution of 1 M NaOH (7.0 mL). The solution was stirred for 7 h at 70 °C and then a solution of 1M HCl was added to make neutralized. The resulting mixture was extracted with EtOAc. The combined organic phases were washed with brine, and then dried over MgSO4, filtered and the solvent was removed under reduced pressure. The orange solid was collected by filtration followed by purification by silica gel column chromatography [eluent: EtOAc / hexane (1:2)]. The solid was recrystallized from EtOH for two times to give the compound 1 (240 mg, 6%) as an orange needle crystal; ^{1}H NMR (270 MHz, CDCl3): δ = 12.7 (s, 1H, OH), 9.68 (s, br, 1H), 9.62 (s, br, 1H), 7.90 (d, 1H, *J* = 8.1 Hz), 7.77 (d, *J* = 16.2 Hz, 1H), 7.56 (d, *J* = 16.2 Hz, 1H), 7.52 (t, *J* = 8.1 Hz, 1H), 7.02-7.05 (m, 2H), 6.97 (t, *J* = 8.1 Hz, 1H), 6.77-6.78 (m, 1H). Anal. Calcd for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.60; N, 5.81. Found: C, 69.90; H, 4.64; N, 5.82.

2,5-Diformylpyrrole[23]



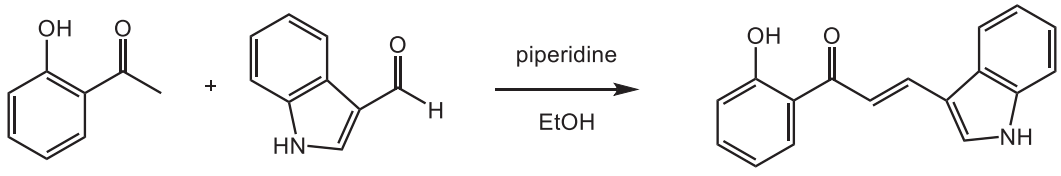
Step 1

To a solution of benzimidazole (5.9 g, 50 mmol) in acetic anhydride (24 mL) at 100 °C was added dropwise pyrrole (2.2 mL, 25 mmol) as a solution in acetic anhydride (15 mL) under atmosphere of nitrogen. The solution was stirred for 7 h at 130 °C, cooled to room temperature, and added hexane (50 mL). The white powder (8.0 g, 68 %) was collected by filtration followed by washing with EtOAc.

Step 2

To a solution of Step 1 product (8.0 g, 17 mmol) in 50 % EtOH (200 mL) at 100 °C was added dropwise 3 M NaOH (30 mL) under atmosphere of nitrogen and the solution was stirred at 100 °C for 3 h. The resulting mixture was extracted with $CHCl_3$ and then a solution of 1 M HCl was added to the combined aqueous phases to make neutralized. The aqueous phase was extracted with EtOAc. The combined organic phases were washed with brine, and then dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The resulting solid purified by silica gel column chromatography [eluent: CH_2Cl_2 / EtOAc (3:1)] to give the desired 2,5-diformylpyrrole as white powder; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 9.53 (s, 2H), 6.98 (d, J = 2.7 Hz, 2H).

(2*E*)-1-(2-Hydroxyphenyl)-3-(1*H*-indol-3-yl)-2-propen-1-one(**3**)[3]



To a mixture of indole-3-carboxaldehyde (0.16 g, 1.1 mmol) and 2'-hydroxyacetophenone (0.12 mL, 1.0 mmol) in EtOH (1.0 mL) was added piperidine (0.10 mL, 1.0 mmol). The solution was stirred for 5 h at 80 °C and the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography [eluent: EtOAc / hexane (1:2)]. The solid was recrystallized from EtOH for two times to give the compound **4** (30.4 mg, 12%) as a yellow needle crystal; ^{1}H NMR(400 MHz, $CDCl_3$): δ = 13.20 (s, 1H, OH), 8.61 (br, 1H), 8.22 (d, *J* = 15.3 Hz, 1H), 8.03 (dd, *J* = 6.2 Hz, 4.1 Hz, 1H), 7.98 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 7.71 (d, *J* = 15.3 Hz, 1H), 7.66 (d, *J* = 2.7 Hz, 1H), 7.50-7.56 (m, 1H), 7.47-7.49 (m, 2H), 7.47-7.45 (m, 1H), 7.03 (dd, *J* = 8.4 Hz, 0.95 Hz, 1H), 6.97 (ddd, *J* = 8.0 Hz, 7.1 Hz, 1.2 Hz, 1H).

MEASUREMENTS

Absorption and fluorescence spectra were measured on a Shimadzu UV-1600 and on a Hitachi F-4500 fluorescence spectrometer, respectively. All solvents of spectral grade for spectroscopy were purchased and used without further purification. All measurements were carried out at 298 K under Ar. The concentration of solution for spectroscopy was adjusted so that the absorption maximum at the excitation wavelength was less than 0.1 for each sample. Fluorescence quantum yields were determined relative to anthracene (Φ_f = 0.27 in ethanol). ^{1}H NMR spectra in $CDCl_3$ with TMS as an internal standard were measured on 270 MHz or 400 MHz NMR spectrometer.

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