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Development of New Pyrrolocoumarin Derivatives with Satisfactory Fluorescent Properties and Notably Large Stokes Shifts

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Small, organic, fluorescent molecules with large Stokes shifts and long emission wavelengths are ideal dyes for various modern fluorescent imaging technologies such as FRET. In this study, we designed and synthesized a number of new fluorescent molecules on the basic structures of two pyrrolocoumarin skeletons where Fischer's indole synthesis and the Suzuki coupling successfully served as the efficient molecular editing protocols. The examination of the fluorescent properties and further structural optimization of these compounds afforded three new pyrrolocoumarin dyes with notably large Stokes shifts and satisfactory fluorescent properties. Among these, **30** showed a large Stokes shift (113 nm) and intense fluorescence (ϕ = 0.55, λ_{em} = 523 nm), and thus showed great potential in biological imaging studies.

Introduction

Biological imaging techniques have been frequently applied in biological, medical and multiple-disciplinary questions. As a representative, fluorescence resonance energy transfer (FRET) is a nonradiative process whereby an excited state (usually a fluorophore) transfers energy to a proximal ground acceptor through long-range, dipole-dipole interactions.[1,2] The transfer efficiency E depends on the inverse sixth power of the distance R between the donor and acceptor obeying the expression $E = 1/(1 + [R/R_0]^6)$, where R_0 is the distance at which 50% of the energy is transferred. In addition, R_0 is a function of the properties of the dyes (including the spectral overlap of donor emission and acceptor absorption, donor quantum yield and the index of medium refraction) and the relative orientation of their dipole moments. Applications of FRET have been widely used in studies of structural biology, biochemistry and polymer science to capture the interactions between the distances from 10 Å to 80 Å.[3] Natural green fluorescent protein (GFP) and its mutants with various spectral properties are frequently used in FRET experiments including the analysis of protein structure,[4] study of protein interactions[5] and immunoassay.[6] However, due to their large sizes, fluorescent proteins may have some undesirable effects on cellular activities. Furthermore, the fluorescent protein-engaged FRET systems often result in practical maximal FRET efficiencies of approximately 40%. Therefore, small-molecule-based organic fluorescent dyes with satisfactory optical properties would be an ideal alternative for modern FRET technology and other fluorescent applications.

FRET-applicable dyes should possess two essential spectral characters. One is a large Stokes shift, and the other is a long emission wavelength. A large Stokes shift could improve the accuracy and sensitivity of the FRET optical ruler in the following aspects: (1) by enhancing the emission intensity of dyes by minimizing the fluorescence self-absorption, and (2) by reducing the mutual interference between excitation and emission wavelength. To date, very few dyes are available with comprehensively satisfactory characteristics, including longer emission wavelength (>500 nm), higher quantum yield (>0.5) and larger Stokes shift (>100 nm). Most commercially available and widely used fluorescent dyes in biological studies usually have a shorter Stokes shift of less than 30 nm, such as rhodamine B (23 nm in methanol), BODIPY (ca. 20 nm), the cyanine dyes (ca. 20 nm) and fluorescein isothiocyanate (28 nm).

Coumarin is a well-known, small, organic molecule. It is also an excellent parent skeleton for organic fluorescent dyes with large Stokes shifts (100–200 nm). Its derivatives have been used in many investigations owing to their intense fluorescence and photochemical stability. However, most coumarin-derived compounds cannot meet the demands for direct application in biological systems due to their relatively short excitation and emission wavelengths (usually in the UV range). This property makes them liable to interference from the background emission and Rayleigh scattering light from biological systems. Relatively little atten-

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tion has been paid to the development of novel and economically available small-molecule fluorescent dyes with satisfactory comprehensive optical properties suitable for FRET experiments. In this paper, we report our design, syntheses, evaluation and optimization of small-molecule fluorescent dyes with notably large Stokes shifts and long emission wavelengths (compatible to fluorescein) on the basic structures of two types of novel pyrrolocoumarin skeletons.

Very recently, Sames and co-workers used several pyrrolocoumarins for the first time as fluorescent probes in their studies of monoamine oxidase.[7] These pyrrolocoumarin derivatives have densely conjugated and aromatic structures and low molecular weights. They were also found to present large Stokes shifts and low to moderate quantum yields (0.03–0.36). If a notable redshift of the excitation/emission wavelength and an enhancement of the quantum yield could be achieved after appropriate modifications, such pyrrolocoumarin derivatives would unambiguously have great potential as FRET dyes. Considering the ease of synthesis, we chose two types of pyrrolocoumarin skeletons (Figure 1, Type I and II) as the basic core structures for further development in this study. By using these two types of basic structures as templates, a sufficient number of new derivatives could be provided for optical property characterizations by diverse molecular editing methods through common precursors.

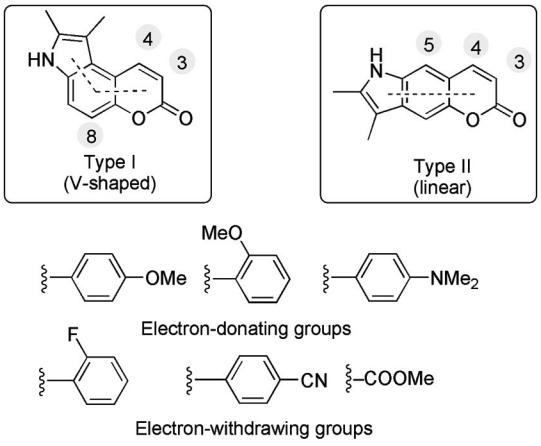


Figure 1. Two types of basic pyrrolocoumarin skeletons, six positions for modification and six representative substituents used in this study.

Results and Discussion

To improve a less than ideal fluorescent compound to a better dye with longer emission wavelength and higher quantum yield, two methods are often used. One is to extend the π-conjugation system, and the other is to introduce either electron-withdrawing group(s) or electron-donating group(s) into the π-conjugation system. Though some helpful experiential principles (PET,[8] ICT,[9] EET and EE[10]) are known, it is still quite difficult to accurately predict the optimal position to attach a functional group for achieving satisfactory fluorescent properties. As the first step, we designed a number of pyrrolocoumarin derivatives based on the above-mentioned two skeletons (**5**–**8** in Scheme 1, **14**–**17** in Scheme 2, **20**–**22** in Scheme 3 and **28**,**29** in Scheme 4) with a focus on synthetic feasibility. Once we obtained the first batch of compounds, we would be able to initiate the primary structure/fluorescence relationship studies, which would then direct further optimizations.

Considering the availability of starting materials, we chose two straightforward strategies for the synthesis of the pyrrolocoumarins. One was to construct a pyrrole moiety fused to the coumarin precursor (Figure 2, Path A), and the other was to elaborate a lactone fused to the indole precursor (Figure 2, Path B). Our initial attempts with Path B failed to generate the desired lactone moiety. After taking into account the lower reaction efficiencies and the relatively high cost of substituted indoles, we turned our efforts to Path A. Fortunately, the Fischer indole synthesis[11] (Path A) was very reliable and successfully applied in this study. Starting from the common and inexpensive starting material coumarin, we efficiently prepared all these pyrrolocoumarins. We achieved the further site-specific introduction of appropriate electron-withdrawing or electron-donating phenyl group(s) with Suzuki couplings in high yields.[12] We describe the details of the synthesis below.

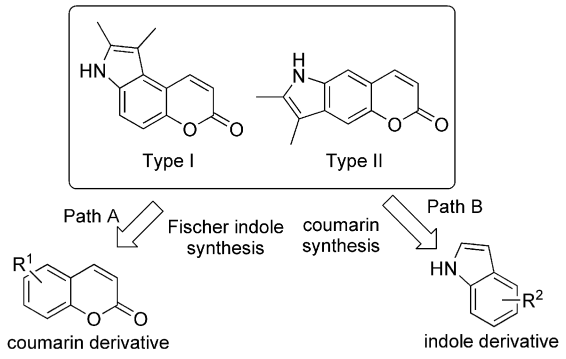
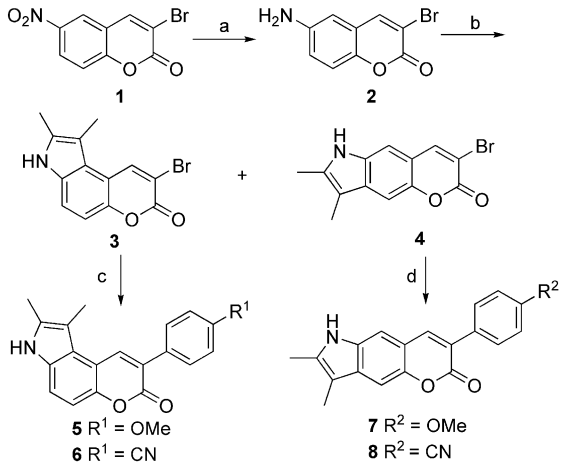


Figure 2. Two synthetic pathways to the designed pyrrolocoumarins.

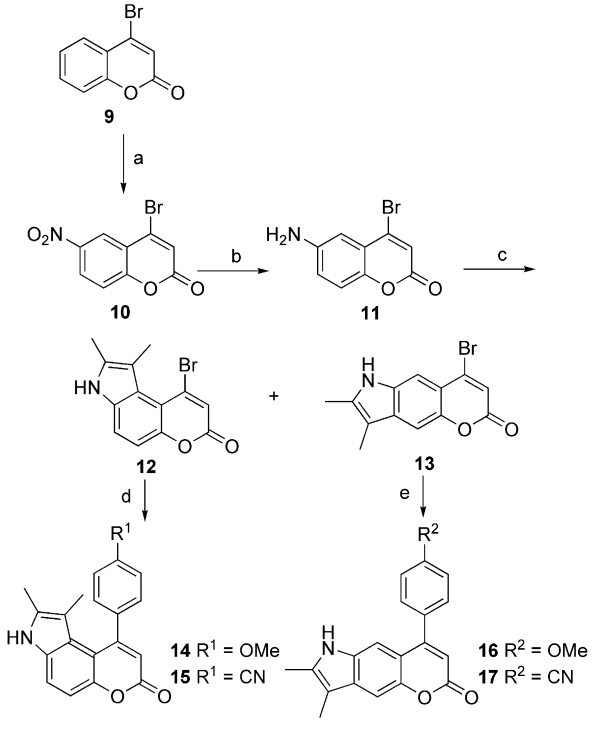
Synthesis of Pyrrolocoumarin Derivatives

2-Bromo-6-nitrocoumarin (**1**), which was readily prepared from coumarin in 2 steps,[13] was reduced to 6-aminocoumarin (**2**) with Fe powder in EtOH and AcOH (Scheme 1). The exposure of aniline **2** to $NaNO_2$/HCl followed by treatment with $SnCl_2$/HCl at 0 °C provided the corresponding hydrazine. This hydrazine immediately reacted with butan-2-one in AcOH at 80 °C for 4 h to give two isomeric pyrrolocoumarin derivatives **3** and **4** in 49% and 16% isolated yield, respectively. Parallel Suzuki couplings of aryl bromide **4** with the corresponding phenylboronic acids afforded the target pyrrolocoumarins **7** and **8** in high yields. Accordingly, Suzuki couplings of the other aryl bromide **3** gave another two pyrrolocoumarins **5** and **6**.



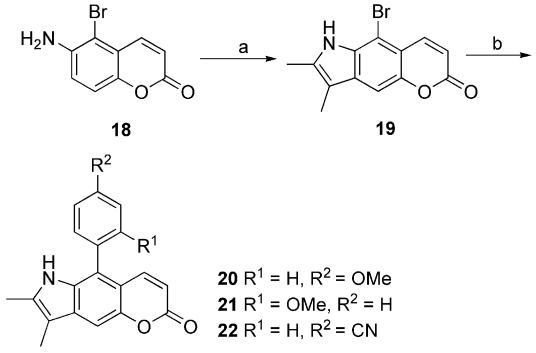
Scheme 1. Reagents and conditions: (a) Fe, AcOH/EtOH, 98%; (b) (i) $NaNO_2$, HCl, (ii) $SnCl_2$, HCl, (iii) butan-2-one, AcOH, 49% for **3**, 16% for **4**; (c) 4-methoxyphenylboronic acid or 4-cyanophenylboronic acid, K_2CO_3, $Pd(PPh_3)_4$, toluene/EtOH/H_2O, 89% for **5**, 82% for **6**; (d) 4-methoxyphenylboronic acid or 4-cyanophenylboronic acid, K_2CO_3, $Pd(PPh_3)_4$, toluene/EtOH/H_2O, 77% for **7**, 62% for **8**.

The synthesis of four more pyrrolocoumarins, **14**–**17**, is outlined in Scheme 2. The nitration of 4-bromocoumarin (**9**)[14] followed by reduction gave aminocoumarin **11**. The Fischer indolization of **11** with butan-2-one afforded major product **12** (56% yield) and minor product **13** (25% yield). We converted both bromides into the corresponding pyrrolocoumarins **14**,**15** and **16**,**17** by parallel Suzuki couplings.

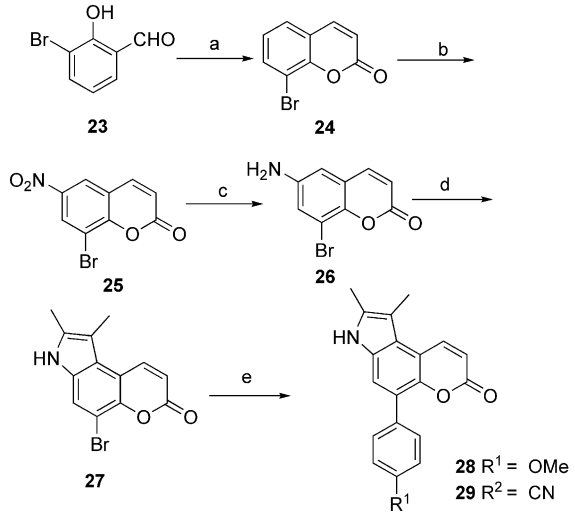


Scheme 2. Reagents and conditions: (a) HNO_3, H_2SO_4, 94%; (b) Fe, AcOH, 93%; (c) (i) $NaNO_2$, HCl, (ii) $SnCl_2$, HCl, (iii) butan-2-one, AcOH, 56% for **12**, 25% for **13**; (d) 4-methoxyphenylboronic acid or 4-cyanophenylboronic acid, K_2CO_3, $Pd(PPh_3)_4$, toluene/EtOH/H_2O, 81% for **14**, 74% for **15**; (e) 4-methoxyphenylboronic acid or 4-cyanophenylboronic acid, K_2CO_3, $Pd(PPh_3)_4$, toluene/EtOH/H_2O, 78% for **16**, 86% for **17**.

We used three additional pyrrolocoumarins, **20**–**22**, with a phenyl substituent at C-5, which were synthesized from the common material 6-amino-5-bromocoumarin (**18**), readily prepared from coumarin.[15] The indolization of **18** proceeded smoothly to afford pyrrolocoumarin derivative **19** in 82% yield (Scheme 3). Again, parallel Suzuki couplings introduced both the 4-methoxyphenyl and 4-cyanophenyl groups into the C-5 position of the target compounds efficiently. In order to investigate the dihedral angle effects in a two-π-conjugate system to pursue better fluorescence,[16] we also designed and synthesized **21** by the installation of a 2-methoxyphenyl group at the C-5 position using the appropriate Suzuki coupling.



Scheme 3. Reagents and conditions: (a) (i) HCl, $NaNO_2$, (ii) $SnCl_2$, HCl, (iii) butan-2-one, AcOH, 80 °C, 82%; (b) 4-cyanophenylboronic acid or 4-methyloxyphenylboronic acid, or 2-methyloxyphenylboronic acid, K_2CO_3, $Pd(PPh_3)_4$, toluene/EtOH/H_2O, 87% for **20**, 74% for **21**, 84% for **22**.



Scheme 4. Reagents and conditions: (a) Ac_2O, AcOK, 82%; (b) HNO_3, H_2SO_4, 83%; (c) Fe, AcOH, 92%; (d) (i) $NaNO_2$, HCl, (ii) $SnCl_2$, HCl, (iii) butan-2-one, AcOH, 45%; (e) 4-methoxyphenylboronic acid, or 4-cyanophenylboronic acid, K_2CO_3, $Pd(PPh_3)_4$, toluene/EtOH/H_2O, 72% for **28**, 54% for **29**.

We prepared the last two pyrrolocoumarins, **28** and **29**, with a C-8 substituent, as outlined in Scheme 4. We synthesized 6-amino-8-bromocoumarin (**26**) from 3-bromosalicylic aldehyde (**23**) for further modifications.[17,18] According to the Fischer indolization conditions described above, we separated 8-bromopyrrolocoumarin (**27**) as a single product and did not detect its linear pyrrolocoumarin isomer. We successfully introduced 4-methoxyphenyl and 4-cyanophenyl functionality into this intermediate by Suzuki reactions to give the target pyrrolocoumarins **28** and **29**, respectively.

Characterization of Fluorescent Properties

We examined all 13 derivatives by standard optical property characterizations (Table 1). To our delight, all these compounds showed large Stokes shifts (109–191 nm), and four pyrrolocoumarins with a C-3 substituent (**5**, **6**, **7** and **8**) presented a very strong fluorescent emission (Table 1, Entries 1, 2, 12 and 13). Among them, the V-shaped **5** gave the highest quantum yield (ϕ = 0.57) despite its relatively short absorption and emission wavelengths (Table 1, Entry 1).

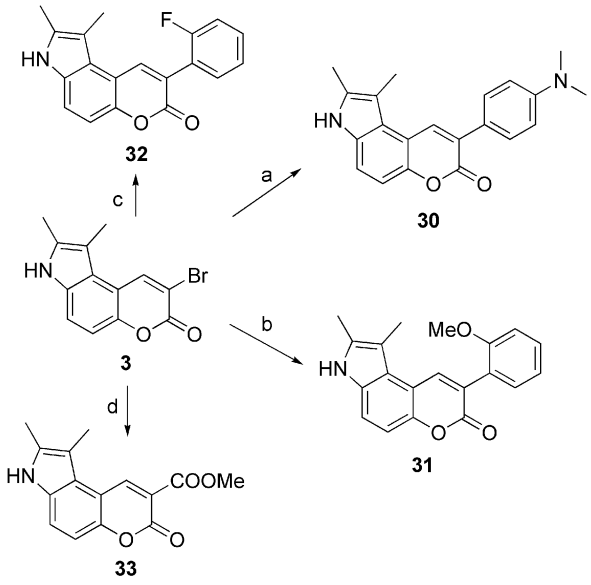
Table 1. Optical properties of the new pyrrolocoumarin derivatives.[a]

Entry	Compound	λ_{ex} [nm]	ε [$cm^{-1}M^{-1}$]	λ_{em} [nm]	ϕ[b,c]	Stokes shift [nm]
1	**5**	388	22198	497	0.57	109
2	**6**	400	17848	520	0.43	120
3	**14**	376	11913	506	0.06	130
4	**15**	388	9295	547	0.03	159
5	**28**	366	13507	501	0.18	135
6	**29**	358	5726	481	0.42	123
7	**20**	348	19588	484	0.19	136
8	**21**	348	19317	485	0.26	137
9	**22**	354	18521	486	0.23	132
10	**16**	352	4684	494	0.19	142
11	**17**	353	7551	544	0.03	191
12	**7**	371	29944	491	0.48	120
13	**8**	378	11573	516	0.36	138

[a] All measurements were performed in dichloromethane. [b] Quantum yields were measured and calculated relative to 9,10-diphenylanthracene in cyclohexane as the standard (excited at 372 nm). [c] Reported quantum yields are the average of three measurements.

Further Optimization

In order to acquire better fluorescent dyes with longer excitation and emission wavelengths, we focused our further optimizations on pyrrolocoumarin **5** and its C-3-substituted analogs (Scheme 5, **30**–**33**). To exclude the effects of the phenyl group, we designed **33** to bear an electron-withdrawing methoxycarbonyl group. Compound **32** contained a fluorine atom aimed at improving photostability and quantum yield.[19] In **30** and **31**, we devised two phenyl groups with electron-donating groups [2-methoxyphenyl and 4-(dimethylamino)phenyl] to replace the previously used 4-methoxyphenyl group in **5**. We quickly synthesized all four compounds from aryl bromide **3** by parallel Suzuki couplings with the corresponding phenylboronic acids (Scheme 5). To our delight, we found **30** was excited by visible light and exhibited intensely green fluorescence (Table 2, Entry 1). Optical property measurements indicated that this compound has a notably large Stokes shift (113 nm). Considering the overall characteristics, we feel that the newly synthesized pyrrolocoumarin **30** has potential applicability in biological FRET devices.



Scheme 5. Reagents and conditions: (a) 4-(dimethylamino)phenylboronic acid, K_2CO_3, $Pd(PPh_3)_4$, toluene/EtOH/H_2O, 85%; (b) 2-methoxyphenylboronic acid, K_2CO_3, $Pd(PPh_3)_4$, toluene/EtOH/H_2O, 81%; (c) 2-fluorophenylboronic acid, K_2CO_3, $Pd(PPh_3)_4$, toluene/EtOH/H_2O, 90%; (d) CO, MeOH, $PdCl_2$(dppf), Et_3N, 83%.

Table 2. Optical properties of the V-shaped pyrrolocoumarin derivatives **30**–**33**.[a]

Entry	Compound	λ_{ex} [nm]	ε [$cm^{-1}M^{-1}$]	λ_{em} [nm]	ϕ[b,c]	Stokes shift [nm]
1	**30**	410	22406	523	0.55	113
2	**31**	374	19598	485	0.46	109
3	**32**	383	18189	495	0.44	112
4	**33**	402	11255	527	0.27	125

[a] All measurements were performed in dichloromethane. [b] Quantum yields were measured and calculated relative to 9,10-diphenylanthracene in cyclohexane as the standard (excited at 372 nm). [c] Reported quantum yields are the average of three measurements.

To analyze the structure/fluorescence relationship of these compounds, we adopted fluorescence intensity ($\phi \times \varepsilon$) as the evaluation standard (Figure 3). In addition to **30**, two other compounds (**5** and **7**) also showed a large fluorescent intensity. Examining the modification positions, we found that the C-3-substituted compounds generally exhibited the best fluorescence intensity (Figure 3, **5**, **6**, **7**, **30**, **31** and **32**), while the corresponding C-4 derivatives showed a relatively poor fluorescence intensity (Figure 3, **14**, **15**, **16** and **17**), and the C-5 and C-8 derivatives exhibited moderate fluores-

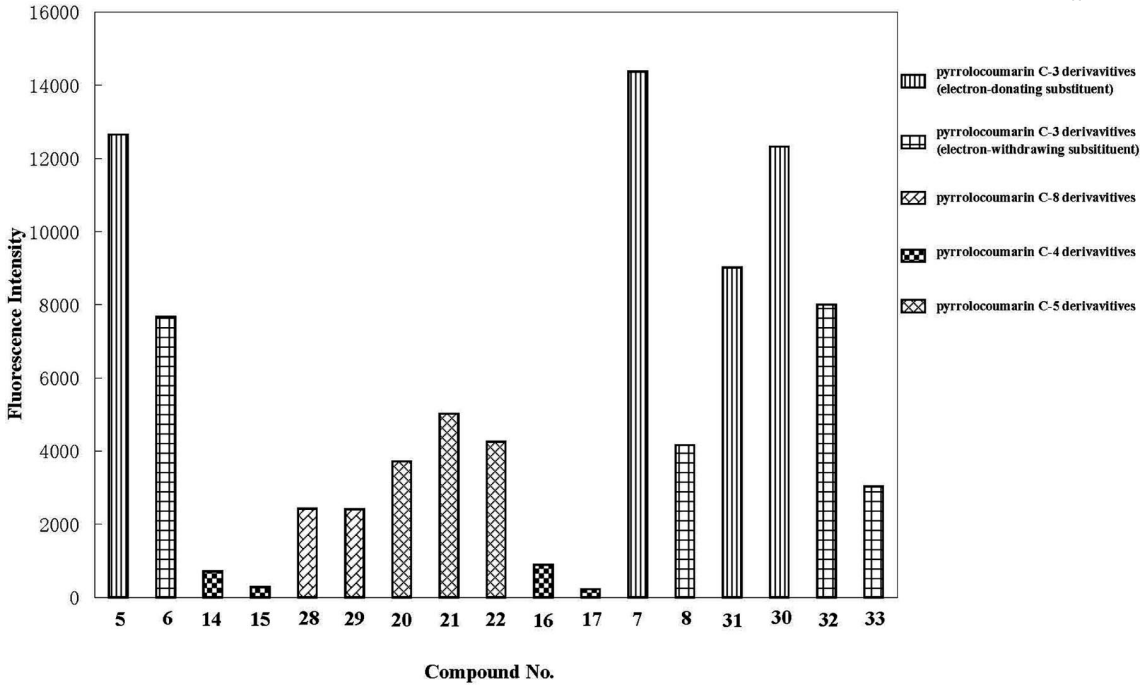


Figure 3. Comparison of fluorescence intensity of new pyrrolocoumarin derivatives.

cence intensities. Thus, in both pyrrolocoumarin skeletons, the C-3 position was the most favorable site for modifications to achieve better fluorescent compounds. As to the electronic effects of the substituent, we observed that electron-withdrawing groups caused remarkable redshifts of the excitation and emission wavelengths (Tables 1 and 2, **6**, **8**, **15**, **17** and **33**), and the electron-donating groups enhanced the fluorescence intensity over that of compounds containing the electron-withdrawing groups (Figure 3, **5** vs. **6**, **7** vs. **8**, **14** vs. **15**, and **16** vs. **17**).

Conclusions

On the basis of two novel pyrrolocoumarin frameworks, we designed and synthesized a number of new pyrrolocoumarin fluorescent dyes. Fischer indolization and Suzuki coupling successfully served as the key methodologies in the synthesis of all the pyrrolocoumarins. The use of inexpensive coumarin as the common starting material was an additional advantage of this study, providing an economic route to future applications of pyrrolocoumarin dyes. We examined and evaluated all synthesized compounds by fluorescent property characterization. Among three intensely fluorescent pyrrolocoumarin dyes with notably large Stokes shifts, we found **30** was excited in the visible-wavelength range and exhibited intense green fluorescence. The further application of this small-molecule organic dye to FRET experiments is underway in this laboratory and will be reported in due course.

Experimental Section

General Methods: IR spectra were recorded with a Perkin–Elmer 983 FTIR spectrophotometer as films on a KBr disk or dispersed in a pressed KBr disk. NMR spectra were recorded with Bruker Avance instruments (300 MHz or 500 MHz for ^{1}H NMR and 75 MHz or 125 MHz for ^{13}C NMR) and are reported in parts per million (δ). HR mass spectra were recorded with an APEX III 7.0 TESLA FTMS instrument. Elemental analyses were preformed with a VARIO EL Elemental Apparatus. Flash column chromatography was performed with silica gel (10–40 μm).

General Procedure for the Fischer Indolizations: A solution of the 6-aminocoumarin derivative (1.0 mmol) in HCl (37%, 1.0 mL) was treated with $NaNO_2$ (83 mg, 1.20 mmol) in H_2O (0.5 mL) at –5 °C. After being stirred at this temperature for 30 min, the resulting mixture was reduced by a pre-cooled (–10 °C to –5 °C) solution of stannous chloride dihydrate (452 mg, 2.0 mmol) in HCl (37%, 0.5 mL). The mixture was stirred at –5 °C for an additional 5 h. The whole mixture was directly used for the next step. To this mixture was added butan-2-one (86 mg, 1.2 mmol) in AcOH (5 mL). The mixture was then heated to 80 °C and stirred for 2–4 h. The solvents were evaporated in vacuo, and the residue was diluted with H_2O (10 mL) and EtOAc (50 mL). The mixture was adjusted to pH = 8 by the addition of saturated aqueous $NaHCO_3$. The organic phase was separated and washed with brine, dried with anhydrous Na_2SO_4 and concentrated. The residue was finally purified by silica gel column chromatography.

8-Bromo-1,2-dimethylpyrano[3,2-*e*]indol-7(3*H*)-one (3): Dark yellow solid (142 mg, 49% yield). Column chromatography mobile phase: CH_2Cl_2/petruleum ether = 2:1–6:1. M.p. 274 °C. IR (KBr): $\tilde{\nu}$ = 3300, 1716, 1689, 1585, 1493, 1426, 1361, 1311, 1207, 1045, 983 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 11.33 (s, 1 H), 8.67 (s, 1 H), 7.53 (d, J = 9.0 Hz, 1 H), 7.02 (d, J = 8.4 Hz, 1 H), 5.75 (s, 1 H), 2.35 (s, 6 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 157.0, 148.9, 142.5, 135.8, 131.6, 122.2, 115.5, 110.7, 108.2, 107.6, 106.7, 11.3, 10.9 ppm. MS (EI): m/z = 291 [M]$^+$. $C_{13}H_{10}BrNO_2$ (292.13): C 53.45, H 3.45, N 4.79; found C 53.36, H 3.50, N 4.82.

7-Bromo-2,3-dimethylpyrano[2,3-*f*]indol-6(1*H*)-one (4): Yellow solid (48 mg, 16%). Column chromatography mobile phase: CH_2Cl_2/pe-

troleum ether = 2:1–6:1. M.p. 258 °C (dec.) IR (KBr): ṽ = 3254, 1694, 1635, 1569, 1546, 1470, 1378, 1289, 1167, 1134, 1041, 975, 912 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 11.15 (s, 1 H), 8.57 (s, 1 H), 7.48 (s, 1 H), 7.28 (s, 1 H), 2.29 (s, 3 H), 2.10 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 157.4, 146.8, 146.7, 138.7, 132.4, 132.1, 113.3, 108.4, 106.4, 105.3, 102.7, 11.7, 8.19 ppm. MS (EI): *m*/*z* = 291 [M]$^+$. $C_{13}H_{10}BrNO_2$ (292.13): calcd. C 53.45, H 3.45, N 4.79; found C 53.48, H 3.73, N 4.94.

9-Bromo-1,2-dimethylpyrano[3,2-*e*]indol-7(3*H*)-one (12): Yellow solid (68 mg, 56%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 3:1. M.p. 258 °C. IR (KBr): ṽ = 1685, 1575, 1348, 1314, 1297, 1103, 1039, 1002 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 11.63 (s, 1 H), 7.60 (d, *J* = 6.6 Hz, 1 H), 7.03 (d, *J* = 6.3 Hz, 1 H), 6.60 (s, 1 H), 2.38 (s, 3 H), 2.36 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 100 MHz): δ = 159.5, 150.7, 149.1, 138.2, 133.6, 122.4, 117.9, 113.3, 110.7, 109.5, 107.5, 16.7, 12.9 ppm. MS (ESI): *m*/*z* = 248 [M + H – 44]$^+$. $C_{13}H_{10}BrNO_2$ (292.13): calcd. C 53.45, H 3.45, N 4.79; found C 53.48, H 3.62, N 4.80.

8-Bromo-2,3-dimethylpyrano[2,3-*f*]indol-6(1*H*)-one (13): Yellow solid (30 mg, 25%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 3:1. M.p. 260–261 °C. IR (KBr): ṽ = 3244, 2916, 1697, 1637, 1594, 1549, 1377, 1237, 1213, 1133, 915, 824 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 11.31 (s, 1 H), 7.63 (s, 1 H), 7.37 (s, 1 H), 6.62 (s, 1 H), 2.38 (s, 3 H), 2.17 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 100 MHz): δ = 159.8, 150.1, 146.6, 140.0, 133.3, 132.9, 111.8, 111.3, 106.8, 106.1, 103.7, 12.2, 8.64 ppm. MS (EI): *m*/*z* = 247 [M – 44]$^+$. $C_{13}H_{10}BrNO_2$ (292.13): calcd. C 53.45, H 3.45, N 4.79; found C 53.29, H 3.36, N 5.06.

9-Bromo-2,3-dimethylpyrano[2,3-*f*]indol-6(1*H*)-one (19): Yellow solid (239 mg, 82%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 5:1–10:1. M.p. 257 °C. IR (KBr): ṽ = 3295, 1704, 1635, 1604, 1568, 1544, 1498, 1200, 1133, 1110, 1039, 821 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 11.28 (s, 1 H), 8.16 (d, *J* = 9.3 Hz, 1 H), 7.39 (s, 1 H), 6.39 (d, *J* = 9.9 Hz, 1 H), 2.39 (s, 3 H), 2.17 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 100 MHz): δ = 160.3, 147.4, 142.6, 139.6, 131.8, 131.6, 113.4, 111.2, 107.4, 102.6, 101.8, 11.4, 8.11 ppm. MS (ESI): *m*/*z* = 292 [M + H]$^+$. $C_{13}H_{10}BrNO_2$ (292.13): calcd. C 53.45, H 3.45, N 4.79; found C 53.54, H 3.65, N 4.81.

5-Bromo-1,2-dimethylpyrano[3,2-*e*]indol-7(3*H*)-one (27): Yellow solid (274 mg, 45%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 1:1–10:1. M.p. >300 °C. IR (KBr): ṽ = 3275, 2924, 1698, 1590, 1448, 1348, 1190, 1133, 926, 816 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 11.33 (s, 1 H), 8.42 (d, *J* = 9.9 Hz, 1 H), 7.72 (s, 1 H), 6.43 (d, *J* = 10.2 Hz, 1 H), 2.34 (s, 6 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 100 MHz): δ = 159.7, 145.0, 141.3, 136.4, 131.6, 122.8, 117.4, 113.8, 111.9, 106.7, 100.0, 11.2, 10.9 ppm. MS (ESI): *m*/*z* = 314 [M + Na]$^+$. $C_{13}H_{10}BrNO_2$ (292.13): calcd. C 53.45, H 3.45, N 4.79; found C 53.34, H 3.59, N 4.93.

General Procedure for the Suzuki Couplings: To a mixture of pyrrolocoumarin bromide (1 mmol), boric acid (2.0 mmol), K_2CO_3 (3.0 mmol) and $Pd(PPh_3)_4$ (0.05 mmol) in a round flask was added EtOH/toluene/H_2O (1:1:2, 4 mL) under nitrogen. The mixture was then heated to 80 °C. The reaction progress was monitored by TLC. After the pyrrolocoumarin bromide was consumed (after 4–24 h), the solvent was evaporated in vacuo. The residue was redissolved in EtOAc (50 mL). The organic solution was washed with saturated brine, dried with anhydrous Na_2SO_4 and concentrated. The residue was finally purified by silica gel column chromatography.

8-(4-Methoxyphenyl)-1,2-dimethylpyrano[3,2-*e*]indol-7(3*H*)-one (5): Bright yellow solid (146 mg, 89%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 1:1–10:1. M.p. 253 °C. IR (KBr): ṽ = 3278, 1685, 1595, 1514, 1363, 1336, 1288, 1250, 1180, 1135, 1105, 1031 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 11.22 (s, 1 H), 8.41 (s, 1 H), 7.73 (d, *J* = 8.1 Hz, 2 H), 7.46 (d, *J* = 8.7 Hz, 1 H), 7.02 (d, *J* = 9.0 Hz, 2 H), 7.01 (d, *J* = 8.4 Hz, 1 H), 3.80 (s, 3 H), 2.41 (s, 3 H), 2.35 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 100 MHz): δ = 160.1, 159.2, 148.6, 136.5, 135.0, 131.3, 129.5, 127.8, 123.3, 122.9, 114.4, 113.6, 111.1, 107.9, 106.7, 55.1, 11.1, 11.0 ppm. MS (ESI): *m*/*z* = 320 [M + H]$^+$. $C_{20}H_{17}NO_3$ (319.35): calcd. C 75.22, H 5.37, N 4.39; found C 75.42, H 5.28, N 4.18.

4-(1,2-Dimethyl-7-oxo-3,7-dihydropyrano[3,2-*e*]indol-8-yl)benzonitrile (6): Dark yellow solid (106 mg, 82%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 1:1–5:1. M.p. >300 °C. IR (KBr): ṽ = 3331, 2923, 2236, 1701, 1589, 1498, 1363, 1336, 1207, 1106, 953 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 11.32 (s, 1 H), 8.60 (s, 1 H), 8.02 (d, *J* = 8.4 Hz, 2 H), 7.92 (d, *J* = 8.1 Hz, 2 H), 7.55 (d, *J* = 8.7 Hz, 1 H), 7.05 (d, *J* = 8.4 Hz, 1 H), 2.44 (s, 3 H), 2.38 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 159.6, 149.5, 140.3, 139.6, 135.8, 132.1, 131.5, 129.1, 123.3, 121.7, 118.8, 115.8, 110.9, 110.3, 108.0, 107.1, 11.3, 11.0 ppm. HRMS: calcd. for $C_{20}H_{15}N_2O_2$ [M + H]$^+$ 315.1128; found 315.1125.

9-(4-Methoxyphenyl)-1,2-dimethylpyrano[3,2-*e*]indol-7(3*H*)-one (14): Yellow solid (89 mg, 81%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 4:1–10:1. M.p. 245 °C. IR (KBr): ṽ = 1687, 1610, 1579, 1512, 1349, 1296, 1249, 1174, 1026, 1000 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 11.35 (s, 1 H), 7.57 (d, *J* = 8.4 Hz, 1 H), 7.34 (d, *J* = 8.7 Hz, 2 H), 7.07 (d, *J* = 9.0 Hz, 1 H), 7.02 (d, *J* = 8.4 Hz, 2 H), 3.81 (s, 3 H), 2.20 (s, 3 H), 1.06 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 100 MHz): δ = 160.9, 160.6, 156.3, 151.1, 136.5, 133.4, 133.2, 129.9, 124.1, 116.4, 114.7, 113.0, 110.6, 109.2, 108.4, 55.8, 12.2, 11.5 ppm. MS (ESI): *m*/*z* = 342 [M + Na]$^+$. $C_{20}H_{17}NO_3$ (319.35): calcd. C 75.22, H 5.37, N 4.39; found C 75.18, H 5.58, N 4.44.

4-(1,2-Dimethyl-7-oxo-3,7-dihydropyrano[3,2-*e*]indol-9-yl)benzonitrile (15): Dark yellow solid (80 mg, 74%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 10:1–100:1. M.p. >300 °C. IR (KBr): ṽ = 3219, 2228, 1689, 1575, 1469, 1357, 1319, 1299, 1240, 1127, 1001 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 11.44 (s, 1 H), 7.95 (d, *J* = 8.4 Hz, 2 H), 7.62 (d, *J* = 8.7 Hz, 1 H), 7.61 (d, *J* = 8.4 Hz, 2 H), 7.11 (d, *J* = 8.7 Hz, 1 H), 6.31 (s, 1 H), 2.20 (s, 3 H), 0.97 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 159.9, 154.0, 150.7, 144.8, 136.5, 132.8, 132.7, 129.1, 123.1, 118.5, 116.3, 113.9, 111.6, 109.1, 108.8, 107.2, 11.6, 11.2 ppm. HRMS: calcd. for $C_{20}H_{15}N_2O_2$ [M + H]$^+$ 315.1128; found 315.1123.

5-(4-Methoxyphenyl)-1,2-dimethylpyrano[3,2-*e*]indol-7(3*H*)-one (28): Yellow solid (63 mg, 72%). Column chromatography mobile phase: CH_2Cl_2/MeOH = 150:1–100:1. M.p. 251 °C (dec.). IR (KBr): ṽ = 3389, 1691, 1589, 1516, 1340, 1242, 1176, 1128, 1030, 826 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 11.26 (s, 1 H), 8.55 (d, *J* = 9.9 Hz, 1 H), 7.51 (d, *J* = 8.7 Hz, 2 H), 7.44 (s, 1 H), 7.05 (d, *J* = 8.7 Hz, 2 H), 6.42 (d, *J* = 9.6 Hz, 1 H), 3.82 (s, 3 H), 2.41 (s, 3 H), 2.38 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 160.2, 158.4, 146.4, 141.8, 135.6, 131.4, 130.6, 129.4, 122.4, 121.3, 115.3, 113.7, 113.2, 110.6, 106.3, 55.1, 11.2, 11.1 ppm. MS (ESI): *m*/*z* = 342 [M + Na]$^+$. $C_{20}H_{17}NO_3$ (319.35): calcd. C 75.22, H 5.37, N 4.39; found C 75.10, H 5.29, N 4.44.

4-(1,2-Dimethyl-7-oxo-3,7-dihydropyrano[3,2-*e*]indol-5-yl)benzonitrile (29): Dark yellow solid (58 mg, 54%). Column chromatography mobile phase: CH_2Cl_2/MeOH = 150:1–100:1. M.p. >300 °C. IR (KBr): ṽ = 2921, 2860, 2225, 1684, 1605, 1591, 1349, 1155, 1133, 826 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 11.41 (s, 1 H),

8.55 (d, J = 9.6 Hz, 1 H), 7.95 (d, J = 8.7 Hz, 2 H), 7.81 (d, J = 8.4 Hz, 2 H), 7.53 (s, 1 H), 6.45 (d, J = 9.6 Hz, 1 H), 2.41 (s, 3 H), 2.40 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 100 MHz): δ = 159.7, 146.1, 142.1, 141.6, 136.8, 131.9, 131.2, 130.3, 123.4, 119.4, 118.7, 115.3, 113.4, 110.5, 109.5, 106.6, 11.1, 10.9 ppm. HRMS: calcd. for $C_{20}H_{15}N_2O_2$ [M + H]$^+$ 315.1128; found 315.1132.

9-(4-Methoxyphenyl)-2,3-dimethylpyrano[2,3-*f*]indol-6(1*H*)-one (20): Yellow solid (114 mg, 87%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 1:1–10:1. M.p. >300 °C. IR (KBr): $\tilde{\nu}$ = 3249, 1692, 1625, 1604, 1554, 1513, 1493, 1247, 1171, 1145, 1035, 835 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 10.58 (s, 1 H), 7.64 (d, J = 9.9 Hz, 1 H), 7.36 (d, J = 8.7 Hz, 2 H), 7.33 (s, 1 H), 7.14 (d, J = 8.1 Hz, 2 H), 6.16 (d, J = 9.9 Hz, 1 H), 3.86 (s, 3 H), 2.31 (s, 3 H), 2.19 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]-DMSO, 100 MHz): δ = 161.2, 159.6, 148.4, 143.4, 139.4, 132.0, 131.5, 126.6, 122.5, 114.8, 112.0, 111.1, 106.9, 102.4, 55.6, 11.9, 8.59 ppm. MS (ESI): m/z = 320 [M + H]$^+$. $C_{20}H_{17}NO_3$ (319.35): calcd. C 75.22, H 5.37, N 4.39; found C 75.14, H 5.59, N 4.34.

9-(2-Methoxyphenyl)-2,3-dimethylpyrano[2,3-*f*]indol-6(1*H*)-one (21): Yellow solid (123 mg, 74%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 1:1–10:1. M.p. 260–261 °C. IR (KBr): $\tilde{\nu}$ = 3269, 1691, 1552, 1503, 1309, 1243, 1135, 1030, 815 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 10.53 (s, 1 H), 7.57–7.51 (m, 1 H), 7.42 (d, J = 9.6 Hz, 1 H), 7.34 (s, 1 H), 7.24 (d, J = 7.8 Hz, 1 H), 7.14 (t, J = 7.8 Hz, 1 H), 6.15 (d, J = 9.9 Hz, 1 H), 3.67 (s, 3 H), 2.30 (s, 3 H), 2.19 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]-DMSO, 100 MHz): δ = 160.9, 157.2, 147.7, 143.3, 138.6, 131.9, 131.6, 131.2, 130.1, 122.4, 120.6, 118.9, 111.8, 111.5, 111.0, 106.1, 102.0, 55.3, 11.4, 8.18 ppm. MS (ESI): m/z = 320 [M + H]$^+$. $C_{20}H_{17}NO_3$ (319.35): calcd. C 75.22, H 5.37, N 4.39; found C 75.41, H 5.39, N 4.31.

4-(2,3-Dimethyl-6-oxo-1,6-dihydropyrano[2,3-*f*]indol-9-yl)benzonitrile (22): Yellow solid (90 mg, 84%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 1:1–5:1. M.p. >300 °C. IR (KBr): $\tilde{\nu}$ = 3255, 2229, 1686, 1603, 1554, 1506, 1491, 1384, 1309, 1195, 1145, 842 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 10.70 (s, 1 H), 8.06 (d, J = 8.1 Hz, 2 H), 7.66 (d, J = 8.4 Hz, 2 H), 7.58 (d, J = 9.6 Hz, 1 H), 7.43 (s, 1 H), 6.21 (d, J = 9.9 Hz, 1 H), 2.31 (s, 3 H), 2.20 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 100 MHz): δ = 160.6, 147.8, 142.3, 139.4, 139.3, 132.7, 131.8, 131.6, 130.6, 120.3, 118.8, 112.4, 111.0, 110.3, 106.6, 103.2, 11.4, 8.13 ppm. HRMS: calcd. for $C_{20}H_{15}N_2O_2$ [M + H]$^+$ 315.1128; found 315.1123.

8-(4-Methoxyphenyl)-2,3-dimethylpyrano[2,3-*f*]indol-6(1*H*)-one (16): Yellow solid (46 mg, 78%). Column chromatography mobile phase: CH_2Cl_2/MeOH = 100:1. M.p. 294 °C. IR (KBr): $\tilde{\nu}$ = 3195, 1677, 1635, 1607, 1512, 1381, 1243, 1174, 1136, 1022, 968, 830 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 10.93 (s, 1 H), 7.45 (d, J = 8.4 Hz, 2 H), 7.32 (s, 1 H), 7.24 (s, 1 H), 7.07 (d, J = 8.4 Hz, 2 H), 6.06 (s, 1 H), 3.79 (s, 3 H), 2.27 (s, 3 H), 2.11 (s, 3 H) ppm. MS (ESI): m/z = 320 [M + H]$^+$. $C_{20}H_{17}NO_3$ (319.35): calcd. C 75.22, H 5.37, N 4.39; found C 75.18, H 5.60, N 4.24.

4-(2,3-Dimethyl-6-oxo-1,6-dihydropyrano[2,3-*f*]indol-8-yl)benzonitrile (17): Yellow solid (46 mg, 86%). Column chromatography mobile phase: CH_2Cl_2/MeOH = 100:1. M.p. >300 °C. IR (KBr): $\tilde{\nu}$ = 2231, 1686, 1637, 1542, 1378, 1358, 1242, 1138, 1037, 970 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 10.99 (s, 1 H), 8.06 (d, J = 6.6 Hz, 2 H), 7.78 (d, J = 6.9 Hz, 2 H), 7.43 (s, 1 H), 7.08 (s, 1 H), 6.24 (s, 1 H), 2.34 (s, 3 H), 2.18 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]-DMSO, 100 MHz): δ = 160.4, 154.6, 147.3, 140.6, 138.5, 132.7, 132.3, 132.1, 129.6, 118.4, 112.1, 111.6, 111.6, 107.0, 106.0, 103.5, 11.6, 8.19 ppm. HRMS: calcd. for $C_{20}H_{15}N_2O_2$ [M + H]$^+$ 315.1128; found 315.1125.

7-(4-Methoxyphenyl)-2,3-dimethylpyrano[2,3-*f*]indol-6(1*H*)-one (7): Bright yellow solid (42 mg, 77%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 2:1–3:1. M.p. 280–282 °C. IR (KBr): $\tilde{\nu}$ = 3248, 1665, 1610, 1517, 1294, 1264, 1244, 1176, 1036, 832 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 11.13 (s, 1 H), 8.24 (s, 1 H), 7.69 (d, J = 8.4 Hz, 2 H), 7.60 (s, 1 H), 7.32 (s, 1 H), 7.00 (d, J = 9.0 Hz, 2 H), 3.79 (s, 3 H), 2.36 (s, 3 H), 2.18 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 100 MHz): δ = 161.2, 159.5, 147.2, 141.5, 138.2, 132.9, 132.0, 130.0, 128.2, 122.5, 114.1, 114.0, 109.2, 106.5, 102.6, 55.6, 12.0, 8.67 ppm. MS (ESI): m/z = 320 [M + H]$^+$. $C_{20}H_{17}NO_3$ (319.35): calcd. C 75.22, H 5.37, N 4.39; found C 75.22, H 5.64, N 4.46.

4-(2,3-Dimethyl-6-oxo-1,6-dihydropyrano[2,3-*f*]indol-7-yl)benzonitrile (8): Dark yellow solid (55 mg, 62%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 1:1–10:1. M.p. >300 °C. IR (KBr): $\tilde{\nu}$ = 3241, 2223, 1678, 1633, 1595, 1548, 1315, 1181, 1138, 1037, 846 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 11.21 (s, 1 H), 8.47 (s, 1 H), 7.96 (d, J = 8.4 Hz, 2 H), 7.89 (d, J = 9.0 Hz, 2 H), 7.63 (s, 1 H), 7.33 (s, 1 H), 2.37 (s, 3 H), 2.18 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 160.2, 147.2, 144.2, 140.3, 138.9, 132.5, 132.5, 132.0, 128.9, 120.3, 118.9, 113.2, 110.0, 109.6, 106.4, 102.3, 11.7, 8.21 ppm. HRMS: calcd. for $C_{20}H_{15}N_2O_2$ [M + H]$^+$ 315.1128; found 315.1123.

8-[4-(Dimethylamino)phenyl]-1,2-dimethylpyrano[3,2-*e*]indol-7(3*H*)-one (30): Bright yellow solid (111 mg, 85%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 1:1–5:1. M.p. 250–252 °C. IR (KBr): $\tilde{\nu}$ = 3233, 2919, 1677, 1610, 1590, 1522, 1361, 1202, 1133, 995, 948, 814 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 11.21 (s, 1 H), 8.39 (s, 1 H), 7.67 (d, J = 8.7 Hz, 2 H), 7.44 (d, J = 8.4 Hz, 1 H), 7.01 (d, J = 8.7 Hz, 1 H), 6.78 (d, J = 9.0 Hz, 2 H), 2.94 (s, 6 H), 2.43 (s, 3 H), 2.36 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]-DMSO, 100 MHz): δ = 161.1, 150.9, 149.0, 135.6, 135.4, 132.1, 129.6, 124.6, 123.6, 123.5, 114.7, 112.5, 112.2, 108.7, 107.4, 11.9 ppm. MS (ESI): m/z = 333 [M + H]$^+$. $C_{21}H_{20}N_2O_2$ (332.40): calcd. C 75.88, H 6.06, N 8.43; found C 75.60, H 5.95, N 8.30.

8-(2-Methoxyphenyl)-1,2-dimethylpyrano[3,2-*e*]indol-7(3*H*)-one (31): Yellow solid (117 mg, 81%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 1:1–5:1. M.p. 265–266 °C. IR (KBr): $\tilde{\nu}$ = 3373, 1703, 1596, 1494, 1441, 1363, 1254, 1235, 1137, 1012, 962 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 11.26 (s, 1 H), 8.42 (s, 1 H), 7.52–7.37 (m, 3 H), 7.12 (d, J = 8.1 Hz, 1 H), 7.06–7.01 (m, 2 H), 3.79 (s, 3 H), 2.36 (s, 6 H) ppm. MS (ESI): m/z = 320 [M + H]$^+$. $C_{20}H_{17}NO_3$ (319.35): calcd. C 75.22, H 5.37, N 4.39; found C 75.29, H 5.17, N 4.19.

8-(2-Fluorophenyl)-1,2-dimethylpyrano[3,2-*e*]indol-7(3*H*)-one (32): Bright yellow solid (124 mg, 90%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 1:1–5:1. M.p. 298 °C. IR (KBr): $\tilde{\nu}$ = 3269, 1682, 1598, 1494, 1434, 1398, 1361, 1335, 1211, 1101, 1046, 995, 972, 751 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 400 MHz): δ = 11.31 (s, 1 H), 8.50 (s, 1 H), 7.67 (dt, J = 5.7, 1.2 Hz, 1 H), 7.54 (d, J = 6.6 Hz, 1 H), 7.50–7.44 (m, 1 H), 7.33–7.28 (m, 2 H), 7.07 (d, J = 6.6 Hz, 1 H), 2.38 (s, 3 H), 2.37 (s, 3 H) ppm. ^{19}F NMR ([D$_6$]DMSO, 282 MHz): δ = 114.37 (m) ppm. ^{13}C NMR ([D$_6$]DMSO, 100 MHz): δ = 160.2 (d, J = 245.6 Hz), 159.9, 159.0, 149.9, 141.1, 136.2, 132.1 (d, J = 9.7 Hz), 130.9 (d, J = 8.2 Hz), 124.9, 124.1 (d, J = 14.2 Hz), 123.7, 119.9, 116.2 (d, J = 22.4 Hz), 116.0, 111.0, 108.7, 107.3, 11.8, 11.6 ppm. MS (ESI): m/z = 308 [M + H]$^+$. $C_{19}H_{14}FNO_2 \cdot 0.045CH_2Cl_2$ (307.32): calcd. C 73.51, H 4.56, N 4.50; found C 73.49, H 4.53, N 4.53.

Methyl 1,2-Dimethyl-7-oxo-3,7-dihydropyrano[3,2-*e*]indole-8-carboxylate (33): Dark yellow solid (54 mg, 83%). Column chromatography mobile phase: CH_2Cl_2/petroleum ether = 1:1–10:1. M.p.

>300 °C. IR (KBr): $\tilde{\nu}$ = 3315, 1768, 1742, 1589, 1561, 1491, 1365, 1299, 1245, 1228, 1122, 1052, 796 cm^{-1}. ^1H NMR ([D_6]-DMSO + $CDCl_3$, 300 MHz): δ = 11.37 (s, 1 H), 9.09 (s, 1 H), 7.62 (d, J = 8.4 Hz, 1 H), 6.99 (d, J = 8.4 Hz, 1 H), 3.85 (s, 3 H), 2.40 (s, 6 H) ppm. HRMS: calcd. for $C_{15}H_{13}NO_4$ $[M + Na]^+$ 294.0737; found 294.0734. $C_{15}H_{13}NO_4$ (271.27): calcd. C 66.41, H 4.83, N 5.16; found C 66.01, H 4.78, N 4.88.

Supporting Information (see footnote on the first page of this article): General methods, experimental details and characterization of new compounds that are not described in the Exp. Sect. and copies of NMR spectra of all new compounds.

Acknowledgments

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