The colourful fluorescence from readily-synthesised 3,4-diaryl-substituted maleimide fluorophores

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A new synthesis procedure has been developed for a series of maleimide-based fluorophores, exhibiting a large variation of emission spectra spanning the entire visible range.

Fluorophores tethered with unsubstituted maleimide, a fluorescence quencher *per se*, are thiol-reactive probes for protein labelling[1] or micromorphological probes[2] for monitoring bulk polymerization. On the other hand, 3,4-bisindole-substituted maleimides, the common structure of natural products found for red-fluorescent alkaloids from slime moulds, are of interest as potent inhibitors of protein kinase C (PKC).[3]

Unlike the larger members of the carboxylic imide family, such as phthalimides, naphthalimide, and perylenebisimide, aryl-substituted maleimide compounds have received much less attention in the field of colorants or fluorescence dyes.[4] Fluorescence metal sensors based on monoindole-substituted maleimides have recently been reported.[5] Nevertheless, absorption and fluorescence spectroscopic properties of diaryl-substituted maleimide have been neglected and remained unexplored. Just recently, we reported the first efficient and bright red organic light-emitting diode (OLED) based on nondoping red emitter, **NPAMLMe**,[6] a naphthylphenylamino substituted *N*-methyl-3,4-diphenylmaleimide. **NPAMLMe** is a deep red fluorophore with relatively large Stokes shifts (Δ) in both solution and solid state.[6] Noteworthy, in addition to its unusual spectroscopic behavior, 3,4-bis(4-bromophenyl)maleimide, a precursor to **NPAMLMe**, was prepared handily in one-step (similar to that shown in Scheme 1) employing 4-bromobenzyl cyanide (or 4-bromophenylacetonitrile) as the starting material. In this communication, we apply the newly found one-step synthesis to prepare a series of 3,4-diarylmaleimide compounds carrying varied functionality, employing a broad class of different aryl-substituted acetonitrile as starting materials. We examine the spectroscopic properties of these new maleimide derivatives in evaluating further electrooptical application.

To our knowledge, there are several synthetic procedures known for preparing either symmetrical or unsymmetrical 3,4-substituted maleimides.[7–10] Among them, the most recognized one is through an indirect method of the ammonolysis of maleic anhydrides, which in turn are best prepared from the reaction of glyoxylic acids with acetic acids.[7] However, glyoxylic acid derivatives are not widely available commercially. An efficient one-step synthesis of maleimides can be achieved by condensation of glyoxylate esters with acetamides.[9] Once again, desired glyoxylate esters often require synthetic preparation. In the context of synthesis, it has been known for some time that diphenylmaleimde can be prepared from diphenylfumaronitrile.[10] However, we found that the synthesis of diphenylfumaronitrile from phenylacetonitrile is often troublesome and requires tedious purification. Difficulties or unsatisfactory yields were often reported in preparing diaryl-substituted fumaronitrile.[11] Therefore, to serve the purpose of spectroscopic studies, the direct and one-step synthesis of maleimides reported here is quite valuable, particularly for the symmetrical 3,4-diaryl-substituted fluorescent maleimides. This is because the starting materials, aryl-substituted acetonitrile derivatives are abundant either commercially available or readily synthesizable. Maleimides **MLH**, **3-CF₃MLH**, **4-CF₃MLH**, **3-PYDMLH**, **2-THPMLH**, **4-MeOMLH, 1-NPHMLH**, and **2-NPHMLH** were synthesized directly from acetonitrile derivatives (Scheme 1). The yields of such direct and one-step syntheses of maleimides are highly dependent on the acetonitrile derivatives. Without optimizing the individual maleimide syntheses, we obtained reaction yields ranging from low (such as < 10% of **2-THPMLH**) to reasonably good (such as > 60% of **3-PYDMLH**). Following methylation with an excess amount of methyl iodide provided *N*-methylated derivatives **MLMe**, **3-CF₃MLMe**, **4-CF₃MLMe**, **2-THPMLH**, **4-MeOMLMe**, **1-NPHMLMe**, and **2-NPHMIMe**. Diamino-substituted derivatives **TPAMLMe**, **PhAMLMe,** and **EtAMLMe** were obtained by a method similar to that for **NPAMLMe** by coupling *N*-methyl-3,4-bis(4-bromophenyl-)maleimide with appropriate secondary amines catalyzed by palladium.[6] All new compounds were purified by column chromatography. They were fully characterized by ¹H and ¹³C NMR, FAB-MS, and elemental analysis, and were consistent with proposed structures.†

Depending on the substituent on diaryl-substituted maleimide, a large variation in fluorescence colour was observed (Fig. 1, Table 1). The emission wavelength maxima (λ_{max}^{em}) of both **MLH** and **MLMe** clearly show bathochromic shifts with electron-donating (such as 4-methoxy and 4-diarylamino groups) or electon-rich aryl (such as 2-thienyl) substituents and hypsochromic shifts with electron-withdrawing (such as 4-trifluoromethyl) or electron-deficient aryl (such as 3-pyridyl) substituents. Except for the quite similar **3-CF₃MLH** and **3-CF₃MLMe**, all maleimide compounds exhibit larger Stokes
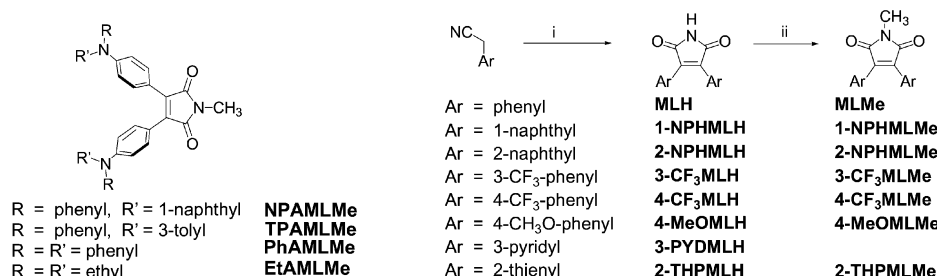
Scheme 1 *Reagents and conditions*: i, I₂ (1 equiv.) in THF, NaOCH₃ (3 equiv.) in CH₃OH, 2 h at −78 °C, 14 h at 25 °C, then 3% HCl(aq) (7 ~ 65%). ii, CH₃I (5 equiv.), KOBu^t, DMF, 25 °C, 6 ~ 12 h (70 ~ 90%).
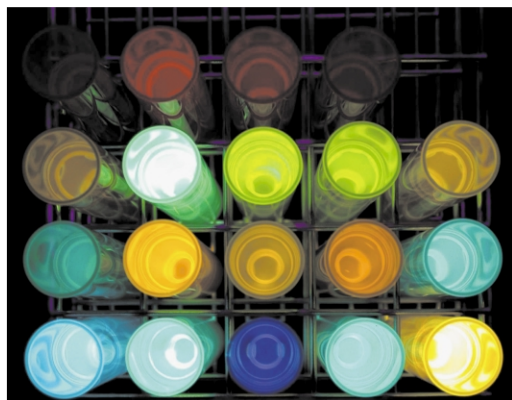
Fig. 1 Fluorescence image of 3,4-diaryl-substituted maleimide derivatives in dichloromethane showing varied colours. From left to right, the first row **EtAMLMe**, **NPAMLMe**, **PhAMLMe**, and **TPAMLMe**; the second row **1-NPHMLH**, **MLMe**, **1-NPHMLMe**, **2-NPHMLH**, and **2-NPHMLMe**; the third row **3-PYDMLH**, **4-MeOMLMe**, **2-THPMLH**, **2-THPMLMe**, and **MLH**; the fourth row **3-CF₃MLH**, **3-CF₃MLMe**, **4-CF₃MLH**, **4-CF₃MLMe**, and **4-MeOMLH**.

Table 1 Spectroscopic data of 3,4-diaryl-substituted maleimides

	λ_{max}^{abs}, ε (nm/nm)^a, (M^{-1}cm^{-1})^b	λ_{max}^{em} (nm/nm)^a	Δ (cm^{-1}/cm^{-1})^a	ϕ_f (%)
MLH	350/357, 6030	471/493	7300/7700	21^c
MLMe	361363, 4010	490/503	7300/7700	31^c
1-NPHMLH	373/384, 4690	497/544	6700/7700	2^c
1-NPHMLMe	377/383, 4410	507/547	6800/7700	3^c
2-NPHMLH	391/392, 10510	488/523	5100/6400	12^c
2-NPHMLMe	395/398, 9250	499/526	5300/6100	22^c
3-CF₃MLH	339/344, 5710	460/471	7800/7800	30^d
3-CF₃MLMe	352/359, 3630	477/490	7400/7400	53^d
4-CF₃MLH	339/340, 2180	459/470	7700/8100	8^d
4-CF₃MLMe	350/353, 3220	475/487	7500/7800	26^d
4-MeOMLH	387/404, 7560	506/548	6100/6500	25^c
4-MeOMLMe	399/408, 7140	518/551	5800/6400	26^c
3-PYDMLH	340/346, 5640	464/482	7900/8200	6^d
2-THPMLH	414/421, 7650	514/545	4700/5400	7^c
2-THPMLMe	423/428, 6400	530/552	4800/5300	5^c
NPAMLMe	474/485, 13900	572/642	3600/5000	13^e
TPAMLMe	476/485, 14830	575/650	3600/5200	11^e
PhAMLMe	480/485, 13690	581/653	3600/5300	10^e
EtAMLMe	481/512, 11050	581/659	3600/4400	5^e

^{a} In hexane and dichloromethane solutions, respectively. ^{b} In dichloromethane solution. ^{c} Fluorescence quantum yields relative to Coumarin 6 in acetonitrile (63%).[12] ^{d} Fluorescence quantum yields relative to Coumarin 1 in acetonitrile (100%).[12] ^{e} Fluorescence quantum yields relative to Nile Red in 1,4-dioxane (68%).[13]

shifts in more polar solvents (dichloromethane vs. hexane in Table 1). A similar electronic push–pull effect on spectra shifting has been commonly found on other fluorophores with intramolecular-charge-transfer (ICT) characteristics.[4] The apparent indication of ICT observed for maleimides is somewhat to our surprise, considering the unavoidable nonplanar conformation of the adjacent 3,4-disubstituted phenyl rings that partially block the interaction of substituents to the five-member maleimide ring. Nevertheless, there are some general trends in comparing the fluorescence data of maleimides with and without the *N*-methyl group. With few exceptions, after *N*-methylation, maleimides have a longer wavelength λ_{max}^{em} (such as 470 nm for purple blue **4-CF₃MLH** vs. 487 nm for sky blue **4-CF₃MLMe**), a higher solution fluorescence quantum yield‡ (ϕ_f) (such as 30% for **3-CF₃MLH** vs. 53% for **3-CF₃MLMe**), and a smaller Stokes shift (such as 6534 cm^{-1} for **4-MeOMLH** vs. 6361 cm^{-1} for **4-MeOMLMe**).

The simple energy gap law does not work well for 3,4-diaryl-substituted maleimides in term of ϕ_f. However, the magnitude of Stokes shift seems to obey, *i.e.*, those emitting light in the green to blue region tend to show larger Stokes shifts than those in the yellow to red region. It is intriguing to ask what is the other factor, in addition to energy gap law, in controlling the fluorescence intensity and Stokes shift of these maleimides, which are key properties in the application of fluorophores for OLEDs. Spectroscopic data of **1-NPHMLMe** and **2-NPHMLMe** may provide a clue to the answer. **2-NPHMLMe** has a much higher ϕ_f and extinction coefficient (ε) than **1-NPHMLMe**. Here the electronic factor is unlikely to be decisive because both maleimides are relatively similar in absorption and emission energy (Table 1). Steric hindrance appears to be a possible reason for the affect on the magnitude of ϕ_f in **1-NPHMLMe** and **2-NPHMLMe**. The sterically hindered **1-NPHMLMe** shows one of the lowest fluorescence intensities on the list (Table 1). It is also interesting to note that the sterically less hindered **2-NPHMLMe** has a shorter λ_{max}^{em} wavelength than that of **1-NPHMLMe**, although the former has a longer λ_{max}^{ab} wavelength. Insightful structure–property relationships are currently being pursued through theoretical calculations and we are preparing more maleimide derivatives for spectroscopic examination.

In summary, we have developed a one-step synthesis of 3,4-diaryl-substituted maleimides directly from easily-accessible acetonitrile derivatives. Our preliminary examination indicates that steric factors in addition to electronic effects play an important role in determining the fluorescence energy and intensity of these colourful fluorophores.

Notes and references

† Full synthesis details and characterization data will be given elsewhere.
‡ ϕ_f of each maleimide was determined by the literature procedure of J. N. Demas and G. A. Crosby, *J. Phys. Chem.*, 1971, **75**, 991.

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