Synthesis of New Imidazoanthraquinol Fluorophores and Their Fluorescence and Solid-State Inclusion Properties

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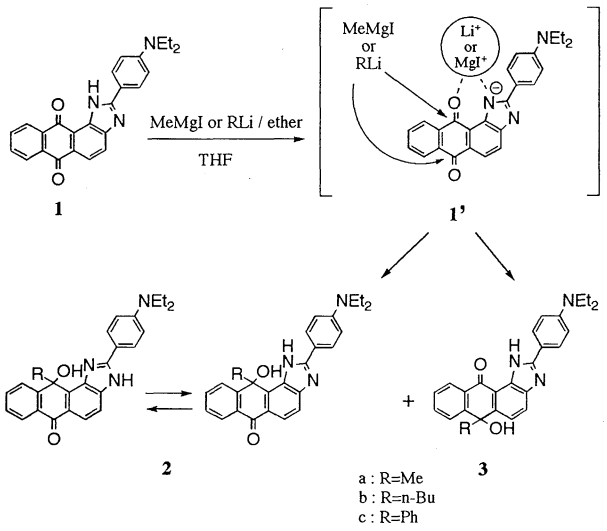
Isomeric pairs of new imidazoanthraquinol-type fluorophores have been synthesized by reaction of a imidazoanthraquinone dye with organometallic reagents. One of a pair was found to exhibit an intense fluorescence in solutions and to form clathrate crystals that contained various kinds of solvent molecules as guest species.

Much attention has long been paid to fluorescent compounds because of their many uses in both the basic and applied research fields.[1,2] Though enormous types of organic fluorophors have already been developed, research for new fluorophores having special characteristics is still of great interest in developing new applications.[3] In this study, we have synthesized isomeric pairs of new imidazoanthraquinol-type fluorophores (**2** and **3**) by the reaction of 2-[4-(diethylamino)-phenyl]imidazo[5,4-a]anthraquinone (**1**) with organometallic reagents (Scheme 1). One of the pair was found to exhibit an intense fluorescence in solutions and form clathrate crystals[4] that contained various kinds of solvent molecules as guest species. The details are described herein.



Scheme 1.

We first prepared the starting heterocyclic quinone (**1**)[5] by refluxing an equimolar amount of 1,2-diaminoanthraquinone with p-(diethylamino)benzaldehyde in acetic acid in the presence of copper(II) acetate, and then examined the reaction of **1** with organometallic reagents at low temperatures to get quinols. Liotta et al.[6] reported in detail the studies of additions of organo-lithium or magnesium reagents to unsymmetrical p-benzoquinones and confirmed that the regioselectivity of 1,2-monoaddition was influenced not only by electronic differences between the carbonyl carbons but also by steric factors including the organometallic reagents. In our case of reaction of **1** with 2.2 equivalent of organo-lithium or magnesium reagents, the isomeric two products (**2** and **3**)[7] were obtained. Two tautomeric forms are possible for each of **2** and **3**. We could not determine a predominant form for **2**. The ^{1}H NMR spectra of **2** did not exhibit clear signals for the 11-hydroxyl proton and the imidazole NH proton. On the other hand, in the case of **3**, the structure shown in Scheme 1 was confirmed by ^{1}H NMR spectra: a broad singlet signal observed at around δ=11.0 ppm supported the formation of intramolecular hydrogen bonding between the NH of imidazole ring and the neighboring quinone carbonyl group. The ratios of the products (**2**/**3**) were greatly dependent on steric factors of the organometallic reagents as shown in Table 1. For example, the reaction with MeMgI afforded a **2a**/**3a** ratio of 31/69 (run 1), whereas the reaction with MeLi afforded a **2a**/**3a** ratio of 83/17 (run 2) : the selectivity of **2a** to **3a** being quite reverse. These results suggest that relatively small MeLi could preferentially attack the more electrophilic carbonyl carbon to give **2a**, while relatively large and heavily solvated MeMgI reagent [6] attack the less-hindered carbonyl carbon to give **3a**. The results given by runs 2-4 in Table 1 also suggest that the isomer (**2**) becomes difficult to be prepared as the counteranion (R^-) of organo-lithium reagents becomes bulky. It is considered that the organometallic reagents abstract firstly the imidazole ring proton of **1** to form a metal chelate (**1'**) which has significant steric influence on the following 1,2-addition step (Scheme 1).

Table 1. Reactions of **1** with organometallic reagents[a]

Run	Reagent	Temp /°C	Yield /%[b] **2+3**	Ratio[b] **2 / 3**
1	MeMgI	-78	82.1	31 / 69
2	MeLi	-108	66.5	83 / 17
3	n-BuLi	-108	73.6	34 / 66
4	PhLi	-108	33.3	0 / 100

[a] To a THF solution of **1** in Ar atmosphere was added an ethereal solution of organometallic reagent (2.2 equiv). [b] The yields and ratios of the products were determined after isolation by column chromatography on silica gel.

Table 2 summarizes absorption and fluorescence spectral data of two kinds of isomers (**2a** and **2b**, and **3a** to **3c**) in solution. The relative fluorescence intensities (RFI) to the fluorescence intensity of 7-diethylamino-4-methylcumarin (DEMC), which is a well-known excellent fluorophore, are also shown in Table 2. It is interesting to see that these two isomers exhibited quite different spectral characteristics, though they have similar structures. The two kinds of isomers have a donor-acceptor chromogen but there is a marked difference in a conjugated interaction between the electron-releasing and electron-withdrawing groups, which results in significant effects on the absorption and fluorescence properties. The quinols (**2a** and **2b**) exhibit an intense absorption band at around λ_{max}=369 nm (ε_{max}>25000) and an intense fluorescence emission band at

Table 2. Absorption and fluorescence spectral properties of **2** and **3**

Compound	Solvent	Absorption λmax nm	Absorption εmax $dm^3mol^{-1}cm^{-1}$	Fluorescence λmax nm	Fluorescence RFI[a]
2a	1,4-dioxane	371	27900	472	49.0
	benzene	369	25300	469	21.9
	acetonitrile	368	24500	593	1.25
	95%ethanol	386	24900	585	0.10
2b	benzene	368	26200	468	20.8
DEMC[b]	benzene	360	25500	411	100
3a	benzene	416	13000	480	0.08
3b	benzene	415	15000	468	0.09
3c	benzene	420	14000	519	0.04

[a] RFI; Relative fluorescence intensity. DEMC (in benzene) =100.
[b] 7-Diethylamino-4-methylcoumarin.

around λ_{max}=469 nm in benzene, whereas the quinols (**3a-3c**) exhibit an absorption band at around λ_{max}=416 nm ($\varepsilon_{max} \leq$ 15000) with only slight fluorescence emission. In addition, the fluorescence spectrum of **2a** was found to undergo drastic changes in the wavelength and intensity depending on the nature of solvents. A large bathochromic shift in the fluorescence maxima and a drastic reduction in the fluorescence intensities were observed on going from 1,4-dioxane to 95%-ethanol.

Furthermore, we have found that the isomers (**2a** and **2b**) can form host-guest inclusion crystals in stoichiometric ratios with various kinds of solvents. The ratio of the host to guest of inclusion crystals prepared by recrystallization of **2a** from solutions of the corresponding guest solvents was determined by means of ^{1}H NMR integration as follows; 2:1 (acetone), 2:1 (benzene), 2:1 (1,4-dioxane), 1:1 (ethanol), 1:1 (1-butanol). Thermogravimetry (TG) was performed to investigate thermal stability of the clathrate crystals and the resulting thermograms are shown in Figure 1. The guest release patterns were considerably different depending on the kinds of solvents. After releasing solvent molecules, the host began to decompose at near 180 °C without melting. The guest release temperatures for 1,4-dioxane and alcohols were higher than their original boiling points. The acetone and benzene inclusion crystals did not show a sharp weight loss process. The percentage weight loss showed good agreement with the data obtained by ^{1}H NMR for benzene, dioxane, and alcohol inclusion crystals but not for acetone inclusion crystal. Crystalline inclusion compounds have recently attracted much attention because of their potential uses in analytical and material sciences.[8] Since the isomers (**2**) exhibit not only inclusion ability but also intense fluorescence, these compounds are expected to have high applicabilities in these fields. The details of inclusion ability of the fluorophors (**2**) and the fluorescence emission characteristics of clathrate crystals are of great interest in both basic and applied points of view and are now under investigations.

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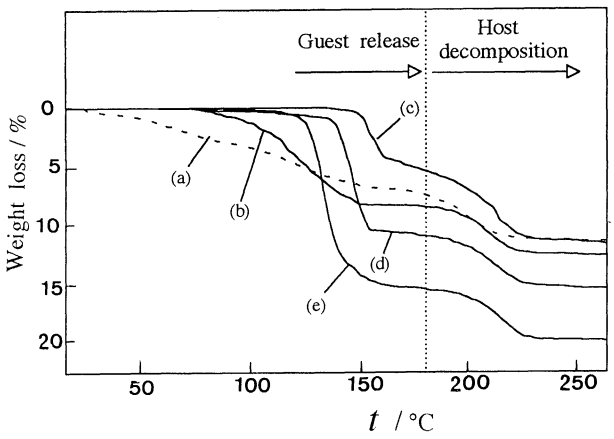

Figure 1. TG curves for host-guest inclusion crystals at a heating rate of 5 °C min^{-1}. Host(**2a**):guest ; (a) 2:1(acetone), (b) 2:1(benzene), (c) 2:1(1,4-dioxane), (d) 1:1(ethanol), (e) 1:1(1-butanol)

References and Notes

1 "Molecular Luminescence Spectroscopy: Method and Applications," ed by S. G. Schulman, John & Sons, New York (1985), (1988), and (1993), Parts. 1, 2, and 3.
2 B. M. Krasovitskii and B. M. Bolotin, "Organic Luminescent Materials," VCH Verlagsgesellschaft, Weinheim (1988).
3 R. M. Christie, *Rev. Prog. Coloration*, **23**, 1 (1993).
4 Crystalline host-guest inclusion complexes are generally known as clathrate crystals.
5 **1:** mp 228-229 °C. ^{1}H NMR(90MHz, $CDCl_3$) δ 1.24 (6H, t), 3.45(4H, q), 6.76 (2H, d), 7.7-8.4 (8H, m), 11.02(1H, br) ; MS m/z 395 (M^+).
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7 Selected physical data for **2** and **3** ; *2-[(4-diethylamino)-phenyl]-11-hydroxy-11-methylimidazo-[5,4-a]anthracen-6(11H)-one (**2a**)*: mp(decomp) 146-147 °C. ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.20 (6H, t), 1.76 (3H, s), 3.37 (4H, q), 6.51 (2H, d), 7.3-7.8 (6H, m), 7.8-8.2 (3H, m); MS m/z 411(M^+). *2-[(4-diethylamino)phenyl]-11-butyl-11-hydroxyimidazo[5,4-a]-anthracen-6(11H)-one (**2b**)* : mp (decomp) 165-166 °C. ^{1}H NMR($CDCl_3$) δ 0.58 (3H, t), 0.94 (4H, m), 1.19 (6H, t), 2.16 (2H, m), 3.37 (4H, q), 6.52 (2H, d), 7.3-7.8(6H, m), 7.8-8.3 (3H, m); MS m/z 453 (M^+). *2-[(4- diethylamino)phenyl]-6-hydroxy-6-methylimidazo[5,4-a]-anthracen-11(6H)-one (**3a**)*: mp 223-224 °C. ^{1}H NMR ($CDCl_3$) δ 1.17 (6H, t), 1.60 (3H, s), 3.36 (4H, q), 4.22 (1H, br), 6.56 (2H, d), 7.0-7.9 (8H, m), 10.62 (1H, br); MS m/z 411 (M^+). *2-[(4-diethylamino)phenyl]-6-butyl-6-hydroxyimidazo-[5,4-a]-anthracen-11(6H)-one (**3b**)* : mp 185-187 °C. ^{1}HNMR ($CDCl_3$) δ 0.60 (3H, t), 0.90 (4H, m), 1.25(6H, t), 2.10 (2H, m), 3.44 (4H, q), 4.10 (1H, br), 6.66 (2H, d), 7.1-8.3 (8H, m), 10.78 (1H, br); MS m/z 453 (M^+). 2-[(4-*diethylamino)-phenyl]-6-hydroxy-6-phenylimidazo[5,4-a]-anthracen-11(6H)-one (**3c**)* : mp 228-230 °C. ^{1}H NMR ($CDCl_3$) δ 1.26 (6H, t), 3.43 (4H, q), 6.52 (2H, d), 6.8-7.9 (14H, m), 10.80 (1H, br); MS m/z 473 (M^+).
8 I. Csoregh, O. Gallardo, E. Weber, and N. Dorpinghaus, J. *Chem. Soc., Perkin Trans. 2*, **1994**, 303, and references cited therein.