Design and Microwave-Assisted Synthesis of Naphtho[2,3-*f*]quinoline Derivatives and Their Luminescent Properties

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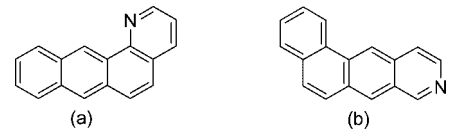
A sequential three-component reaction of an aromatic aldehyde with an equimolar amount of 2-aminoanthracene and cyclic 1,3-dicarbonyl compounds (such as tetronic acid, 5,5-dimethyl,3-cyclohexanedione, 1,3-indanedione, 3*H*-chromene-2,4-dione, quinoline-2,4(1*H*, 3*H*)-dione and barbituric acid) in acidic medium under microwave irradiation has been developed. In this one-pot reaction, a series of unusual fused heterocyclic compounds, naphtho[2,3-*f*]quinoline derivatives, were synthesized. This method has the advantages of operational simplicity, increased safety for small-scale fast synthesis, and minimal environmental impact. Most distinctively, this new class of naphtho[2,3-*f*]quinoline derivatives exhibit good luminescent properties in the ethanol solution, which can be used potentially as organic electroluminescent (EL) media.

Introduction

Organic light-emitting diodes (OLED) are a class of electronic devices that emit light in response to an electrical current applied to the device. The structure of an OLED device generally includes an anode, an organic electroluminescent (EL) medium, and a cathode. The term, organic EL medium, herein refers to organic materials or layers of organic materials disposed between the anode and the cathode in the OLED device. Organic electroluminescent media comprising a single layer of anthracene film had been described by Dresner in 1969.[1] In 1987 and 1989, an EL medium with a multilayer structure of organic thin film, which was demonstrated highly efficient OLED devices, was reported by Tang et al.[2] Furthermore, it was shown in patents that codoping of luminescent layer with anthracene derivatives resulted in devices with better stability.[3] With anthracene as the parent nucleus, azabenz[*a*]anthracene derivatives have strong rigidity and big π-conjugation systems. To the best of our knowledge, of the twelve possible isomeric monoazabenz[*a*]anthracenes, all but 1-azabenz[*a*]anthracene (a) and 9-azabenz[*a*]anthracene (b) have been synthesized.[4] However, this method was still not satisfactory in view of the narrow scope of substrates, harsh reaction conditions, generality, and operational complexity. Thus, a simple, rapid, and efficient procedure is still strongly desired for the synthesis of rigid ring-framework heterocyclic compounds.

The diversity generating potential of multicomponent reactions (MCRs) has been recognized and their utility in preparing libraries to screen for functional molecules is well-appreciated.[5,6] Microwave irradiation of organic reactions has rapidly gained popularity as it accelerates a variety of synthetic transformations.[7] The microwave enhanced procedures without the use of catalyst are particularly ecofriendly, and the protocol has the advantages of short reaction time and high yield.[8]



(a) (b)

To pursue this idea, in this paper, we design and develop feasible strategies for the preparation of rigid ring-framework of azabenz[*a*]anthracene derivatives from an equimolar amount of aromatic aldehyde (**1**), 2-aminoanthracene (**2**), and cyclic 1,3-dicarbonyl compounds (containing **3**, **5**, **7**, **9**, **10**, and **13**; Scheme 1) in acidic media, under microwave irradiation, and without catalyst. Most importantly, these previously unreported naphtho[2,3-*f*]quinoline derivatives may display interesting luminescent behavior that makes the compound more diverse for organic electroluminescent media.

In addition to having potential utility as organic luminescent media mentioned above, these products contain many useful integral skeletons which have significant biological activities. For example, podophyllotoxin derivatives (**4**) are used as an antitumor lignan that inhibits microtubule assembly.[9] Acridines (**6**) as anticancer drugs, antimalarial, and antitumor agents have attracted the attention of organic chemists.[10] Indenoquinoline derivatives (**8**) acted as antitumor agents,[11] steroid reductase inhibitors,[12] acetylcholinesterase inhibitors,[13] antimalarials,[14] and new potential topo I/II inhibitors.[15] In addition, chromenes and their derivatives (**11**) and (**12**) are found to possess the activities of antiestrogenic,[16] hypotensive,[17] vasodilator, antihypertensive,[18] β-a-

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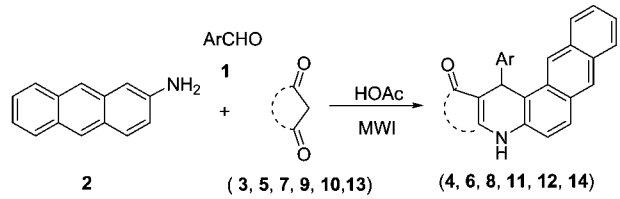
Scheme 1. Synthesis of Naphtho[2,3-*f*]quinoline Derivatives **4a**−**m**, **6a**−**g**, **8a**−**e**, **11a**−**f**, **12a**−**f**, and **14a**−**f**



1,3-dicarbonyl compounds	3	5	7	9	10	13
Product	4	6	8	11	12	14

Table 1. Solvent and Temperature Optimization for the Synthesis of **4b**

entry	solvent	*T* (°C)	time (min)	yield[a] (%)
1	ethylene glycol	140	5	88
2	DMF	130	5	89
3	HOAc	120	4	94
4	EtOH	140	6	80
5	HOAc	100	4	92
6	HOAc	110	4	93
7	HOAc	120	4	94
8	HOAc	130	4	93
9	HOAc	140	4	93
10	HOAc	150	4	91

[a] Isolated yields.

Table 2. Synthesis of **4** under Microwave Irradiation at 120 °C

entry	product (**4**)	Ar	time (min)	yield[a] (%)
1	**4a**	4-ClC_6H_4	4	93
2	**4b**	4-BrC_6H_4	4	94
3	**4c**	3-$NO_2C_6H_4$	4	91
4	**4d**	4-$NO_2C_6H_4$	4	90
5	**4e**	3,4-$(OCH_2O)C_6H_3$	4	93
6	**4f**	C_6H_5	4	93
7	**4g**	4-$MeOC_6H_4$	4	93
8	**4h**	4-$CH_3C_6H_4$	4	91
9	**4i**	4-OH-3-$NO_2C_6H_3$	5	93
10	**4j**	3.4-$CH_3OC_6H_3$	4	94
11	**4k**	2-Thienyl	5	92
12	**4l**	2,4-$Cl_2C_6H_3$	5	92
13	**4m**	4-$(CH_3)_2NC_6H_4$	5	94

[a] Isolated yields.

drenolytic,[19] antimicrobial,[20] and biological activity of high-affinity retinoic acid receptor antagonist.[21] Moreover, dihydropyrimidinone derivatives (**14**) serve as the integral backbones of several calcium channel blocks, antihypertensive agents, and NPY antagonists.[22] Therefore, the synthesis of azabenz[*a*]anthracene derivatives is of great significance.

Results and Discussion

We first chose tetronic acid **3** to react with equimolar amount of aromatic aldehyde **1** and 2-aminoanthracene **2** (Scheme 1) for the formation of that skeleton and investigate the optimized conditions.

To search for the optimal reaction solvent, the reaction of 4-bromophenylaldehyde (**1b**), 2-aminoanthracene (**2**), and tetronic acid (**3**) was examined in ethylene glycol, DMF, glacial acetic acid, and ethanol respectively (Table 1, entries 1−4) under microwave irradiation conditions at the maximum power of 200 W. It was shown in Table 1 that the reaction using glacial acetic acid (Table 1, entry 3) as solvent resulted in higher yields and shorter reaction times than those using ethylene glycol, DMF, and ethanol. So, glacial acetic acid was chosen as the solvent. To further optimize the reaction condition, the same reaction was carried out in glacial acetic acid at temperatures ranging from 100 to 150 °C (Table 1, entries 5−9), with an increment of 10 °C. As shown in Table 1, further increase of the temperature to 130−150 °C failed to improve the yield of product **4b** (Table 1, entries 9 and 10). It implied that further increase of the temperature above 120 °C has no obvious influence on this reaction. Therefore, 120 °C was chosen as the reaction temperature for all further microwave-assisted reactions.

The use of these optimal microwave experimental conditions [glacial acetic acid, 120 °C, 200 W (maximum power)] to the reactions of different aromatic aldehydes afforded good yields of naphtho[2,3-*f*]quinoline (Table 2).

This new class of naphtho[2,3-*f*]quinoline derivatives display very favorable fluorescence profiles (Table 4). To further expand the scope of the application of this reaction and make organic electroluminescent media more diverse, the replacement of **3** with **5**, **7**, **9**, **10**, and **13** (Scheme 1) was examined respectively. To our delight, under the above optimized conditions, the reactions proceeded smoothly. As a result, five other kinds of naphtho[2,3-*f*]quinoline derivatives were obtained (Table 3). Although the active hydrogen of cyclic 1,3-dicarbonyl compounds in **5** ($pK_a = 5.2$),[23] **7** ($pK_a = 7.2$),[23] **9**, **10** ($pK_a = 5.86$),[24] and **13** ($pK_a = 3.9$)[24] is different from that of tetronic acid **3** ($pK_a = 3.76$),[25] experimental results indicated that the pK_a of the active

Table 3. Synthesis of **6**, **8**, **11**, **12**, and **14** under Microwave Irradiation at 120 °C

entry	product	Ar	time (min)	yield[a] (%)
1	**6a**	4-$CH_3C_6H_4$	4	90
2	**6b**	4-$CH_3OC_6H_4$	5	88
3	**6c**	3,4-$CH_3OC_6H_4$	5	90
4	**6d**	4-BrC_6H_4	4	91
5	**6e**	3,4-$(OCH_2O)C_6H_3$	5	89
6	**6f**	2-Thienyl	5	86
7	**6g**	4-OH-3-$NO_2C_6H_3$	4	90
8	**8a**	4-BrC_6H_4	5	91
9	**8b**	3-$NO_2C_6H_4$	5	92
10	**8c**	4-$CH_3C_6H_4$	4	92
11	**8d**	2,4-$Cl_2C_6H_3$	4	93
12	**8e**	3,4-$(OCH_2O)C_6H_3$	5	90
13	**11a**	4-$CH_3OC_6H_4$	6	92
14	**11b**	3.4-$CH_3OC_6H_3$	6	91
15	**11c**	4-$NO_2C_6H_4$	5	94
16	**11d**	3-$NO_2C_6H_4$	5	95
17	**11e**	3,4-$(OCH_2O)C_6H_3$	6	91
18	**11f**	2-Thienyl	6	93
19	**12a**	4-$CH_3C_6H_4$	5	92
20	**12b**	3.4-$CH_3OC_6H_3$	5	90
21	**12c**	4-$NO_2C_6H_4$	5	89
22	**12d**	2,4-$Cl_2C_6H_3$	4	89
23	**12e**	3,4-$(OCH_2O)C_6H_3$	5	91
24	**12f**	4-OH-3-$NO_2C_6H_3$	4	90
25	**14a**	4-$CH_3OC_6H_4$	5	92
26	**14b**	3.4-$CH_3OC_6H_3$	5	91
27	**14c**	4-OH-3-$NO_2C_6H_3$	4	93
28	**14d**	2,4-$Cl_2C_6H_3$	5	92
29	**14e**	3,4-$(OCH_2O)C_6H_3$	4	90
30	**14f**	2-ClC_6H_4	4	91

[a] Isolated yields.

Table 4. Date of Luminescence and Purities of Some Products ($c = 10^{-5}$ mol·L^{-1})

entry	λ_{max} (nm)	λ_{em} (nm)	purity[a] (%)	entry	λ_{max} (nm)	λ_{em} (nm)	purity[a] (%)
4b	330.0	455.8	97.8	**11a**	332.0	488.8	100
4d	311.0	439.8	98.1	**11b**	333.0	488.4	86.1
4e	329.0	458.4	92.1	**11c**	331.0	466.4	100
4f	330.0	454.8	97.3	**11d**	330.0	461.0	87.1
4h	330.0	458.4	90.6	**11e**	333.0	485.0	87.9
4i	311.0	446.8	98.6	**11f**	332.0	486.6	82.9
4j	295.0	456.8	97.6	**12a**	342.0	458.2	99.4
4k	328.0	456.0	97.2	**12b**	342.0	457.2	91.8
4l	303.0	451.0	97.5	**12c**	332.0	452.0	97.6
6a	347.0	464.2	98.2	**12d**	344.0	453.4	97.8
6b	346.0	462.6	96.4	**12e**	341.0	455.8	97.1
6d	347.0	459.2	98.2	**12f**	330.0	455.2	98.3
6e	347.0	460.0	100	**14a**	329.0	459.0	94.7
6g	329.0	459.0	99.3	**14b**	329.0	459.0	90.5
8a	330.0	456.8	89.4	**14c**	330.0	466.8	90.5
8b	330.0	456.6	89.5	**14d**	332.0	466.6	94.6
8d	330.0	456.6	94.8	**14e**	328.0	455.0	91.9
8e	330.0	454.8	94.4	**14f**	330.0	463.0	93.7

[a] HPLC purity.

hydrogen of the 1,3-dicarbonyl compounds had no significant influence to the success of the reactions.

The structures of all the synthesized compounds were based on their spectroscopic data. As shown in Tables 2 and 3, this protocol could be applied not only to aromatic aldehydes with either electron-withdrawing or electron-donating groups, but also to heterocyclic aromatic aldehydes. Bearing the same active methylene in **3**, **5**, **7**, **9**, **10**, and **13**, the mechanism of the above reactions should have similar mechanism via sequential condensation, addition, cyclization, and elimination as that we have previously reported.[26]

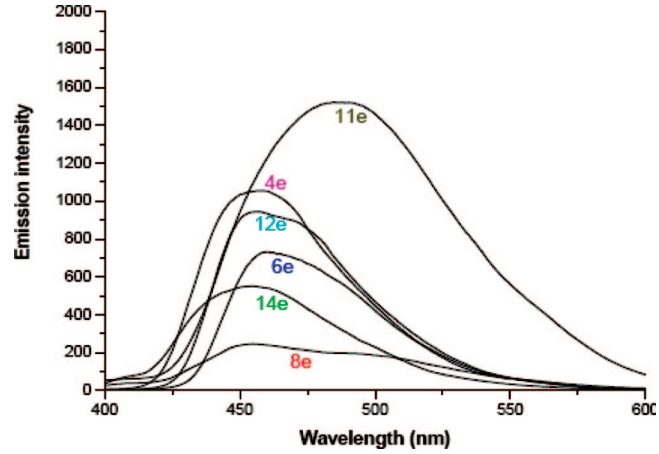


Figure 1. Emission spectra of the compounds of **4e**, **6e**, **8e**, **11e**, **12e**, and **14e** which contain the same substituent group.

The naphtho[2,3-*f*]quinoline derivatives exhibit good luminescent properties in 95% ethanol solution and the corresponding luminescence data are listed in Table 4.

As shown in Table 4, naphtho[2,3-*f*]quinoline derivatives exhibit good luminescent properties with emission wavelengths at the range of 439.8−488.8 nm in the blue region. Except **11c** and **11d**, the emission wavelengths of **11** were slightly longer than those of other compounds. As shown in Figure 1, with the same substituent group, we can make a conclusion that the emission intensity of **11e** is stronger than that of **4e**, **6e**, **8e**, **12e**, and **14e**. All of these maybe mainly ascribe to their stronger rigidity and bigger π-conjugation systems. Although **11e** and **12e** have similar structure, the different emission wavelength between them may be caused by the molecular polarity.

Conclusion

In summary, we have provided an effective route for the synthesis of a series of naphtho[2,3-*f*]quinoline derivatives which are promising candidates for organic electroluminescent media because of their good luminesent properties in the blue region and maybe also display important biological activities for biomedical screening. This work is currently in progress and the results will be reported in due course.

Experimental Section

Microwave irradiation was carried out with a microwave oven (Emrys Creator from Personal Chemistry, Uppsala, Sweden). Melting points were determined in open capillaries and are uncorrected. IR spectra were taken on a FT-IR-Tensor 27 spectrometer in KBr pellets and reported in inverse centimeters. ^{1}H NMR (^{13}C NMR) spectra were measured on a Bruker DPX 400 MHz (100 MHz) spectrometer in DMSO-d_6 with chemical shifts (δ) given in parts per million relative to TMS as an internal standard. ESI-MS was determined by using the LCQ Advantage HPLC/MS instrument (Thermo Finnigan). All fluorescence intensity measurements were made with a LS-50B spectrometer. HPLC chromatograms were measured with Agilent 1100 series equipment.

General Procedure. The reactions were performed in a monomodal Emrys Creator from Personal Chemistry, Uppsala, Sweden. In a 10 mL Emrys reaction vial, aldehyde

(0.05 mmol) and 2-aminoanthracene (0.05 mmol), with an equimolar amount of cyclic 1,3-dicarbonyl compounds separately (tetronic acid **3**, 5,5-dimethyl-1,3-cyclohexanedione **5**, barbituric acid **7**, 3*H*-chromene-2,4-dione **9**, quinoline-2,4(1*H*, 3*H*)-dione **10**, and barbituric acid **13**) and glacial acetic acid (3 mol), were mixed and then capped. The mixture was irradiated for a desired time (monitored by TLC) at 200 W and at 120 °C. The reaction mixture was cooled to room temperature and then poured into water. The solid products were filtered, washed with water and EtOH (95%), and recrystallized from EtOH to give the pure products (**4a**−**m**, **6a**−**g**, **8a**−**e**, **11a**−**f**, **12a**−**f**, and **14a**−**f**).

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Supporting Information Available. Representative experimental procedures, spectral data of compounds **4a**−**m**, **6a**−**g**, **8a**−**e**, **11a**−**f**, **12a**−**f**, and **14a**−**f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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