Synthesis of Carbonyl Dyes from 1-Hydroxy-2-Acetonaphthone and 2-Fluorobenzophenone
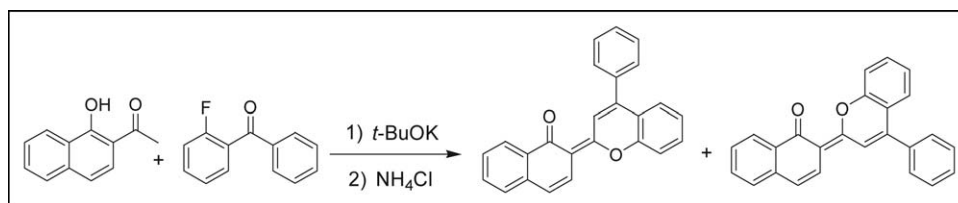
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The reaction between 1-hydroxy-2-acetonaphthone and 2-fluorobenzophenone in basic medium afforded two diastereoisomeric carbonyl dyes whose structures were unambiguously established using spectroscopic methods. A mechanism for the formation of these dyes involving a base-catalysed addition followed by dehydration and intramolecular aromatic nucleofilic substitution is proposed.
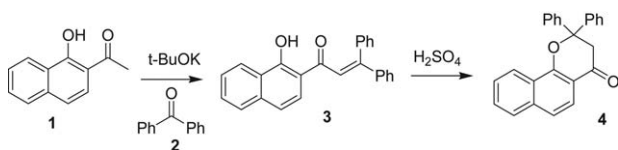
INTRODUCTION

Reaction between 1-hydroxy-2-acetonaphthone **1** and benzophenone **2** in the presence of sodium *tert*-butoxide is known to produce, after acid treatment, mainly 2,2-diphenylnaphthopyran-4-one **4**, a useful compound in the synthesis of photochromic naphthopyrans [1,2]. The reaction involves a base-catalysed addition of **1** to **2** followed by dehydration that provides the yellow intermediate **3**. Then the acid catalyzed intramolecular 1,4-addition of the phenolic hydroxyl group to the α,β-conjugated ketone produces the diphenylnaphthopyran-4-one **4** (Scheme 1) [3]. This low yielding reaction (56%) requires an excess of base and ketone and is thus far limited to diarylketones [4–6].

Recently, we have reported that the reaction between **1** and 2-fluorobenzophenone **5** in the presence of 5 equivalents of potassium *tert*-butoxide in toluene under reflux, followed by reflux in AcOH/HCl gives rise to a small amount of a blue dye (5.7%). Spectroscopic characterization using high-resolution NMR techniques established the highly conjugated structure **6** for this product [7].

RESULTS AND DISCUSSION

To improve the yield and understand how this dye is formed, we re-investigated this reaction and found out that, in fact, two different dyes are formed after the first step of the reaction between **1** and **5** (*t*-BuOK in toluene under reflux). NH₄Cl(aq) hydrolysis of the basic reaction mixture afforded a yellow dye **7** (less polar, 63% yield) as well as a small amount of the already known dye **6** (more polar, 7% yield) (Scheme 2).

Spectroscopic characterization of the new yellow dye **7** using DEPT, COSY, HMBC, HSQC provided the complete assignment of all proton and carbon resonances and showed that this compound is a diastereoisomer of the previously isolated dye **6** (Table 1). Long-range C—H correlations in the HMBC spectrum established the connectivity between all atoms and are shown in Figure 1.

The spectroscopic data for compounds **7** and **6** are quite similar. Both exhibit the same molecular formula and similar patterns in the Mass spectra and in the ^{1}H and ^{13}C NMR spectra. The main differences between these two diastereoisomeric dyes in the NMR spectra were the chemical shifts of protons H-3′ found at 6.04 (s) for dye **7** and at 9.12 (s) for dye **6** and the chemical shift of the carbonyls found at 195.36 ppm for **7** and at 183.58 ppm for **6**. The NOESY spectrum showed an important correlation between H-3′and H-3 for compound **7**, which was not observed for compound **6** and thus establishes a *Z*-configuration for the double bond between carbons 2 and 2′ of dye **7**.

Scheme 1. Synthesis of 2,2-diphenylnaphthopyran-4-one **4**.

Scheme 2. Synthesis of dyes **6** and **7**.
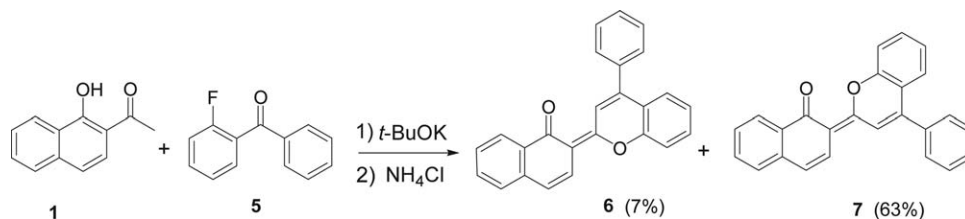
The UV-vis spectra of these two dyes are very different. While the blue dye **6** exhibits a large band in the visible spectrum with a maximum at 538 nm (ε 1.1 $\times$ 10^4), a sub-maximum at 577 nm (ε 1.1 $\times$ 10^4), and two shoulders at 504 nm (ε 0.83 $\times$ 10^4) and 630 nm (ε 0.50 $\times$ 10^4), the yellow dye **7** presents a maximum at 394 nm (ε 0.74 $\times$ 10^4) (Figure 2). The lower λ_{max} for dye **7** suggests a less efficient conjugation that may be due to the repulsion between the oxygen atoms at C-2′ and C-1 that would led to a less planar structure of this Z-isomer.

The formation of both dyes under basic medium led us to propose the following mechanism: subsequent to the base-catalyzed addition between **1** and **5**, proton transfer and dehydration would form the phenolate **A**, which might adopt two configurations, that upon intra-molecular nucleophilic aromatic substitution would lead to the two diastereoisomeric dyes **6** and **7** (Scheme 3) [8,9].

Although both dyes were formed under basic conditions, a small amount of the blue dye **6** was also formed when the yellow dye **7** was refluxed in acid medium (AcOH/HCl). This can be explained through an acid catalyzed isomerization of **7** to **6** (Scheme 4).

EXPERIMENTAL

The reagents were obtained from Aldrich and were used as supplied. Solvents were of analytical grade. The reactions were monitored by thin-layer chromatography on aluminum plates precoated with Merck silica gel 60 F254 (0.25 mm). Melting point was determined in capillary tubes and are

Table 1

NMR spectral data for dyes **6** and **7**.

Atom	Dye **6**		Dye **7**	
	1H (*J* in Hz)	13C	1H (*J* in Hz)	13C
1		183.58, *s*		195.36, *s*
2		111.21, *s*		113.96, *s*
3	7.66, *d* (9.6)	123.18, *d*	7.80, *d* (8.8)	124.59, *d*
4	6.73, *d* (9.6)	119.53, *d*	7.25[a]	118,11, *d*
4a		137.78, *s*		137.28, *s*
5	7.42, *d* (7.6)	127.25, *d*	7.74, *d* (8.0)	127.35, *d*
6	∼7.55[a]	131.84, *d*	7.62, *ddd* (1.3,6.9, 8.0)	130.04, *d*
7	7.36, *dd* (7.5; 8.0)	126.38, *d*	7.51, *ddd* (1.0,7.0, 8.0)	125.77, *d*
8	8.34, *d* (8.0)	126.90, *d*	8.45, *d* (8.0)	124.35, *d*
8a		132.59, *s*		125.18, *s*
2′		162.44, *s*		163.54, *s*
3′	9.12, *s*	120.74, *d*	7.48, *s*	124.15, *d*
4′		150.14, *s*		147.72, *s*
4′a		121.38, *s*		126.59, *s*
5′	∼7.55[a]	126.47, *d*	7.10[a]	128.18, *d*
6′	7.25, *dd* (7.5; 7.6)	124.81, *d*	7.15, *d* (8.9)	123.96, *d*
7′	∼7.58[a]	132.03, *d*	7.20[a]	131.20, *d*
8′	∼7.51[a]	117.12, *d*	7.05[a]	115.50, *d*
8′a		153.34, *s*		148.52, *s*
1″		136.05, *s*		140.28, *s*
2″ and 6″	∼7.52[a]	128.77, *d*	7.45[a]	128.58, *d*[b]
3″ and 5″	∼7.62[a]	128.98, *d*	7.45[a]	127.86, *d*[b]
4″	∼7.52[a]	129.54, *d*	7.40[a]	129.70, *d*

All [1]H-^{13}C connectivities were assigned by HMBC and HSQC and the multiplicities were determined by DEPT experiments.
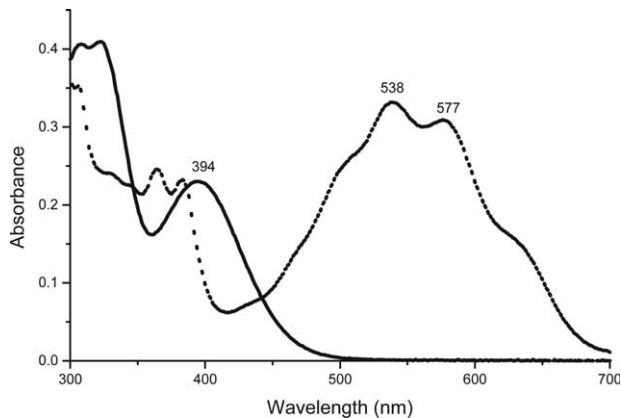[a] Approximate central values due to overlapped signals.
[b] The values may be interchanged.
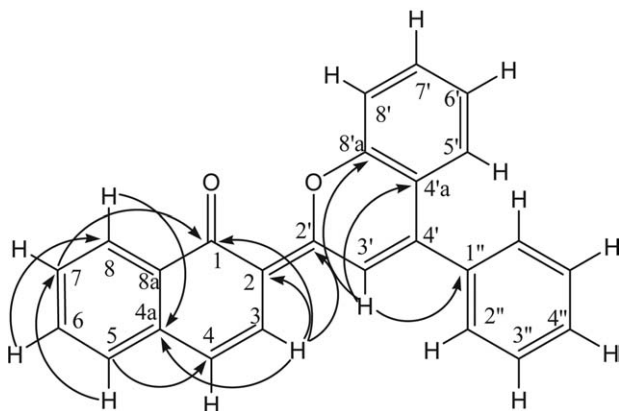
Figure 1. Long-range C—H correlations obtained from HMBC for dye **7**.

Figure 2. UV/vis spectra of compounds **6** and **7** (3.1×10^{-5} M, CH_2Cl_2).

uncorrected. The new compounds were determined to be >95% pure by ^{1}H NMR spectroscopy. UV-Vis spectra were recorded on a CARY 50 Varian spectrophotometer. IR spectra were obtained on a Perkin-Elmer FTIR 1600 spectrometer using KBr disks (wavenumbers in cm^{-1}). Electronic impact mass spectra were measured on a AutoSpecE spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded at 298 K in CDCl$_3$ using a Bruker ARX400 spectrometer (at 400.13 for ^{1}H and 100.62 MHz for ^{13}C). Chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz. Resonance multiplicities for ^{13}C were established via the acquisition of DEPT spectra. Heteronuclear ^{1}H-^{13}C HSQC and HMBC experiments were carried out using standard procedures.

General procedure for the synthesis of dyes (6) and (7). 1-Hydroxy-2-acetonaphthone **1** (0.186 g, 1.0 mmol) and potassium *tert*-butoxide (0.336 g, 3 mmol) in toluene (15 mL) were refluxed for 20 min. 2-Fluorobenzophenone **2** (0.400 g, 2.0 mmol) was added and the reaction mixture was refluxed

for another 40 min. The dark red solution was hydrolyzed with NH$_4$Cl (aq) and then extracted with Et$_2$O (3 $\times$ 20 mL). The organic extracts were dried over anhydrous Na$_2$SO$_4$ and evaporated leaving a deep red residue, which was purified by column chromatography (2–10% ethyl acetate/petroleum ether) over silica gel. Two compounds were isolated: **7**, 0.220 g (63%) and **6**, 0.025 g (7%).

(2Z)-2-(4′-phenyl-2H-chromen-2′-ylidene)naphthalene-1(2H)-one (7). This compound was obtained as a yellow powder, mp 130°C dec. IR: 3060, 3026, 2976, 1620, 1594, 1569, 1450, 1320, 1254, 1203, 1059. For ^{1}H NMR and ^{13}C NMR data see Table 1. MS: *m/z* (%): 348 (75), 331 (12), 291 (8), 271 (14), 170 (100). Exact mass for C$_{25}$H$_{16}$O$_2$: 348.1150; Found 348.1146.

(2E)-2-(4′-phenyl-2H-chromen-2′-ylidene)naphthalene-1 (2H)-one (6). This compound was obtained as blue needles, mp 155–158°C. IR: 3050, 2923, 2852, 1624, 1593, 1541, 1505, 1468, 1371, 1315, 1273, 1235, 955, 923. For ^{1}H NMR

Scheme 3. Mechanism for the formation of dyes **6** and **7** from 1-hydroxy-2-acetonaphthone **1** and 2-fluorobenzophenone **5**.
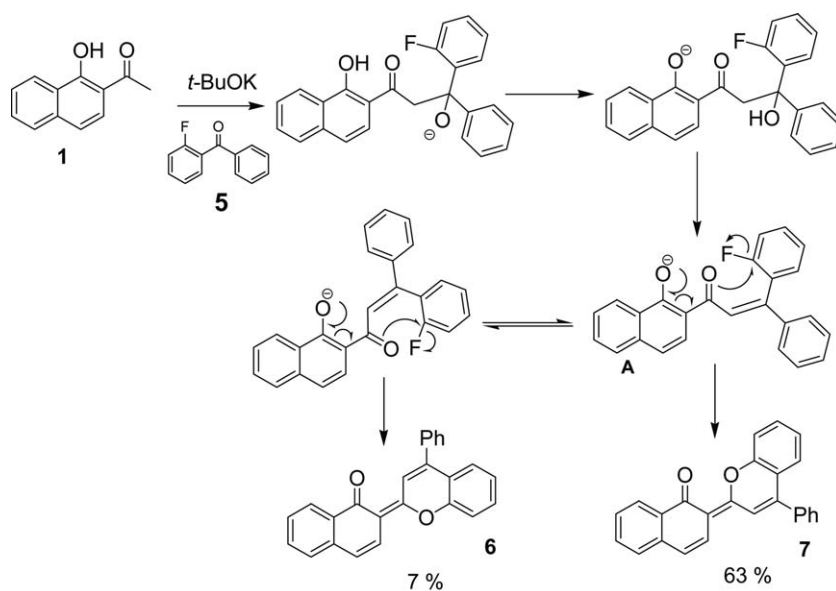
Scheme 4. Acid catalysed isomerization of dye **7** to dye **6**.
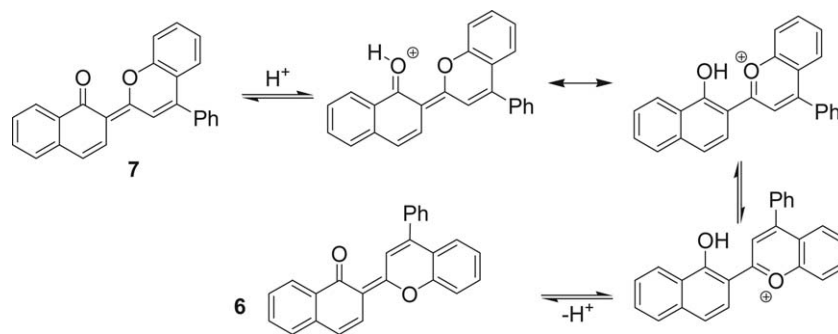
and ^{13}C NMR data see Table 1. MS: *m/z* (%): 348 (100), 331 (25), 289 (10), 271 (40). Exact mass for $C_{25}H_{16}O_2$: 348.1150; Found 348.1148.

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