Dyes and Pigments 80 (2009) 26–29

Contents lists available at ScienceDirect

Dyes and Pigments

journal homepage: www.elsevier.com/locate/dyepig

Deuterated dicondensed indolinobenzospiropyran formed from the reaction of Fischer base-d_2 and salicylaldehyde: Mechanism involving a carbinol intermediate

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ARTICLE INFO

Article history:
Received 4 February 2008
Received in revised form 15 April 2008
Accepted 19 April 2008
Available online 30 April 2008

Keywords:
Dicondensed indolinobenzospiropyran
Carbinol intermediate
Merocyanine intermediate
Michael-type addition
Simultaneous reaction pathway
Consecutive reaction pathway

ABSTRACT

From the deuterium content (*x*-value) of deuterated molecules obtained from the reaction of an excess of Fischer base-d_2 with salicylaldehydes, it is found that the formation of the dicondensed indolinobenzospiropyrans occurred via a carbinol intermediate, rather than an open merocyanine form of spiropyran. ^{1}H NMR behavior supported this proposed mechanism, indicating that a carbinol intermediate was simultaneously, and not consecutively, formed prior to the transformation to both spiropyrans and dicondensed indolinobenzospiropyran.

1. Introduction

Thermo- and photochromic indolinobenzospiropyrans are typical organic compounds, with high extinction coefficients in the near-infrared region, which have been widely studied from chemical, physical and material points of view [1,2]. Therefore, these spiropyran dyes (SP) have become important in connection with the rapid development of information recording systems, high-density optical data storage, displays, holographic devices and as optical switches [3–10].

Dicondensed indolinobenzospiropyrans (DC) are formed together with monocondensed compounds (SP) from the condensation reaction of an excess amount of Fischer base with substituted salicylaldehydes. Spiropyran molecules are known to be unstable, whereas DC molecules are relatively stable, either thermally or photochemically.

Dicondensed spiropyran molecules are referred to precursors of SP molecules, since those molecules can transform to the corresponding SP molecules thermally [1] or by acid [11], as shown in Fig. 1.

Therefore, DC molecules have been used in many practical applications in various fields, such as additives in silver halide emulsion [12] and as components of thermal papers [13,14], in addition to as precursors of thermo- and photochromic spiropyran dyes.

Although dicondensed products have provoked considerable discussion [15–18], including their X-ray crystal structures and spectroscopic characterization, the mechanism of their formation has not been previously rationalized. Two reasonable variations of a mechanistic pathway were suggested earlier for the formation of DC molecules from reaction of a Fischer base and salicylaldehydes [1,2]. The salicylaldehydes may condense with two molecules of Fischer base via a carbinol intermediate or the Fischer base may undergo a Michael addition to the open MC (merocyanine) form of the spiropyran, but controversy still exists.

The structure of the dicondensed product has been reported in our previous paper [16], along with ^{1}H and ^{13}C NMR spectroscopic data, but the formation mechanism has now been reconsidered. Therefore, the deuterium content (*x*-value) of the deuterated DC (DC-d_x) molecules from reaction of excess Fischer base-d_2 with salicylaldehydes was needed to be evaluated, as this may enable the differentiation of two previously suggested mechanistic pathways (see text).

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doi:10.1016/j.dyepig.2008.04.004

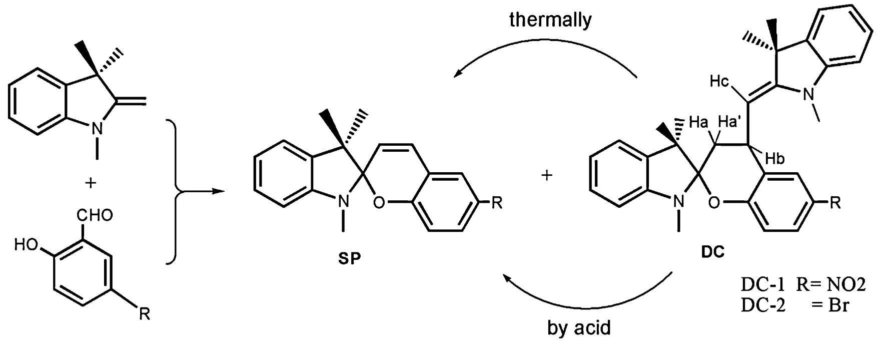

Fig. 1. Synthesis of SP and dicondensed SP (DC) from the reaction of FB and SA.

2. Experimental

2.1. General

Melting points were determined using a Fischer–Jones melting point apparatus, and are reported uncorrected. ^{1}H NMR spectra were obtained in DMSO-d_6 on a Varian 300 NMR spectrophotometer. Chemical shifts were reported in δ (ppm) relative to tetramethylsilane, which was used as the internal standard. High-resolution FAB mass spectra were obtained at the Seoul Campus of the Basic Science Research Institute of Korea University.

2.2. Materials

All reagents were purchased from commercial sources and used without further purification unless otherwise noted. Fischer base (1,3,3-trimethyl-2-ethyleneindoline), 2,3,3-trimethylindolenine, salicylaldehyde derivatives and potassium deuteroxide were available from Aldrich Chemical Co. and used without further purification. Potassium deuteroxide was 40 wt.% solution in D_2O.

2.2.1. 1,2,3,3-Tetramethyl indolenium iodide

2,3,3-Trimethylindolenine (1.00 g, 6.29 mmol), chloroform (10 mL), and methyl iodide (1.28 g, 9.00 mmol) were added into an ampule tube, which was sealed by a torch and heated at 80 °C for 20 h. The resulting pink powder was filtered and washed with ice-cooled chloroform and then repeatedly with diethyl ether to give a 64% yield of a white powder of product (1.21 g, 4.03 mmol). ^{1}H NMR (60 MHz, D_2O): δ 1.70 (s, 3-*Me*, 6H), 2.89 (s, 2-*Me*, 3H), 3.99 (s, N*Me*, 3H), 7.60 (br, aromatic 4H).

2.2.2. 1,3,3-Trimethyl-2-dideuteriomethyleneindoline (FB-d$_2$)

1,2,3,3-Tetramethyl indolenium iodide (901.6 mg, 2.992 mmol) was added to a solution of potassium deuteroxide/D_2O (1.0 M, 10 mL). The suspension was stirred for 1 h at room temperature, during which time the suspension turned into a yellow oil. The resulting oil was extracted with Et_2O, repeatedly washed with saturated NaCl (aqueous) and then dried over anhydrous sodium sulfate. Evaporation of the solvent gave a 50% yield of 1,3,3-trimethyl-2-dideuteriomethyleneindoline as a light orange liquid (286.8 mg, 655 mmol). On the basis of integration of the ^{1}H NMR spectrum, the deuterium content of deuterium was found to be 35% for indoline-d_2. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.34 (s, 6-*Me*, 3H), 3.03 (s, N*Me*, 3H), 3.89 (d, =C*H*$_2$, 2H), 6.58 (d, 7-C*H*, *J* = 7.8 Hz, 1H), 6.82 (dd, 5-C*H*, *J* = 7.2, 7.4 Hz, 1H), 7.13 (d, 4-C*H*, *J* = 7.2 Hz, 1H), 7.16 (dd, 6-C*H*, *J* = 7.4, 7.8 Hz, 1H).

*2.2.3. Deuterated 4-(1,3,3-trimethyl-2-methyleneindoline-2′-yl)-6-nitro-1′,3′,3′-trimethylspiro[3,4-dihydro-2*H*-1-benzopyran-2,2′-indoline] (DC-1-d$_x$)*

5-Nitrosalicylaldehyde (1.0 g, 5.98 mmol) was added to an ethanolic solution (10 ml) of isotope-labeled Fischer base (2.6 g, 15.0 mmol) and refluxed for 4 h. The yellow precipitate was filtered from the hot solution and washed thoroughly with cold diethyl ether. Purification was carried out either by recrystallization from acetone or by precipitation from chloroform/diethyl ether. Evaporation of the solvent gave an 82% yield of 4-(1,3,3-trimethyl-2-methyleneindoline-2′-yl)-6-nitro-1′,3′,3′-trimethylspiro[3,4-dihydro-2*H*-1-benzopyran-2,2′-indoline] as a yellow solid. M.p. 176 (dec.137) °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.31 (s, 3H), 1.33 (s, 3H), 1.62 (s, 6H), 2.23 (dd, *J* = 14.3, 13.0 Hz, 1H), 2.85 (s, 3H), 3.00 (dd, *J* = 14.3, 4.87 Hz, 1H), 3.05 (s, 3H), 4.15 (d, *J* = 10.1 Hz, 1H), 4.32 (m, *J* = 13.0, 10.1, 4.87 Hz, 1H), 6.83 (t, 1H), 6.59 (d, 1H), 6.60 (d, *J* = 7.43 Hz, 1H), 6.75 (d, 1H), 6.86 (t, 1H), 7.06 (t, 1H), 7.07 (d, 1H), 7.09 (t, *J* = 7.43 Hz, 1H), 7.11 (d, 1H), 7.96 (d, 1H), 8.23 (s, 1H).

*2.2.4. 4-(1,3,3-Trimethyl-2-methyleneindoline-2′-yl)-6-bromo-1′,3′,3′-trimethylspiro[3,4-dihydro-2*H*-1-benzopyran-2,2′-indoline] (DC-2-d$_x$)*

The isotope-labeled analogue DC-2 was similarly prepared from the reaction of Fischer base-d_2 and 5-bromosalicylaldehyde in 65% yield. M.p. 175 (dec.137) °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 3H),

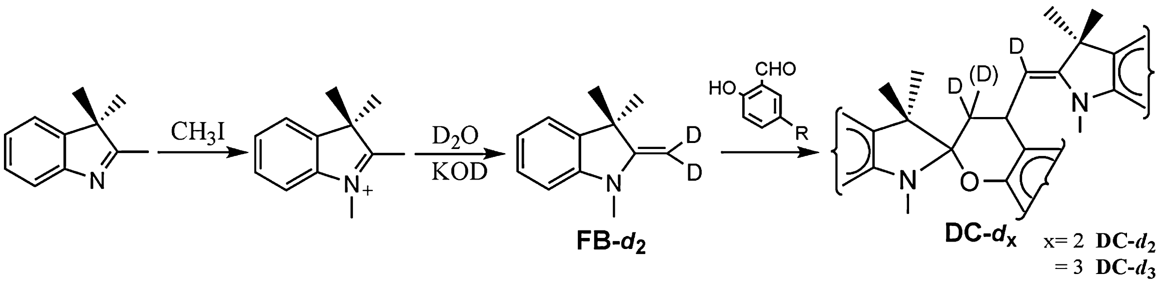

Fig. 2. Synthesis of deutero-FB (FB-d_2) and deutero-DC (DC-d_x).

Table 1
Determination of deuterium content (*x*-value) in DC-d_x formed from FB-d_2

Starting FB	Via intermediate	$\text{Product}_{\text{expected}}$	*x*-Values [(Ha + Ha′)/Hc]		Note[b]
			Calculated[a]	Experimental	
FB-d_2 (34 atom% D)	Carbinol	DC-d_3	2.0		
				1.82 (DC-1)	Close to 2.0
				1.90 (DC-2)	
	Merocyanine	DC-d_2	2.5		

[a] Sum of Ha and Ha′ peak intensity, relative to Hc, in ^{1}H NMR spectrum of deuterated DC compounds. Since 35% of the 2′-methylene of FB molecule was deuterated, the ratio can be calculated as follows: [(0.65 + 0.65)/0.65 = 2.0 for DC-d_3 and (0.65 + 1.0)/0.65 = 2.5 for DC-d_2].

[b] Values are close to 2.0, which imply that the mechanism undergoes via a carbinol intermediate.

1.33 (s, 3H), 1.62 (s, 6H), 2.23 (dd, *J* = 14.3, 13.0 Hz, 1H), 2.85 (s, 3H), 3.00 (dd, *J* = 14.3, 4.87 Hz, 1H), 3.05 (s, 3H), 4.15 (d, *J* = 10.1 Hz, 1H), 4.32 (m, *J* = 13.0, 10.1, 4.87 Hz, 1H), 6.83 (t. 1H), 6.59 (d, 1H), 6.60 (d, *J* = 7.43 Hz, 1H), 6.75 (d, 1H), 6.86 (t, 1H), 7.06 (t, 1H), 7.07 (d, 1H), 7.09 (t, *J* = 7.43 Hz, 1H), 7.11 (d, 1H), 7.96 (d, 1H), 8.23 (s, 1H).

3. Results and discussion

3.1. Synthesis

The isotope-labeled 4-(1,3,3-trimethyl-2-methyleneindoline-2′-yl)-6-nitro-1′,3′,3′-trimethylspiro[3,4-dihydro-2*H*-1-benzopyran-2,2′-indoline] (DC-d_x) was prepared in a 34–38% yield from the reaction of Fischer base-d_2 and 5-nitro and 5-bromosalicylaldehyde, as shown in Fig. 2. Deuteration of the Fischer base was carried out by the reaction of 1,2,3,3-tetramethyl indolenium iodide with potassium deuteroxide in D_2O, as previously reported [15].

The ^{1}H NMR spectrum of DC-d_x clearly indicates a slightly broad signal (likely due to the $^3J_{HD}$ coupling) at 4.34 ppm, while the intensity of the signals at 2.50 and 2.25 ppm for Ha and Ha′ were significantly decreased due to the partial deuteration.

3.2. Determination of deuterium content in deuterated DC-d$_x$

On the basis of integration of the ^{1}H NMR spectrum, the deuterium content of deuterium (*x*-value) can be determined. For the evaluation of the extent (*x*-value) of the deuterated DC (DC-d_x) formed, ratios of (Ha + Ha′)/Hc were obtained from ^{1}H NMR data of the deuterated DC. With the knowledge of the structure of the dicondensed product and ^{1}H and ^{13}C NMR spectroscopic data previously reported [16], the experimental *x*-values were able to be obtained and compared with calculated values. Since 35% of the 2′-methylene of FB molecule was deuterated, the residual Hc is 65% in ^{1}H NMR data. Thus the ratio (Ha + Ha′)/Hc for the Path I and Path II could be calculated. The *x*-values were 1.82 and 1.90 for DC-1 and DC-2, respectively, as shown in Table 1. These values are closer to 2.00 (from the mechanism via DC-d_3) not to 2.50 (from the mechanism via DC-d_2), which imply that the mechanism undergoes via a carbinol intermediate (Path II).

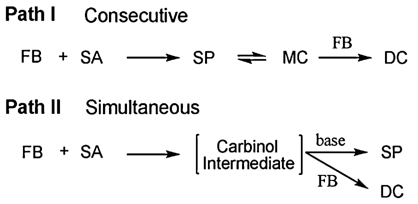

Fig. 3. Two plausible pathways for the reaction of excess FB with salicylaldehyde: Michael-type addition (Path I) of the second FB molecule to an α,β-unsaturated iminium intermediate versus nucleophilic substitution (Path II) by the second FB molecule to a carbinol intermediate.

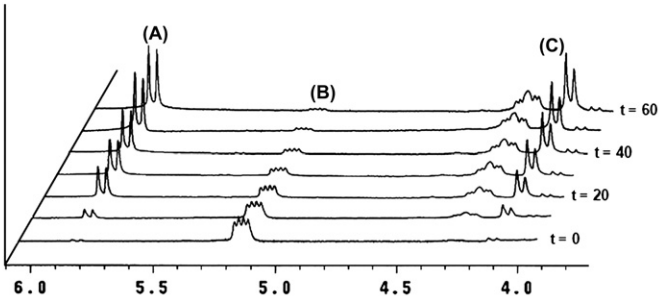

Fig. 4. Simultaneous increase or decrease of ^{1}H NMR peaks corresponding to SP (A), carbinol intermediate (B) and DC (C) species versus time, during the reaction.

Dicondensed products can be formed from the reaction of Fischer base and salicylaldehydes by either of two reasonable variations of a mechanistic pathway, consecutive or simultaneously, as in Fig. 3. The salicylaldehydes may condense with the first molecule of the Fischer base to form an intermediate carbinol, which can then react with a second Fischer base molecule to form a DC molecule (Path II) or a second Fischer base molecule may undergo a Michael addition to an α,β-unsaturated iminium group of the open MC form of the spiropyran, formed from the reaction of the first Fischer base molecule with salicylaldehydes (Path I).

The most plausible mechanism for its formation may be the Path II, which involves dehydration of a carbinol intermediate, via a cyclic transition state with the aid of intramolecular H-bonding, as suggested earlier by Keum et al. [11,17]. Path I which involves capture of the open merocyanine intermediate prior to ring closure to the spiropyran would not lead to the stereoselective formation of DC molecules. Therefore, Path I as a mechanistic pathway has been ruled out.

The time-dependant ^{1}H NMR spectroscopic behavior of the reaction mixture of excess FB and salicylaldehydes *in situ* showed the formation of a carbinol intermediate (5.12 ppm), when salicylaldehydes were added to an ethanolic solution of excess Fischer base, which was followed by the formation of both SP and DC molecules. ^{1}H NMR peaks corresponding to SP (A), a carbinol intermediate (B) and DC (C) species were simultaneously increased or decreased depending on time. This simultaneous formation/deformation behavior is shown in Fig. 4.

This is a further strong evidence for pathway II being the correct mechanism. The ^{1}H NMR spectral behavior clearly indicates that a carbinol intermediate (B) was initially first, followed by the simultaneous, not consecutive, transformation of B to both SP (A) and DC (C). This clearly shows that the reaction proceeds simultaneously via a carbinol intermediate, rather than consecutively via a Michael addition to MC form of spiropyrans, as shown in Fig. 5.

In our separate experiment [18], authentic compounds such as **1** and **2** turned out to be inert with an excess molear of FB. Compound **1** is structurally similar to the MC form of spiropyrans, with the exception of the position of O^-. To decrease the stability of the zwitter ionic MC form, compound **2** was obtained by tosylation of **1**. The authentic compound **1** was also inert with excess FB molecules, as shown in Fig. 6.

In conclusion, the most plausible mechanism for the DC formation from excess FB with salicylaldehydes is via Path II (in Figs. 3 and 5), which involves the dehydration of a carbinol intermediate to simultaneously form SP and DC molecules. SP can

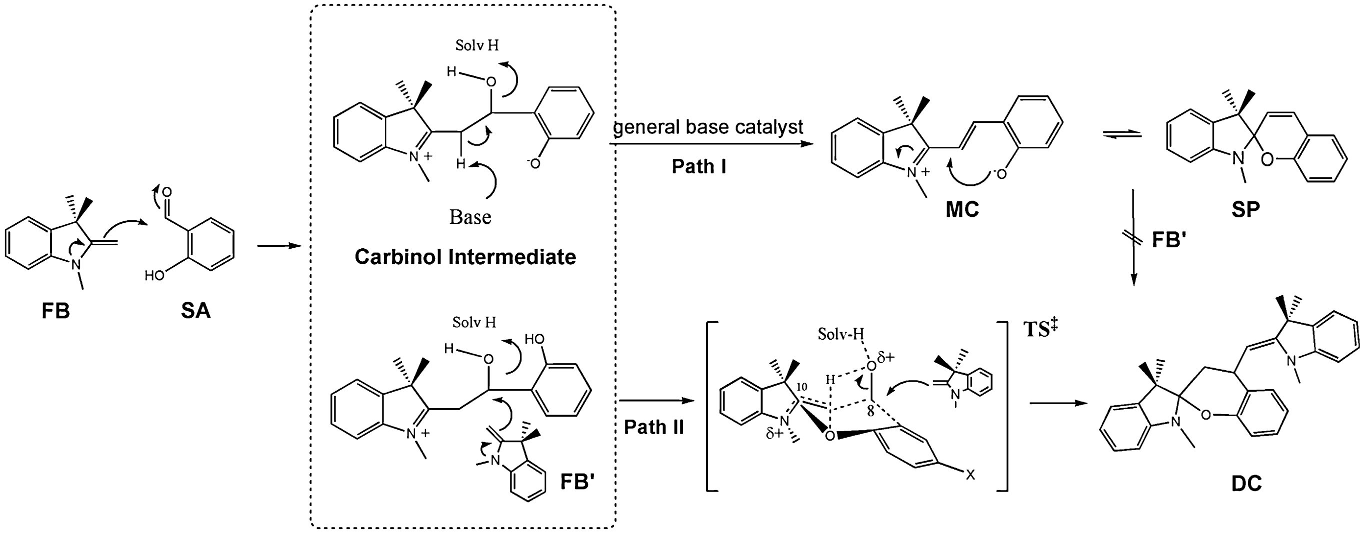

Fig. 5. Mechanistic pathways for the simultaneous formation of SP and DC molecules from reaction of excess Fischer base and salicylaldehydes.

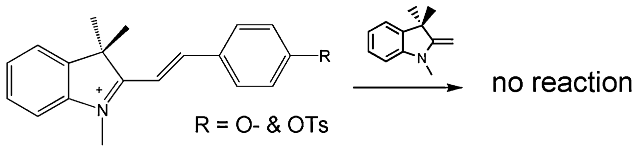

Fig. 6. Authentic compounds turned out to be inert with an excess of FB.

be formed from a carbinol intermediate by a general base catalyzed dehydration and DC via nucleophilic attack.

Acknowledgement

We are grateful to the Brain Korea 21 project in 2006 and partly to the Korea University Grant 2007.

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