Available online at www.sciencedirect.com
ScienceDirect
Dyes and Pigments 78 (2008) 111–116
DYES and PIGMENTS
www.elsevier.com/locate/dyepig

Preparation of 6-benzyloxo-spirobenzopyran-indoline compounds and the evaluation of their optical activities

Luis E. Elizalde*, Gladys de los Santos

Centro de Investigación en Química Aplicada, Blvd. Enrique Reyna no. 140, Saltillo, Coahuila, Mexico

Received 8 June 2007; received in revised form 10 October 2007; accepted 28 October 2007
Available online 6 November 2007

Abstract

Substituted derivatives of spiropyran compounds bearing a benzyloxo fraction at the 6-position were prepared by direct Friedel–Crafts acylation. The novel compounds exhibited maximum absorption at 580 nm. According to the activation energy and kinetic rate constants, the Cl and Br derivatives were more stable in the open form than their analogues which did not contain the benzyloxo fraction.

Keywords: Spiropyrans; Photochromism; Benzophenone; Friedel–Crafts acylation

1. Introduction

The preparation of functional optical materials with photoactive properties has become one of the most promising topics in materials science. These materials are used in the fabrication of several optoelectronic devices such as optical memories, switches, and holograms. These integrated systems are basically formed by two components: the support media and the photoactive material, most of them are polymers doped with photoactive molecules [1].

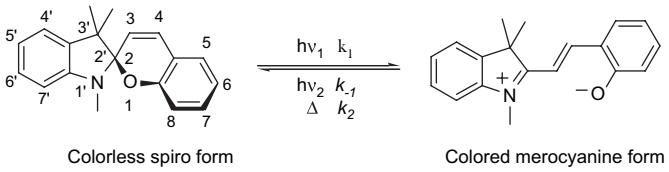
Since the last decade, the development of such optoelectronic devices has included the photochromic compounds as the active ingredient [2]. It is well known that the photochromic compounds support their activities in a reversible photochemical reaction induced by electromagnetic radiation, mainly in the ultraviolet region to provoke a visible color change of the original colorless molecule. An important characteristic of this optical change is the clear difference in the absorption spectra shown by these two species. Additionally, the most important feature of photochromic compounds is the magnitude of the photochemical reversible equilibrium (k_1/k_{-1} ratio in Scheme 1) between the color–colorless species and the thermal ring closure reaction (k_2 on the same scheme).

There exist several families of compounds that exhibit photochromism, such as spiropyrans, spirooxazines, fulgides, diarylethenes, viologens, and azo compounds. Among them, those which contain a spiro carbon, such as benzopyrans and oxazines, are especially appealing since they have found applications in electronic storage media as well as in optoelectronic devices [3–6]. The spiro group consists of two orthogonal systems linked by a tetrahedral spiro carbon. Under ultraviolet irradiation it triggers a ring opening reaction by a $4n + 2$ photochemical route. The open form of the molecule, also called photomerocyanine, which have ionic or quinonic resonant forms, the contribution of one can predominate over the other depending on the temperature or the solvent used [7]. In several applications, like for the fabrication of optical devices, the merocyanine is required to be reasonably stable in the absence of radiation in order to be reversible only by the effect of visible light [8]. Nevertheless, this kind of compounds has shown poor stability in the colored form. This is due to the ring closure reaction (k_2) which is able to follow a thermal pathway with relatively low activation energy. This process can be present even at room temperature (thermal fade reaction).

The stability of the colored form of merocyanine can be significantly improved by the substitution of several groups

* Corresponding author. Tel.: +52 844 4389830; fax: +52 844 4389463.
E-mail address: elizalde@ciqa.mx (L.E. Elizalde).

0143-7208/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.dyepig.2007.10.011



Scheme 1. Isomerization reaction of spirobenzopyran-indolines.

on its benzopyran ring. This substitution modifies the electronic configuration into the zwitterionic–quinonic form, thus improving its stability and also resulting in a better control over the coloration–colorless cycles [5]. Another method to improve thermal stability of the merocyanine is by the formation of complex with metals [9–11].

Recently, we reported the synthesis and properties of novel spiropyrans, derivatives of 1′,3′,3′-trimethylspiro[2*H*-1]-benzopyran-6-benzyloxo-2,2′-indoline which can eventuate to a photomerocyanine with a maximium absorption beyond 560 nm [12]. In these novel molecules, the benzyloxo fraction at position 6 can improve the thermal stability of the merocyanine to enhance the potential application in optical devices. In this report, a new synthesis method for the preparation of novel spiropyrans is proposed and new evidence is offered, supported by photokinetic data, to substantiate the stability of the merocyanine.

2. Experimental section

All inorganic reagents and solvents were of analytical grade and used as purchased (Aldrich, Merck). Sulfuryl chloride, 2-methylene-1,3,3-trimethylindoline (97%), 2-hydroxybenzaldehyde (98%), benzoyl chloride and aluminum chloride were purchased from Aldrich. The reference photochromic compounds **5a–d** were synthesized and purified according to previously reported methods [8,9]. ^{1}H and ^{13}C NMR spectra at room temperature were collected in a 300-MHz Jeol-JNM-ECP300 spectrometer, employing $CDCl_3$ as solvent and tetramethylsilane as standard reference. Routine infrared spectra were obtained in a Magna Nicolet 550 infrared spectrometer. Elemental analyses were determined in a Perkin Elmer 2400 series analyzer and UV–vis spectra in a HP 8452 spectrometer. The chromatograms were run in a GC–MS Hewlett Packard HP-5971.

2.1. Synthesis of 2-formylphenyl benzoate

A mixture of 1.23 mL (8.84 mmol) of 2-hydroxybenzaldehyde, 20 mL of dichloromethane, 1.09 mL (0.014 mol) of pyridine was placed in a three-necked round-bottomed flask and kept under inert atmosphere. Benzoyl chloride, 1.5 mL (8.84 mmol), was added dropwise over a 45-min period at room temperature, and then the reaction mixture was heated to 60 °C and kept at this temperature for at least 4 h. After this time, it was acidified by the addition of 30 mL of a hydrochloric acid aqueous solution (10% w/w) and extracted twice with 50 mL of chloroform. The organic layer was dried by the addition of anhydrous magnesium sulfate. After the evaporation of the solvent, 1.86 g (93% yield) of the dark yellow powder was recovered. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 10.2 (s, 1H), 8.3 (m, 3H,), 6.9 (m, 5H). ^{13}C (50 MHz, $CDCl_3$) δ: 191.45, 165.23, 154.22, 135.34, 134.78, 133.25, 130.16, 128.15, 127.89, 124.87. FT-IR (KBr) ν_{max} (cm^{-1}): 1742, 1701, 1178. EI-MS *m/z*: (intensity, %), 105 (100), 226 (40).

2.2. Synthesis of 3-formyl-4-hydroxybenzophenone by Fries rearrangement (**2a**)

Dry nitrobenzene (20 mL) and 0.442 g (3.316 mmol) of anhydrous aluminum chloride were placed in a three-necked round-bottomed flask. The solution was heated to 50 °C, and 0.5 g (2.21 mmol) of 2-formylphenyl benzoate was carefully added. After the addition, the temperature was increased to 85 °C and maintained constant for 10 h. Then the reaction mixture was added carefully, to a 100 mL HCl aqueous solution (10% w/w) under vigorous stirring and extracted with 100 mL of ethyl ether. The organic layer was washed with 100 mL of a potassium hydroxide aqueous solution (5% w/w). The aqueous layer was acidified with hydrochloric acid (35% w/w) until the solution reached a pH of 1, and again extracted with ethyl ether. The organic layer was dried with anhydrous magnesium sulfate. After the solvent had evaporated, 0.42 g (84%) of the white powder was recovered. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.08 (d, 1H, $J = 9$ Hz), 7.53 (m, 2H), 7.61 (tt, 1H, $J = 6$ Hz, $J = 1.38$ Hz), 7.76 (m, 2H), 8.06 (dd, 1H, $J = 2$ Hz, $J = 9$ Hz), 8.13 (d, 1H, $J = 2$ Hz), 9.95 (s, 1H), 11.48 (s, 1H). ^{13}C (50 MHz, $CDCl_3$) δ: 196, 165, 161, 138, 136, 133, 132.65, 132, 129.78, 129.6, 128.5, 128.2, 117.97, 115. FT-IR (KBr) ν_{max} (cm^{-1}): 1642, 1600; EI-MS *m/z*, (intensity, %), 226. Anal. calcd. for $C_{14}H_{10}O_3$: C, 74.03%; H, 4.45%. Found: C, 74.09%; H, 4.55%.

2.3. Synthesis of 3-formyl-4-hydroxybenzophenone by Friedel and Crafts acylation

Benzoyl chloride, 0.83 mL (1 g, 5.92 mmol), was placed in a three-necked round-bottomed flask under inert atmosphere at room temperature. Nitrobenzene (15 ml) and 1.89 g (14.2 mmol) of aluminum chloride was then added. After the addition, 0.75 mL (5.92 mmol) of 2-hydroxbenzaldehyde was added dropwise over a 45-min period and the temperature was increased to 80 °C for at least 5 h. Thereafter, the reaction mixture was acidified by the addition of 50 mL of an aqueous solution of HCl (10%) and extracted twice with 50 mL of ethyl ether. The organic layer was extracted with 100 mL of KOH aqueous solution (7.5% w/w). The aqueous layer was acidified with concentrated HCl to a pH of 1 and extracted twice with 50 mL of ethyl ether. The extract was dried over $MgSO_4$. After the solvent evaporation, 1.24 g of a white powder was recovered (93% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.08 (d, 1H, $J = 9$ Hz), 7.53 (m, 2H), 7.61 (tt, 1H, $J = 6$ Hz, $J = 1.38$ Hz), 7.76 (m, 2H), 8.06 (dd, 1H, $J = 2$ Hz, $J = 9$ Hz), 8.13 (d, 1H, $J = 2$ Hz), 9.95 (s, 1H), 11.48 (s, 1H). ^{13}C (50 MHz, $CDCl_3$) δ: 196,

165, 161, 138, 136, 133, 132.65, 132, 129.78, 129.6, 128.5, 128.2, 117.97, 115. FT-IR (KBr) ν_{max} (cm^{-1}): 1642, 1600; EI-MS *m/z*: (intensity, %), 226. Anal. calcd. for $C_{14}H_{10}O_3$: C, 74.03%; H, 4.45%. Found: C, 74.09%; H, 4.55%.

2.4. Synthesis of 2-chloro-3-formyl-4-hydroxybenzophenone (**2b**)

3-Formyl-4-hydroxybenzophenone (**2a**), 1.51 g (6.7 mmol), dissolved in 20 mL of dry CH_2Cl_2 was placed in a reactor. Then 0.65 mL (8 mmol) of sulfuryl chloride was carefully added under vigorous stirring. The reaction mixture was kept at 25 °C for 24 h. Then it was washed with 20 mL of distilled water and 10% $NaHCO_3$ aqueous solution. The organic layer was finally dried over $MgSO_4$. The product was recovered by precipitation in ether. Yield 30%, mp 156 °C, ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.53 (m, 2H), 7.61 (tt, 1H, $J = 6$ Hz, $J = 1.38$ Hz), 7.76 (m, 2H), 8.06 (d, 1H, $J = 2$ Hz,), 8.13 (d, 1H, $J = 2$ Hz), 9.95 (s, 1H), 11.92 (s, 1H). ^{13}C (50 MHz, $CDCl_3$) δ: 198.17, 198.5, 161.51, 141.83, 138.56, 137.65, 136.42, 130.32, 129.12, 127.63, 120.1, 112.96. FT-IR (KBr) ν_{max} (cm^{-1}): 1631, 1605; EI-MS *m/z*, (intensity, %), 260 (100), 262 (30). Anal. calcd. for $C_{14}H_9ClO_3$: C, 64.5%; H, 3.5%, Cl, 13.6%. Found: C, 64.75%; H, 3.43%, Cl, 13.57%.

2.5. Synthesis of 2-bromo-3-formyl-4-hydroxybenzophenone (**2c**)

Dry CH_2Cl_2 (15 mL) and 1.51 g (6.74 mmol) of 3-formyl-4-hydroxybenzophenone (**2a**) were placed in a three-necked round-bottomed flask under inert atmosphere. The flask was cooled in an acetone–CO_2 bath to −78 °C. Then 8.11 mmol of bromine was added through a dropping funnel. As soon as the addition was completed, a few crystals of anhydrous $FeCl_3$ were added. After 30 min, the temperature was allowed to reach room temperature, and the mixture was stirred for 6 h. The reaction mixture was then washed with distilled water. The organic phase was extracted with 10% NaOH aqueous solution to remove the product as sodium salt. The aqueous phase was acidified and extracted with chloroform, and then dried over anhydrous $MgSO_4$. After evaporation of the solvent, the final product was crystallized in ethyl ether yielding 0.78 g (38%) of a white solid with a melting point of 166 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.53 (m, 2H), 7.61 (tt, 1H, $J = 6$ Hz, $J = 1.38$ Hz), 7.76 (m, 2H), 8.06 (d, 1H, $J = 2$ Hz), 8.32 (d, 1H, $J = 2$ Hz), 9.95 (s, 1H), 12.08 (s, 1H). ^{13}C (50 MHz, $CDCl_3$) δ: 196.07, 193.15, 151.51, 141.33, 135.32, 135.55, 132.07, 130.70, 128.84, 128.5, 120.49, 111.32. FT-IR (KBr) ν_{max} (cm^{-1}): 1655, 1618. EI-MS *m/z*, (intensity, %), 304 (50), 306 (50). Anal. calcd. for $C_{14}H_9BrO_3$: C, 55.1%; H, 3.0%; Br, 26.2%. Found: C, 54.37%; H, 2.98%; Br, 26.37%.

2.6. Synthesis of 2-nitro-3-formyl-4-hydroxybenzophenone (**2d**)

A mixture of 0.3 g of ammonium nitrate (3.7 mmol), 0.42 g of 3-formyl-4-hydroxybenzophenone (1.85 mmol), and 25 mL of dry chloroform was placed in a 100 mL three-necked, round-bottomed flask under inert atmosphere. After complete dissolution of the reactants, 3.25 g (15.5 mmol) of trifluoroacetic anhydride was added. The mixture was refluxed in chloroform for 2 h. Then it was washed with distilled water. The organic phase was separated and dried over anhydrous magnesium sulfate, followed by purification by column chromatography (hexane–ethyl acetate 7:3), and 0.29 g of a yellow powder were recovered (57% yield). Mp 96 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.53 (m, 2H), 7.61 (tt, 1H, $J = 6$ Hz, $J = 1.38$ Hz), 7.76 (m, 2H), 8.55 (d, 1H, $J = 2$ Hz), 8.83 (d, 1H, $J = 2$ Hz), 9.95 (s, 1H), 12.08 (s, 1H). ^{13}C (50 MHz, $CDCl_3$) δ: 189.67, 188.15, 158.51, 138.47, 136.32, 133.64, 133.07, 130.70, 129.92, 129.15, 125.49, 116.32. FT-IR (KBr) ν_{max} (cm^{-1}): 1650, 1595, 1534; EI-MS *m/z*; (intensity, %), 271. Anal. calcd. for $C_{14}H_9NO_5$: C, 62.0%; H, 3.3%; N, 5.2%. Found: C, 61.01%; H, 3.29%; N, 5.48%.

2.7. General procedure for the preparation of derivatives of 1′,3′,3′-trimethylspiro-[2H-1-benzopyrane-8-benzyloxo-2,2′-indoline] (Benzyloxo-BIPS)

A mixture of 3 g of 3-formyl-4-hydroxybenzophenone (**2a**), 2.475 mL of 2-methylene-1,3,3-trimethylindoline, and 50 mL of distilled ethanol was boiled for 4 h. The reaction mixture was filtered and washed with cold ethanol. The precipitate was recovered, washed with cold ethanol, and then recrystallized in ethanol.

2.7.1. Characterization of 1′,3′,3′-trimethylspiro-[2H-1-benzopyran-6-benzyloxo-2,2′-indoline] (**1a**)

^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.23 (d, 1H, $J = 2$ Hz), 8.059 (dd, 1H, $J = 9$ Hz, $J = 2$ Hz), 7.66 (tt, 1H, $J = 6$ Hz, $J = 1.38$ Hz), 7.55 (m, 2H), 7.78 (m, 2H), 7.28 (m, 2H), 7.15 (d, 1H, $J = 8$ Hz), 7.01 (d, 1H, $J = 9$ Hz), 6.82 (d, 1H, $J = 12$ Hz), 6.38 (d, 1H, $J = 8$ Hz), 5.75 (d, 1H, $J = 12$ Hz), 3.05(s, 3H), 1.25 (s, 3H), 1.15 (s, 3H). ^{13}C (50 MHz, $CDCl_3$) δ: 190.54, 156.15, 149.8, 143.47, 138.52, 136.64, 134.07, 131.70, 130.92, 129.15, 129.04, 122.49, 122.13, 119.32, 118.95, 109.53, 108.32, 97.51, 52.8, 30.41, 18.63. EI-MS D.I.P. *m/z*, (intensity, %) 159 (100), 381 (1). FT-IR (KBr film) ν_{max} cm^{-1}: 1648, 1285, 885, 732. Anal. calcd. for $C_{26}H_{23}NO_2$: C, 81.9%; H, 6.1%; N, 3.7%. Found: C, 82.10%; H, 6.23%; N, 3.25%.

2.7.2. Characterization of 6-benzyloxo-8-chloro-1′,3′,3′-trimethylspiro-[2H-1-benzopyran-2,2′-indoline] (**1b**)

^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.18 (d, 1H, $J = 2$ Hz), 8.05 (d, 1H, $J = 2$ Hz), 7.66 (tt, 1H, $J = 6$ Hz, $J = 1.38$ Hz), 7.55 (m, 2H), 7.78(m, 2H), 7.28 (m, 2H), 7.15 (d, 1H, $J = 8$ Hz), 6.82 (d, 1H, $J = 12$ Hz), 6.38 (d, 1H, $J = 8$ Hz), 5.75 (d, 1H, $J = 12$ Hz) 3.05 (s, 3H), 1.25 (s, 3H), 1.15 (s, 3H). ^{13}C (50 MHz, CDC_{l3}) δ: 191.50, 156.15, 149.8, 146.47, 139.32, 136.64, 134.07, 131.70, 130.92, 129.15, 129.04, 122.49, 122.13, 119.32, 115.92, 111.23, 108.32, 97.35, 51.45, 30.41, 18.63. EI-MS D.I.P *m/z*, (intensity, %), 159 (100), 415 (5), 417 (2). FT-IR (KBr film) ν_{max}: 1649, 1286, 892, 733 cm^{-1}.

Anal. calcd. for $C_{26}H_{22}ClNO_2$: C, 75.1%; H, 5.3%; Cl, 8.5%; N, 3.4%. Found: C, 75.31%; H, 5.45%; N, 3.27%; Cl, 8.35%.

*2.7.3. Characterization of 6-benzyloxo-8-bromo-1′,3′, 3′-trimethylspiro-[2H-1-benzopyran-2,2′-indoline] (**1c**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.33 (d, 1H, $J = 2$ Hz), 8.19 (d, 1H, $J = 2$ Hz), 7.66 (tt, 1H, $J = 6$ Hz, $J = 1.38$ Hz), 7.55 (m, 2H), 7.78(m, 2H), 7.28 (m, 2H), 7.15 (d, 1H, $J = 8$ Hz), 6.82(d, 1H, $J = 12$ Hz), 6.38 (d, 1H, $J = 8$ Hz), 5.75 (d, 1H, $J = 12$ Hz), 3.05 (s, 3H), 1.25 (s, 3H), 1.15 (s, 3H). ^{13}C (50 MHz, $CDCl_3$) δ: 193.54, 156.15, 149.8, 146.47, 139.32, 136.64, 134.07, 131.70, 130.92, 129.15, 129.04, 122.49, 122.13, 119.32, 118.95, 111.23, 108.32, 97.31, 51.83, 30.41, 18.63. EI-MS D.I.P. *m/z*, 159 (100), 459 (2), 461 (2). FT-IR (KBr Film) ν_{max} cm^{-1}: 1648, 1285, 885, 732. Anal. calcd. for $C_{26}H_{22}BrNO_2$: C, 67.8%; H, 4.8%; Br, 17.4%; N, 3.0%. Found: C, 68.23%; H, 4.91%; N, 2.85%; Br, 17.36%.

*2.7.4. Characterization of 6-benzyloxo-8-nitro-1′, 3′,3′-trimethylspiro-[2H-1-benzopyran-2,2′-indoline] (**2d**)*

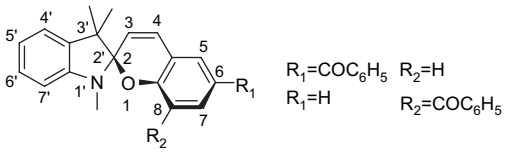
^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.85 (d, 1H, $J = 2$ Hz), 8.55 (d, 1H, $J = 2$ Hz), 7.66 (tt, 1H, $J = 6$ Hz, $J = 1.38$ Hz), 7.55 (m, 2H), 7.78 (m, 2H), 7.28 (m, 2H), 7.15 (d, 1H, $J = 8$ Hz), 6.82 (d, 1H, $J = 12$ Hz), 6.38 (d, 1H, $J = 8$ Hz), 5.75 (d, 1H, $J = 12$ Hz), 3.05 (s, 3H), 1.25 (s, 3H), 1.15 (s, 3H). ^{13}C (50 MHz, $CDCl_3$) δ: 190.54, 156.15, 149.8, 146.47, 139.32, 136.64, 134.07, 131.70, 130.92, 129.15, 129.04, 122.49, 122.13, 119.32, 118.95, 116.23, 108.32, 97.81, 51.35, 30.41, 18.63. EI-MS D.I.P. *m/z* 159 (100), 426 (2). FT-IR (KBr Film) ν_{max} cm^{-1}: 1650, 1595, 1279, 710. Anal calcd. for $C_{26}H_{22}N_2O_2$: C, 73.2%; H, 5.2%; N, 6.6%. Found: C, 73.7%; H, 5.45%; N, 6.32%.

3. Results and discussion

Our research group has previously reported the preparation of a new kind of pigments which are substituted derivatives of the 6-benzyloxo-1′,3′,3′-trimethylspiro-[2*H*-1-benzopyran-2,2′-indoline] [13]. The introduction of the benzyloxo group in the spirobenzopyran molecule in this kind of molecules, results in three changes: (1) photochromic activity is modified, (2) the maximum absorption wavelength in the UV spectra is shifted and (3) a higher color density (higher molar extinction coefficient) is observed. All of these have better photochromic properties than those obtained with common 1′,3′,3′-trimethylspiro[2*H*-1-benzopyran-2,2′-indoline] molecules (BIPS derivatives).

To announce more breakthroughs to our previous results, we are currently in a position to report some new synthesis methods to prepare 1′,3′,3′-trimethylspiro[2*H*-1-benzopyran-2,2′-indoline] molecules and also to report on the evaluation of the effect of the substitution over the benzyloxo moiety through the evaluation of the photokinetic data.

In order to evaluate the photochromic properties of the 8-benzyloxo-1′,3′,3′-trimethylspiro[2*H*-1-benzopyran-2,2′-indoline] and to establish the effect on the substitution compared with the 6-benzyloxo derivative (Scheme 2), we now propose



Scheme 2. 6 or 8-Benzyloxo-spirobenzopyran-indoline.

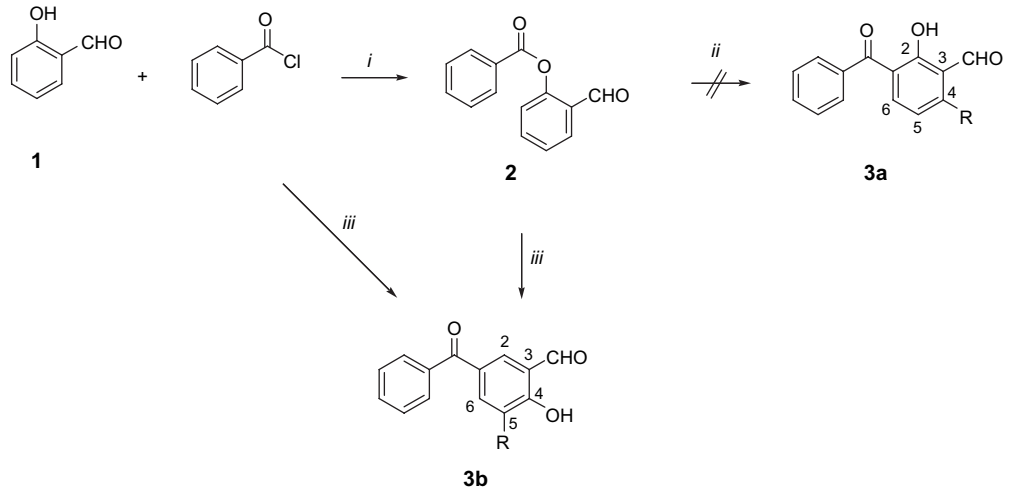
an alternative synthesis route to produce substituted benzyloxo-1′,3′,3′-trimethyl spiro[2*H*-1-benzopyran-2,2′-indoline molecules that would involve the interaction between 2-methylene-1,3,3-trimethylindoline and the corresponding substituted formyl-hydroxy-benzophenone.

The preparation of such derivates was performed by two synthesis methods (Scheme 3): (a) the Fries rearrangement strategy which offers the possibility, in accordance with the literature, to choose between *ortho* or *para* isomers, depending on the experimental conditions employed [14,15] and (b) the Friedel–Crafts approach, which can result in the preparation of a mixture of isomers. According to Scheme 3, **2** was obtained after the esterification of 2-hydroxybenzaldehyde with benzoyl chloride. The yield was quantified and FT-IR, GC–MS and ^{1}H NMR properly characterized the presence of the desired compound.

In order to obtain **3a**, the *ortho* isomer, via the Fries rearrangement, of 2-formylphenyl benzoate was reacted with aluminum chloride as Lewis acid using a temperature higher than 120 °C and chlorobenzene or nitrobenzene as solvent. After several attempts even at 150 °C and employing several Lewis acids (like tin tetrachloride, titanium tetrachloride or zinc chloride) 2-hydroxybenzaldehyde and benzoic acid were recovered as the main products. Using the same experimental conditions, but changing the temperature to 80 °C the 3-formyl-4-hydroxy-benzophenone **3b** (*para* isomer) was recovered in quantitative yield. This product was purified by liquid chromatography and characterized by GC–MS (molecular weight of 226), FT-IR and ^{1}H NMR was used to confirm the substitution from the characteristic signal of the hydrogen located at position 6 (**3b**, Scheme 3). This position had a chemical shift of 8.06 ppm and appeared as a doublet of doublets with a coupling constant of 9 Hz (coupled with hydrogen at position 5), and another coupling constant of 2 Hz (coupled with the hydrogen at position 2 of the aromatic ring).

The second method of direct Friedel–Crafts benzoylation [16] was used as an alternative for the preparation of the 2-formyl-4-hydroxy-benzophenone and was carried out using the same experimental conditions, i.e. nitrobenzene as solvent, molar ratio 2-hydroxybenzaldehyde:aluminum chloride of 1:1.5, at 80 °C. After 5 h of reaction, surprisingly only the *para* isomer was recovered. After that result, the next step was to block position 4 with chloro, bromo or nitro substituted 2-hydroxybenzaldehyde, in order to orientate the reaction to the formation of the *ortho* isomers. However, this methodology did not work well as the results showed a system with a poor reactivity.

In spite of the disappointing results, the direct Friedel–Crafts benzoylation methodology does offer a very good alternative for

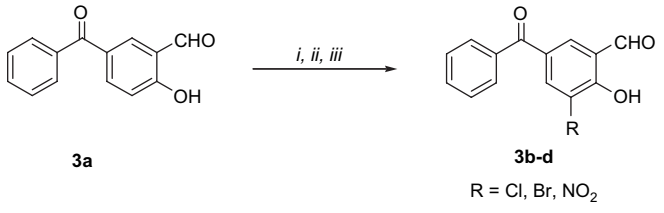


Scheme 3. Preparation of substituted hydroxy-formyl-benzophenones by Fries rearrangement and Friedel–Crafts benzoylation. (i) Py, DMAP cat, acetone, 40 °C, 24 h, 98%; (ii) Chlorobenzene, $AlCl_3$, 150 °C, 72 h; (iii) Nitrobenzene, $AlCl_3$, 70 °C, 10 h, 90%.

the preparation of the 3-formyl-4-hydroxybenzophenones and similar derivatives (Scheme 4). The main advantage of this methodology lies in the sufficient quantitative yield exclusively for the *para* isomer which could be easily isolated. The Fries rearrangement methodology gives the same isomer as the main product, but it requires an additional synthesis step which consumes time and reagents.

According to our previous work, these molecules (**3b–d** in Scheme 4) were further used to complete the synthesis of the photochromic compound by their reactions with 2-methylene-1,3,3-trimethylindoline by the synthesis route shown in Scheme 5. All four molecules **4a–d**) of 6-benzyloxo-1′,3′,3′-trimethylspiro-[2*H*-1-benzopyran-2,2′-indoline] were fully characterized by spectroscopic techniques as described in Section 2.

In order to evaluate the thermodynamic stability of these pigments under ultraviolet irradiation, the kinetic data on the ring closure reaction (k_2 on Scheme 1) were evaluated at several temperatures from 288 to 303 K, measuring the absorbance at 568 nm using an ultraviolet spectrophotometer equipped with photodiode array detector. A special program was used to recover one data point each 100 μs. The first step was the irradiation of the 10^{-4} M solutions with an ultraviolet lamp with an intensity of 1.5 μJ/cm^2. Samples were irradiated for 2 min, to be sure that all the molecules had reached the colored excited state. The experiments were performed in complete absence of visible light in order to ascertain that the only pathway for the ring closure reaction was through the unimolecular process by a pure thermal mechanism. With this consideration, the first order kinetic model can be used for the determination of the kinetic rate constant by the graph of $\ln(C/C_o)$ versus time. In order to evaluate the photochromic behavior of the 6-benzyloxo-1′,3′,3′-trimethylspiro-[2*H*-1-benzopyran-2,2′-indoline] derivatives, some compounds which did not contain the benzyloxo moiety were employed as references. These compounds were synthesized by a previously reported method [7].

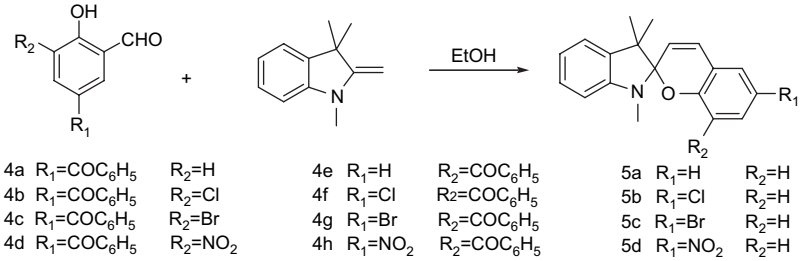


Scheme 4. Preparation of Cl, Br or NO_2 substituted formyl-hydroxy-benzophenones. (i) **3b**: $SOCl_2$, CH_2Cl_2, 24 h, 25 °C, 30%; (ii) **3c**: CH_2Cl_2, Br_2, $FeCl_3$ cat, 6H, −78 °C, 38%; (iii) **3d**: NH_4NO_3, trifluoroacetic anhydride, $CHCl_3$, 60 °C, 2 h, 57%.

The activation energy (E_a) can be calculated following the Arrhenius theory, considering the experimentally obtained kinetic rate constants and the absolute temperature. The results are shown in Table 1. By analyzing the kinetic rate constant and activation energy values, it is possible to note significant differences on the stability of the open form between those compounds bearing the benzyloxo fraction (**4b–d**) and those without such fraction (**5b–d**). When the chloro and bromo substituted derivatives (**5b** and **c**) are compared with **4b** and **c**, it was found that the presence of the benzyloxo group lowers the rate of the ring closure reaction by a factor of 10^{-1} and increases 1.6 times the energy required for this reaction. Such behavior makes the molecules **4b** and **c** more stable in the open form than **5b** and **c**. A special situation occurs when the nitro derivatives are analyzed. Both **4d** and **5d** show the lowest rate on the ring closure reaction while the activation energy presents the same behavior previously described for **4b** and **c**. This means that **4d** requires 1.6 times more energy than the required energy for the reference compound **5d**.

4. Conclusions

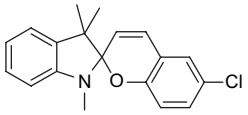
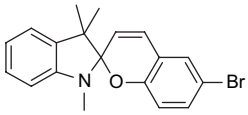
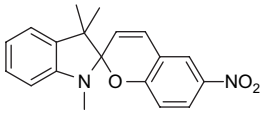
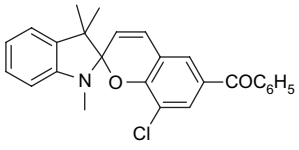
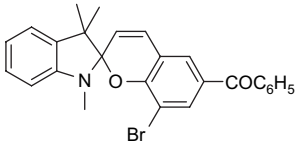
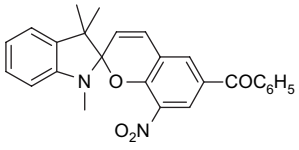
A new synthesis approach for the preparation of the substituted derivatives of 3-formyl-4-hydroxybenzophenone



Scheme 5. Preparation of substituted benzyloxo-spirobenzopyran-indolines.

based on the direct Friedel–Crafts benzoylation was described. By comparing the results with those following the Fries strategy, Friedel–Crafts offered a better alternative for the preparation of similar molecules. By using the latter technique, several 6-benzyloxo-spirobenzopyran-indoline derivatives were prepared and most of them had shown good color stability based on the experimentally obtained data from evaluation with UV spectroscopy. The results offered clear evidence about the importance of the substitution at position 6 of the benzyloxo group which can significantly improve the photochromic properties of this kind of pigments.

Table 1
Kinetic data determined for the ring closure reaction of benzyloxo-spirobenzopyran-indolines at different temperatures

Molecule	T (K)	$k_{-1} \times 10^{-4}$ (s^{-1})	Energy of activation (kcal/mol)
 **5b**	283	174.40	10.326
	288	216.27	
	293	326.80	
 **5c**	283	181.20	9.329
	288	225.80	
	293	348.60	
 **5d**	283	1.29	21.072
	288	1.89	
	293	6.89	
	303	13.34	
 **4b**	283	26.82	16.326
	288	34.21	
	293	73.31	
	303	155.70	
 **4c**	283	13.44	16.874
	288	31.58	
	293	33.95	
	303	110.05	
 **4d**	283	0.81	33.959
	288	1.03	
	293	2.20	
	303	4.67	

Acknowledgements

The authors are grateful to the Mexican Council of Science and Technology (CONACYT) for financial support through the project number 53186, to Lourdes Guillen and Julieta Sanchez for their helpful collaboration during the characterization of the reported molecules and also to M.C. Sion NG from Peace Corps for his valuable collaboration.

References

[1] (a) Mizokuro T, Mochizuki H, Kobayashi A, Horiuchi S, Yamamoto N, Tanigaki N, et al. Chem Mater 2004;16:3469–75;
(b) Mizokuro T, Mochizuki H, Xiaoliang M, Horiuchi S, Tanaka N, Tanigaki N, et al. Jpn J Appl Phys 2003;42:983–5.
[2] Hirshberg Y, Fischer E. J Chem Soc 1953:629–36.
[3] Persano L, Mele E, Athanassiou A, Cingolani R, Psignano D. Chem Mater 2006;18:4171–5.
[4] Kanakkanatt SV. Proc SPIE Int Soc Opt Eng 1997;3227:218–24.
[5] Berkovic G, Krongauz V. Chem Rev 2000;100:1741–54.
[6] Uznanski P. Langmuir 2003;19:1919–22.
[7] Guglielmetti R, Durr H, Bouas-Laurent H. Spiropyranes: photochromism, molecules and systems. New York: Elsevier; 1990. p. 314–466.
[8] Yagi S, Maeda K, Nakazumi H. J Mater Chem 1999;9:2991–7.
[9] Tanaka M, Kamada K, Ando H, Kitagaki T, Shibutani Y, Yajima S, et al. Chem Commun 1999;16:1453–4.
[10] Wojtyk JT, Buncel E, Kazmaier PM. Chem Commun 1998;16:1703–4.
[11] Tanaka M, Nakamura M, Salhin MAA, Ikeda T, Kamada K, Ando H, et al. J Org Chem 2001;66:1533–7.
[12] Keum SR, Ahn SM, Lee SH. Dyes Pigments 2004;60:55–9.
[13] Elizalde LE, de los Santos G, Garcia AE, Medellín DI, Acosta R. Synth Commun 2005;35:1–11.
[14] Ralston AW, McCorkle MR, Bauer ST. J Org Chem 1940;5(6):645–59.
[15] Organic reactions, vol. 5; 1949. p. 388–412.
[16] Campbell BN, Spaeth JEC. J Am Chem Soc 1959;81(22):5933–6.