
Synthesis of 2,6-Diethyl-3-methacroyloxymethyl-1,5,7,8-tetramethylpyrromethene-BF₂ for the Preparation of New Solid-State Laser Dyes

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ABSTRACT

The synthesis of 2,6-diethyl-3-methacroyloxymethyl-1,5,7,8-tetramethylpyrromethene-BF₂ (2) was carried out in straightforward fashion from 2,6-diethyl-1,3,5,7,8-pentamethylpyrromethene-BF₂ (1) in three steps. The monomer unit 2 has been shown to be useful for copolymerization with methyl methacrylate for the synthesis of new solid-state optical materials. In addition, the synthesis of 1 has been modified to give greater yields of this useful laser dye. © 1997 John Wiley & Sons, Inc.

INTRODUCTION

Recent advances in the synthesis of novel, strongly fluorescing laser dyes have renewed interest in dye-laser technology. The pyrromethene-BF₂ complex dye molecules have been shown to possess laser performances that are superior to that of rhodamine-6G [1,2]. In 1993, 2,6-diethyl-1,3,5,7,8-pentamethylpyrromethene-BF₂ complex (1, DEPMP-BF₂) was found to exhibit twice the power efficiency of rhodamine-6G. Since their initial discovery, pyrromethene-BF₂ derivatives have been useful as fluorescent probes in

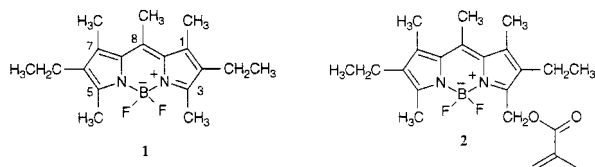
medical and biological research and as photodynamic therapeutic agents for cancer [3,4].

Although laser-dye solutions are easy to prepare, dyes dissolved in organic solvents are not attractive for use in nonlaboratory environments due to high flammability and other potential health hazards associated with the solvent. The advent of pyrromethene-BF₂ dyes together with new plastics has led to the development of solid-state laser-dye materials. The use of dye-doped solid-state laser materials offers advantages over nonlinear techniques (e.g., Raman scattering and optical parametric oscillation), such as virtually thresholdless operation, relative insensitivity to fluctuations in pump laser intensity, continuous tunability over the gain region, the lack of a need for the excitation source to be coherent, and a low chemical hazard. DEPMP-BF₂ (1) dispersed in a 16% hydroxypropyl acrylate/methyl methacrylate polymer matrix gave a material with dye-lasing absolute efficiency equivalent to 77% of 1 in solution [5]. Rhodamine-6G under similar treatment gave an unsatisfactory performance and sulfarhodamine-B gave only 37% efficiency [5]. However, very few pyrromethene-BF₂ dyes were found to be stable to the high-temperature polymerization process required to prepare the dispersed polymer matrix [6].

In a continuing search to develop new solid-state laser-dye materials based on pyrromethene-BF₂ complexes, 1,5,7,8-tetramethyl-2,6-diethyl-3-methacroyloxymethylpyrromethene-BF₂ complex (2) was envisaged as the first in a series of monomeric dyes

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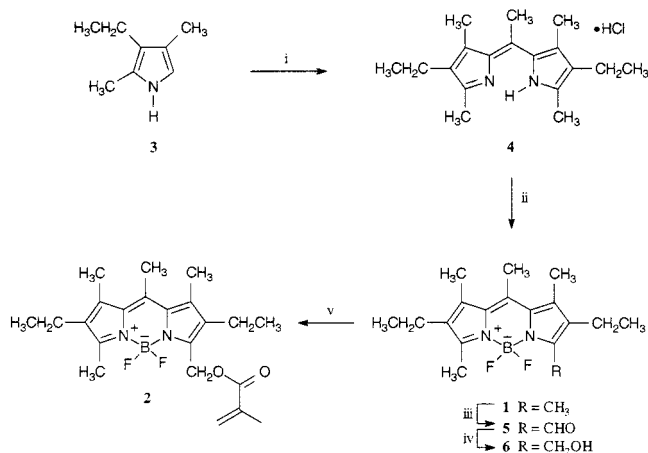
that contain polymerizable functional groups. With a polymerizable appendage, the dye **2** could be homogeneously copolymerized in a suitable matrix to form new solid-state laser-dye materials that might give better performance and longer lifetime than the dispersed counterparts.



RESULTS AND DISCUSSION

The synthesis of the monomeric pyrromethene-BF₂ unit **2** was envisaged to proceed from **1** using methodology previously developed in these laboratories [1]. The preparation of **1** was achieved in straightforward fashion using slightly modified experimental conditions. As shown in Scheme 1, the condensation of acetyl chloride with 2,4-dimethyl-3-ethylpyrrole (**3**) in freshly distilled dichloromethane gave the pyrromethene derivative **4** in 94% yield. The use of freshly distilled dichloromethane greatly improved the yield and purity of this labile intermediate. Conversion of **4** into **1** was also achieved with much greater efficiency (65% yield) when all reagents and solvents were carefully dried prior to use. This improved procedure greatly enhanced the efficiency of the synthesis and readily furnished multi-gram quantities of **1**.

With **1** in hand, oxidation of the C(3)-methyl group to the corresponding C(3)-formyl group was



SCHEME 1 Reagents: (i) CH₃COCl, CH₂Cl₂, 40°C. (ii) BF₃·Et₂O, Et₃N, toluene. (iii) DDQ, THF. (iv) H₂, 5% Pd/C EtOH. (v) methacryloyl chloride, pyridine, room temperature.

achieved with DDQ, using previously reported procedures [7]. This provided **5** in 80% yield (Scheme 1). Subsequent conversion of **5** into the alcohol **6** was achieved by hydrogenation over 5% palladium on carbon under ambient conditions. This furnished **6** in 56% yield based on recovery of **1** (21%) due to over reduction. Unfortunately, complete hydrogenation of the carbonyl to the methyl group was found to be a competing side reaction. A detailed investigation of the hydrogenation reaction revealed that any attempt to increase the selectivity of the reaction for **6** and minimize the formation of **1** failed. However, the two compounds, **1** and **6**, could be easily separated by flash chromatography on silica gel and **1** recycled back into the earlier oxidation step.

The final esterification step of **6** was found to be very sensitive to the base employed. The presence of base was required to drive the reaction to completion; however, triethylamine resulted in competitive displacement of the BF₂ moiety and destroyed the pyrromethene-BF₂ complex **6**. The hindered base, *N,N*-diisopropyl-*N*-ethylamine was found to greatly retard the rate of decomposition of the complex, but no esterification was observed. Finally, pyridine was found to be the base of choice for the acylation of **6** to give **2** in 46% yield. The controlled addition of methacryloyl chloride was also required to be carried out at room temperature in order to avoid the excessive heat generated by the reaction that was found to accelerate the decomposition of the pyrromethene-BF₂ complex **2**.

With **2** in hand, the absorbance in methanol [λ_{max} (log ϵ) 513 nm (5.74)] and fluorescence (λ_f 530.5 nm, Φ 0.59) properties were measured. It was interesting to note that comparison of the fluorescence quantum yields for the pyrromethene-BF₂ derivatives **1** (Φ 0.83) [1], **5** (Φ 0.12) [8], **7** (Φ 0.70) [8], and **2** (Φ 0.59) correlated well with the electron-withdrawing nature associated with the substituent on C(3) of the pyrromethene-BF₂ nucleus. The greater the electron-withdrawing ability of the C(3)-substituent, the lower was the fluorescence quantum yield.

Preliminary studies by Jones et al. [9] have recently demonstrated that **2** is covalently incorporated into several polymethacrylate-derived matrices. The concentration of dye **2** was determined to be on the average equal to one dye-tagged residue per 1600 polymer residues [9]. The copolymers have been found to exhibit fluorescent and absorption properties very similar to an ethanolic solution of the monomer **2**. In addition, the fluorescent quantum yield of the covalently bound chromophore was not affected by variation of the copolymer structure [9]. Further investigation of the synthesis, photophysical properties (laser), and structural properties of co-

polymers of **2** are underway and will be reported in due course.

SUMMARY

The methacrylate ester **2** was easily prepared from the readily available pyrromethene-BF₂ complex **1** in good overall yield. The monomer **2** was found to be chemically stable to the polymerization process and has furnished polymethacrylate copolymers with nearly identical photophysical properties to the solvated monomer. These results clearly demonstrate the potential of this strategy for the development of new solid-state fluorescence and laser-dye materials.

EXPERIMENTAL

Instruments for spectroscopic measurements included the following: Perkin-Elmer 1600 FTIR, Perkin-Elmer LS-5B luminescence spectrometer, and Perkin-Elmer Lambda 6 (UV/VIS) Spectrometer. Melting points were obtained by use of a Mel-Temp II apparatus and were uncorrected. Elemental analysis was obtained from Midwest Micro Lab, Indianapolis, IN. Hydrogenation reactions were carried out on a Parr 3911 Hydrogenation Apparatus. ¹H- and ¹³C-NMR spectra were recorded on a Varian 300 MHz NMR spectrometer in CDCl₃ with tetramethylsilane as an internal standard.

All chemicals unless otherwise noted were purchased from Aldrich Chemical Company. Dichloromethane and triethylamine were distilled from calcium hydride, and toluene was distilled from sodium/benzophenone. Pyridine was dried by distillation from potassium hydroxide pellets.

4,4'-Diethyl-3,5,3',5',6-pentamethylpyrromethene Hydrochloride 4

Acetyl chloride (7.44 g, 94.7 mmol) was added dropwise with stirring over a period of 15 minutes to a solution of **3** (5.00 g, 40.6 mmol) in dichloromethane (25 mL). The reaction mixture was heated (40°C, 1 hour), cooled to room temperature, diluted with petroleum ether (290 mL), and triturated for 12 hours to bring about the separation of 4,4'-diethyl-3,5,3',5',6-pentamethylpyrromethene hydrochloride **4** as a crystalline, red-brown solid (5.84 g, 93.8%), mp 186–187°C (Ref. [1] mp 185–186°C).

2,6-Diethyl-1,3,5,7,8-pentamethylpyrromethene-BF₂ Complex 1

Triethylamine (7.75 g, 76.7 mmol) was added at room temperature to a suspension of 4,4'-diethyl-

3,5,3',5',6-pentamethylpyrromethene hydrochloride **4** (5.11 g, 16.3 mmol) in toluene (500 mL). The mixture was stirred for 15 minutes and boron trifluoride etherate (13.6 mL, 111 mmol) was added dropwise with stirring as a green fluorescence developed. The reaction mixture was heated (80°C, 15 minutes), cooled to 40°C, washed with warm water (3 × 100 mL), and dried (magnesium sulfate). The solvent was removed under reduced pressure to give the complex **1** as a dark brown solid. The crude material was purified by chromatography (silica gel) to give **1** as an orange crystalline solid (3.35 g, 65%), mp 208.5–209°C (Ref. [1] mp 207–208°C).

2,6-Diethyl-3-hydroxymethyl-1,5,7,8-tetramethylpyrromethene-BF₂ Complex 6

2,6-Diethyl-3-formyl-1,5,7,8-tetramethylpyrromethene-BF₂ complex **5** [7] (0.509 g, 1.63 mmol) was dissolved in hot anhydrous ethanol (200 mL) and hydrogenated over palladium on carbon (5%, 0.29 g) at room temperature until the red color disappeared. Purification by gradient flash chromatography (silica gel-dichloromethane, dichloromethane/ethyl acetate, 9:1) gave 2,6-diethyl-1,3,5,7,8-pentamethylpyrromethene-BF₂ complex **1** as an orange, crystalline solid (0.102, 21%), mp 208.5–209°C and 2,6-diethyl-3-hydroxymethyl-1,5,7,8-tetramethylpyrromethene-BF₂ complex **6** as an orange, crystalline solid (0.234 g, 45%), mp 182–183°C (dec) (Ref. [7] mp 182–183°C).

2,6-Diethyl-3-methacroyloxymethyl-1,5,7,8-tetramethylpyrromethene-BF₂ Complex 2

2,6-Diethyl-3-hydroxymethyl-1,5,7,8-tetramethylpyrromethene-BF₂ complex **6** (0.623 g, 1.87 mmol) was dissolved in anhydrous pyridine (5 mL). Methacroyl chloride (0.520 g, 5.00 mL) was added dropwise to the mixture. After the mixture had been stirred for 5 minutes water (10 mL) was added with vigorous stirring. The precipitate that had formed was allowed to settle in an ice bath for 10 minutes, and the supernatant liquid was decanted. The residue was stirred thoroughly with aqueous sodium carbonate (5%, 5 mL), collected by filtration, and purified by gradient flash chromatography (silica gel-hexane, hexane/dichloromethane, 1:1). The 2,6-Diethyl-3-methacroyloxymethyl-1,5,7,8-tetramethylpyrromethene-BF₂ complex **2** was obtained as a crystalline solid (0.364 g, 46%), mp 158–159°C; IR (KBr) ν 2377, 2344, 1726, 1561 cm⁻¹; ¹H NMR (deuteriochloroform) δ 6.15 (s, 1H), 5.41 (s, 2H), 2.65 (s, 3H), 2.53 (s, 3H), 2.47 (m, 4H), 2.35 (s, 6H), 1.95 (s, 3H), 1.05 (m, 6H); ¹³C NMR (deuteriochloroform) δ 167.1,

157.2, 142.9, 141.7, 139.3, 136.2, 134.6, 134.5, 133.5, 133.0, 131.6, 125.8, 57.3, 18.4, 17.3, 17.1, 17.2, 17.0, 16.9, 15.5, 14.6, 14.1, 12.8; UV (methanol) λ_{\max} (log ϵ) 513 nm (5.74); λ_f (methanol) 530.5 nm, Φ 0.59 (acridine orange); EI MS (70 eV) m/e 402 (M^+). Anal. calcd for $C_{22}H_{29}N_2O_2BF_2$: C, 65.68; H, 7.27; N, 6.96; F, 9.44. Found: C, 65.75, H, 7.45; N, 6.76; F, 9.41.

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