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REPORT DOCUMENTATION PAGE

Form Approved
OMB NO. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	April 26, 1996	Technical Report

4. TITLE AND SUBTITLE
Synthesis of 2,6-Diethyl-3-methacroyloxymethyl-1,5,7,8-tetramethylpyrromethene-BF_2 for the Preparation of New Solid-State Laser Dyes.

5. FUNDING NUMBERS
DAAH04-95-1-0078

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8. PERFORMING ORGANIZATION REPORT NUMBER
NA

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Research Office
P.O. Box 12211
Research Triangle Park, NC 27709-2211

10. SPONSORING / MONITORING AGENCY REPORT NUMBER
ARO 33588.1-CH

11. SUPPLEMENTARY NOTES
The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision, unless so designated by other documentation.

12a. DISTRIBUTION / AVAILABILITY STATEMENT
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12 b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 words)*

The synthesis of 2,6-diethyl-3-methacroyloxymethyl-1,5,7,8-tetramethylpyrromethene–BF_2 (**2**) was prepared in straightforward fashion from 2,6-diethyl-1,3,5,7,8-pentamethylpyrromethene–BF_2 (**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.

14. SUBJECT TERMS	15. NUMBER IF PAGES
Laser Dyes, pyrromethene-BF_2 complexes	16
	16. PRICE CODE: NA

17. SECURITY CLASSIFICATION OR REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
UNCLASSIFIED	UNCLASSIFIED	UNCLASSIFIED	UL

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TECHNICAL REPORT

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APRIL 26, 1996

U.S. ARMY RESEARCH OFFICE

GRANT NUMBER: DAAH04-95-1-0078

DEPARTMENT OF CHEMISTRY

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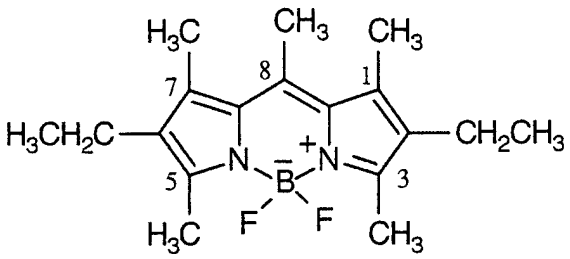
1. FOREWORD

The synthesis of 2,6-diethyl-3-methacroyloxymethyl-1,5,7,8-tetramethylpyrromethene–BF_2 (**2**) was prepared in straightforward fashion from 2,6-diethyl-1,3,5,7,8-pentamethylpyrromethene–BF_2 (**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.



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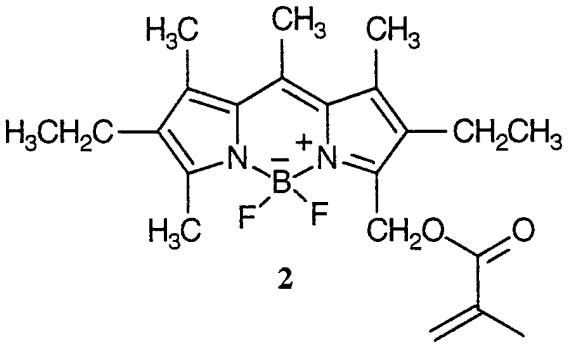

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4. BODY OF REPORT

A. STATEMENT OF THE PROBLEM STUDIED

Recent advances in the synthesis of novel strongly fluorescing laser dyes have renewed interest in dye-laser technology. The pyrromethene–BF_2 complex family of dye molecules have been shown to possess a laser performance that is superior to that of rhodamine–6G [1,2]. In 1993, 2,6-diethyl-1,3,5,7,8-pentamethylpyrromethene–BF_2 complex (**1**, DEPMP–BF_2) was found to exhibit twice the power efficiency of rhodamine–6G. Since their initial discovery, pyrromethene–BF_2 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 non-laboratory environments due to high flammability and other potential health hazards associated with the solvent. The advent of pyrromethene–BF_2 dyes together with new plastics has lead to the development of solid-state laser dye materials. Dye-doped solid-state laser materials offer 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 excitation source need not be coherent and low chemical hazard. DEPMP–BF_2 (**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–BF_2 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–BF_2 complexes, 1,5,7,8-tetramethyl-2,6-diethyl-3-methacroyloxymethylpyrro-methene–BF_2 complex (**2**) was envisaged as the first in a series of monomeric dyes which 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 which might give better performance and longer lifetime than the dispersed counterpart.

RESULTS AND DISCUSSION

The synthesis of the monomer pyrromethene–BF_2 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 synthetic procedure greatly enhanced the efficiency of the synthesis and readily furnished multigram quantities of **1**.

With **1** in hand, oxidation of the *C(3)*-methyl group to the corresponding *C(3)*-formyl group was 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 at 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 BF_2 moiety and destroyed the pyrromethene–BF_2 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 at room temperature in order to avoid the excessive heat generated by the reaction which was found to accelerate the decomposition of the pyrromethene–BF_2 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–BF_2 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–BF_2 nucleus. The greater the electron-withdrawing ability of the *C(3)*-substituent the lower the fluorescence quantum yield.

Preliminary studies by Jones *et al.* [9] have recently demonstrated that **2** is convalently 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 copolymers of **2** are underway and will be reported in due course.

B. SUMMARY OF THE MOST IMPORTANT RESULTS

The methacrylate ester **2** was easily prepared from the readily available pyrromethene–BF_2 complex **1** in good overall yield. The monomer **2** clearly 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, Perkin Elmer Lambda 6 (UV/VIS) Spectrometer. Melting points were obtained from a Mel–Temp II and were uncorrected. Elemental analysis was obtained from Midwest Micro Lab, Indianapolis, IN. Hydrogenation reactions were carried out on a Parr 3911 Hydrogenation Apparatus. ^{1}H and ^{13}C nmr spectra were recorded on a Varian 300 MHz nmr spectrometer in $CDCl_3$ 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 min to a solution of **3** (5.00 g, 40.6 mmol) in dichloromethane (25 mL). The reaction mixture was heated (40 °C, 1 h), cooled to room temperature, diluted with petroleum ether (290 mL) and triturated for 12 h 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 – BF_2 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 min 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 min), cooled to 40 °C, washed with warm water (3 × 100 mL), 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–BF_2 Complex **6**.

2,6-Diethyl-3-formyl-1,5,7,8-tetramethylpyrromethene–BF_2 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–BF_2 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–BF_2 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 – BF_2 Complex **2**.

2,6-Diethyl-3-hydroxymethyl-1,5,7,8-tetramethylpyrromethene–BF_2 complex **6** (0.623 g, 1.87 mmol) was dissolved in anhydrous pyridine (5 mL). Methacryloyl chloride (0.520 g, 5.00 mL) was added dropwise to the mixture. After stirring for 5 min, water (10 mL) was poured into the mixture with vigorous stirring. The precipitate was allowed to settle in an ice bath for 10 min 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–BF_2 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); ^{13}C 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.

ACKNOWLEDGEMENT. We wish to thank the U.S. Army Missile Command for support of this research.

C. LIST OF ALL PUBLICATIONS AND TECHNICAL REPORTS

5. REPORT OF INVENTIONS: N/A

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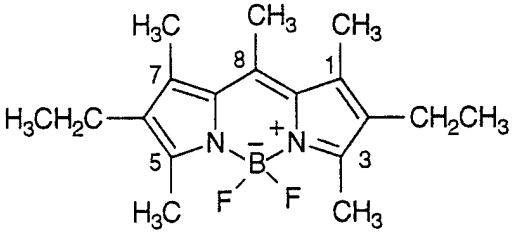
7. APPENDICES

Drawing **1**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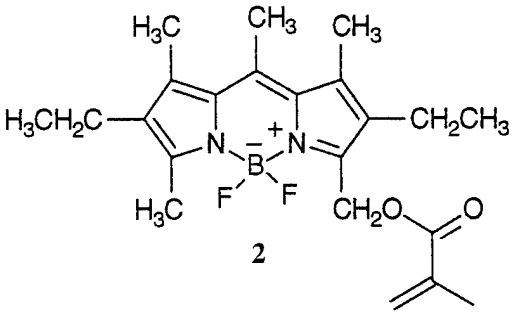
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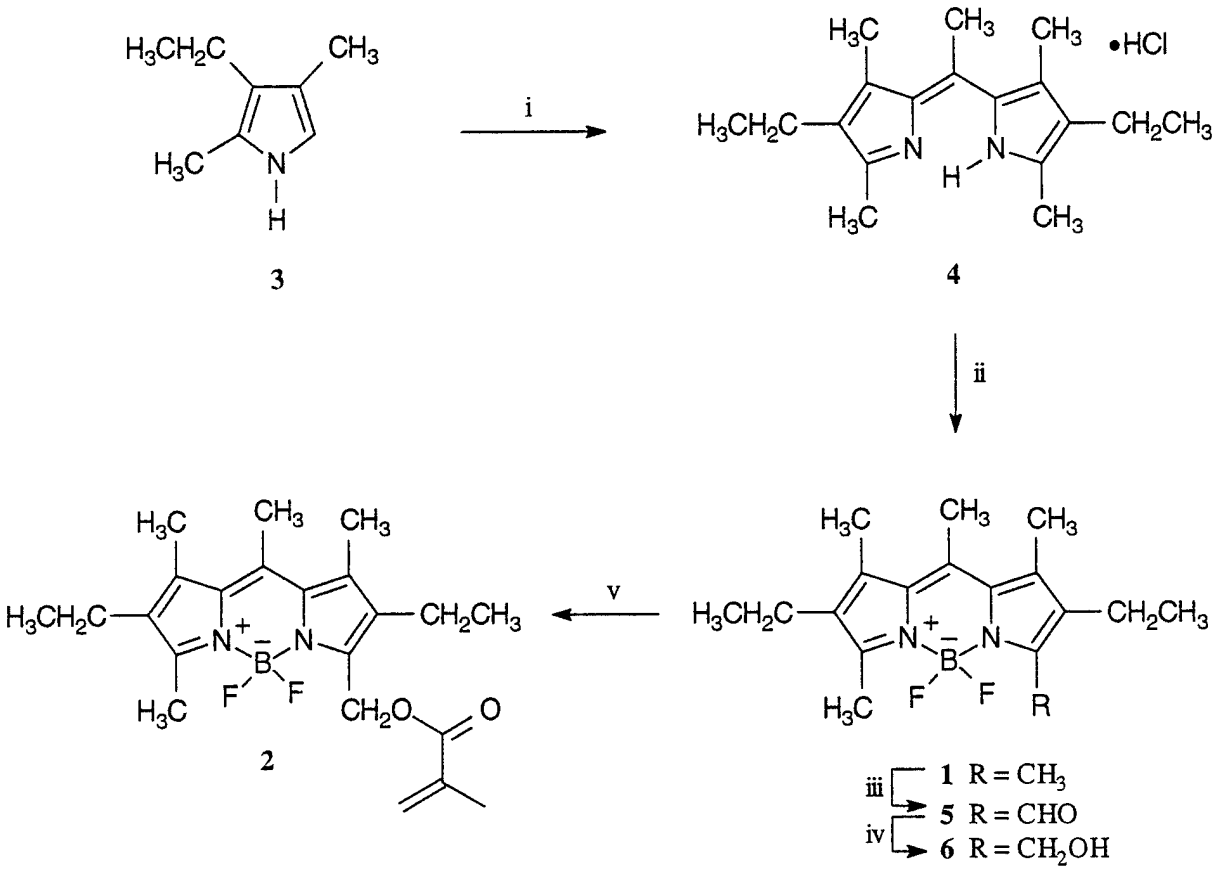
Scheme 1



Reagents: i) CH_3COCl, CH_2Cl_2, 40 °C. ii) $BF_3 \bullet Et_2O$, Et_3N, toluene. iii) DDQ, THF. iv) H_2, 5% Pd/C EtOH. v) methacroyl chloride, pyridine, room temperature.