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Synthesis of Isomers of Rhodamine 575 and Rhodamine 6G as New Laser Dyes

Claudine Scala-Valéro[a,b], Denis Doizi[a], Gérald Guillaumet[b]

[a]*Commissariat à l'Energie Atomique, CEN Saclay, DPE/SLCS/LLCP, 91191 Gif sur Yvette cedex, France.*

[b]*Institut de Chimie Organique et Analytique, associé au CNRS, Université d'Orléans, BP 6759, 45067 Orléans cedex 2, France.*

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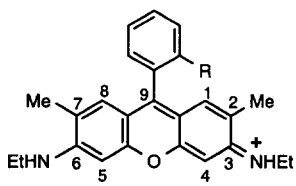
Abstract : Two new laser dyes of the rhodamine family, substituted at C-1 and C-8, were prepared by condensation of phthalic anhydride with 3-ethylamino-5-methylphenol. Two methodologies have been investigated for the preparation of the latter.

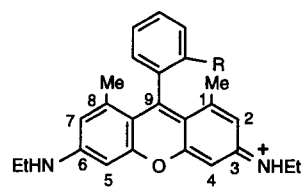
Keywords : Xanthenes, Rhodamines, Dyes.

Rhodamines are very efficient laser dyes for the red region of the visible spectrum[1]. In order to improve the laser efficiency of rhodamine 6G, we have investigated a new type of substitution of its basic skeleton. We present here the synthesis of new dyes **1**, isomers of rhodamine 575 and rhodamine 6G, bearing methyl groups at C-1 and C-8 of the xanthene skeleton (Figure 1) :



R = COO^- Rhodamine 575

R = COOEt Rhodamine 6G



R = COO^- **1a**

R = COOEt **1b**

Figure 1

Structural flexibility is known to be an important cause of non-radiative deactivation in rhodamines[1-3]. With such a substitution we expect to reduce the non-radiative processes due to the free rotation of the carboxyphenyl fragment, and hence to have an improved laser efficiency.

Rhodamine dyes are prepared by heating phthalic anhydride and an appropriate *m*-aminophenol, here the 3-ethylamino-5-methylphenol **2**.[4-7] Compound **2** is not commercially available and it

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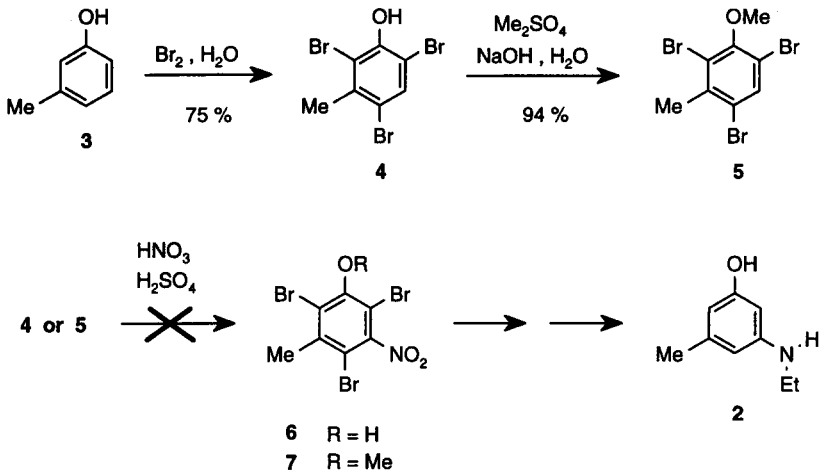
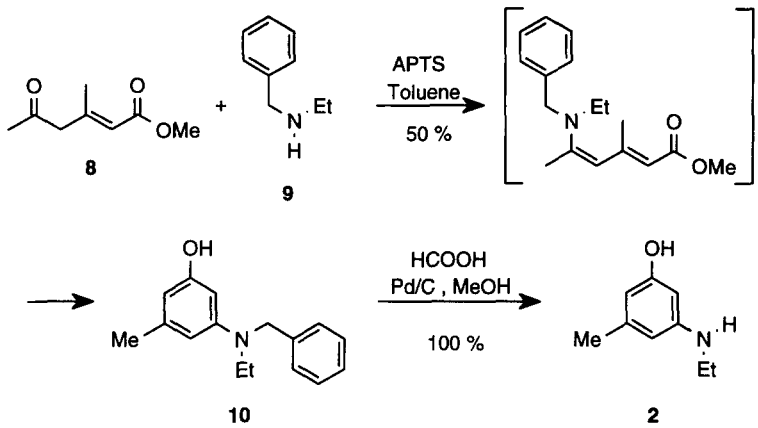
cannot be easily prepared by using classical aromatic chemistry involving direct electrophilic substitution. Two different methods have been investigated for the preparation of this compound.

The first method (Scheme 1) has been introduced by Adachi[8] for the synthesis of orcinol monomethyl ether. Bromination of *m*-cresol **3** using bromine in water at 40°C gave the 2,4,6-tribromo-*m*-cresol **4** in 75 % yield. Nitration of this intermediate by means of a mixture of concentrated nitric and sulfuric acids did not give **6** as expected, but a by-product probably resulting from oxidation of the aromatic skeleton into a quinone derivative. This failure led us to protect the phenolic group of **4** as a methyl ether by means of dimethyl sulfate as described by Adachi. Thus the compound **5** was obtained in 94 % yield. Nitration of this compound to give **7** also failed.



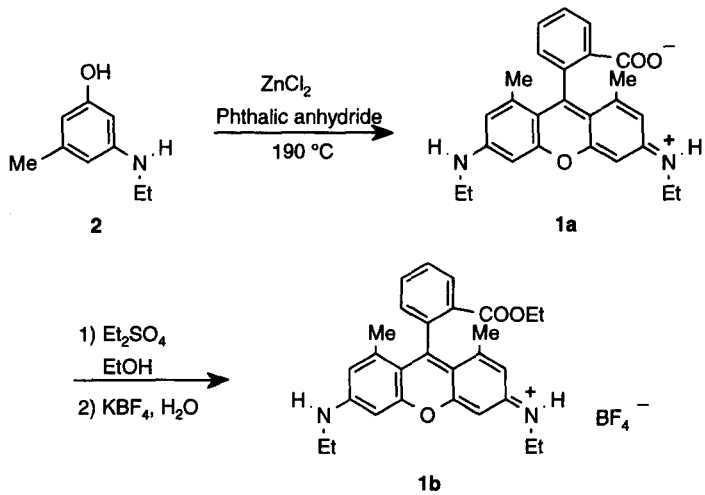
Scheme 1

The second method (Scheme 2) is based on intermolecular cyclisation between methyl 3-methyl-5-oxo-2-hexenoate **8** and an amine catalysed by *p*-toluenesulfonic acid to produce compound **10**.[9] Only secondary amines can be used in this reaction. We chose *N*-benzyl-*N*-ethylamine **9** for the possibility of the *N*-benzyl group to be cleaved, giving the required *N*-ethylamino group. The starting ketoester **8** was prepared following the procedure described by Alkonyi,[10] consisting in acetylation of methyl 3,3-dimethylacrylate. Reaction of this intermediate with *N*-benzyl-*N*-ethylamine **9** in the presence of *p*-toluenesulfonic acid as a catalyst gave 3-(*N*-benzyl-*N*-ethylamino)-5-methylphenol **10** in 50 % yield. This compound was debenzylated by means of formic acid and palladium on activated carbon in methanol following the procedure described by Means *et al.*[11] to give 3-ethylamino 5-methylphenol **2** in quantitative yield (35 % overall yield)[12].



Scheme 2

Several experimental conditions were investigated for the condensation of **2** with phthalic anhydride to obtain the dye **1a**. Steric hindrance due to the methyl groups seemed to make the reaction difficult : operating in dichlorobenzene according to the procedure described by Aburada and Akagi[4] failed, as well as Hammond's procedure using phosphoric acid as a catalyst[7]. Finally, the use of zinc chloride as a catalyst gave **1a**. The dye was precipitated from the reaction mixture by addition of aqueous tetrafluoroboric acid. The solid thus obtained was recristallised from methanol and purified by column chromatography[13]. The compound **1a** was obtained in less than 5 % yield, a value lower compared to those obtained in the case of Rhodamine 575. The dye **1a** was then esterified using diethyl sulfate in anhydrous ethanol to form the ester **1b** which has been obtained as tetrafluoborate salt (Scheme 3). The chemical shift of the methyl groups attached to the carbons C-1 and C-8 confirm unequivocally the structures of new dyes **1a** and **1b**.



Scheme 3

In conclusion, two new dyes of the rhodamine family, with two methyl groups at C-1 and C-8 of the xanthene skeleton, have been synthetised. Their optical properties will be presented elsewhere.

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12. All new compounds were characterised by ^{1}H-NMR, ^{13}C-NMR, IRFT and mass spectral analysis.

13. Spectral data for **1a** : ^{1}H-NMR (DMSO d_6, 200 MHz) : δ 1.13 (t, *J* = 7.3 Hz, 6H, CH_3), 1.52 (s, 6H, CH_3), 3.00 (q, *J* = 7.3 Hz, 4H, CH_2), 5.90 (brs, 2H, NH), 6.10 (d, *J* = 2.2 Hz, 2H, H_{arom}), 6.16 (d, *J* = 2.2 Hz, 2H), 7.04 (d, *J* = 7.4 Hz, 1H, H_{arom}), 7.55-7.68 (m, 2H, H_{arom}), 7.85 (d, *J* = 7.4 Hz, 1H, H_{arom}) ; ^{13}C-NMR (DMSO d_6, 200 MHz) : δ 14.2, 25.0, 39.0, 97.6, 131.2, 131.3, 134.2, 134.2 ; IR (KBr) : ν 3500, 3100, 2973, 1721, 1610, 1491, 1270, 1227 cm^{-1} ; UV (EtOH) : λ max = 513 mm, ∈ = 36 000 dm^3 mol^{-1} cm^{-1} ; MS (FAB) : *m/z* = 415 (MH^+) ; Anal. $C_{26}H_{26}N_2O_3$ (C, H, N).

14. Spectral data for **1b** : ^{1}H-NMR (acetonitrile-d_3, 200 MHz) : δ 1.06 (t, *J* = 7.1 Hz, 3H, CH_3), 1.33 (t, *J* = 7.2 Hz, 6H, CH_3), 1.57 (s, 6H, CH_3), 3.42 (m, 4H, CH_2N), 4.14 (q, *J* = 7.1 Hz, 2H, OCH_2), 6.68 (m, 4H, H_{arom}), 6.75 (br s, 2H, NH), 7.43 (d, *J* = 4.4 Hz, 1H, H_{arom}), 7.82 (m, 2H, H_{arom}), 8.22 (d, *J* = 4.4 Hz, 1H, H_{arom}) ; IR (KBr) : ν 3434, 3100, 2919, 1716, 1641, 1609, 1494, 1270, 1099 cm^{-1} ; UV (EtOH) : λ max = 529 mm, ∈ = 74800 dm^3 mol^{-1} cm^{-1} ; MS (FAB) : *m/z* = 443 (M^+) ; Anal. $C_{28}H_{31}N_2O_3BF_4$ (C, H, N).