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Xanthenes: Fluorone Derivatives II

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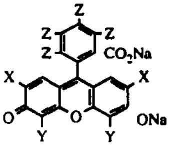
Abstract: A series of 9-hydrogen and 9-cyano substituted xanthenes was synthesized and their absorption spectra compared. It was found that the cyano group at the C-9 position can produce large bathochromic shifts (about 100 nm).

The xanthene dyes are among the oldest synthetic dyes and have many important applications.[2] These compounds, which include eosin, phloxin, erythrosin and rose bengal, have the same ring skeleton and absorb, in general, around 500 nm depending on the different ring substituents, Table 1.[3]

Table 1



Xanthenes	X	Y	Z	λmax nm in EtOH	
Rose bengal	I	I	Cl	557	Δλ 25 nm
Erythrosin	I	I	H	532	
Phloxin	Br	Br	Cl	548	Δλ 25 nm
Eosin	Br	Br	H	523	

Table 1: Example Xanthene Dyes

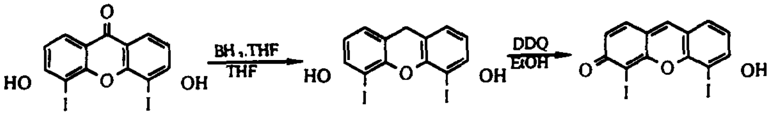
For many applications, it is desirable to extend the spectral sensitivity to longer wavelengths while retaining the general structure. As a part of fundamental studies of the xanthene dyes, we have recently synthesized new xanthene derivatives, the hydroxyfluorones.[4] Though the substitution of hydrogen for phenyl at C-9 has only a minor influence on the absorption and emission spectra, the maximum absorptions of erythrosin and Rose Bengal differ by 20+ nm so that it is clear that the substitution pattern at the C-9 position has an important influence (See Table 1, compare also eosin/phloxin). We were intrigued by the observation that the presence of an electron acceptor such as tetrachlorophenyl at the C-9 position could cause such a bathochromic shift.. As crystal structures of typical xanthenes have shown,[5] the large phenyl substituent at the C-9 position is severely twisted out of the plane of the fluorone and should have a limited effect on the delocalization of π-electron density from the fluorone ring.

One approach to producing a large bathochromic shift in the absorption of the basic fluorone skeleton may involve intramolecular charge-transfer (CT) chromophores. Examples of such are generally found in quinoid, azo, and indigo chromophores.[6] It is notable that the xanthene dyes, in spite of their importance, have not been evaluated in term of this substituent effect. It seemed reasonable to us that the introduction of a stronger electron acceptor, such as a cyano group, at the C-9 position could produce a large bathochromic shift.

Herein, we report the synthesis of a series of novel C-9 hydrogen and cyano substituted xanthene dyes for exploring this matter.

Compounds **1, 3, 5** were synthesized by the previous method.[4] Compound **9** was obtained by treatment of 3,6-dihydroxyxanthane and 2-methyl-2-propanol with 15-18% fuming sulfuric acid. Iodination of **9** produced **11**. The synthesis of compound **7** started from 3,6-dihydroxy-4,5-diiodoxanthone **13**.[7] A salient feature of the synthesis was the reduction of the carbonyl group in compound **13** without effecting the iodo substituent by using the borane tetrahydrofuran complex. Dye **7** was obtained by treatment of reduction product **14** with DDQ in ethanol. Scheme I.

Scheme I



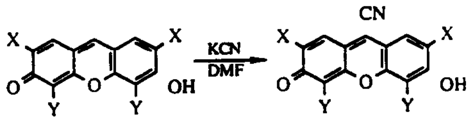
13 **14** **7**

To prepare the cyano derivatives, the C-9 hydrogen substituted hydroxyfluorones **1, 3, 5, 7, 9, 11** were treated with potassium cyanide in dimethylformidey. The reaction likely started with a 1,6-conjugated addition followed by oxidation, Scheme II.

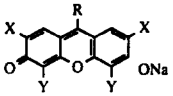
A typical procedure for preparing the compound **8** was described as follows:

Potassium cyanide (19 mg, 0.3 mmol.) was added to the solution of **7** (70 mg, 0.15 mmol.) in 1.5 ml of DMF. The reaction was monitored by visible spectrum until compound **7** was completely consumed. The reaction solution was treated with 25.0 ml of 4:1 hexane:dichloromethane, after which the precipitate was filtered, dried and treated with 5% HCl (should be done in the hood with pre-cautions: take care!) then washed with water. 4,5-Diiodo-9-cyano-3-hydroxy-6-fluorone **8** (70 mg) was obtained in 95% yield. ^{1}HNMR (DMSO): 7.38 (2H, d, J=9.2 Hz), 6.46 (2H, d, J=9.2 Hz).

Scheme II



A comparison of the absorption spectra of these novel dyes showed that the 9-cyano substituted xanthene dye, in general, demonstrates about a 100 nm (or larger) bathochromic shift relative to the 9-hydrogen substituted compounds. (Table 2) This permits the design and synthesis of a new class of xanthene dyes with absorption, in general, near 600 nm which is the ideal region to use with He/Nd lasers as light sources for many application purposes.

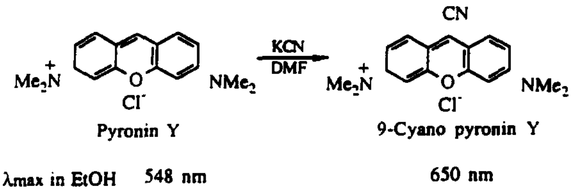


No.	R	X	Y	λmax in EtOH	ε
1	H	H	H	504	24700
2	CN	H	H	594, 548	50300, 24700
3	H	Br	Br	530	39300
4	CN	Br	Br	626, 576	51400, 24500
5	H	I	I	536	91200
6	CN	I	I	638, 586	80000, 35000
7	H	H	I	520	86000
8	CN	H	I	618, 570	30500, 16600
9	H	t-Bu	H	518	101000
10	CN	t-Bu	H	614, 564	47400, 23200
11	H	t-Bu	I	532	90800
12	CN	t-Bu	I	636, 582	68300, 33600

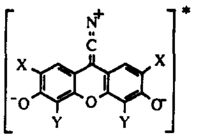
Table 2

To test the generality of this larger bathochromic shift in other xanthene analogs, 9-cyano pyronin Y was synthesized.[8] Its absorption spectrum was compared with pyronin Y and the same large bathochromic shift was observed, Scheme III.

Scheme III



It is anticipated that the introduction of the cyano group at the C-9 position will generate the lower energy excited state **15** which could be responsible for this large bathochromic shift.



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References and notes

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1. Contribution # 154 from the Center for Photochemical Sciences
2. See, for example: (a) Valdes-Aguilera, O.; Pathak, C.P.; Shi, J.; Watson, D. and Neckers, D.C. *Macromolecules*, **1992**, *25*, 541. (b) Wang, C.J.; Stroupe, S.D.; Jolley, M.E. U.S. patent 4,585,862, **1986**. (c) Eaton, D.F., *Adv. Photochem.*, **1986**, *13*, 427.
3. Neckers, D.C. *J. Photochem. and Photobio.*, **1989**, *47*, 1.
4. Shi, J.; Zhang, X. and Neckers, D.C. *J. Org. Chem.*, (submitted) **1992**.
5. Valdes-Aguilera, O.M., and Neckers, D.C., *Advances in Photochemistyr*, Vol. 18, Wiley, N.Y. **1993.**
6. (a) Kim, S.H.; Matsuoka, M.; Yodoshi, T.; Suga, K. and Kitao,T. *J..Soc. Dyes Colourists*, **1989**, *105*, 212. (b) Kubo, Y.; Mori, F. and Yoshida, K. *Chem. Lett.*, **1987**, 1761. (c) Bello, K.A.; and Griffths, J. *J. Chem. Soc., Chem. Commun.*, **1986,** 1639. (d) Bello, K.A.; Cheng, L. and Griffiths,J. *J. Chem. Soc. Perkin Trans. II*, **1987**, 815. (e) Kubo, Y.; Mori, F.; Komatsu, K. and Yoshida, K. *J. Chem. Soc. Perkin Trans. I*, **1988**, 2439.
7. Gaekwad, Y.G. and Sethna, S. *J. Indian Chem. Soc.*, **1978**, *LV*, 794.
8. The 9-cyano pyronin Y was difficult to purify.

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