Synthesis and Fluorescence Analysis of 3-Substituted 7-Dialkylamino-2*H*-1,4-benzoxazin-2-ones

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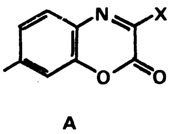
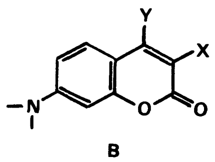
New benzoxazinone type dyes have been synthesized by the reaction of α-keto esters on 2-amino-5-(dialkylamino)phenols. The obtained 7-dialkylamino-2*H*-1,4-benzoxazin-2-ones show a strong fluorescence and a large Stokes shift, reaching 183 nm. An effect of 15 various substituents in position 3, together with a solvent effect have been characterized on their absorption and emission bands. Linear free energy relationships allow the tuning of their spectroscopic characteristics over a large spectral range.

The 2*H*-1,4-benzoxazin-2-ones, abusively called "azacoumarins," have been described by Wislicenus[1] in 1897, and more recently by Biekert[2] and Moffett.[3] They have synthesized many heterocyclic compounds of this kind by the reaction of an acid or a keto ester with an *o*-aminophenol. Actually, only a few derivatives of benzoxazinones with an amino group in the position 7 have been described in the literature.[4] These compounds (**A**) show a strong fluorescence which, due to the bathochromic effect of the heterocyclic nitrogen, is shifted towards the red when compared to the analogous 7-aminocoumarins (**B**). In order to better understand the spectroscopic properties of these highly fluorescent dyes (**A**), we have synthesized a large serie of 3-substituted 7-aminobenzoxazinones, and analyzed the substituent effect together with the solvent effect on their absorption and emission spectra.

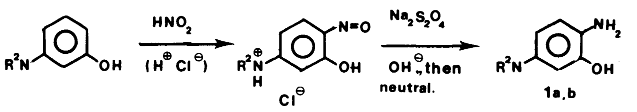


A

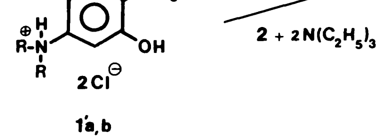


B

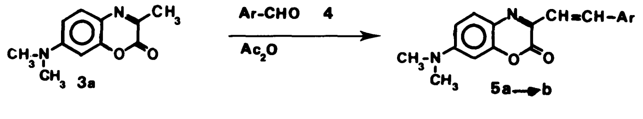
Synthesis of 2*H*-1,4-Benzoxazin-2-ones. The 7-amino derivatives of benzoxazinones are poorly described because of the difficulty to synthesize the starting 2,5-diaminophenols. These compounds are easily oxidized, and their fast degradation leads to highly-blue-colored products, whose structure is still unknown. Nevertheless, taking great care to avoid this oxidation, we isolated 2-amino-5-(dialkylamino)phenols **1a,b** by reducing 5-dialkylamino-2-nitrosophenols with sodium dithionite in basic medium (**a**, R=Me; **b**, R=Et).



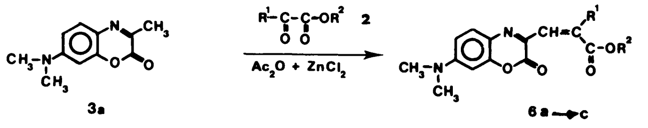
The 7-dialkylamino-2*H*-1,4-benzoxazin-2-ones, **3a,b** substituted in the position 3, have been obtained by the action of α-keto esters **2** on the 2-amino-5-(dialkylamino)phenols **1a,b**, or on the corresponding dihydrochloride **1a,b**, in the presence of a tertiary amine.



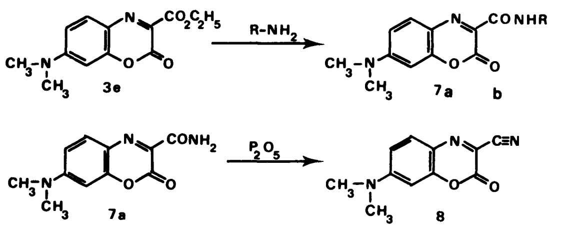
The reactivity of the methyl group on the position 3 in the 7-dimethylamino-3-methyl-2*H*-1,4-benzoxazin-2-ones **3a** allows the formation of 3-styrylbenzoxazinone **5**, by using the method described by Le Bris[4d] which involves the condensation of aromatic aldehydes.



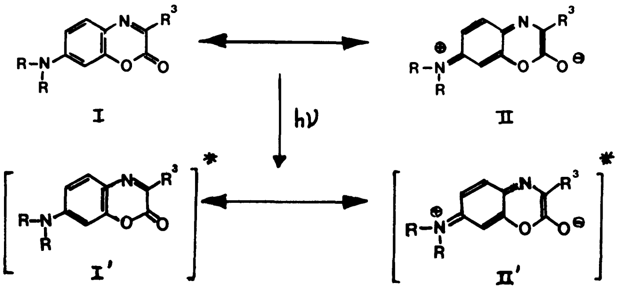
Moreover, a Lewis acid such as anhydrous zinc chloride allows the condensation of a few α-keto esters **2** on the activated methyl group on the position 3.



An ester function on the position 3 can also be easily substituted into an amide function, the unsubstituted amide leading to the corresponding nitrile by dehydration.



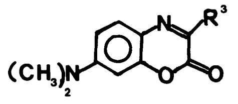
Spectral Properties of 3-Substituted Benzoxazinones. As shown on Table 1, 3-substituted benzoxazinones (**A**) thus obtained showed very interesting fluorescence properties, which can be explained on the basis of the following mesomeric forms (**I**) and (**II**).



In the ground state, the π-electron distribution in this essentially neutral molecule closely relates to the form (**I**), with a minor contribution of the dipolar form (**II**). On the other hand, the first excited singlet state S₁ can be described by a predominant dipolar form (**II'**). Consequently, a large increase in the dipole moment of the molecule can be expected during the excitation $S_0 \rightarrow S_1$, which will result in a large rearrangement of the surrounding solvent molecule around the excited state. Thus the energy level of this excited state will be markedly lowered before the emission takes place, with regard to the energy level of its Franck-Condon excited state. These considerations explain the unusually large Stokes shift observed for these molecules (**A**), as compared to others dyes such as xanthenes or even the parent coumarins (**B**).

The dipolar moment variation will be controlled by

Table 1. Effect of R³ Substituent on the Spectral Properties of Compounds of Type **3**



R^3	Solvents								
	$(C_2H_5)_2O$			$CHCl_3$			DMF		
	Abs	Em nm	SS	Abs	Em nm	SS	Abs	Em nm	SS
CH_3	384	484	100	400	502	102	395	525	130
$CH_2\text{-}C(CO_2C_2H_5)(OCOCH_3)\text{-}CO_2C_2H_5$	408	486	78	422	502	80	423	525	102
$C_6H_4OCH_3(p\text{-})$	428	512	84	444	530	86	445	550	105
$\alpha\text{-}C_{10}H_7$	429	510	81	445	528	83	449	557	108
C_6H_5	427	506	79	440	520	80	443	551	108
$CH{=}C(CO_2C_2H_5)(CO_2C_2H_5)$	475	546	71	500	557	57	510	592	82
$CH{=}C(CH_3)(CO_2CH_3)$	450	521	71	469	536	67	476	572	96
$CH{=}C(C_6H_5)(CO_2CH_3)$	464	533	69	483	551	68	488	583	85
$C_6H_4N(CH_3)_2(p\text{-})$	450	548	98	467	584	117	468	586	118
$CO_2C_2H_5$	426	502	76	457	517	60	455	538	83
$CONH_2$	502	578	76	470	513	43	445	540	95
$CONHC_6H_5$	446	511	65	476	524	48	454	522	68
CN	457	512	55	476	523	47	478	548	70
$CH{=}CH\text{-}C_6H_4N(CH_3)_2(p\text{-})$	472	560	88	500	616	116	499	634	135
$CH{=}CH\text{-}C_6H_4NO_2(p\text{-})$	475	566	91	496	591	95	499	682	183

Abs = absorption maximum, Em = emission maximum, SS = Stokes Shift

Table 2. Effect of Solvent on Spectroscopic Properties of Compound **3a**

Solvent	Abs/nm	Em/nm	SS/cm^{-1}	Parameter E_T
Benzene	390	478	4721	34.5
Diethyl ether	384	484	5381	34.6
Dioxane	383	482	5363	36
Chloroform	400	502	5080	39.1
Pyridine	398	506	5363	40.2
Acetone	391	510	5968	42.2
DMF	395	525	6269	43.8
DMSO	399	532	6266	45
Acetonitrile	392	519	6242	46
Methanol	398	558	7204	55.5

the extent of the contribution of the dipolar forms (**II**, **II′**) to the S_0 and S_1 states, and thus governed by external parameters which are able to modify the electronic distribution in the molecule. For instance substituent as well as solvent can be expected to affect on the position of the absorption and emission bands. For instance, if the small contribution of the polar form (**II**) in the ground state is increased by an electronic effect of the R^3 substituent, a shift of the main absorption band to longer wavelength will occur. A stabilization of (**II**) can also be achieved by the increase of the solvent polarity. The energy level of the S_1 excited state will also be affected by these effects, resulting in an even larger shift of the emission band towards longer wavelength.

In order to go into more details, we have analyzed the effects of the R^3 substituent and of the solvent on the spectral properties of this class of compounds (Tables 1 and 2). The R^3 substituent effect determined in three different solvents shows that shifts of the absorption band higher than 100 nm can be obtained by varying the electronic distribution in the molecule. Using the parameter σ_I which represents the polar nature of a substituent,[5] a satisfying correlation with absorption frequency is obtained for a few substituents for which σ_I is given (Fig. 1). The emission maximum is also shifted by the substituents but to a smaller extent, as could be expected for a state in which the dipolar form (**II′**) is predominant, even for unsubstituted molecule.

Solvents can also affect on the energy levels of the S_0 and S_1 states. As already shown in the literature, the spectroscopic properties of such type of molecules possessing two limit forms, a neutral and a dipolar one, are governed by the solvent polarity.[6] Solvent parameters have been proposed for representing this effect, as for instance E_T on the basis of the spectral behavior of the pyridinium derivative (**C**).[7] Ten solvents of varying polarity have been used to analyze the solvent effect on the absorption and emission bands of one representative molecule of (**A**), with R=Me. The very large shift observed, which obey to a linear relationship with E_T (Fig. 2), emphasizes the significance of the dipolar form contribution to the

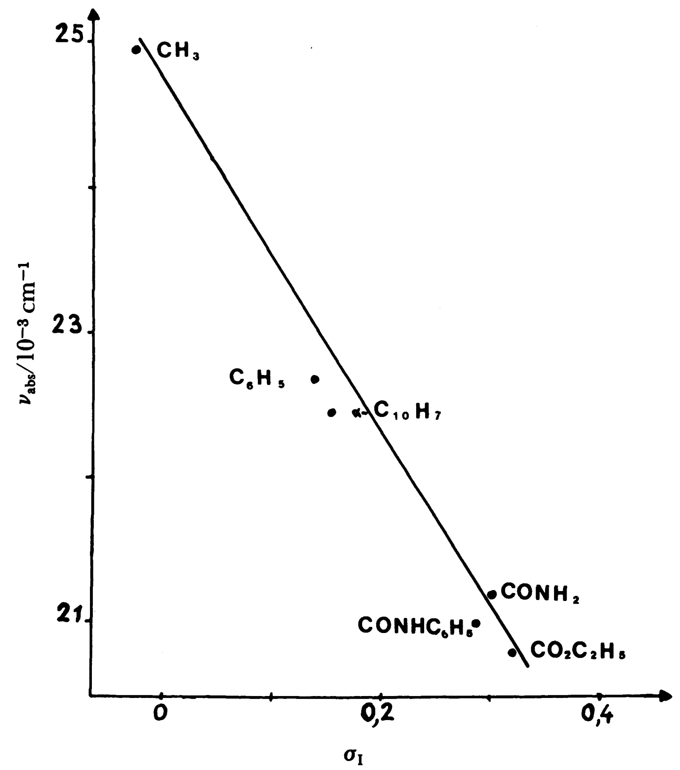


Fig. 1. Free energy relationship between absorption frequency ν_{abs} and substituent parameter σ_I. Solvent: CHCl$_3$.

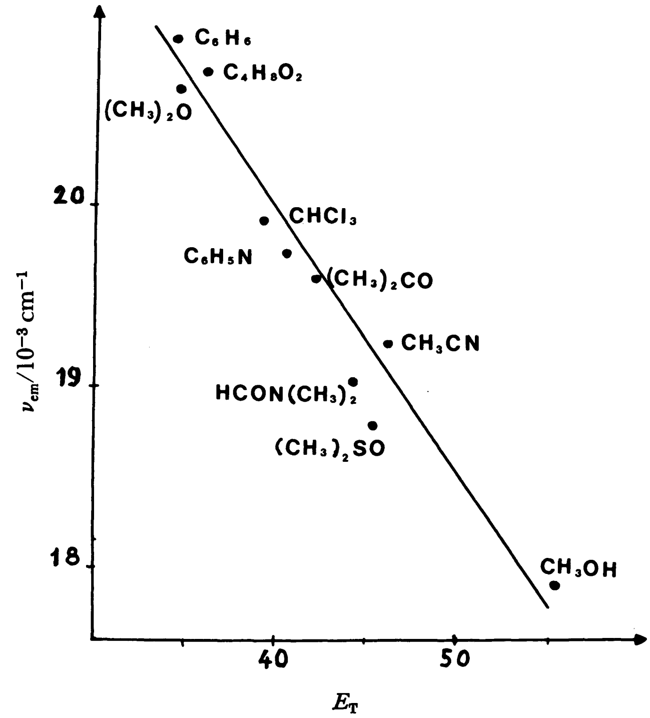
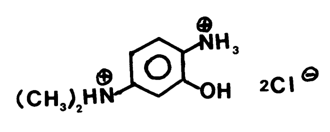
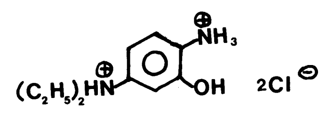
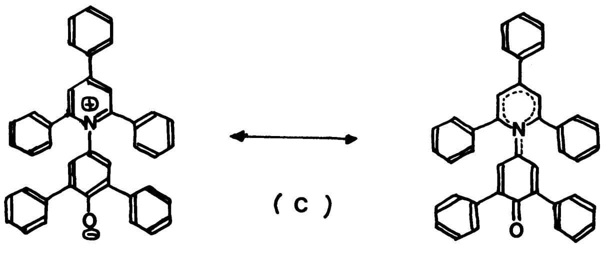


Fig. 2. Relationship between emission frequency (cm^{-1}) and the polarity parameter E_T in various solvents.





structure of these molecules. The observed Stokes shift reaches unusual value as high as 183 nm, compared with the 100 nm obtained with the parent coumarin dyes (**B**) when studied in the same range of solvent polarity. Furthermore, these benzoxazinone dyes possess a high fluorescence yield, as shown by the quantum yield $\eta=0.93$ obtained for R=CH_3 in chloroform, using Rhodamine 101 as standard.


(C)

In conclusion, the position of the absorption and emission bands of these news benzoxazinone dyes can be tuned over a very large spectral range by the use of a substituent and (or) a solvent effect. Taking also account for their strong fluorescence, this new class of material appears promising for a large field of applications and particularly as laser dyes.

Experimental

Melting points were not corrected and were determined on a Koffler apparatus. The IR spectra were recorded on a Pye Unicam SP 200 spectrophotometer, the ^{1}H NMR spectra on a JNM-FX 100 JEOL spectrometer (the chemical shifts were reported as δ values in parts per million employing tetramethylsilane as an internal standard). The absorption spectra were obtained on a Cary 219 spectrophotometer and the fluorescence spectra on a MPF-44R Perkin Elmer spectrophotometer. Elemental analyses were carried out by the CNRS Microanalysis Laboratory.

Preparation of 2-Amino-5-(dialkylamino)phenols (1a,b). The hydrochloride of 5-dialkylamino-2-nitrosophenols have been obtained in yields of 90% following Ref. 8, then reduced into 2-amino-5-(dialkylamino)phenols by sodium dithionite in basic medium.[9]

We have isolated the compounds **1a** and **1b** by operating under nitrogen atmosphere to avoid of oxidative degradation, and using them readily for subsequent cyclization into benzoxazinones **3**. Besides, the dihydrochlorides **1'a** and **1'b** are stable under solid state. **1'a**: Gray crystals; mp 230 °C (decomp). ^{1}H NMR (D_2O) δ=3.37 (s, 6H, $N(C\underline{H}_3)_2$), 7.20—7.37 (m, 2H, H_4+H_6), 7.63 (d, J=9 Hz, 1H, H_3). **1'b**: Slightly blue crystals; mp 220 °C (dec). ^{1}H NMR (D_2O) δ=1.10 (t, J=7 Hz, 6H, $N(CH_2C\underline{H}_3)_2$), 3.57 (q, J=7 Hz, 4H, $N\text{-}(C\underline{H}_2\text{-}CH_3)_2$), 6.80—7.10 (m, 3H, H_3+H_4+H_6).

Preparation of 3-Substituted 7-Dialkylamino-2*H*-1,4-benzoxazin-2-ones. Metod A. To a solution of 20 mmol of α-ketoester **2**[†] in 50 ml of dry toluene and under nitrogen atmosphere, 20 mmol of 2-amino-5-(dialkylamino)phenols (**1**) were added with stirring. This reaction mixture was refluxed for 1 h and the water produced during the cyclization was eliminated by azeotropic distillation. After cooling, the organic layer was separated and concentrated to dryness. The benzoxazinone **3** was purified by chromatography on deactivated alumina or on silica gel, then by recrystallization. **2d** p-$(CH_3)_2N\text{-}C_6H_4\text{-}CO\text{-}CO_2C_2H_5$: Yellow-green crystals, mp 95 °C (lit,[10] mp 95 °C), **2e** p-$CH_3O\text{-}C_6H_4\text{-}CO\text{-}CO_2C_2H_5$: Slightly yellow oil, bp 195 °C/2 mmHg,[††] **2f** $C_{10}H_7\text{-}CO\text{-}CO_2C_2H_5$: Yellow oil, bp 155—160 °C/1 mmHg, (lit,[11] bp 213—215°/23 mmHg).

Method B. Under a nitrogen atmosphere and while stiring, a mixture of 20 mmol of dihydrochloride **1'** and 20 mmol of α-keto ester **2** in 50 ml of dry toluene was refluxed; then 40 mmol of triethylamine were gradually added. The reflux was continued for 1 h with elimination of water as azeotrope. The cooled solution was filtered, the solid triethylammonium chloride was washed two times by 15 ml of toluene. All the organic layers were then treated as above.

7-Dimethylamino-3-methyl-2*H*-1,4-benzoxazin-2-ones (3a). Orange yellow crystals mp 125—126 °C (benzene-ethanol), yield 60% (method A); 70% (method B). Found: C, 64.59; H, 5.97; N, 13.81%. Calcd for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72%. ^{1}H NMR ($CDCl_3$) δ=2.47 (s, 3H, CH_3-3), 3.02 (s, 6H, $N(CH_3)_2$-7, 6.32 (d, J=2.5 Hz, 1H, H_8), 6.60 (dd, J=9 and 3 Hz, 1H, H_6), 7.42 (d, $J={}^1H$, H_5). UV-visible: λ_{max} 400 ($CHCl_3$), 395 nm (DMF); fluorescence: 502 ($CHCl_3$), 525 nm (DMF). IR (KBr): 1725 (s), 1624 cm^{-1} (s) (s=strong).

7-Diethylamino-3-methyl-2*H*-1,4-benzoxazin-2-one (3b). Yellow crystals mp 63—64 °C (cyclohexane). Yield: 50% (Method A); 54% (Method B). Found: C, 67.35; H, 5.94; N, 12.18. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. ^{1}H NMR ($CDCl_3$) δ=1.16 (t, J=7 Hz, 6H, $N(CH_2C\underline{H}_3)_2$-7), 2.37 (s, 3H, CH_3-3), 3.29 (q, J=7 Hz, 4H, $N(C\underline{H}_2CH_3)_2$-7), 6.16 (d, J=3 Hz, 1H, H_8), 6.39 (dd, J=9 and 3 Hz, 1H, H_6), 7.47 (d, J=9 Hz, 1H, H_5). UV-visible: λ_{max} 397 ($CHCl_3$), 402 nm (DMF); fluorescence: 500 ($CHCl_3$), 520 nm (DMF). IR (KBr): 1733 (s), 1633 cm^{-1} (s).

7-Dimethylamino-3-phenyl-2*H*-1,4-benzoxazin-2-one (3c). Orange crystals, mp 182 °C ($CHCl_3$-ethanol). Yield 40% (method A). Found: C, 72.14; H, 5.15; N, 10.51%. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52%. ^{1}H NMR ($CDCl_3$) δ=3.07 (s, 6H, $N(C\underline{H}_3)_2$-7), 6.33 (d, J=3 Hz, 1H, H_8), 6.68

[†] α-Ketoesters **2** used are commercial (methyl pyruvate **2a**, methyl benzoylformate **2b**, diethyl mesoxalate **2c**) or have been prepared by a Friedel–Crafts reaction between the ester chloride of oxalic acid ($ClCOCO_2C_2H_5$) and the appropriate aromatic derivative. The structure of these α-keto esters has been verified by ^{1}H NMR.

[††] 1 mmHg=133.322 Pa.

(dd, J=9 and 3 Hz, 1H, H_6), 7.37—7.50 (m, 3H, $H'_3+H'_4+H'_5$), 7.62 (d, J=9 Hz, 1H, H_5), 8.17—8.33 (m, 2H, $H'_2+H'_6$). UV-visible: λ_{max} 440 ($CHCl_3$), 443 nm (DMF); fluorescence: 520 ($CHCl_3$), 551 nm (DMF). IR (KBr): 1728 (s), 1620 cm^{-1} (s).

7-Diethylamino-3-phenyl-2*H*-1,4-benzoxazin-2-one (3d). Yield: 60% (Method B). Yellow crystals, mp 101 °C (cyclohexane). Found: C, 73.22; H, 6.21; N, 9.48%. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52%. ^1H NMR ($CDCl_3$) δ=1.19 (t, J=7 Hz, 6H, $N(CH_2C\underline{H}_3)_2$-7), 3.35 (q, J=7 Hz, 4H, $N(C\underline{H}_2CH_3)_2$-7), 6.25 (d, J=3 Hz, 1H, H_8), 6.47 (dd, J=9 and 3 Hz, 1H, H_6), 7.15—7.37 (m, 5H, H aromatic phenyl-3), 7.40 (d, J=9 Hz, 1H, H_5). UV-visible: λ_{max} 450 ($CHCl_3$), 462 nm (DMF); fluorescence: 520 ($CHCl_3$), 550 nm (DMF). IR (KBr): 1730 (s), 1620 cm^{-1} (s).

7-Dimethylamino-3-ethoxycarbonyl-2*H*-1,4-benzoxazin-2-one (3e). Yield: 70% (Method A); red crystals, mp 153—154 °C (ethanol). Found: C, 59.77; H, 5.39; N, 10.65% Calcd for $C_{13}H_{14}N_2O_4$: C, 59.53; H, 5.38; N, 10.68%. ^1H NMR ($CDCl_3$) δ=1.43 (t, J=7 Hz, 3H, $CO_2CH_2C\underline{H}_3$-3), 3.15 (s, 6H, $N(C\underline{H}_3)_2$-7), 4.43 (q, J=7 Hz, 2H, $CO_2C\underline{H}_2CH_3$), 6.35 (d, J=3 Hz, 1H, H_8), 6.72 (dd, J=9 and 3 Hz, 1H, H_6), 7.64 (d, J=9 Hz, 1H, H_5). UV-visible: λ_{max} 457 ($CHCl_3$), 455 nm (DMF); fluorescence: 517 ($CHCl_3$), 538 nm (DMF). IR (KBr): 1760 (s), 1625 cm^{-1} (s).

7-Diethylamino-3-ethoxycarbonyl-2*H*-1,4-benzoxazin-2-one (3f). Yield: 27% (Method B); orange crystals, mp 68—69 °C (ethanol-water). Found: C, 62.13; H, 6.28; N, 9.33%. Calcd for $C_{15}H_{18}N_2O_4$: C, 62.06; H, 6.26; N, 9.65%. ^1H NMR ($CDCl_3$) δ=1.22 (t, J=7 Hz, 6H, $N(CH_2C\underline{H}_3)_2$-7), 1.39 (t, J=7 Hz, 3H, $CO_2CH_2C\underline{H}_3$-3), 3.47 (q, J=7 Hz, 4H, $N(C\underline{H}_2CH_3)_2$-7), 4.47 (q, J=7 Hz, 2H, $CO_2C\underline{H}_2CH_3$-3), 6.40 (d, J=3 Hz, 1H, H_8), 6.75 (dd, J=9 and 3 Hz, 1H, H_6), 7.65 (d, J=9 Hz, 1H, H_5). UV-visible: λ_{max} 420 ($CHCl_3$), 462 nm (DMF); fluorescence: 450 ($CHCl_3$), 538 nm (DMF). IR (KBr): 1770 (s), 1628 cm^{-1} (s).

7-Dimethylamino-3-(*p*-(dimethylamino)phenyl)-2*H*-1,4-benzoxazin-2-one (3q). Yield: 75% (Method A); red crystals, mp 222 °C ($CHCl_3$–ethanol). Found: C, 69.18; H, 6.17; N, 13.44%; Calcd for $C_{18}H_{19}N_3O_2$: C, 69.88; H, 6.99; N, 13.58%. ^1H NMR ($CDCl_3$) δ=3.07 (s, 12H, $N(C\underline{H}_3)_2$-7 and -4′); 6.37 (d, J=3 Hz, 1H, H_8), 6.60 (dd, J=9 and 3 Hz, 1H, H_6), 6.70 (d, J=9 Hz, 2H, $H'_3+H'_5$), 7.52 (d, J=9 Hz, 1H, H_5), 8.25 (d, J=9 Hz, 2H, $H'_2+H'_6$). UV-visible: λ_{max} 467 ($CHCl_3$), 468 nm (DMF); fluorescence: 584 ($CHCl_3$), 586 nm (DMF). IR (KBr): 1725 (s), 1615 cm^{-1} (s).

7-Dimethylamino-3-(*p*-methoxyphenyl)-2*H*-1,4-benzoxazin-2-one (3h). Yield: 40% (Method A); red crystals, mp 177—178 °C ($CHCl_3$–ethanol). Found: C, 68.40; H, 5.45; N, 9.35%. Calcd for $C_{17}H_{16}N_2O_3$: C, 68.91; H, 5.44; N, 9.35%. ^1H NMR ($CDCl_3$) δ=3.07 (s, 6H, $N(C\underline{H}_3)_2$-7), 3.87 (s, 3H, OCH_3-4′), 6.40 (d, J=3 Hz, 1H, H_8), 6.63 (dd, J=9 and 3 Hz, 1H, H_6), 5.97 (d, J=9 Hz, 2H, $H'_3+H'_5$), 7.55 (d, J=9 Hz, 1H, H_5), 8.23 (d, J=9 Hz, 2H, $H'_2+H'_6$). UV-visible: λ_{max} 444 ($CHCl_3$), 445 nm (DMF); fluorescence: 530 ($CHCl_3$), 550 nm (DMF). IR (KBr): 1726 (s), 1630 (s), 1605 cm^{-1} (s).

7-Dimethylamino-3-(naphthyl)-2*H*-1,4-benzoxazin-2-one (3i). Yield: 59% (Method A); orange red crystals, mp 182 °C ($CHCl_3$–ethanol). Found: C, 75.90; H, 5.08; N, 8.75%. Calcd for $C_{20}H_{16}N_2O_2$: C, 75.93; H, 5.10; N, 8.86%. ^1H NMR ($CDCl_3$) δ=3.05 (s, 6H, $N(C\underline{H}_3)_2$-7); 6.42 (d, J=9 Hz, 1H, H_5), 6.66 (dd, J=9 and 3 Hz, 1H, H_6), 7.64 (d, J=9 Hz, 1H, H_5), 8.35 (dd, J=9 and 3 Hz, 1H, H_2), 7.40—8.12 (m, 6H, $H'_3+H'_4+H'_5+H'_6+H'_7+H'_8$). UV-visible: λ_{max} 445 ($CHCl_3$), 449 nm (DMF); fluorescence: 528 ($CHCl_3$), 557 nm (DMF). IR (KBr): 1728 (s); 1625 cm^{-1} (s).

Preparation of 7-dimethylamino-3-styryl-2*H*-1,4-benzoxazin-2-ones (5). A solution of 10 mmol of **3a** and 20 mmol of aromatic aldehyde **4** in 20 ml of acetic anhydride was refluxed for 7 h. In the case of *p*-nitrobenzaldehyde **4b**, the compound **5b** was obtained by filtration of the cooled mixture. In the case of the *p*-(dimethylamino)benzaldehyde **4a**, the compound **5a** was isolated after concentration and chromatography on silica gel using the chloroform as eluent.

7-Dimethylamino-3-(*p*-(dimethylamino)styryl)-2*H*-1,4-benzoxazin-2-one (5a). Yield: 6%; red crystals, mp 252 °C ($CHCl_3$–ethanol). Found: C, 71.53; H, 6.28; N, 12.58%. Calcd for $C_{20}H_{21}N_3O_2$: C, 71.62; H, 6.31; N, 12.53%. ^1H NMR ($CDCl_3$) δ=3.02 (s, 6H, $N(C\underline{H}_3)_2$-4′), 3.07 (s, 6H, $N(C\underline{H}_3)_2$-7), 6.43 (d, J=3 Hz, 1H, H_8), 6.67 (dd, J=9 and 3 Hz, 1H, H_6), 6.68 (d, J=9 Hz, 2H, $H'_3+H'_5$), 7.25 (d, J=16 Hz, 1H, H_β), 7.53 (d, J=9 Hz, 3H, $H_5+H'_2+H'_6$), 7.92 (d, J=16 Hz, 1H, H_α). UV-visible: λ_{max} 500 ($CHCl_3$), 495 nm (DMF); fluorescence: 616 ($CHCl_3$), 634 nm (DMF). IR (KBr): 1730 (s), 1632 (m), 1600 cm^{-1} (s).

7-Dimethylamino-3-(*p*-nitrostyryl)-2*H*-1,4-benzoxazin-2-one (5b). Yield: 64%; dark red crystals, mp 260 °C ($CHCl_3$). Found: C, 64.10; H, 4.54; N, 12.44%. Calcd for $C_{18}H_{15}N_3O_4$: C, 64.59; H, 4.48; N, 12.46%. This compound is nearly insoluble in NMR solvents and the spectrum cannot be registered. UV-visible: λ_{max} 496 ($CHCl_3$), 499 nm (DMF); fluorescence: 591 ($CHCl_3$), 682 nm (DMF). IR (KBr): 1737 (s), 1630 (s), 1615 (s), 1595 cm^{-1} (s).

Condensation of 3a with α-Ketoesters 2. A mixture of 5 mol of **3a**, 10 mmol of α-keto ester **2** and 5 mmol of anhydrous zinc chloride in 10 ml of acetic anhydride was refluxed for 1 h. After the removal of the solvent, the residue was washed with boiling methanol; the methanolic solution was evaporated and the residual oil was submitted to column chromatography on silica gel using the dichloromethane as eluent.

Methyl 3-(7-Dimethylamino-2-oxo-2*H*-1,4-benzoxazin-3-yl)-2-methylpropenoate (6a). Yield: 42%; red crystals, mp 174—175 °C ($CHCl_3$–methanol). Found: C, 62.27; H, 5.52; N, 9.22%. Calcd for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72%. ^1H NMR ($CDCl_3$) δ=2.42 (d, J=1.6 Hz, 3H, $C=C-C\underline{H}_3$): 3.08 (s, 6H, $N(C\underline{H}_3)_2$-7), 3.82 (s, 3H, $CO_2C\underline{H}_3$), 6.37 (d, J=3 Hz, 1H, H_8), 6.66 (dd, J=9 and 3 Hz, 1H, H_6), 7.52 (d, J=9 Hz, 1H, H_5), 7.88 (q, J=6 Hz, 1H, $\underline{H}C=C-CH_3$). UV-visible: λ_{max} 469 ($CHCl_3$), 476 nm (DMF); fluorescence: 536 ($CHCl_3$), 572 nm (DMF). IR (KBr): 1730 (s), 1710 (s), 1630 cm^{-1} (s).

Methyl 3-(7-Dimethylamino-2-oxo-2*H*-1,4-benzoxazin-3-yl)-2-phenylpropenoate (6b). Yield: 21%; red crystals, mp 188 °C ($CHCl_3$–methanol). Found: C, 67.92; H, 5.17; N, 7.96%. Calcd for $C_{20}H_8N_2O_4$: C, 68.56; H, 5.18; N, 8.00%. ^1H NMR ($CDCl_3$) δ=3.08 (s, 6H, $N(C\underline{H}_3)_2$-7), 3.95 (s, 3H, $CO_2C\underline{H}_3$), 6.38 (d, J=3 Hz, 1H, H_8), 6.65 (dd, J=9 and 3 Hz, 1H, H_6), 7.20—7.70 (m, 7H, 5H aromatic+H_5+$\underline{H}C=C$-3). UV-visible: λ_{max} 483 ($CHCl_3$), 488 nm (DMF); fluorescence: 551 ($CHCl_3$), 583 nm (DMF). IR (KBr): 1740 (s), 1730 (s), 1620 cm^{-1} (s).

Diethyl (7-Dimethylamino-2-oxo-2*H*-1,4-benzoxazin-3-yl)-methylenemalonate. Yield: 47%; red crystals, mp 175 °C ($CHCl_3$–methanol). Found: C, 60.00; H, 5.57; N, 7.61%.

Calcd for $C_{18}H_{20}N_2O_6$: C, 59.59; H, 5.59; N, 7.77%. ^{1}H NMR ($CDCl_3$) δ=1.35 (t, J=7 Hz, 6H, $C(CO_2CH_2C\underline{H}_3)_2$), 3.13 (s, 6H, $N(C\underline{H}_3)_2$-7), 4.38 (q, J=7 Hz, 4H, $C(CO_2C\underline{H}_2CH_3)_2$), 6.38 (d, J=3 Hz, 1H, H_8), 6.67 (dd, J=9 and 3 Hz, 1H, H_6), 7.33 (d, J=9 Hz, 1H, H_5), 7.96 (s, 1H, $\underline{H}$-C=C($CO_2C_2H_5)_2$). UV-visible: λ_{max} 500 ($CHCl_3$), 510 nm (DMF); fluorescence: 557 ($CHCl_3$), 592 nm (DMF). IR (KBr): 1745 (s), 1700 (s), 1628 cm^{-1} (s).

Reactivity of the Ester Group on the 3 Position of the 1,4-Benzoxazin-2-one. 3-Carbamoyl-7-dimethylamino-2*H*-1, 4-benzoxazin-2-one (7a). A solution of 10 mmol of **3e** in a mixture of 50 ml of methanol and 5 ml of concentrated aqueous ammonia was refluxed during 15 min.

The amide **7a** was obtained by filtration of the cooled mixture. Yield: 86%; red crystals, mp>280 °C. Found: C, 56.82; H, 4.73; N, 18.16%. Calcd for $C_{11}H_{11}N_3O_3$: C, 56.65; H, 4.75; N, 18.02%. This compound is nearly insoluble in NMR solvents and so the spectrum cannot be registered. UV-visible: λ_{max} 470 ($CHCl_3$), 445 nm (DMF); fluorescence: 530 ($CHCl_3$), 540 nm (DMF). IR (KBr): 3420 and 3285 (-NH), 1710, 1620, 1595 cm^{-1} (s).

7-Dimethylamino-3-phenylcarbamoyl-2*H*-1,4-benzoxazin-2-one (7b). To a refluxed solution of 5 mmol of **3e** in 10 ml of xylene, 10 mmol of aniline were slightly added while azeotrope ethanol–xylene issued from the reaction is eliminated. After cooling the compound **7b** is isolated by filtration. Yield: 50%; red crystals, mp 241 °C ($CHCl_3$–methanol). Found: C, 65.77; H, 4.68; N, 13.54%. Calcd for $C_{17}H_{15}N_3O_3$: C, 66.01; H, 4.89; N, 13.59%. ^{1}H NMR ($CDCl_3$) δ=3.18 (s, 6H, $N(C\underline{H}_3)_2$-7), 6.46 (d, J=3 Hz, 1H, H_8), 6.80 (dd, J=9 and 3 Hz, 1H, H_6), 7.0—7.6 (m, 3H, H_5+2H (*o*)N-aromatic group), 7.7—8.0 (m, 3H, 2H(*m*)+1H(*p*)N-aromatic group), 10.60 (s, large, 1H, $N\underline{H}C_6H_5$). UV-visible: λ_{max} 476 ($CHCl_3$), 474 nm (DMF): fluorescence: 524 ($CHCl_3$), 522 nm (DMF). IR (KBr): 3285 (s, -NH), 1710 (s), 1625 (s), and 1598 cm^{-1} (s).

3-Cyano-7-dimethylamino-2*H*-1,4-benzoxazin-2-one (8). A mixture of 10 mmol of amide **7a** and of 10 mmol of P_2O_5 was heated cautiously on the flame until near 100 °C. At this temperature the reaction starts violently and it can be slowed by rapid cooling. The residue was then extracted by boiling chloroform, the compound **8** then purified by submitting to column chromatography on silica gel, using the chloroform as eluent. Yield: 23%; red crystals, mp 260 °C. Found: C, 61.30; H, 4.31; N, 19.02%. Calcd for $C_{11}H_9N_3O_2$: C, 61.39; H, 4.22; N, 19.53%. ^{1}H NMR (DMSO-d_6) δ=3.22 (s, 6H, $N(C\underline{H}_3)_2$-7), 6.43 (d, J=3 Hz, 1H, H_8), 6.77 (dd, J=9 and 3 Hz, 1H, H_6), (7.68 (d, J=9 Hz, 1H, H_5). UV-visible: λ_{max} 476 ($CHCl_3$), 478 nm (DMF); fluorescence: 523 ($CHCl_3$), 548 nm (DMF). IR (KBr) 2212 (s, C≡N), 1722 (s), 1625 cm^{-1} (s).

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