Synthesis of Some Coumarin Derivatives as Potential Laser Dyes

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With a view to extend the tunability range and maximum output of the coumarin series of dyes, 15 new 3-substituted 7-hydroxycoumarins emitting in the blue-green region of the visible spectrum are synthesized, some of which show laser activity.

Several 3-substituted 7-hydroxycoumarins rank among the most efficient photostable laser dyes emitting in the blue-green region of the visible spectrum. The lasing range covered by coumarin dyes is appreciably extended when the 3-substituent is a heterocyclic moiety.[1,2] Therefore it seemed relevant to design and synthesize 7-hydroxycoumarins bearing different heterocycles at the 3-position with the aim to obtain a new photostable laser dyes having rigid structures that are tunable over a wide wavelength range within the visible spectrum.

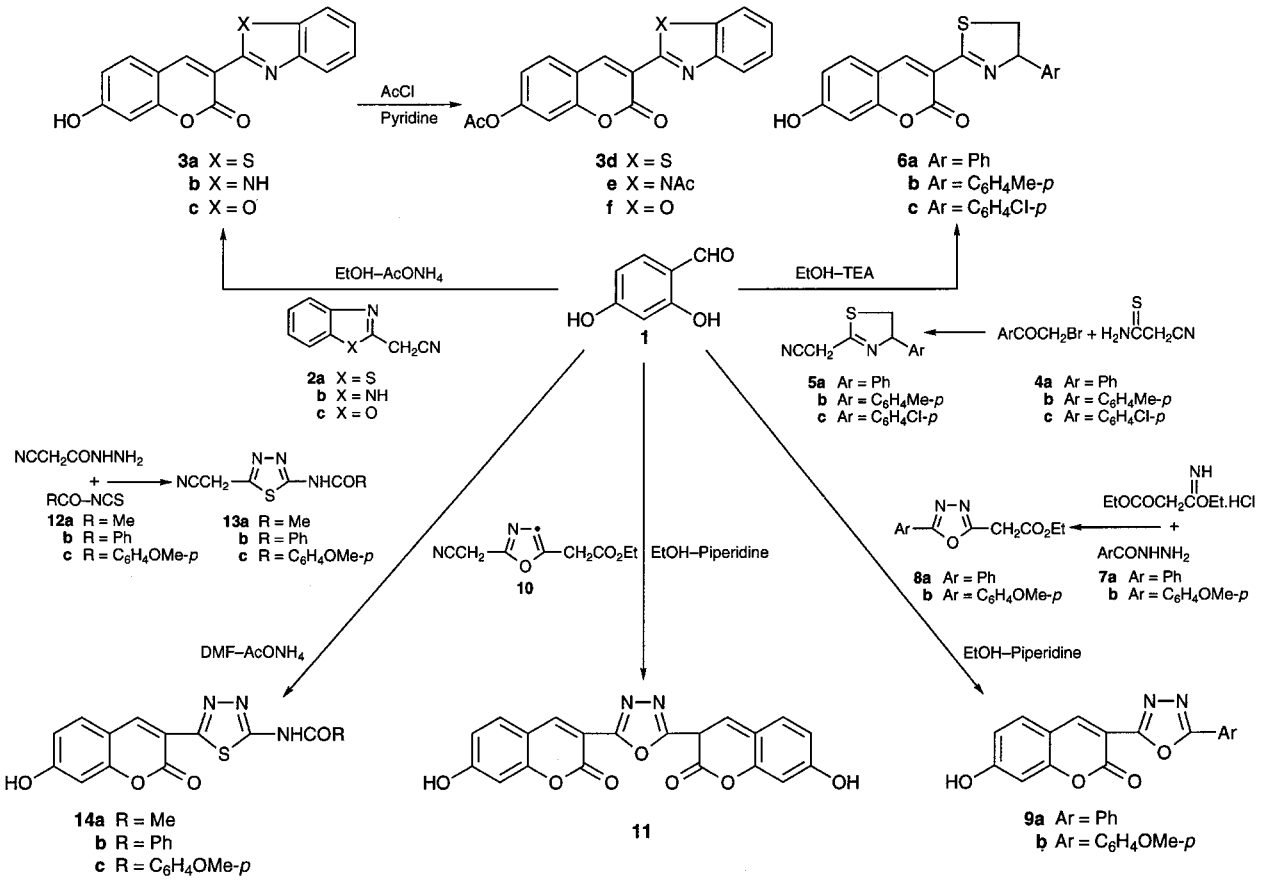
This approach was also stimulated by the assumption that the introduction of biologically active heterocycles at the 3-position of 7-hydroxycoumarin may lead to physiologically active fluorescent compounds of general and analytical biological interest.

The syntheses of the new 3-substituted 7-hydroxycoumarins from *β*-resorcylaldehyde (2,4-dihydroxybenzaldehyde; **1**) are outlined in the Scheme.

The 3-benzothiazolyl, 3-benzimidazolyl and 3-benzoxazolyl derivatives of 7-hydroxycoumarin **3a–c** were synthesized *via* condensation of *β*-resorcylaldehyde (**1**) with benzothiazol-2-ylacetonitrile (**2a**),[3] 1*H*-benzimidazol-2-ylacetonitrile (**2b**)[4] and benzoxazol-2-ylacetonitrile (**2c**),[5] respectively.

Solutions of these 7-hydroxycoumarins in different organic solvents were found to be strongly fluorescent. In order to investigate the effect of introducing an acetoxy group at position 7 on the fluorescence properties of these compounds, the 3-(benzazol-2-yl)-7-acetoxycoumarins **3d–f** were prepared by acetylating compounds **3a–c**.

The strongly fluorescent 3-thiazolyl-7-hydroxycoumarins **6a–c** were obtained by the reaction of **1** with 4-aryl-2-cyanomethyl-1,3-thiazoles **5a–c**. 2-Cyanomethyl-4-phenyl-1,3-thiazole (**5a**)[6] was obtained by the reaction of *ω*-bromoacetophenone (**4a**) with cyanothioacetamide. Likewise, the same method was adopted for the preparation of the novel 2-cyanomethyl-4-*p*-tolyl-1,3-thiazole (**5b**) and 4-*p*-chloro-



Scheme

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phenyl-2-cyanomethyl-1,3-thiazole (**5c**), using ω-bromo-4-methylacetophenone (**4b**) and ω-bromo-4-chloroacetophenone (**4c**), respectively.

Condensing **1** with ethyl (5-aryl-1,3,4-oxadiazol-2-yl)acetate **8a–b** in ethanol containing piperidine as a catalyst afforded the 3-(5-aryl-1,3,4-oxadiazol-2-yl)-7-hydroxycoumarins **9a–b**. Compound **8a**[7] was obtained by the reaction of ethyl 3-ethoxy-3-iminopropanoate hydrochloride with benzoylhydrazine (**7a**). The same method was used to prepare the unreported ethyl (5-*p*-anisyl-1,3,4-oxadiazol-2-yl)acetate (**8b**) utilising *p*-anisoylhydrazine (**7b**).

Many dicoumarins show intensive anticoagulant activity and are used in the therapy of thromboembolisms. Hence it seemed worth synthesizing the dicoumarin **11**, which was accomplished by condensing **1** with ethyl (5-cyanomethyl-1,3,4-oxadiazol-2-yl)acetate (**10**)[8] in a 2:1 molar ratio in ethanol in presence of piperidine as a catalyst.

The preparation of the 3-thiadiazolyl-7-hydroxycoumarins **14a–c** was achieved by reacting **1** with the appropriate 2-acylamino-5-cyanomethyl-1,3,4-thiadiazoles **13a–c**. The thiadiazoles **13a**[9] and **13b**[10] were synthesized by treating 2-cyanoacetohydrazide with acetyl isothiocyanate (**12a**) and benzoyl isothiocyanate (**12b**), respectively. The novel 2-*p*-anisoylamino-5-cyanomethyl-1,3,4-thiadiazole (**13c**) was prepared in a similar manner using *p*-anisoyl isothiocyanate (**12c**).

With a view to standardize the parameters to make the present dyes effective in the field of lasers, a study of their electronic absorption emission and excitation spectra in different organic solvents was carried out. The effects of acidity and temperature as well as dye concentration on their optical properties were also explored. The fluorescence quantum yields (ϕ_f) of these dyes are high and some showed lasing activity upon pumping with an N_2 laser.

The newly synthesized compounds showed variable antibacterial activities against some Gram positive, Gram negative and acid fast bacteria. Only the thiazole and the thiadiazole derivatives **3a**, **6a–c** and **14a–c** showed significant activity against the acid fast *Mycobacterium phlei*, probably due to their ability to penetrate the lipid-rich cell wall which is resistant to acids, alkalis and chemical disinfectants. However, all compounds showed no significant activity against *Pseudomonas* fluorescence which is resistant to most antimicrobial agents.

Techniques used: ^{1}H NMR, IR, UV–VIS, MS

References: 10

Scheme: 1

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