

## PHOTOCHEMICAL REACTIONS OF 7-AMINOCOUMARINS.

### 10.\* REACTION OF 3-IODO-4-METHYL-7-DIETHYLAMINOCOUMARIN WITH HETEROAROMATIC COMPOUNDS

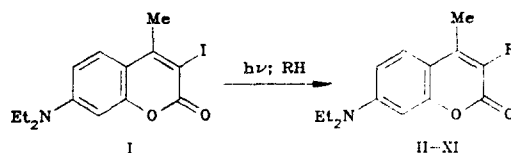
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UDC 547.587.51

*Photolysis of 3-iodo-4-methyl-7-diethylaminocoumarin in the presence of N-methylpyrrole, furan, thiophene, selenophene, pyridine, indole, imidazole, and benzimidazole results in the formation of a series of 3-hetaryl-7-aminocoumarins. The spectral luminescence characteristics of these newly synthesized compounds have been investigated.*

We have previously [2, 3] reported that photochemical reactions of 3-iodo-4-methyl-7-diethylaminocoumarin (I) with olefins and monosubstituted benzenes lead to the formation of 3-substituted 7-aminocoumarins. In the present paper we have examined the analogous reactions with heteroaromatic compounds, for the purposes of preparing 3-hetaryl-7-aminocoumarin derivatives, which are potential laser dyes [4].

Treatment of coumarin I with N-methylpyrrole, furan, thiophene, selenophene, pyridine, indole, imidazole, and benzimidazole in solutions with these heteroaromatic compound solvents, or in acetonitrile or DMSO solution in the case of crystalline reagents, leads to the formation of 3-hetaryl-substituted coumarins II-XI in yields of 10-40% at 60-100% conversion. The side products in the photolysis of coumarin I are 4-methyl-7-diethylaminocoumarin and N-deethylation products [5].



II R = 2-(N-methylpyrrolyl); III R = 2-furyl; IV R = 2-thienyl; V R = 2-selenienyl VI R = 2-pyridyl; VII R = 3-pyridyl; VIII R = 4-pyridyl; IX R = 3-indolyl; X R = 2-imidazolyl; XI R = 2-benzimidazolyl

In the case of reaction with imidazole and benzimidazole, products resulting from substitution at the 4-CH<sub>3</sub> group were isolated as the predominant products, in addition to coumarins X and XI [6]. In all of the reactions the formation of a small amount of iodine was observed. The use of solvents (CH<sub>3</sub>CN, DMSO, CH<sub>2</sub>Cl<sub>2</sub>, 1,4-dioxane, etc.) reduced the yields of the desired products; we therefore excluded, to the degree possible, the use of solvent.

The structures of these newly synthesized compounds were established spectroscopically (Tables 1-3). The presence in the IR spectra of coumarins II-XI of absorption bands for a lactonic carbonyl group in the 1670-1710 cm<sup>-1</sup> region provides evidence for the retention of the coumarin structure. The pattern for dissociative ionization of hetaryl coumarins II-XI under elec-

\*For communication 9, see [1].

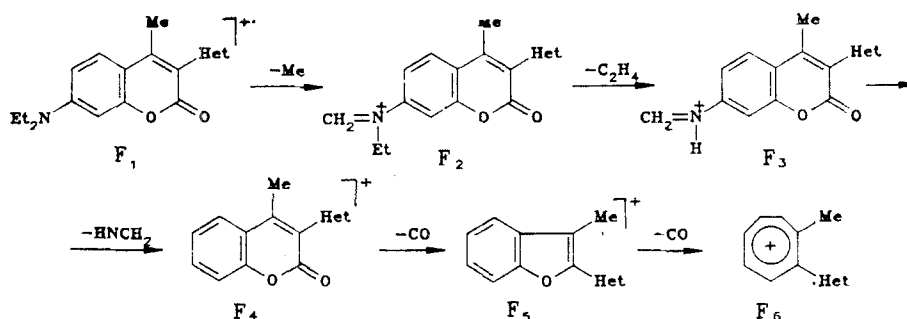
TABLE 1. Physical Characteristics of Newly Synthesized Compounds\*

Compound	Molecular formula	mp, °C	$R_f^{**}$ (system)	$\nu_{C=O}$ , cm <sup>-1</sup>	UV spectrum		$\lambda_{max}^{em}$ , nm	$\phi_f$	Quantum reaction yield	Yield, %	Conversion, %
					$\lambda_{max}^{ab}$ , nm	lg $\epsilon$					
II	C <sub>19</sub> H <sub>22</sub> N <sub>2</sub> O <sub>2</sub>	171	0,15 A	1690	390	4,56	490	0,63	0,335	31	90
III	C <sub>18</sub> H <sub>19</sub> NO <sub>3</sub>	65	0,35 A	1700	397	4,43	495	0,60	0,288	21	50
IV	C <sub>18</sub> H <sub>19</sub> NO <sub>2</sub> S	116	0,35 A	1700	395	4,49	500	0,37	0,221	40	100
V	C <sub>18</sub> H <sub>19</sub> NO <sub>2</sub> Se	101	0,35 A	1685	397	4,53	510	0,24	0,183	22	60
VI	C <sub>19</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub>	73	0,24 B	1700	390	4,56	475	0,67	—	8	80
VII	C <sub>19</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub>	124	0,18 B	1695	390	4,50	475	0,65	0,004	26	80
VIII	C <sub>19</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub>	160	0,13 B	1705	394	4,51	485	1,00	—	10	80
IX	C <sub>22</sub> H <sub>22</sub> N <sub>2</sub> O <sub>2</sub>	202	0,37 A	1670	397	4,48	510	<0,1	—	29	90
X	C <sub>17</sub> H <sub>19</sub> N <sub>3</sub> O <sub>2</sub>	196	0,38 C	1710	396	4,51	490	0,88	—	15	75
XI	C <sub>21</sub> H <sub>21</sub> N <sub>3</sub> O <sub>2</sub>	237	0,58 C	1675	400	4,47	495	0,90	—	10	60

\*UV and luminescence spectra were measured in ethanol solution.

\*\*A) Benzene-acetone, 20:1; B) hexane-acetone, 1:1; C) hexane-acetone, 3:1.

iron impact condition is typical of 7-diethylaminocoumarins [7], and involves fragmentation of the diethylamino group (with subsequent cleavage of CH<sub>3</sub>, C<sub>2</sub>H<sub>4</sub>, CH<sub>3</sub>N groups) and disruption of the benzopyran structure (via loss of two CO groups); cleavage of the coumarin-heterocycle bonds was not detected.



In the PMR spectra of these 3-hetaryl-substituted coumarin derivatives II-XI (Table 2) the signals for the protons in the coumarin fragment appear in their normal range [8]. The 4-CH<sub>3</sub> and 5-H proton signals in coumarins X and XI are shifted strongly downfield relative to 4-methyl-7-diethylaminocoumarin; this can be attributed apparently to planarization of the bis(hetaryl) system. An analogous downfield shift for the 4-H signal in 3-(2-benzimidazolyl)-7-diethylaminocoumarin may be the result of intramolecular hydrogen bond formation, since in the case of the N-methylbenzimidazolyl derivative this effect is not observed [8]. The significant downfield shift observed for the methyl protons in coumarin IX may be due to the deshielding effect of the benzene ring in the indolyl substituent group.

Previous <sup>13</sup>C-NMR studies of 3-(2-benzimidazolyl)-, 3-(2-N-methylbenzimidazolyl)-, and 3-(2-benzthiazolyl)-7-diethylaminocoumarins have demonstrated that these hetaryl substituents effect only a weak change in the  $\pi$ -electron density distribution of the coumarin ring [8]. We assumed, therefore, that the presence of a methyl group in the 4-position of the coumarin ring would lead to an even greater reduction in  $\pi$ , $\pi$ -conjugation between the heterocyclic systems, due to an increase in the angle at which they are turned away from one another. Based on this scenario, we anticipated the  $\sigma$ -acceptor (electron withdrawing) character of the 3-coumarinyl substituent to predominate. It was found, in fact, that the distant  $\gamma$ - and  $\delta$ -protons in coumarins II-IX are deshielded ( $\Delta\delta$  0.2-0.4 ppm) relative to their heterocycle precursors, which means that the 3-coumarinyl substituent approaches a phenyl group substituent in terms of its electronic effect on heterocycles [9].

The weak degree of  $\pi$ , $\pi$ -conjugation in coumarins II-XI was also confirmed by their electronic absorption spectra (Table 1); their long-wavelength maxima were found in a narrow range (390-400 nm), regardless of the nature of the heterocyclic substituent. The large bathochromic and bathofluoric shifts observed in the series of coumarins II  $\rightarrow$  IV  $\rightarrow$  V may be rationalized in terms of enhanced conjugative stabilization in this series due to increased polarizability of the heteroatom electron

TABLE 2. PMR Spectra of Compounds II-XI

Com- pound	Chemical shifts, $\delta$ , ppm (SSCC, Hz)						
	5-H, d (9.0)	6-H, dd	8-H, d (2.5)	NCH <sub>3</sub> , q (7.0)	CH <sub>2</sub> , t (7.0)	4-CH <sub>3</sub> , s	Other protons
II	7.47	6.63	6.52	3.43	1.20	2.29	3.49 (3H, s, NCH <sub>3</sub> ); 6.08 (1H, dd, $J=3.5$ ); $J=1.7$ ; 3'-H); 6.19 (1H, dd, $J=3.5$ ; $J=3.0$ ); 4'-H); 6.72 (1H, dd, $J=3.0$ ; $J=1.7$ ; 5'-H)
III	7.52	6.63	6.52	3.43	1.22	2.48	6.52 (1H, dd, $J=3.4$ ; $J=1.6$ ; 4'-H); 6.77 (1H, d, $J=3.4$ ; 3'-H); 7.64 (1H, d, $J=1.6$ ; 5'-H)
IV	7.46	6.62	6.51	3.42	1.20	2.36	7.03 (1H, dd, $J=3.5$ ; $J=1.0$ ; 3'-H); 7.07 (1H, dd, $J=3.5$ ; $J=5.0$ ; 4'-H); 7.41 (1H, dd, $J=5.0$ ; $J=1.0$ ; 5'-H)
V	7.47	6.64	6.54	3.43	1.20	2.43	7.21 (1H, dd, $J=3.5$ ; $J=1.2$ ; 3'-H); 7.31 (1H, dd, $J=3.5$ ; $J=5.9$ ; 4'-H); 8.13 (1H, dd, $J=5.9$ ; $J=1.2$ ; 5'-H)
VI	7.53	6.66	6.57	3.45	1.24	2.30	7.30 (1H, ddd, $J=8.0$ ; $J=5.0$ ; $J=1.5$ ; 5'-H); 7.52 (1H, dd, $J=8.0$ ; $J=1.5$ ; 3'-H); 7.82 (1H, ddd, $J=8.0$ ; $J=8.0$ ; $J=1.5$ ; 4'-H); 8.75 (1H, dd, $J=5.0$ ; $J=1.5$ ; 6'-H)
VII	7.57	6.75	6.52	3.51	1.20	2.25	7.42 (1H, dd, $J=7.6$ ; $J=5.0$ ; 5'-H); 7.72 (1H, ddd, $J=7.6$ ; $J=2.4$ ; 2'-H); 8.54 (1H, dd, $J=5.0$ ; $J=1.8$ ; 6'-H)
VIII	7.47	6.63	6.52	3.43	1.22	2.26	8.52 (1H, d, $J=2.4$ ; 2'-H); 8.68 (2H, br. s, 2'-H, 6'-H)
IX	7.57	6.67	6.55	3.45	1.23	2.71	6.66 (1H, dd, $J=2.5$ ; $J=1.0$ ; 2'-H); 7.12 (1H, ddd, $J=8.0$ ; $J=1.0$ ; 5'-H); 7.44 (1H, ddd, $J=8.0$ ; $J=7.0$ ; $J=1.0$ ; 4'-H); 10.02 (1H, br. s, NH)
X	7.63	6.67	6.49	3.42	1.21	3.01	$J=1.0$ ; 7'-H); 7.64 (1H, ddd, $J=8.0$ ; $J=1.0$ ; $J=1.0$ ; 4'-H); 10.02 (1H, br. s, NH)
XI	7.68	6.69	6.51	3.45	1.21	3.19	7.27 (2H, dd, $J=6.5$ ; $J=3.0$ ) } 4'-H, 5'-H, 6'-H, 7'-H 7.68 (2H, m)

TABLE 3. Mass Spectra of Compounds II-XI

Compound	M <sup>+</sup>	Characteristic peak intensities <sup>**</sup>					
		F <sub>1</sub>	F <sub>2</sub>	F <sub>3</sub>	F <sub>4</sub>	F <sub>5</sub>	F <sub>6</sub>
II	310	100	100	15	19	5	7
III	297	85	100	10	7	5	5
IV	313	86	100	11	9	5	5
V	360	78	100	13	12	6	5
VI <sup>**</sup>	308	82	75	15	6	5	7
VII	308	54	100	17	13	8	9
VIII	308	61	100	17	10	6	8
IX	346	98	100	24	25	7	6
X	297	16	100	12	9	6	8
XI	347	100	83	8	8	5	8

\*In percent of maximum.

\*\*The 100% peak is at m/z 188.

pairs, and, consequently, to the feasibility of a higher degree of planarity of the (heterocyclic) systems. This assumption is at least qualitatively supported by the small, yet nonetheless systematic, downfield shifts observed for the 4-methyl group proton signals in the PMR spectra of these compounds (Table 2). Coumarin III appears to be an exception to this pattern; based on its spectral characteristics (Tables 1 and 2) the efficiency of resonance conjugation in this compound appeared to be higher than expected on the basis of the electron donating ability of the furyl substituent [10]. This fact would seem to be related to decreased steric hindrance in the transition to a more compact hetaryl substituent fragment.

The emission bands in the luminescence spectra of these compounds are more sensitive to the effect of the hetaryl substituent. Coumarins II-XI fluoresce in the range 475-510 nm; compounds VIII, X, and XI display especially strong fluorescence ( $\phi_f^{C_2H_5OH}$  0.9-1.0). In the series of coumarins III  $\rightarrow$  IV  $\rightarrow$  V a fluorescence quenching effect due to the presence of heavy atoms is apparent [11]. In a somewhat unexpected effect, coumarins VI-VIII exhibited a hypsofluoric shift of their emission bands, compared to the other compounds in the series. These data suggest a weak interaction of the 3-pyridyl substituents with the electron density distribution in the singlet excited state, in analogy with the behavior of 3-aryl-substituted 7-aminocoumarins [12]. The observation of practically complete luminescence quenching in the case of the 3-indolyl-coumarin IX can be interpreted in terms of internal singlet-triplet energy transfer in this bis(hetaryl) system.

The same characteristic principles governing the photosubstitution reactions of 3-iodocoumarin I with olefins and mono-substituted benzenes [2, 3] apply to the photohetarylation reaction studied herein: the formation of significant amounts of iodine during the course of the reactions, process quenching upon the addition of polyhalomethanes and hydrogen donors, and the fact that the reactions take place despite differences in the electronic properties of the reagents. We postulate, therefore, that a radical mechanism involving 3-coumarinyl radicals is operative in this case as well. Measurement of the quantum yields for the formation of coumarins II-V and VII (Table 1) has provided the data to show that photochemical substitution occurs an order of magnitude faster (or more) with electron-rich five-membered ring heterocycles than with pyridine. Comparison of the reaction of coumarin I with N-methylpyrrole, furan, thiophene, and selenophene indicates that the efficiency of this photosubstitution process decreases in the same order as the reduction in reactivity of these enumerated heterocycles with respect to electrophilic substitution reactions [13], which is consistent with data reported previously concerning the electrophilic properties of the coumarinyl radical [2, 3].

## EXPERIMENTAL

The IR spectra were recorded on a Perkin-Elmer 577 spectrophotometer (using KBr pellets); the UV spectra and luminescence spectra were measured on an EPS-3T spectrophotometer equipped with a luminescence accessory G3. The relative quantum yields for luminescence were determined based on 3-aminophthalimide [14]. The PMR spectra were recorded on a Bruker WM (250 MHz) spectrometer using CDCl<sub>3</sub> solutions versus HMDS as internal standard. Mass spectra were obtained on a Varian MAT-311A spectrometer (at an ionizing electron energy of 70 eV). The reaction products were isolated by column chromatography (40  $\times$  3.5 cm columns) filled with Silpearl UV-254 sorbent. Product purity was monitored by TLC on Silu-foi plates, which were visualized with UV light and iodine. The degree of conversion in each reaction was determined based

on the amount of residual unreacted coumarin I after column chromatography of the reaction mixture. Differential reaction quantum yields were calculated according to a previously published procedure [15] and were determined for solutions of coumarin I at a concentration of 0.05 mole/liter in the appropriate heterocyclic compounds as solvents, upon irradiation with 370-nm wavelength light, which was obtained using a Shimadzu NGF-16 monochromator. The source intensity  $I_0$  was determined using a standard method [15] and was equal to  $3.72 \cdot 10^{-10}$  einstein/sec. Quantitative estimates of the reaction products formed were made using a Shimadzu CS-930 densitometer after separation of the reaction mixtures on Kieselgel 60 (Merck).

**General Method for the Preparation of Coumarins II-IX.** A solution of 1 g coumarin I in 100 ml of the appropriate heteroaromatic compound (or, in the case of reaction with indole, in 100 ml, a saturated solution of indole in  $\text{CH}_3\text{CN}$ ) was irradiated with a medium pressure mercury lamp PRK-2 in a glass reactor (100-ml volume); the solution was stirred under nitrogen and irradiated for 12-24 h. The reaction mixture was evaporated and the residue separated by chromatography (for compounds II-V and IX with benzene eluent, for VI-VIII with hexane-acetone, 5:1); the products isolated by chromatography were then crystallized from a mixture of hexane and acetone.

**3-(2-Imidazolyl)-4-methyl-7-diethylamino-2H-benzopyran-2-one (X).** A solution of 1 g (3 mmoles) coumarin I and 21 g (0.3 mole) imidazole in 100 ml acetonitrile was irradiated for 18 h. The reaction mixture was evaporated and the residue dissolved in 100 ml ethyl acetate and washed with water ( $4 \times 50$  ml). The ethyl acetate layer was evaporated and the residue separated by column chromatography with hexane-acetone eluent (10:1)  $\rightarrow$  (1:1).

**3-(2-Benzimidazolyl)-4-methyl-7-diethylamino-2H-benzopyran-2-one (XI).** A solution of 1 g (3 mmoles) coumarin I and 36 g (300 mmoles) benzimidazole in 100 ml DMSO was irradiated for 24 h; the reaction mixture was then diluted twofold with water and extracted with chloroform. The chloroform layers were combined, evaporated, and the residue separated by column chromatography with hexane-acetone eluent (10:1)  $\rightarrow$  (2:1).

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