PHOTOCHEMICAL REACTIONS OF 7-AMINOCOUMARINS.

6.* REACTION OF 7-DIALKYLAMINOCOUMARINS WITH HALO DERIVATIVES

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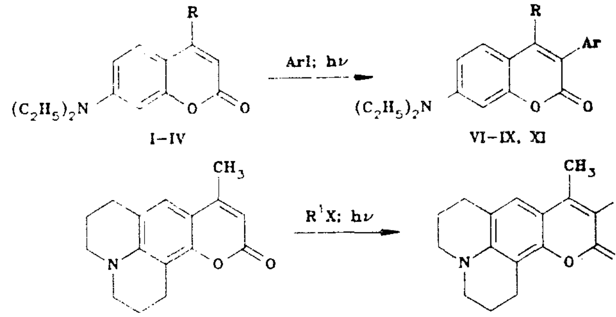
3-Substituted 7-dialkylaminocoumarins were synthesized as a result of the photoreaction of 7-diethylaminocoumarin, 4-trifluoromethyl-7-diethylaminocoumarin, 4-chloro-7-diethylaminocoumarin, 4-(N-morpholino)-7-diethylaminocoumarin, and coumarin-102 (2,3,6,7-tetrahydro-9-methyl-1H,5H,11H-[1]-benzopyrano[6,7,8-ij]quinolizin-11-one) with iodobenzene, 3,4-dimethoxyiodobenzene, isopropyl iodide, and ethyl a-bromoacetate. It was established that electron-acceptor and electron-donor substituents in the 4 position accelerate photosubstitution. The spectral-luminescence characteristics of the compounds obtained were investigated.

We have previously investigated [2] the photochemical reactions of 4-methyl-7-diethylaminocoumarin with alkyl and aryl halides and found that they lead to the synthesis of 3-substituted 7-aminocoumarins. It was shown that reactions of this type are accelerated by the addition of triethylamine and proceed via a radical (or ion-radical) mechanism.

In order to study the effect of a substituent in the 4 position on the effectiveness of photosubstitution we investigated the reaction of coumarins I-V with iodobenzene, as a result of which we obtained 3-phenylcoumarins VI-X in 15-20% yields vis-a-vis 50-70% conversion. The use of triethylamine as an additive makes it possible to increase the preparative yields of VI, IX, and X to 30-40% and the conversion to 70-90% (Table 1). In the case of coumarins II and III, the use of triethylamine did not lead to an increase in the yields of 3-phenyl derivatives VII and VIII. A common feature of the photoreactions under consideration is the formation of side products of N-de-ethylation [3].



I-IV

VI-IX, XI

V

X, XII, XIII

I, VI R=H; II, VII, XI R=CF_3; III, VIII R=Cl; IV, IX R=$N(CH_2CH_2)_2O$; VI—IX Ar=C_6H_5; XI Ar=3,4-$(CH_3O)_2C_6H_3$; X $R^1=C_6H_5$; XII $R^1=i\text{-}C_3H_7$; XIII $R^1=CH_2CO_2C_2H_5$; X=Br, I

The structures of VI-IX as 3-substituted coumarins follow from the PMR spectra (Table 2) in which, as compared with the starting coumarins I-IV, a signal of a 3-H proton is absent. The signals of the remaining "coumarin" protons retain their structure and show up in the characteristic 6.6-7.7 ppm region [4]. A $^5J_{5\text{-H,F}}$ spin-spin coupling constant (SSCC) shows up distinctly in the PMR spectrum of coumarin VII, as a result of which the signal of the 5-H proton has the form of a doublet

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*For Communication 5, see [1].

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TABLE 1. Characteristics of Coumarins VI-XIII

Compound	Empirical formula	mp, °C	R_f*	$\nu_{C=O}$, cm^{-1}	Yield, %	Conversion, %	φ**
VI	$C_{19}H_{19}NO_2$	151***	0,46	1700	29	70	0,035
VII	$C_{20}H_{18}F_3NO_2$	120	0,53	1710	41	60	0,120
VIII	$C_{19}H_{18}ClNO_2$	124	0,48	1710	38	70	0,094
IX	$C_{23}H_{26}N_2O_3$	191	0,42	1690	33	85	0,077
X	$C_{22}H_{21}NO_2$	141	0,43	1695	35	90	0,063
XI	$C_{22}H_{22}F_3NO_4$	139	0,45	1715	27	75	0,022
XII	$C_{19}H_{23}NO_2$	128	0,59	1690	20	75	—
XIII	$C_{20}H_{23}NO_4$	116	0,47	1720, 1695	29	70	—

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*Hexane–acetone (3:1).

**Note that φ is the quantum yield of the reaction.

***Coincides with the data in [5].

TABLE 2. PMR Spectra of Coumarins VI-IX

Compound	Chemical shifts, δ, ppm (SSCC, J, Hz)					
	5-H, d (9,0)	6-H dd (9,0; 2,6)	8-H d (2,6)	7-NCH_2 q (7,0)	7-$N(CH_2CH_3)_2$ t (7,0)	Other protons
VI	7,29	6,63	6,56	3,42	1,21	7,30...7,45 (3H, m 3-H, 4-H and 5-H$_{arom}$); 7,70 (1H, s 4-H); 7,71 (2H, d 8,8, 2-H and 6-H$_{arom}$)
VII	7,60*	6,68	6,58	3,41	1,21	7,25 (2H, m, 3-H and 5-H$_{arom}$); 7,40 (3 H, m, 2-H, 4-H and 6-H$_{arom}$)
VIII	7,70	6,72	6,59	3,43	2,22	7,25...7,45 (5H, m, C_6H_5)
IX	7,54	6,69	6,60	3,41	1,20	2,84 (4H, t, $J=5,6$; 4-$N(CH_2)_2$); 3,70 (4H, t, $J=5,6$; $O(CH_2)_2$); 7,25...7,45 (5H, m, C_6H_5)

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*A doublet of quartets (J = 9.0 Hz, J = 2.5 Hz).

of quartets. In the case of IX the chemical shifts of the methylene protons of the morpholino substituent are found at stronger field as compared with coumarin IV; this constitutes evidence that they fall within the cone of the anisotropy of the aromatic ring and, consequently, indicates an out-of-plane orientation of the phenyl group.

The electronic spectra of VI-X in ethanol or acetonitrile contain an intense (log ε ~ 4.5) band of long-wave absorption at 380-415 nm and, as a rule, somewhat less-intense bands at 250-320 nm (Table 3). Compounds VI-X have fluorescence at 470-480 nm (Table 3). Coumarins VI and X fluoresce most intensely (φ_f ~ 0.7-0.9), while the fluorescence quantum yields (φ_f) do not exceed 0.1 for coumarins VII, VIII, and IX. The loss of luminescence properties in the case of coumarin VIII is reproduced regularly in a number of other 4-chloro-7-aminocoumarins [6]; however, the fact of the absence of luminescence for the 4-morpholino derivative is quite unexpected, since 4-morpholino-7-aminocoumarins usually are effective luminophores [7]. A common peculiarity of the examined absorption and emission bands in the spectra of 3-phenylcoumarins VI-X, as well as 3-phenyl-4-methyl-7-diethylaminocoumarin [2], is their shift to the long-wave region on passing from electron-donor to electron-acceptor substituents in the 4 position in the order $N(CH_2CH_2)_2O \rightarrow CH_3 \rightarrow H \rightarrow Cl \rightarrow CF_3$.

It was established that the investigated photoarylation reactions proceed most effectively in the case of irradiation with short-wave monochromatic light in the region of the absorption band of iodobenzene (255 nm) and virtually do not take place in the case of irradiation in the region of the absorption bands of 7-aminocoumarins I-V. In analogy with the photoreactions of 4-methyl-7-diethylaminocoumarin [2] it should be assumed that the key step in the photoreactions under consideration is the photodissocation of iodobenzene, which is accompanied by the formation of a phenyl radical. The latter can attack the 7-aminocoumarin molecules, which exists in the ground state (S_0) or, which is less likely, in an excited (S_1 or T_1) state. A possible pathway consists in reaction of the starting 7-aminocoumarin with a molecule of iodobenzene in the photoexcited

TABLE 3. Spectral-Luminescence Characteristics of Coumarins VI-XIII

Compound	Solvent	UV spectrum, λ_{max}, nm (log ε)	Luminescence, λ, nm		φ_f
			excit	max.	
VI	C_2H_5OH	243 (3,98), 269 (4,24), 312 (3,46), 326 (3,54), 401 (4,62)	400	484	0,92
	CH_3CN	241 (3,90), 268 (4,12), 312 (3,36), 328 (3,52), 397 (4,53)	400	480	0,73
VII	C_2H_5OH	263 (4,07), 415 (4,23)	400	545	<0,10
	CH_3CN	264 (4,28), 408 (4,46)	400	545	<0,10
VIII	C_2H_5OH	249 (4,11), 259 (4,14), 307 (3,40), 320 (3,42), 394 (4,47)	390	490	<0,10
	CH_3CN	248 (4,13), 255 (4,09), 318 (3,35), 385 (4,40)	390	485	<0,10
IX	C_2H_5OH	260 (4,23), 314 (4,03), 382 (4,50)	380	470	<0,10
	CH_3CN	260 (4,17), 314 (4,44), 375 (4,46)	380	470	<0,10
X	C_2H_5OH	265 (4,02), 400 (4,38)	390	484	0,84
	CH_3CN	256 (4,02), 391 (4,40)	390	480	0,66
XI	C_2H_5OH	263 (4,37), 410 (4,51)	400	535	0,53
	CH_3CN	265 (4,25), 407 (4,42)	400	530	0,53
XII	C_2H_5OH	251 (4,29), 386 (3,82), 320 (3,75), 386 (4,54)	390	476	0,97
	CH_3CN	249 (4,20), 284 (3,69), 318 (3,75), 377 (4,47)	390	466	0,73
XIII	C_2H_5OH	253 (4,06), 288 (3,59), 312 (3,45), 395 (4,38)	390	470	0,70
	CH_3CN	250 (3,99), 296 (3,43), 318 (3,41), 383 (4,35)	380	466	0,66

state with the formation of the cation radical (CR) of the coumarin and an anion radical (AR) of iodobenzene. In turn, the iodobenzene AR is a source of phenyl radicals [8], which can recombine with the aminocoumarin CR or attack a neutral molecule of the dye.

Measurement of the quantum yields of the reactions involved in the formation of VI-X, as well as 3-phenyl-4-methyl-7-diethylaminocoumarin (Table 1), showed that in the series of investigated compounds the photosubstitution proceeds most effectively for coumarin II (φ 0.12) and least effectively for coumarin I. An interpretation of the data obtained that is based on the stability of the radical intermediates formed as a result of the primary radical attack is the most probable. This is in agreement with the increased quantum yields of coumarins VIII and IX (stabilization of the radical center by the heteroatom [9]) and for VII (analogy with the capto-dative effect [10]) and also explains the high quantum yield for 3-phenyl-4-methyl-7-diethylaminocoumarin (0.070) as compared with coumarin VI (stabilization by an alkyl group [11]). It also follows from the data in Table 1 that the effectiveness of the photosubstitution reactions under consideration is not associated unambiguously with the electron density on the $C_{(3)}$ reaction center. In fact, for example, the quantum yields of the phenylation reactions have comparable values for coumarins II and IV, which contain groups in the 4 position with different electronic properties. This is particularly appreciable if one takes into account the unavoidable steric hindrance during the photoarylation of IV.

For an indirect evaluation of the effect of charge control on the step involving addition of an aryl radical we studied the reaction of coumarin II with 3,4-dimethoxyiodobenzene under similar conditions. Coumarin XI was obtained in 27% yield in this reaction. The quantum yields for the formation of XI show that, as compared with photophenylation, a decrease in the rate of the process by a factor of approximately five is observed in this case. Thus, it might be assumed that in the investigated photoreactions coulombic interactions of the substrate and the attacking radical of the donor–acceptor (or nucleophile–electrophile) type do not have decisive significance.

To evaluate the range of application of the photosubstitution reactions we also studied the reaction of coumarin V with alkyl halides, viz., isopropyl iodide and ethyl α-bromoacetate. The reactions were carried out under conditions similar to those used in photoarylation, viz., with an excess of the halo derivative and with the addition of triethylamine. As a result, coumarins XII and XIII were synthesized in 20 and 29% yields (see Tables 1, 3, and 4). Both compounds absorb intensely in ethanol and acetonitrile over a somewhat shorter-wave range (377-395 nm) than coumarin X and are effective luminophores at 465-475 nm ($\varphi_f \sim 0.7$-0.9).

On the whole, on the basis of the data in [2] and the results of our investigation, it may be asserted that the photochemical reactions of 7-dialkylaminocoumarins with iodo or bromo derivatives should be regarded as a general method for the synthesis of 3-substituted 7-aminocoumarins.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a Perkin–Elmer 577 spectrometer. The UV and luminescence spectra were obtained with a Hitachi EPS-3T spectrophotometer equipped with a G-3 luminescence adapter. The

TABLE 4. PMR Spectra of Coumarins X-XIII

Compound	Chemical shifts, δ, ppm (SSCC, J, Hz)					
	$1\text{-}CH_2$	$2\text{-}CH_2$, $6\text{-}CH_2$	$3\text{-}CH_2$, $5\text{-}CH_2$	$7\text{-}CH_2$	8-H	other protons
X	2,82 (t, 6,1)	2,03 (q, 6,1)	2,27 (q, 6,1)	2,94 (t, 6,1)	7,09 (s)	2,15 (3H, s, $9\text{-}CH_3$); 7,25 ... 7,40 (5H, m, C_6H_5)
XI	7,79 (dq, 9,0; 2,2)	6,68 (dd, 9,0; 2,7	6,50 (q, 2,7)	3,49 (q, 7,0)	1,21 (t, 7,0)	6,55 (1H, dd, $J = 8,2$; 2,5; 6′-H$_{arom}$); 6,60 (1H, d, $J = 2,5$; 2′-H$_{arom}$); 7,10 (1H, d 8,2; 5′-H$_{arom}$)
XII	2,77 (t, 6,1)	1,97 (q, 6,1)	3,20 (q 6,1)	2,86 (t, 6,1)	7,00 (s)	1,31 (6H, d $J = 6,5$, 2 CH_3); 1,95 (1H, m, CH); 2,30 (3-H, s 9-CH_3)
XIII	2,79 (t, 6,1)	2,01 (q, 6,1)	3,27 (q, 6,1)	2,88 (t, 6,1)	7,05 (s)	1,25 and 4,15 (3H, t, $J = 7,0$ and 2H, q $J = 7,0$; OCH_2CH_3); 2,41 (3H, s, 9-CH_3); 3,68 (2H, s, CH_2CO)

relative luminescence quantum yields were determined with respect to quinine bisulfate or 3-aminophthalimide by the method in [12]. The PMR spectra of solutions in $CDCl_3$ were recorded with a Bruker WM spectrometer (250 MHz) with hexamethyldisiloxane (HMDS) as the internal standard.

The reaction products were isolated by chromatography with a column (30 × 2.5 cm) packed with Silpearl UV silica gel by elution with a hexane–acetone system. Monitoring of the course of the photoreactions and the purity of the substances was accomplished by means of TLC on Silufol UV-254 plates. The conversion was determined from the amount of unchanged coumarin isolated after chromatographic separation of the mixture.

The differential quantum yields of the photochemical reactions were calculated taking into account the absorption of 7-aminocoumarins II-V with respect to iodobenzene (or 3,4-dimethoxyiodobenzene for XI) in accordance with [13] and were determined for solutions of the coumarins (0.050 mole/liter) and solutions of iodobenzene (1.50 moles/liter) in acetonitrile by means of a Shimadzu CS-930 densitometer. In the determination of the quantum yields we used UV light with a wavelength of 255 nm obtained by means of a Shimadzu NGF-16 monochromator. The intensity of the source was determined by the standard method [12] and was $I_0 = 5.81 \cdot 10^{-10}$ ergs/sec.

General Method for Obtaining Coumarins VI-XIII. A mixture of 5 mmoles of coumarin I-V and 50 mmoles of the corresponding halo derivative (with the addition of 10 mmoles of triethylamine for VI, IX, X, XII, and XIII) in solution in acetonitrile was irradiated with the total light of a PRK-2 medium-pressure mercury lamp in a 100-ml quartz reactor with stirring by means of a stream of nitrogen for 8-20 h. The reaction mixture was evaporated in vacuo, and the residue was separated by chromatography. The products isolated were recrystallized from hexane–acetone.

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