PHOTOCHEMICAL REACTIONS OF 7-AMINOCOUMARINS.

8*. REACTION OF 3-IODO-4-METHYL-7-DIETHYLAMINOCOUMARIN WITH MONOSUBSTITUTED BENZENES

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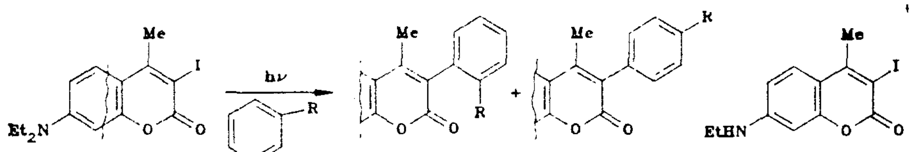
A number of 3-aryl-4-methyl-7-diethylaminocoumarins were obtained as a result of the photolysis of 3-iodo-4-methyl-7-diethylaminocoumarin in the presence of benzene, chlorobenzene, fluorobenzene, benzonitrile, toluene, and diphenyl ether. On the basis of an analysis of the PMR spectra it was established that photosubstitution leads to o- and p-isomeric products. The mechanism of the reaction was studied.

We have previously reported [1] the photoreactions of 3-iodo-4-methyl-7-diethylaminocoumarin (I) with olefins leading to 3-substituted 7-aminocoumarins.

In the present research we investigated similar reactions of coumarin I with benzene and monosubstituted benzenes in order to develop a new photochemical method for the synthesis of 3-aryl-substituted 7-aminocoumarins, which are promising laser dyes [2]. The regioselectivity of such reactions and the electronic effect of the substituent in the benzene ring on the effectiveness of photosubstitution should also be studied.

Compounds II-XII were isolated in 10-30% yields (40-80% conversions) as a result of the photochemical reactions of coumarin I with benzene, benzonitrile, fluorobenzene, chlorobenzene, toluene, diphenyl ether, and nitrobenzene.



I   II, III, V, VII, IX   IV, VI, VIII, X, XI   XII

II R=H; III, IV R=CN; V, VI R=F; VII, VIII R=Cl; IX, X R=CH_3; XI R=OC_6H_5

For the monosubstituted benzenes in most cases we obtained two isomeric 3-arylcoumarins (ortho and para). Diphenyl ether, in the reaction with which an ortho isomer was not detected, and nitrobenzene, in the reaction with which only N-deethylation product XII was isolated constituted exceptions. This is in agreement with data on the oxidative properties of nitrobenzene, which is capable of acting as an electron acceptor [3]. The principal side product in the investigated reactions (up to 20%) was 4-methyl-7-diethylaminocoumarin, as well as its de-ethylation products [4]. The use of organic solvents (acetonitrile, dioxane, DMSO, etc.), as in reactions with olefins, led to an increase in the relative percentage of this side product.

Compounds II-XII were isolated by means of column chromatography (see Table 1). Since the separation of the mixture of 3-tolylcoumarins IX and X proved to be rather difficult, these compounds were obtained in individual form also by alternative synthesis from 4-methyl-7-diethylaminocoumarin by irradiation in acetonitrile solutions with o- and p-iodotoluene in the presence of triethylamine [5].

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*See [1] for Communication 7.

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TABLE 1. Characteristics of the Synthesized Compounds

Compound	Empirical formula	mp, °C	$\nu_{C=O}$, cm^{-1}	φ*	Conversion, %	Yield, %
II	$C_{20}H_{21}NO_2$	133	1690	0,090	70	33
III	$C_{21}H_{20}N_2O_2$	147	1700	0,004	60	23
IV	$C_{21}H_{20}N_2O_2$	137	1690	0,002	60	11
V	$C_{20}H_{20}FNO_2$	126	1700	0,022	90	24
VI	$C_{20}H_{20}FNO_2$	113	1695	0,010	90	15
VII	$C_{20}H_{20}ClNO_2$	153 . . . 154	1700	0,034	70	24
VIII	$C_{20}H_{20}ClNO_2$	95 . . . 96	1700	0,018	70	10
IX	$C_{21}H_{23}NO_2$	118	1700	0,037	50	22
X	$C_{21}H_{23}NO_2$	146	1700	0,020	50	11
XI	$C_{26}H_{25}NO_3$	164 . . . 165	1695	0,063**	80	34
XII	$C_{12}H_{12}INO_2$	155	1690		40	21

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*φ pertains to the quantum yield of the reaction.

**Measured at 40°C.

The structure of 3-arylcoumarins II-XI were established on the basis of an analysis of the PMR spectra (Table 2). The presence of the residue of a coumarin fragment is confirmed by the presence of signals of 5-H, 6-H, and 8-H protons with characteristic spin-spin coupling constants (SSCC) [6]. The structure of para isomers was assigned to IV, VI, VIII, and X, since characteristic symmetrically situated signals of an AA'BB' system were observed in the aromatic region of the spectra of these compounds (in the case of VI, the spectrum is complicated by additional splitting of the lines of the multiplets due to spin-spin coupling of the ^1H and ^{19}F nuclei). Thus, the spectrum of 3-arylcoumarin VIII contains two intense multiplets (pseudodoublets, each with an intensity of two protons) at 7.23 and 7.41 ppm with a clearly expressed "roof effect." It was more difficult to isolate the AA'BB' part in the spectrum of XI because of superimposition of the signals of the protons of the second benzene ring, and we therefore carried out a differential double-resonance experiment for the assignment of the signals of the protons of the p-substituted phenyl fragment. Additional irradiation of the sample with the frequency corresponding to the multiplet at 7.29 ppm (the pseudodoublet of the AA' part) made it possible to isolate the corresponding components of the multiplet at 6.94 ppm (the BB' part) in the differential spectrum.

In the spectra of ortho isomers III and V we carried out the complete assignment of all of the signals of the aromatic protons. The chemical shifts (CS) and SSCC of the aromatic protons of III (Table 2) were measured directly from the spectrum within the approximation of first-order spectra and were confirmed by complete coincidence of the simulated (by means of the PANIC program) theoretical and experimental spectra. The form of the signals of the protons of the aromatic substituent of V proved to be more complex even at a spectrometer operating frequency of 400 MHz (ABMNX spin system); this is explained by additional splitting of the signals of the protons due to spin-spin coupling with fluorine (the X nucleus) and the close CS of the 3-H and 4-H protons (the A and B nuclei) with $\Delta\delta_{AB} = 0.042$ ppm. The CS and SSCC of the indicated protons (Table 2) were obtained by iteration (with the PANIC program). The theoretical and experimental spectra of V were simulated by means of the PANIC program (see Fig. 1). The part of the spectrum of coumarin VII that is related to the aryl substituent is strongly coupled, and the accurate assignment of the signals in this case is difficult. A comparison of the CS of the protons of the 3-aryl substituents in the spectra of II, VIII, and VII, as well as the relative intensities of the signals in the spectrum of coumarin VII, made it possible to assign the structure of the ortho isomer to the latter. A multiplet signal with a relative intensity of one proton, the CS of which is close to the CS of the 2'-H and 4'-H protons of coumarin VIII, is recorded in the spectrum of VII at weak field (Table 2). If VII were the meta isomer, signals of two protons should have been recorded in the indicated region of the spectrum.

All of the synthesized 3-arylcoumarins luminesce intensely in ethanol and acetonitrile at 450-490 nm (φ_f 0.6-1.0).

On the basis of the previously obtained results [1], it may be assumed that the investigated photosubstitution reactions are realized via a radical mechanism that includes the formation of a 3-coumarinyl radical. In fact, we observed quenching of the processes when hydrogen-atom donors (hydrocarbons, alcohols, etc.) or active radical carriers (CCl_4, $CHCl_3$) were added to the reaction mixtures. Evidence in favor of a radical mechanism is also provided by the formation, as a result of photolysis, of iodine, the amount of which does not change substantially with the addition of organic bases (pyridine, triethylamine).

As a result of measurement of the quantum yields of the reactions involving the formation of coumarins II-XI it was established that the effectiveness of photosubstitution decreases on passing from electron-donor to electron-acceptor substituents in the order $C_6H_5O > CH_3 > Cl > F > CN$ (Table 1); the quantum yields of the reactions involved in the formation of the ortho isomers are greater by a factor of 1.5-2 than for the para isomers. This distribution corresponds approximately to

TABLE 2. PMR Spectra of Coumarins II-XII in $CDCl_3$

Compound	Chemical shifts, δ, ppm (SSCC, J, Hz)							
	5-H, d (J=9,0)	6-H dd	8-H, d (J=2,5)	4-CH_3, s	NCH_2, q (J=7,0)	CH_2CH_3, t (J=7,0)	protons of the aryl substituent	other protons
II	7,46	6,66	6,57	2,22	3,42	1,20	7,24 . . . 7,44 (5H, m, 1'-H—5'-H)	—
III	7,47	6,65	6,55	2,21	3,13	1,22	7,42 (1H, m, J=7,5, J=1,3, 5'-H); 7,46 (1H, m, J=7,5, J=7,5, J=1,3, 3'-H); 7,65 (1H, m, J=7,5, J=7,5, J=1,3, 4'-H); 7,75 (1H, m J=7,5, J=1,3, 2'-H)	—
IV	7,50	6,75	6,62	2,20	3,40	1,20	7,43 (2H, m, 1'-H, 5'-H); 7,72 (2H, m, 2'-H, 4'-H)	—
V	7,48	6,67	6,56	2,13	3,44	1,22	7,07 (1H, m, J=9,7, J=9,0, J=1,4, 2'-H); 7,14 (1H, m, J=7,9, J=1,5, J=8,1, 5'-H); 7,25 (1H, m, J=0,4, J=1,4, J=7,8, J=8,1, 4'-H); 7,29 (1H, m, J=5,9, J=9,0, J=7,8, J=1,5, 3'-H)	—
VI	7,48	6,65	6,57	2,21	3,43	1,22	6,99 (2H, m 2'-H, 4'-H); 7,09 (2H, m, 1'-H, 5'H)	—
VII	7,47	6,65	6,56	2,13	3,41	1,21	7,24 . . . 7,35 (3H, м, 3'-H, 5'-H); 7,54 . . . 7,62 (1H, m, 2'-H)	—
VIII	7,50	6,77	6,65	2,25	3,45	1,23	7,23 (2H, m, 1'-H, 5'-H); 7,41 (2H, m 2'-H, 4'-H)	
IX	7,18	6,65	6,55	2,16	3,44	1,22	7,08 . . . 7,13 (1H, m) } 2'-H—5'-H 7,20 . . . 7,30 (3H, m) } 2'-H—5'-H	2,12 (3H, s 1-CH_3)
X	7,50	6,72	6,68	2,25	3,43	1,22	7,19 (2H, m 1'-H, 5'-H); 7,25 (2H, m 2'-H, 4'-H)	2,38 (3H, s, 3-CH_3)
XI	7,52	6,70	6,45	2,20	3,47	1,20	6,91 (2H, m, 2'-H, 4'-H); 7,29 (2H, m, 1'-H, 5'-H)	6,95 . . . 7,40 (5H, m, 6'-H—10'-H)
XII	7,42	6,47	6,42	2,55	3,20	1,27		4,75 (1H, br.s, NH)

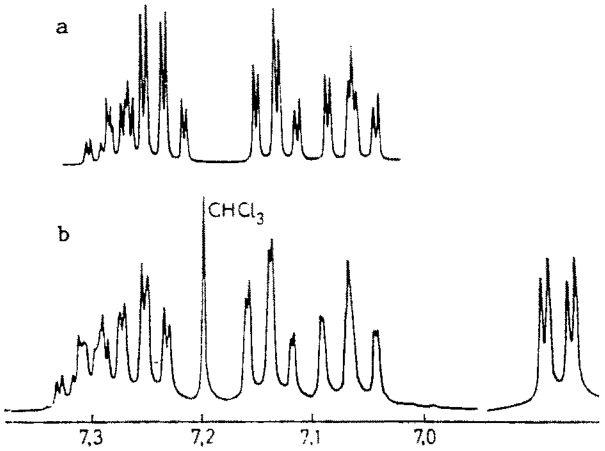

Fig. 1. Theoretical (a) and experimental (b) spectra of the aryl substituent of coumarin V:

$\delta_{2'\text{-H}}$ 7.073 ppm., $J_{2'F} = 9.73$; $J_{2'3'} = 8.95$; $J_{2'4'} = 1.36$ Hz
$\delta_{3'\text{-H}}$ 7.294 ppm. $J_{3'F} = 5.94$; $J_{3'2'} = 8.95$; $J_{3'4'} = 7.80$; $J_{3'5'} = 1.50$ Hz
$\delta_{4'\text{-H}}$ 7.252 ppm $J_{4'F} = -0.40$; $J_{4'2'} = 1.36$; $J_{4'3'} = 7.80$; $J_{4'5'} = 8.08$ Hz
$\delta_{5'\text{-H}}$ 7.144 ppm . $J_{5'F} = 7.94$; $J_{5'3'} = 1.50$; $J_{5'4'} = 8.08$ Hz

the statistical distribution and denotes close reactivities of the ortho and para positions. On the basis of these data it can be concluded that the coumarinyl radical is an electron-deficient particle and is evidently a σ radical [7], the electrophilic properties of which are the result of the electron-acceptor effect of the lactone carbonyl group.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a Perkin–Elmer 577 spectrometer. The PMR spectra of $CDCl_3$ solutions were obtained with Bruker WM spectrometers (250 and 400 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. The isolation of the reaction products was carried out by chromatography with columns (40 × 3.5 cm) packed with Silpearl UV-254 sorbent in benzene and hexane–ethyl acetate systems. Monitoring of the purity of the substances was realized by means of TLC on Silufol plates with development with UV light and iodine. The degree of conversion was determined from the amount of unchanged 3-iodocoumarin I isolated after column chromatography. The differential quantum yields of the reactions were calculated by the method in [7] and were determined for solutions of coumarin I in the corresponding aromatic compounds (0.05 mole/liter) in the case of irradiation of them with UV light with a wavelength of 370 nm obtained by means of a Shimadzu NGF-16 monochromator. The intensity of the source determined by the standard method [8] was $3.72 \cdot 10^{-10}$ ergs/sec. The quantitative evaluation of the reaction products formed was carried out by means of a Shimadzu CS-930 densitometer after separation of the reaction masses on Merck Kieselgel 60 plates.

General Method for Obtaining Coumarins II-XII. A solution of 1 g of 3-iodocoumarin I in 100 ml of the corresponding aromatic compound was irradiated with the light of a medium-pressure PRK-2 mercury lamp for 10-20 h in a 100-ml glass reactor with stirring by means of a stream of nitrogen, after which the reaction mass was evaporated. The residue was separated by column chromatography [elution with benzene for II and IX-XII, with hexane–ethyl acetate (10:1) for III and IV, and with hexane–ethyl acetate (15:1) for V-VIII], and the isolated products were recrystallized from hexane–acetone.

3-(o-Tolyl)-4-methyl-7-diethylamino-2H-benzopyran-2-one (IX) and 3-(p-Tolyl)-4-methyl-7-diethylamino-2H-benzopyran-2-one (X). A 0.15-g sample (21% yield, 50% conversion) of X was obtained after irradiation of 1 g of 4-methyl-7-diethylaminocoumarin, 10 g of p-iodotoluene, and 2 g of triethylamine in 100 ml of acetonitrile for 15 h and separation of the reaction mass in benzene. Under similar conditions, 0.12 g (17% yield, 50% conversion) of IX was obtained by reaction with o-iodotoluene.

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2-BENZOPYRYLIUM SALTS.

40*. ADDITION OF AZOMETHINES TO 2-BENZOPYRYLIUM SALTS – NEW METHOD FOR THE SYNTHESIS OF ISOQUINOLINIUM SYSTEMS

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The addition of azomethines to 2-benzopyrylium salts, which leads to derivatives of 3,4-dihydroisoquinolinium salts, was observed. An assumption regarding the mechanism of the reaction is expressed on the basis of its stereoselectivity. Dehydrogenation of the compounds obtained to completely aromatic isoquinolinium salts and reduction to tetrahydroisoquinolines were realized.

The reaction of monocyclic pyrylium salts with azomethines, which hypothetically proceeds via a four-center mechanism, concludes with the simple exchange of an oxygen atom for the amino fragment of the Schiff base, i.e., with the formation of pyridinium salts and the elimination of an aldehyde [2, 3]. With the same reagents, 2-benzopyrylium salts with a methyl group in the 1 position add the residue of an aromatic aldehyde at this substituent and form, with retention of the oxonium atom, 1-styryl-substituted derivatives [4].

We have observed the stereoselective addition of azomethines to 2-benzopyrylium salts that do not contain an alkyl substituent in the 1 position, as a result of which trans isomers of 3,4-dihydroisoquinolinium salts IVa-d are formed in quantitative yields. The configuration of the compounds obtained can be judged from the spin-spin coupling constants (SSCC) of the methylidine protons, viz., $J_{3,4} = 0$ Hz, while this value should be on the order of 6 Hz for the cis isomers [5].

As compared with the well-known conversion of 2-benzopyrylium salts to completely aromatic isoquinolinium salts under the influence of primary amines [6], which proceeds via the ANRORC scheme [7], a fundamentally different recyclization mechanism, viz., cycloaddition of the C=N bond of the azomethine to the 1 and 4 positions of the pyrylium fragment of salts Ia, b with subsequent opening of the ring containing the onium heteroatom in intermediates IIIa-d, is, in our opinion, realized in the case being described here.

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*See [1] for Communication 39.

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