PHOTOCHEMICAL CYCLIZATION OF ANILS OF POLYFLUOROAROMATIC KETONES

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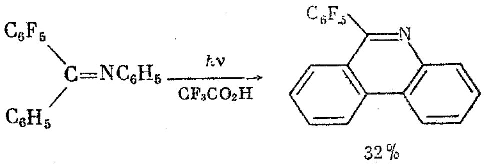
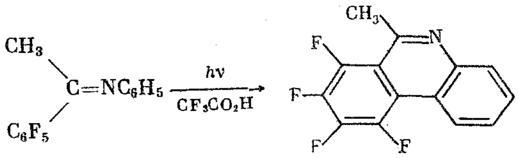
Aromatic Schiff bases when exposed to UV light in strongly acidic media undergo oxidative cyclization to phenanthridines [1]. Photocyclization reactions of anils of the nonoxidative type, with the cleavage of HX and not of two H atoms, are unknown. Previously we found a new type of photocyclization of fluorinated N-alkyldiarylamines to carbazoles, with the cleavage of F atom from the aromatic ring [2]. In the present paper we studied the possibility of effecting a similar reaction for the anils of polyfluoroaromatic carbonyl compounds.

It proved that the anil of pentafluorobenzaldehyde, in contrast to the unfluorinated analog [3], remains unchanged when exposed to UV light in conc. H_2SO_4 or CF_3CO_2H. The anil of 2,3,4,5,6-pentafluorobenzophenone under similar conditions undergoes oxidative photocyclization to pentafluorophenylphenanthridine.

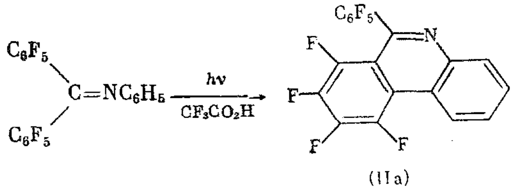


The absence of transformation of the nonoxidative type, with the cleavage of a F atom, can be due to either the theoretical impossibility of accomplishing such a reaction for the anils of polyfluoroaromatic carbonyl compounds or to the low thermodynamic stability of the photoinducible and potentially photolytically active isomer with a cis arrangement of C_6F_5 and N–Ph (cf. [4]). If the latter is true, then photocyclization with the cleavage of a F atom can be expected for the anil of 2,3,4,5,6-pentafluoroacetophenone, which, judging by the ^{19}F NMR spectrum [5], exists as two geometric isomers. Actually, its exposure to UV light in CF_3CO_2H led to the formation of 6-methyl-7,8,9,10-tetrafluorophenanthridine:



The low yield of the latter is probably due to the partial hydrolysis of the starting anil, as is indicated by the presence of a band at 1720 cm^{-1}, which corresponds to the stretching vibrations of the C=O group, in the IR spectrum of the reaction mixture.

Nonoxidative photocyclization with the cleavage of F was also accomplished for the anil of decafluorobenzophenone (Ia), in which a cis orientation of C_6H_5 and N–Ph is authentically realized. 6-Pentafluorophenyl-7,8,9,10-tetrafluorophenanthridine (IIa) was obtained in 80% yield when (Ia) was irradiated in CF_3CO_2H.



(IIa)

(Ia)

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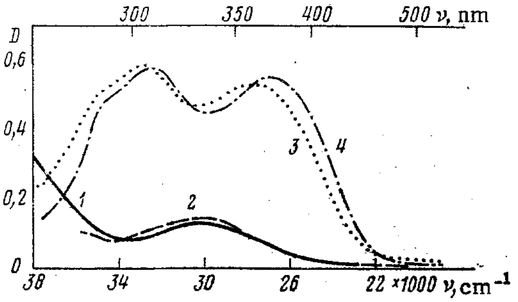
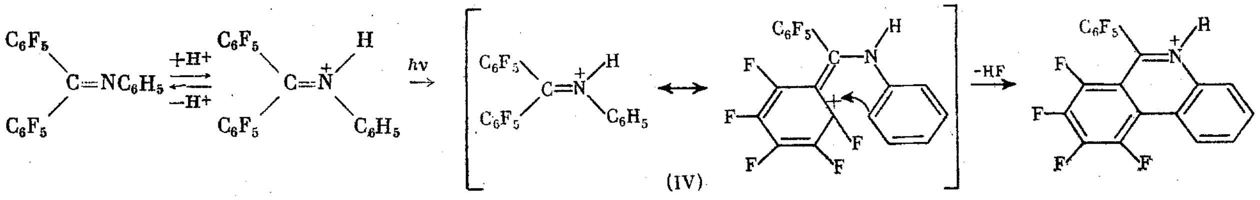


Fig. 1. Ultraviolet spectrum of decafluorobenzophenone anil (Ia), concentration 0.00005 mole/liter, and layer thickness 1 cm: 1) in alcohol; 2) in CH_3CO_2H; 3) in CF_3CO_2H; 4) in conc. H_2SO_4.

As was to be expected, anil (Ia) is stable when refluxed in CF_3CO_2H and when heated in anhydrous DMF in the presence of KF. Evidently, its cyclization to a phenanthridine is actually a photochemical process that proceeds via the photoexcited state.

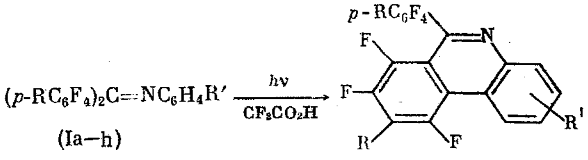
Anil (Ia) remains unchanged when irradiated in neutral solvents (n-hexane, alcohol) and in AcOH. The cyclization reaction is accomplished only in strongly acid media like CF_3CO_2H or conc. H_2SO_4. In the UV spectrum of anil (Ia) in these acids (Fig. 1) is observed, when compared with the spectrum in alcohol or AcOH, a substantial shift toward longer wavelengths and an increase in the intensity of the band at 335 nm, which is caused by electron transition in the central double bond [6]. Such changes in the spectrum indicate that in strong acids anil (Ia) is found mainly as the conjugated acid (III) (cf. [7]). It may be assumed that the photocyclization of anil (Ia) proceeds the same as the cyclization of the unfluorinated analogs [4] via the photoexcited state of the conjugated acid (IV), in which the N—Ph moiety attacks the C_6F_5 group at the o-C atom with the cleavage of HF.



(IV)

An efficient distribution of the positive charge in the excited state of (IV) from the N atom to the polyfluorinated aromatic ring is apparently a necessary condition for photocyclization. The anil of benzophenone and pentafluoroaniline, in the excited state of whose conjugated acid the positive charge is distributed mainly in the unfluorinated ring, is stable to irradiation.

A study of the photolysis of polyfluoroaromatic ketone anils of type $(p\text{-}RC_6F_4)_2C = NC_6H_4R'$, which contain various substituents in the aromatic rings, attached to either the C or N atom, disclosed that in all cases the sole type of transformation that can be recorded is photocyclization to the corresponding phenanthridines.



(Ia—h)

(IIa-h)

R = F, R′ = H (a); R = F, R′ = p-Me (b);
R = F, R′ = o-Me (c);
R = F, R′ = p-MeO (d);
R = F, R′ = m-MeO (e);
R = F, R′ = o-F (f); R = CF_3, R′ = H (g);
R = MeO, R′ = H (h).

TABLE 1. Preparation of Polyfluorinated Phenanthridines (I)→(II)

Starting anil	Irradiation time, h	Yield of (II), %	mp, °C	Found, %				Empirical formula	Calc., %			
				C	H	F	N		C	H	F	N
(Ia)	5	80*	172–173	54,64	1,02	41,38	3,27	$C_{19}H_4F_9N$	54,69	0,92	40,98	3,35
(Ib)	5	85	167,5–168	55,69	1,55	39,62	3,11	$C_{20}H_6F_9N$	55,69	1,40	39,62	3,25
(Ic)	40	60	216–218	55,23	1,53	39,24	3,03	$C_{20}H_6F_9N$				
(Id)	40	53	205–206	53,43	1,46	38,04	2,85	$C_{20}H_6F_9NO$	53,70	1,35	38,23	3,13
(Ie)	40	45	169,5–171	54,12	1,42	37,82	3,22	$C_{20}H_6F_9NO$				
(If)	40	27	140–140,5	52,79	0,71	44,01	3,18	$C_{19}H_3F_{10}N$	52,43	0,69	43,65	3,22
(Ig)	20	78	141,5–142	48,67	0,76	47,72	2,69	$C_{21}H_4F_{13}N$	48,76	0,78	47,75	2,70
(Ih)	25	80	146–148	57,14	2,31	30,00	3,11	$C_{21}H_{10}F_7NO_2$	57,17	2,25	30,14	3,17

*^{19}F NMR spectrum (in DMF, ppm): 137.4; 140.1; 143.0; 149.0; 153.2; 154.2; 162.3; ratio of intensities 1:1:2:1:1:1:2.

TABLE 2. Composition of Reaction Mixtures, Obtained during Photolysis of Anils (I) (in CF_3CO_2H, 20°C, 5 h)

R	R′	Amount, %		Analytical ν, cm^{-1}	
		(I)	(II)	for (I)	for (II)
F	H	3	94	693, 1502	636, 1443
F	*p*-Me	3	94	558, 1500	705, 1505
F	*o*-Me	38	53	1331	1368
F	*p*-MeO	82	18	559, 1250	706, 1271
F	*m*-MeO	78	20	690	1375
F	*o*-F	75	16	1335	1368
CF_3	H	20	80	693	606
MeO	H	73	22	695	640

TABLE 3. Anils of Polyfluoroaromatic Ketones

Starting anil	Amt. of $AlCl_3$, mmoles	Yield of (I), %	mp, °C	λ_{max}, nm (log ε) in alcohol	$\delta^{19}F$ in CCl_4, ppm (ratio of intensities)	Found, %				Empirical formula	Calc., %			
						C	H	F	N		C	H	F	N
(Ib)	20	35	75–76,5	218 sh (4,30), 233 infl.(4,20), 343 (3,98)	138,5, 143,0, 150,9, 151,7, 160,9, 161,9 (2 : 2 : 1 : 1 : 2 : 2)	52,78	1,53	42,05	2,98	$C_{20}H_7F_{10}N$	53,23	1,56	42,10	3,14
(Ic)	20	68	91,5–93	236 infl. (4,18), 343 (3,48)	139,1, 143,0, 150,9, 151,8, 160,9, 161,8 (2 : 2 : 1 : 1 : 2 : 2)	53,07	1,48	42,32	2,99	$C_{20}H_7F_{10}N$				
(Id)	10	60	81,5–82,5	223 (4,29), 236 infl. (4,21), 357 (3,70)	135,5, 139,6, 147,8, 157,1, 158,2 (1 : 1 : : 1 : 1 : 1)	51,35	1,54	40,86	2,99	$C_{20}H_7F_{10}NO$	51,40	1,50	40,66	2,99
(Ie)	15	66	73,5–75	240 infl. (4,16), 340 (3,45)	138,5, 143,1, 150,9, 151,5, 161,0, 161,9 (2 : 2 : 1 : 1 : 2 : 2)	51,74	1,16	40,39	2,97	$C_{20}H_7F_{10}NO$				
(If)	20	77	98,5–99,5	236 sh (4,24), 335 (3,51)	126,5, 139,1, 142,6, 150,4, 151,1, 160,9, 161,8 (1 : 2 : 2 : 1 : : 1 : 2 : 2)	49,65	0,99	45,91	3,11	$C_{19}H_4F_{11}N$	50,13	0,88	45,91	3,07
(Ig)	30	80	110–111,5	222 (4,04), 284 (3,81), 342 (3,49)	57,7, 136,0, 138,5, 139,1, 140,8 (3 : 1 : : 1 : 1 : 1)	46,40	1,00	49,89	2,38	$C_{21}H_5F_{14}N$	45,95	0,94	49,56	2,61
(Ih)	10	67	76–78	240 sh (4,30), 331 (3,60)	140,5, 144,9, 158,0, 158,6 (1 : 1 : 1 : 1)	54,60	2,03	32,98	2,74	$C_{22}H_{11}F_8NO_2$	54,67	2,40	32,95	3,04

The results of the experiments are summarized in Table 1. It can be seen that the irradiation time and yields of isolated phenanthridines vary within wide limits as a function of the structure of the starting anils. To compare their reactivity we analyzed the reaction mixtures via the IR spectra after 5 h of irradiation in CF_3CO_2H (Table 2).

In all cases, except when R' = p-Me, the insertion of substituents in anil (Ia) lowers the transformation rate noticeably. In contrast to the photocyclization of fluorinated diarylamines [2], and in harmony with the phototransformation of aromatic azo compounds [8], a simple relation is not observed between the character of the substituent and its effect on the rate of the process. Nevertheless, the observed effects of the substituents can be interpreted if it is assumed that they are manifested mainly in the cyclization step of the (IV) cation. The acceptor substituents (R = CF_3, R' = o-F) can lower the transformation rate via a decrease in the concentration of the conjugated acid of the anil, and consequently of its excited state, while donor methoxy groups (R = MeO, R' = m-MeO, R' = p-MeO) can lower it by efficient participation in distributing the positive charge in a cation of the (IV) type, which leads to a decrease in the charge on the C atoms of the polyfluorinated aromatic ring. The nociceable retarding effect of a methyl group in the o-position of an N-aryl can have a steric nature. However, it should be mentioned that in most cases the reaction proceeds quite unequivocally and can be used as a method for the preparation of little-studied and difficultly available [9] polyfluorinated phenanthridines.

EXPERIMENTAL

The UV spectra were taken on a Specord UV-VIS instrument, while the ^{19}F NMR spectra were taken on a Varian A-56/60A instrument (56.4 MHz). C_6F_6 was used as the internal standard and the δ ^{19}F values are given in ppm from CCl_3F (the $\Delta\delta$ of C_3F_6 from CCl_3F is equal to 163.0 ppm). The molecular weight was determined on an MS-3301 high-resolution mass spectrometer.

A quantitative analysis of the reaction mixtures was based on the IR spectra employing the method of linear programming [10] on a Minsk-32 electronic computer. The spectra were recorded on a Perkin—Elmer 180 instrument, using 3-4% CCl_4 solutions and a layer thickness of 0.28 cm in the 710-400 cm^{-1} range, and 0.07 cm in the 1700-1100 cm^{-1} range.

The transmittance values were fed into the memory of the computer at 1 cm^{-1} intervals. The analytical points on the spectral curve in the 710-400 and 1700-1100 cm^{-1} regions were selected automatically (see Table 2). The analysis accuracy was 5-10% of the determined value.

Anils of Polyfluoroaromatic Ketones. With vigorous stirring, to a solution of 10 mmoles of the starting ketone and 30 mmoles of the aromatic amine in 80 ml of chlorobenzene, dried over $CaCl_2$, was added the amount of anhydrous $AlCl_3$ indicated in Table 3. The reaction mixture was refluxed for 3.5-5 h, poured into water, and extracted with ether. The ether extract was washed in succession with 10% HCl solution and water, dried over $CaCl_2$, and evaporated. The thus isolated product was recrystallized from alcohol. The yields and characteristics of the anils are given in Table 3.

Photolysis of Anils of Polyfluoroaromatic Ketones. A solution of 0.2 g of the anil in 70 ml of CF_3CO_2H was placed in a 30-mm diameter quartz test tube and irradiated at ∿20° with a DRSh-500 mercury lamp, placed at a distance of 25 cm from the test tube. Then the solution was evaporated, and the residue was treated with 100 ml of water, neutralized with 10% aqueous NH_3 solution, and extracted with ether. The ether solution was washed with water, dried over anhydrous $CaCl_2$, evaporated, and the residue was recrystallized from alcohol. The irradiation time, yields, and characteristics of the obtained phenanthridines (II) are given in Table 1.

A solution of 2,3,4,5,6-pentafluorobenzophenone anil [5] in CF_3CO_2H (0.01 M) was irradiated for 20 h. We obtained the 6-pentafluorophenylphenanthridine in 32% yield, mp 139-141° (from alcohol). ^{19}F NMR spectrum (in DMF, δ, ppm): 141.5; 154.5; 162.1; ratio of intensities 2:1:2. Found: C 65.99; H 2.36; F 27.89; N 4.27%. $C_{19}H_8F_5N$. Calculated: C 66.02; H 2.33; F 27.51; N 4.05%.

A solution of 2,3,4,5,6-pentafluoroacetophenone anil [5] in CF_3CO_2H (0.01 M) was irradiated for 20 h. We obtained 6-methyl-7,8,9,10-tetrafluorophenanthridine in 23% yield, mp 174-176° (from alcohol). ^{19}F NMR spectrum (in CF_3CO_2H, δ, ppm): 128.0; 134.8; 136.0; 150.1 (signals of equal intensity). Found: C 63.36; H 2.61; F 28.61; N 5.27%; mol. wt. 265 (mass spectrometry). $C_{14}H_7F_4N$. Calculated: C 63.40; H 2.66; F 28.65; N 5.28%; mol. wt. 265.

CONCLUSIONS

The UV irradiation of the anils polyfluoroaromatic ketones in strongly acidic media leads to photochemical cyclization to phenanthridines. The insertion of substituents into the anil molecule lowers the phototransformation rate.

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EFFECT OF INTRAMOLECULAR HYDROGEN BOND IN NUCLEOPHILIC AZAHETEROAROMATIC SUBSTITUTION REACTION

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The formation of a strong intramolecular hydrogen bond (IHB) is characteristic for azaheteroaromatic systems that contain an o-hydroxyphenyl group α to the heteroatom [1]. The substantial effect of the H bond on the reactivity of the fragment taking direct part in the IHB is mentioned in the literature [2]. The question of the change in the reactivity of the fragment at a distance from the chelate ring has received less study. Only one paper is known [3] for nucleophilic substitution reactions in which a study was made of the effect of the IHB on the rate of substituting chlorine in sym-triazine derivatives that contain the 2-hydroxynaphthyl moiety. Quite complex compounds and a hydroxyl-containing solvent (water—dioxane mixture) were used in [3]. However, the intermolecular H bond in such solvents can greatly complicate estimating the effect of the IHB on the reactivity.

To obtain more accurate information on the effect of the IHB on the nucleophilic substitution rate in the haloazine series we used aprotic solvents and simpler model compounds. We studied the effect of the IHB on the rate of the piperidinodechlorination reaction for compounds that contain an o-hydroxyphenyl group in one of the even positions of the pyrimidine ring. As model compounds we selected 4-chloro-6-(o-hydroxyphenyl)pyrimidine (I), 2-chloro-4-(o-hydroxyphenyl)pyrimidine (II), and 4-chloro-2-(o-hydroxyphenyl)pyrimidine (III).

As the criterion of change in the reactivity we took the ratio of the reaction rate constants of compounds (I)-(III) to the reaction rate constants of respectively 4-chloro-6-phenylpyrimidine (IV), 2-chloro-4-phenylpyrimidine (V), and 4-chloro-2-phenylpyrimidine (VI) under the same reaction conditions. It possibly would be more rigorous to use the corre-

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