REACTION OF 5-HALOANTHRA[1,9-cd]-6-ISOXAZOLONES WITH AZIRIDINE

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The reaction of 5-haloanthra[1,9-cd]-6-isoxazolones with aziridine gave 5-aziridinoanthra[1,9-cd]-6-isoxazolones. The latter, upon reaction with acids, undergo cleavage of the aziridine ring.

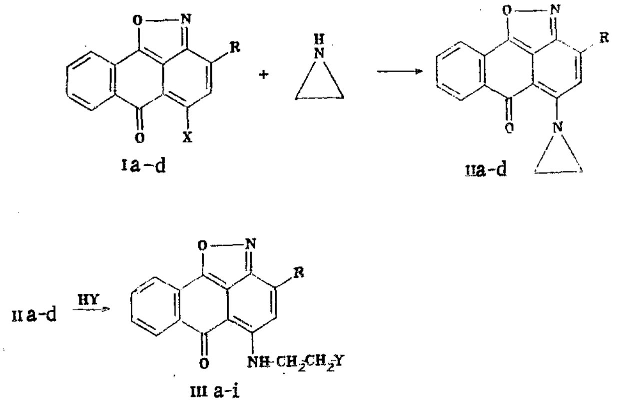
It has been shown that facile nucleophilic substitution of the chlorine atom by amines occurs in 5-chloroanthra[1,9-cd]-6-isoxazolone (Ia) [1]. The lability of chlorine in Ia is even higher than that of fluorine in 1-fluoro-9,10-anthraquinone [2].

We have investigated the reaction of 5-haloanthra[1,9-cd]-6-isoxazolones (Ia-d) with aziridine, the residue of which, as is well known [3], is introduced into the anthraquinone ring only when difficult-to-obtain fluoro anthraquinones are used [4].

It was found that isoxazolones Ia-d are aminated by aziridine at the usual temperature in aprotic polar solvents (DMF, DMA). The decrease in the yield of some of the 5-aziridinoanthra[1,9-cd]-6-isoxazolones (IIb-d) is associated both with the bifunctionality of the starting substances (Ic-d) and with the passivating effect of the methyl group in Ib.

It is characteristic that the absorption maximum in the visible region of the spectra of IIa-d (Table 1) is shifted hypsochromically approximately 50 nm as compared with the similarly constructed 5-ethylamino anthra[1,9-cd]-6-isoxazolone (λ_{max} 490, 522 nm), evidently because of disruption of conjugation with the participation of the unshared electron pair of the aziridine nitrogen atom. This same phenomenon was previously observed in the aziridinoanthraquinone series [3].

The IR spectra of isoxazolones IIa-d contain intense bands of stretching vibrations of C=O and C=N bonds at 1670-1680 and 1620-1630 cm^{-1}, respectively. The low intensity bands of the stretching vibrations of the C-H bonds of the aziridine ring are observed at 3060 cm^{-1}; this is characteristic for this fragment [3, 5].



I a R=H, X=Cl; b R=CH_3, X=Br; c R=X=Cl; d R=X=Br; II a R=H; b R=CH_3; c R=Cl; d R=Br; III a-c R=H; d-f R=CH_3; g, h R=Cl; i R=Br; a, d, g Y=Cl; b, e Y=Br; c, f, h, i Y=$OCOCH_3$

The high strain of the aziridine ring in IIa-d is manifested in the facile cleavage of the ring by hydrogen halides and acetic acids. The mild conditions for the II → III transformation make it possible to retain in them the isoxazole ring, which is cleaved in similar compounds under the influence of hydrohalic acids upon heating [6]. The electronic spectra of products IIIa-i (Table 2) are identical to the spectra of the previously described 5-alkylaminoanthra[1,9-cd]-6-isoxazolones [1].

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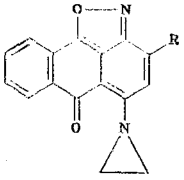
TABLE 1. Characteristics of 5-Aziridinoanthra[1,9-cd]-6-isoxazolones



Compound	R	mp, °C	Electronic spectrum, λ_{max}, nm (log ε)	Found, %		Empirical formula	Calc. %		Yield, %
				Hal	N		Hal	N	
IIa	H	202—204[a]	249 (4,38), 257 (4,41), 454 (4,16), 480 (4,18)		10,2	$C_{16}H_{10}N_2O_2$		10,7	95
IIb	CH_3	196—197[b]	250 (4,41), 257 (4,40), 452 (4,10), 480 (4,11)		9,9	$C_{17}H_{12}N_2O_2$		10,1	53
IIc	Cl	200—202[b]	253 (4,39), 260 (4,42), 460 (4,19), 485 (4,20)	12,0	9,4	$C_{16}H_9ClN_2O_2$	11,9	9,4	56
IId	Br	186—187[c]	256 (4,48), 260 (4,38), 460 (4,19), 488 (4,20)	24,0	7,9	$C_{16}H_9BrN_2O_2$	23,5	8,2	55

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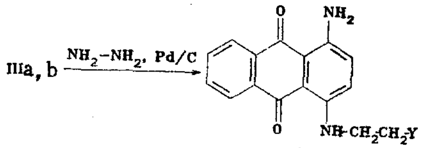
[a] From toluene—ethanol (3:1).
[b] From toluene.
[c] From m-xylene.

On the basis of III one can obtain derivatives of 1-alkylamino-9,10-anthraquinone that contain a labile halogen atom in the side chain and are of interest as active dyes [7].



IVa,b

EXPERIMENTAL

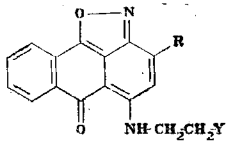
The IR spectra of mineral oil and KBr pellets of the compounds were recorded with a Specord 75-IR Spectrometer. The UV spectra of IV in dioxane and the UV spectra of the remaining compounds in tetrahydrofuran were recorded with a Specord UV-vis spectrophotometer. The molecular mass of IIa was determined with a AEI MS-902 mass spectrometer (Britain), ionizing-electron energy of 70 eV, and a direct input temperature of 170°C. The individuality of the starting and final substances as well as the course of the reactions were monitored by TLC on UV-254 plates. The melting points were determined on a microheated Boetius stage.

Anthra[1,9-cd]-6-isoxazoles I were synthesized by refluxing the corresponding azides in acetic acid [8] or toluene [9]. 3-Methyl-5-bromo anthra[1,9-cd]-6-isoxazolone (Ib) was obtained in 80.8% yield and had mp 236-239°C (from toluene). Found: Br 25.3; N 4.2%. $C_{15}\cdot H_8BrNO_2$. Calculated: Br 25.5; N 4.5%. 3,5-Dibromanthra[1,9-cd]-6-isoxazole (Ic), yield 80%, mp 220-223° (from toluene). Found: Cl 24.3; N 4.7%. $C_{14}H_5Cl_2NO_2$. Calculated: Cl 24.5; N 4.8%.

The 1-azidoanthraquinones were synthesized from the corresponding amines by the method in [8]. 1-Azido-2-methyl-4-bromoanthraquinone was synthesized in 94% yield and had mp 149-151°C. Found: Br 23.7; N 12.9%. $C_{15}H_8BrN_3O_2$. Calculated: Br 23.4; N 12.3%. 1-Azido-2,4-dichloroanthraquinone was synthesized in 90% yield and had mp 216-218°C (in agreement with the melting point of the decomposition products). Found: Cl 22.16; N 13.15%. $C_{14}H_5Cl_2N_3O_2$. Calculated: Cl 22.32; N 13.2%.

5-Ethyl Aminoanthra[1,9-cd]-6-isoxazolone. A 1.63-g (40 mmole) sample of ethylamine hydrochloride, 2 ml of H_2O, and 1.5 g of Na_2CO_3 (crystalline) were added to a suspension of 1.28 g (5 mmole) of isoxazolone Ia in 50 ml of dioxane, and the mixture was stirred at 20°C for 25 h, after which 300 ml of water was added, 30 g NaCl was added, and the precipitate was removed by filtration to give 1.0 g (75.8%) of 5-ethylaminoanthra[1,9-cd]-6-isoxazolone with mp 163-165°C [from ethanol—toluene (3:1)]. UV spectrum (in THF), λ_{max} (log ε): 253 (4.45), 259 (4.52), 490 (4.22), 522 nm (4.28). Found: N 10.5%. $C_{16}H_{12}N_2O_2$. Calculated: N 10.6%.

TABLE 2. Conditions for the Synthesis of and Characteristics of the Products of the Reaction of 5-Aziridinoanthra[1,9-cd]-6-isoxazolones with HY Acids



Compound	R	Y	Reaction temp. °C; time, min	mp, °C	Electronic spectrum, λ_{max}, nm (log ε)	Found, %		Empirical formula	Calc. %		Yield, %
						Hal	N		Hal	N	
IIIa	H	Cl	35—40; 10	152—154[a]	252 (4,44), 258 (4,52), 486 (4,22), 520 (4,26)	12,2	9,6	$C_{16}H_{11}ClN_2O_2$	11,9	9,4	87,1
IIIb	H	Br	35—40; 10	163—165[a]	253 (4,43), 260 (4,51), 488 (4,20), 520 (4,25)	23,5	8,0	$C_{16}H_{11}BrN_2O_2$	23,3	8,2	79,6
IIIc	H	$OCOCH_3$	35—40; 10	175—177[a]	253 (4,48), 260 (4,55), 490 (4,27), 522 (4,35)		8,7	$C_{18}H_{14}N_2O_4$		8,7	84,5
IIId	CH_3	Cl	70—80; 40	197—199[b]	253 (4,47), 259 (4,98), 485 (4,23), 515 (4,29)	11,11	8,7	$C_{17}H_{13}ClN_2O_2$	11,36	9,0	80,0
IIIe	CH_3	Br	60—70; 40	172—175[c]	252 (4,44), 260 (4,48), 483 (4,23), 515 (4,28)	22,9	7,6	$C_{17}H_{13}BrN_2O_2$	22,4	7,8	75,6
IIIf	CH_3	$OCOCH_3$	60—70; 20	176—178[a]	252 (4,50), 259 (4,52), 485 (4,25), 538 (4,30)		8,2	$C_{19}H_{16}N_2O_4$		8,4	80,4
IIIg	Cl	Cl	35—40; 30	188—190[a]	255 (4,43), 261 (4,53), 498 (4,19), 533 (4,23)	20,8	8,6	$C_{16}H_{10}Cl_2N_2O_2$	21,3	8,4	75,0
IIIh	Cl	$OCOCH_3$	60—70; 30	212—216[a]	255 (4,43), 261 (4,53), 498 (4,19), 533 (4,23)	9,5	8,3	$C_{18}H_{13}ClN_2O_4$	10,0	7,8	77,0
IIIi	Br	$OCOCH_3$	90—100; 30	192—195[d]	255 (4,42), 262 (4,54), 496 (4,19), 532 (4,29)	20,2	6,9	$C_{18}H_{13}BrN_2O_4$	20,0	7,0	75,0

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[a] From ethanol—toluene (3:1).
[b] From toluene—m-xylene (3:1).
[c] From toluene.
[d] From m-xylene.

5-Aziridinoanthra[1,9-cd]-6-isoxazolones (IIa-d). A solution of 0.86 g (20 mmole) of aziridine in 10 ml of the solvent used was added with stirring at 20-25°C to a suspension of 5 mmole of isoxazolone Ia-d in 30-40 ml of DNF or DMA, after which the mixture was stirred for another 3 h. It was then cooled to −10°C and maintained at this temperature for 5-10 h. The precipitate was removed by filtration and crystallized.

5-(β-Haloethylamino)anthra[1,9-cd]-6-isoxazolones (IIIa, b, d, e, g). To a suspension of 2.5 mmole of isoxazolone IIa-d in 20 ml of dioxane was added with stirring 10 ml of 36% HCl or 48% HBr. The reaction mixture was maintained at the temperature indicated in Table 2 for 10-40 min, after which it was diluted with water to 300 ml, and the precipitate was removed by filtration and crystallized.

5-(β-Acetoxyethylamino)anthra[1,9-cd]-6-isoxazolones (IIIc, f, h, i). A 2.5-mmole sample of IIa-d was stirred in 20 ml of a mixture of dioxane and 20 ml of acetic acid (10-30 min) at the temperature indicated in Table 2. The mixture was then diluted with 100 ml of water and the precipitate was removed by filtration and crystallized.

1-Amino-4-(β-haloethylamino)-9,10-anthraquinones (IVa, b). A 0.1-g sample of 0.2% of palladium on charcoal and 0.5 ml of hydrazine hydrate were added to a suspension of 2 mmole of isoxazolones IIIa, b in 20 ml of ethanol, and the mixture was stirred at 40-50°C for 2 h. The reaction product and the catalyst were then removed by filtration. This mixture was treated with 30 ml of dioxane at 50-80°C. The ethanol filtrate and the dioxane extract were combined and poured into 200 ml of H_2O at 20-25°C. The precipitated product was removed by filtration and crystallized from m-xylene. The yield of IVa, with mp 201-202°C (from xylene), was 0.52 g (86%). UV spectrum (dioxane), λ_{max} (log ε): 566 (4.14) and 609 nm (4.15). Found: Cl 11.84; N 8.94%. $C_{16}H_{13}ClN_2O_2$. Calculated: Cl 11.81; N 9.32%. The yield of IVb, with mp 158-160°C (from xylene), was 0.64 g (92%). UV spectrum (dioxane), λ_{max} (log ε): 566 (4.10) and 609 nm (4.10). Found: Br 22.5; N 8.2%. $C_{16}H_{13}BrN_2O_2$. Calculated: Br 23.2; N 8.1%.

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