TRANSFORMATIONS OF ANTHRA[1,9-cd]ISOXAZOL-6-ONES IN HYDROHALIC ACIDS

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4-Halo-1-aminoanthraquinones are formed when anthra[1,9-cd]isoxazol-6-ones are refluxed in hydrohalic acids. The 3 position undergoes halogenation when 5-substituted isoxazoles are used. The process takes place via a one-proton mechanism with the participation of halide ion in the rate-determining step, possibly with the intermediate formation of N-haloaminoanthraquinones.

It is known that anthra[1,9-cd]isoxazol-6-one (Ia) is converted to 1-amino-4-hydroxyanthraquinone when it is heated in sulfuric acid [1]. The aim of the present research was to study the behavior of anthra[1,9-cd]-isoxazol-6-ones (Ia-e) with respect to hydrohalic acids.

We observed that Ia-e are converted smoothly to 1-amino-4-haloanthraquinones IIa-g when they are heated in hydrobromic or hydrobromic acid. The corresponding 1-amino-2-haloanthraquinones were formed when 5-substituted compounds (Table 1) are used. The reaction proceeded quite readily in concentrated hydrohalic acids; however, a mixture of equal volumes of the hydrohalic acid and acetic acid was used to increase the solubilities of the starting Ia-e.

In order to ascertain the mechanism of the investigated reaction we studied the kinetics of conversion of anthra[1,9-cd]isoxazol-6-one in 20-40% hydrobromic acid at 80°C; in this case we observed that the rate of the Ia → IIa transformation increases when the hydrobromic acid concentration is increased. The kinetics were studied by spectrophotometry. The reaction was described by a first-order reaction. The rate constants (k_{eff}) coincided when the reaction was followed from both the decrease in the amount of the starting compound (Ia) and from the accumulation of the final product (IIa).

Considering the high thermal stability of anthra[1,9-cd]isoxazol-6-ones [7] in inert solvents, one should have assumed the participation of a protonated molecule of Ia in the reaction. In fact, the rate constants (k_{eff}) of the investigated reaction increased when the hydrobromic acid concentration was increased. The reaction rates differed substantially (the half-conversion periods were 25 and 180 min, respectively) during a study of the conversion of anthra[1,9-cd]isoxazol-6-one in hydrobromic and hydrochloric acids with identical H_0 [values 36% HBr ($H_0 = -2.33$) and 21.74% HCl ($H_0 = -2.33$)] at 80°C. It may be assumed that protonated anthra 1,9-cd isoxazol-6-one is attacked by halide ion in the rate-determining step of the reaction at the instant at which it undergoes ring opening. The dependence of $\log k_{eff}/[Br^-]$ on H_0, which is presented in Fig. 1, also constitutes evidence in favor of this assumption. The slope of the line is close to −1, which confirms a one-proton mechanism for the investigated reaction [8]. It might be expected that in the slow step the halide ion attacks either the nitrogen atom of Ia (process A) or the 5 position (process B), since the conversion of anthra[1,9-cd]isoxazol-6-one in sulfuric acid leads to 1-amino-4-hydroxyanthraquinone. If process A is realized, the formation of the final product should take place as a consequence of bromination of 1-aminoanthraquinone, as shown in the scheme. To confirm this hypothesis we carried out the conversion of anthra[1,9-cd]isoxazol-6-one (Ia) in a mixture consisting of equal volumes of 40% hydrobromic acid and acetic acid in the presence of a threefold excess of an easily brominated phenol, in this case virtually no 1-amino-4-bromoanthraquinone was formed, and Ia was converted completely to 1-aminoanthraquinone. The latter confirms the formation of N-bromoaminoanthraquinone (IV) in the investi-

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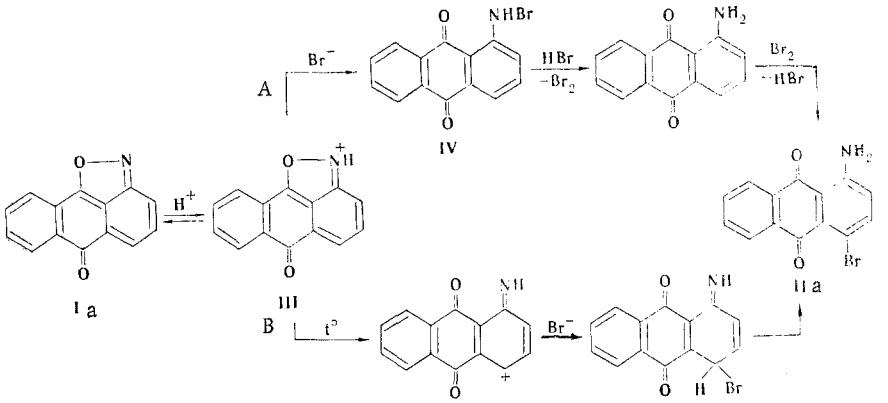
TABLE 1. Aminoanthraquinones

Compound	Starting isoxazole	mp, * °C	Found, % Hal	Found, % N	Empirical formula	Calc., % Hal	Calc., % N	Yield, %
IIa	Ia	177—178 (177,5—179 [2])	26,92 26,80	4,50 4,54	$C_{14}H_8BrNO_2$	26,46	4,64	80
IIb	Ia	177 (177—178 [2])	13,64 13,69	5,60 5,58	$C_{14}H_8ClNO_2$	13,78	5,41	74
IIc	Ib	245 (245—246 [3])	25,57 25,63	4,42 4,38	$C_{15}H_{10}BrNO_2$	25,28	4,43	75
IId	Ib	254 (255—256 [4], began at 245)	13,50 13,55	5,29 5,36	$C_{15}H_{10}ClNO_2$	13,07	5,14	62
IIe	Ic	217 (217 [5])	—	4,20 4,19	$C_{14}H_7BrClNO_2$	—	4,15	78
IIf	Id	211	—	4,08 4,10	$C_{14}H_7BrClNO_2$	—	4,15	70
IIg	Ie	227 (226—227 [6])	42,35 42,32	3,81 3,78	$C_{14}H_7Br_2NO_2$	41,94	3,67	69

*The compounds were recrystallized: IIa-f from acetic acid, and IIg from xylene.

gated reaction. In addition, we observed that unsubstituted anthra[1,9-cd]isoxazol-6-one is converted more rapidly to 1-amino-4-bromoanthraquinone in 30% hydrobromic acid at 80°C ($K_{eff} = 1.8 \cdot 10^{-2}$) than 3-chloro-anthra[1,9-cd]isoxazol-6-one ($k_{eff} = 1.36 \cdot 10^{-4}$) and 3-methyl-



Ia 3-H, 5-H; b 3-CH_3, 5-H; c 3-Cl, 5-H; d 3-H, 5-Cl; e 3-H, 5-Br; II a 2-H, 4-Br; b 2-H, 4-Cl; c 2-CH_3, 4-Br; d 2-CH_3, 4-Cl; e 2-Cl, 4-Br; f 2-Br, 4-Cl; g 2-Br, 4-Br

anthra[1,9-cd]isoxazol-6-one ($k_{eff} - 1.95 \cdot 10^{-4}$), respectively, to IIe and IIc. The latter is probably explained by the steric hindrance created by the substituents in the 3 position at the instant of attack on the nitrogen atom by the bromide ion.

EXPERIMENTAL

Anthra[1,9-cd]isoxazol-6-ones Ia-e were obtained by the method in [1].

1-Aminohaloanthraquinones (IIa-g). A 0.01-mole sample of Ia-e was added to a mixture consisting of equal volumes (50 ml) of 42-45% hydrobromic acid or 36% hydrochloric acid and acetic acid, and the resulting mixture was refluxed for 1-3 h. The course of the reaction was monitored by thin-layer chromatography on Silufol plates. The reaction mixture was poured over ice (150-200 g), and IIa-g were removed by filtration and purified by recrystallization from acetic acid.

The kinetics of the anthraisoxazolone Ia → IIa conversion was studied in the following way. A solution of Ia in 0.21 ml of acetic acid was added to a thermostated (at 80 ± 0.1°C)

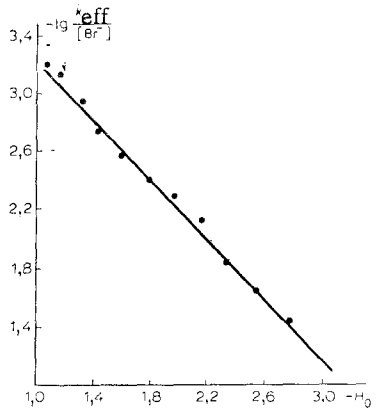


Fig. 1. Dependence of log $k_{eff}/[Br^-]$ on H_o for anthra[1,9-cd]-isoxazol-6-one in hydrobromic acid at 80°C (tan α = −1.037, r = 0.998, S = ± 0.002).

sample of hydrohalic acid with a predesignated concentration in such a way that its final concentration was 10^{-4} mole/liter. At definite intervals the contents of the tightly sealed flasks were mixed with an equal volume of pyridine cooled to 0°C. The solutions were analyzed in 2-cm glass cuvettes with an SF-14 spectrophotometer. In all cases the absorption lines passed through an isobestic point. The optical densities at the absorption maxima of the starting isoxazole (λ_{max} 457 nm) and 1-amino-4-bromoanthraquinone (λ_{max} = 476 nm) were used to calculate the k_{eff} values. The experiments were reproduced two to three times, and the k_{eff} values coincided within the limits of the errors in the measurements. The known H_o values for hydrochloric [9] and hydrobromic [10] acids were used in the research.

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