STUDIES ON QUINONES

VII. Reaction of Anthra[1,2-c]-1,2,5-oxadiazole-6,11-dione with Amines*

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Anthra[1,2-c]-1,2,5-oxadiazole-6,11-dione (I) readily reacts with ammonia and primary and secondary amines, being converted with a yield of about 80—83% into the corresponding 4-amino derivatives of anthra[1,2-c]-1,2,5-oxadiazole-6,11-dione (III).

Anthra[1,2-c]-1,2,5-oxadiazole-6,11-dione (I), the reaction of which with bisulfite has been described previously [2], reacts with amines with even greater readiness than its selena and thia analogs [3, 4]. Even at room temperature and in the absence of oxygen the action of aliphatic amines gives amino derivatives of II with yields of more than 80%. The other part of the initial quinone undergoes far-reaching degradation and is converted into a mixture of resinous substances, obviously by the oxidation of the primary addition products.

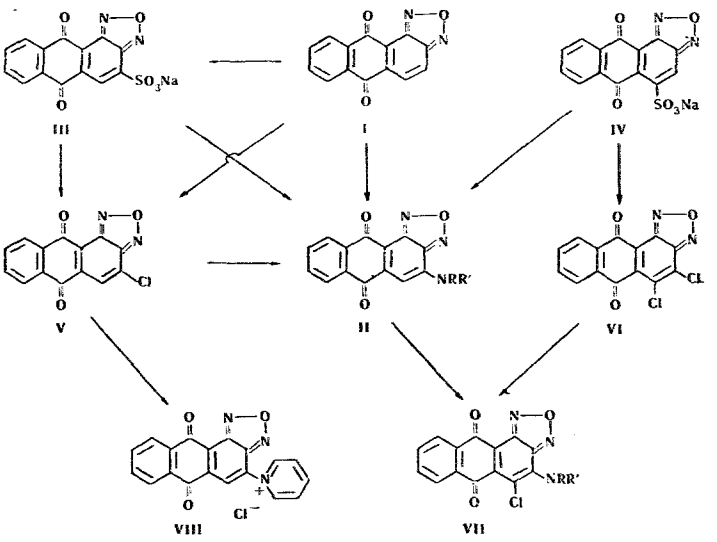
To determine the position of entry of the amine residue into the anthraquinoneoxadiazole molecule, it was first proposed to use its sulfonic acid derivatives III and IV [2]. However, in an aqueous solution of cyclohexylamine both the 4-sulfonic acid III and the 5-sulfonic acid (IV) are converted into the same compound IIf as the unsubstituted quinone I, i.e., the addition of the amine to one of the sulfonic acids is accompanied by the splitting off of the sulfo group from the neighboring carbon atom.

The treatment of the 4-sulfonic acid III with potassium chlorate in hydrochloric acid leads exclusively to 4-chloroanthra[1,2-c]-1,2,5-oxadiazole-6,11-dione (V) [2] while in the case of the 5-sulfonic acid IV, in addition to the replacement of the sulfo group, additional chlorination occurs. Anthraquinoneoxadiazole I itself, as has been established, smoothly chlorinates under these conditions in position 4. Consequently the dichloro derivative isolated in the experiments with the 5-sulfonic acid IV was assigned the structure of 4,5-dichloroanthra[1,2-c]-1,2,5-oxadiazole-6,11-dione (VI).

The reaction with cyclohexylamine of the 4-chloroanthraquinoneoxadiazole V and the unsubstituted quinone I has given one and the same amino derivative IIf, and the 4,5-dichloro substituted compound VI has given compound VII (R = H, R = C_6H_{11}), which has also been synthesized by the chlorination of IIf with sulfuryl chloride. It follows from this that a chlorine atom in position 4 of anthraquinoneoxadiazole is replaced by an amine residue while one in position 5 is not affected and that the products of the reaction of the quinone I with amines are the 4-amino derivatives II.

Chlorine in position 4 of anthraquinoneoxadiazole is so mobile that it is replaced even by a tertiary amine residue. Thus, when 4-chloroanthra[1,2-c]-1,2,5-oxadiazole-6,11-dione (V) is boiled in pyridine, the quaternary pyridinium salt VIII is formed. In the anthraquinone series, this reaction has been described only for the o-nitrohaloanthraquinones [5].

The 4-amino derivatives II were obtained from ammonia and the primary and secondary aliphatic, heterocyclic, and aromatic amines given in the table. The color of the compounds depends considerably on the substituent attached to the amine nitrogen. The position of the absorption maximum shifts from 532 nm



*For part VI, see [1].

4-Amino Derivatives of Anthra[1,2-c]-1,2,5-oxadiazole-6,11-dione (II)

Compound	NRR′	Mp, °C (solvent)	λ_{max}, nm (log ε) (in ethanol)	Empirical formula	Found, %			Calculated, %		
					C	H	N	C	H	N
IIa	NH_2	decomp. 320 (nitrobenzene)	532*	$C_{14}H_7N_3O_3$	63.36 63.15	2.75 2.87	15.64	63.40	2.65	15.84
IIb	$NHCH_3$	279—280 (nitrobenzene)	544 (4.06)	$C_{15}H_9N_3O_3$	64.74 64.66	3.40 3.54	14.88 14.81	64.51	3.25	15.05
IIc	$NH(CH_2)_3CH_3$	222—223 (ethanol)	542 (4.10)	$C_{18}H_{15}N_3O_3$	—	—	12.82 12.97	—	—	13.08
IId	$NH(CH_2)_4CH_3$	218—219 (ethanol)	540 (4.10)	$C_{19}H_{17}N_3O_3$	68.27 68.07	5.04 5.05	12.58 12.77	68.05	5.11	12.53
IIe	$NH(CH_2)_5CH_3$	235.5—236 (ethanol)	543 (4.10)	$C_{20}H_{19}N_3O_3$	68.58 68.54	5.53 5.44	11.90 11.85	68.75	5.48	12.03
IIg	NHC_6H_{11}	245.6—246 (dioxane)	545 (4.10)	$C_{20}H_{17}N_3O_3$	69.25 69.41	4.98 5.22	12.02 12.03	69.15	4.93	12.10
IIf	$NHCH_2CH_2OH$	270 (decomp.) (dimethylformamide)	535*	$C_{16}H_{11}N_3O_4$	—	—	13.38 13.29	—	—	13.59
IIh	$N(CH_3)_2$	280—281 (ethanol)	560 (4.12)	$C_{16}H_{11}N_3O_3$	65.45 65.38	4.02 3.95	14.28 14.15	65.52	3.78	14.33
IIi	$N(C_2H_5)_2$	236—237 (ethanol)	564 (4.16)	$C_{18}H_{15}N_3O_3$	—	—	13.04 13.29	—	—	13.08
IIj	$N(n\text{-}C_4H_9)_2$	153—154 (ethanol)	566 (4.18)	$C_{22}H_{23}N_3O_3$	69.90 69.85	6.05 5.93	11.17 11.25	70.01	6.14	11.13
IIk	$N(CH_2CH_2OH)_2$	209—210 (ethanol)	560 (4.10)	$C_{18}H_{15}N_3O_5$	—	—	11.70 11.62	—	—	11.89
III		259—261 (ethanol)	565 (4.12)	$C_{19}H_{15}N_3O_3$	68.54 68.47	4.62 4.58	12.72 12.64	68.46	4.54	12.61
IIm		265—267 (chlorobenzene)	570 (4.06)	$C_{20}H_{17}N_3O_3$	—	—	11.92 12.15	—	—	12.10
IIn		258—259.5 (ethanol)	540 (4.09)	$C_{18}H_{13}N_3O_4$	64.39 64.71	4.11 3.83	12.60 12.74	64.47	3.91	12.53
IIo	NHC_6H_5	252—253.5 (chlorobenzene)	547 (4.14)	$C_{20}H_{11}N_3O_3$	70.16 70.22	3.34 3.15	12.11 12.02	70.38	3.25	12.31
IIp	$NHC_6H_4CH_3\text{-}p$	284.5—286 (trichlorobenzene)	550 (4.15)	$C_{21}H_{13}N_3O_3$	71.19 70.90	3.68 3.92	11.91 11.79	70.98	3.69	11.83
IIq	$NHC_6H_4Cl\text{-}p$	303—304 (dioxane)	545 (4.06)	$C_{20}H_{10}ClN_3O_3$**	—	—	10.93 11.07	—	—	11.19
IIr	$NHC_6H_4OH\text{-}p$	decomp. 305 (aqueous dioxane)	567 (4.13)	$C_{20}H_{11}N_3O_4$	67.41 67.35	3.28 3.15	11.54 11.63	67.22	3.10	11.76
IIs	$NHC_6H_4NH_2\text{-}p$	290 (decomp.) (dioxane)	572 (4.11)	$C_{20}H_{12}N_4O_3$	—	—	15.81 15.88	—	—	15.72

*Saturated solution

**Found, %: Cl 9.32, 9.24. Calculated, %: Cl 9.45.

for the unsubstituted amine IIa to 540–545 nm for the monoalkylamino and to 560–570 nm for the dialkylamino derivatives. The phenyl radical exerts approximately the same influence as the cyclohexyl radical, but the introduction of an amino or a hydroxy group into the para position of the phenyl causes a bathochromic shift by 20–25 nm. From the value of λ_{max} in the long-wave region, the 4-amino derivatives of the anthraquinoneoxa-, -thia-, and -selenadiazoles are arranged in the sequence: S < O < Se, although the anthradiazoles themselves have a different sequence: O < S < Se.

The rate of the reaction of the anthraquinonediazoles with amines rises on passing from a selenadiazole to a thiadiazole and further to an oxadiazole in agreement with the increase in the electronegativity of the heteroatom.

EXPERIMENTAL

4-Aminoanthra[1,2-c]-1,2,5-oxadiazole-6,11-dione (IIa). A solution of 2.50 g (0.01 mole) of I in 80 ml of dioxane at 80° C was treated with 20 ml of 25% ammonia and the mixture was boiled for 3 min. After cooling, the precipitate was separated off from the blue solution and was washed with 200 ml of 30% aqueous dioxane and with ethanol. This gave 1.92 g (70%) of the red-violet compound **IIa**, sparingly soluble in organic solvents.

Similarly, the amino derivatives IIb and IIh (table) were synthesized using methylamine and dimethylamine, respectively.

The acetyl derivative **IIa** forms yellow tetrahedral prisms (from trichlorobenzene), mp 330° C (decomp). In concentrated sulfuric acid, the substance dissolves with a yellow coloration which changes on heating into blue-violet as a result of the transformation into **IIa**. Found, %: N 13.45, 13.30. Calculated for $C_{16}H_9N_3O_4$, %: N 13.67.

4-Cyclohexylaminoanthra[1,2-c]-1,2,5-oxadiazole-6,11-dione (IIf). a) A mixture of 2.50 g of I and 25 ml of cyclohexylamine was boiled for 10 min and was poured into 400 ml of 5% hydrochloric acid. The precipitate (3.38 g) was filtered off, washed with water, dried, and chromatographed on alumina, being eluted with chloroform. The yield of IIf was 2.83 g (81%). Under the same conditions, 2.85 g (0.01 mole) of V gave 2.90 g (83%) of **IIf**, mp 245–245.5° C; mixture of the specimens mp 245–245.8° C. The substance is insoluble in water and dilute mineral acids and dissolves in chloroform, dioxane, and chlorobenzene with a pink coloration and a strong yellow fluorescence, and in sulfuric acid, ethanol, aqueous dioxane, acetic acid, and dimethylformamide with a red-violet coloration.

Compounds IIc–g, i–n were obtained similarly using the appropriate amines (table).

b) A solution of 1.500 g (0.006 mole) of I in 15 ml of dimethylformamide and a solution of 0.9 g (0.009 mole) of cyclohexylamine in 4 ml of dimethylformamide through which a current of hydrogen or a current of nitrogen freed from oxygen had previously been passed for several hours were mixed at 20° C. A violet coloration immediately appeared. After being stirred for 4 hr in a current of gas, the solution was poured into dilute hydrochloric acid. Chromatography on alumina in chloroform yielded 1.280 g (61.5%) of IIf and 0.402 g (26.6%) of the initial I; yield 83% calculated on the quinone I that had reacted.

c) A solution of 0.002 mole of the sodium salt of the sulfonic acid III or IV in 12 ml of water was treated with 2 ml of cyclohexylamine and heated at 95° C for 30 min. The precipitate was filtered off, washed with hot water, and recrystallized from dioxane. In both cases, 0.41–0.42 g (~60%) of compound IIf was obtained with mp 244.5–245.5° C, giving no depression of the melting point in admixture with the substance synthesized from I.

4-Phenylaminoanthra[1,2-c]-1,2,5-oxadiazole-6,11-dione (IIo). a) A mixture of 1.25 g (0.005 mole) of I and 20 g of aniline was heated at 130° C for 1 hr. The excess of aniline was eliminated by treatment with 5% hydrochloric acid and the residue (1.56 g) was chromatographed on alumina, being eluted with chloroform. This gave 0.25 g (20%) of the initial I and 1.14 g (65%) of the amino derivative **IIo**; the yield calculated on the I that had reacted was 81%.

The amino derivatives IIp and IIq (table) were obtained similarly.

b) A mixture of 0.57 g (0.002 mole) of V, 20 ml of ethylene glycol, and 0.56 g (0.006 mole) of aniline was heated at 160° C for 30 min and was then cooled to 80° C and diluted with hot water; the precipitate was filtered off, washed with water, and dried; blue prisms (from chlorobenzene); yield 0.62 g (about 90%). The amino derivatives IIr and IIs (table) were obtained similarly.

4-Chloroanthra[1,2-c]-1,2,5-oxadiazole-6,11-dione (V). A solution of 0.50 g (0.002 mole) of I in 15 ml of acetic acid at 90° C was treated with 40 ml of hot water and 5 ml of concentrated hydrochloric acid. Over 45 min, a solution of 1.5 g of potassium chlorate in 20 ml of water was added to the boiling suspension, after which the mixture was boiled for another 4 hr and the precipitate (0.52 g) was separated off. After crystallization from acetic acid, mp 245–245.5° C; a mixture with a specimen obtained from the 4-sulfonic acid III [2] had mp 245.6–245.9° C.

4,5-Dichloroanthra[1,2-c]-1,2,5,-oxadiazole-6,11-dione (VI). As described for the sodium salt III [2], 1.55 g (0.004 mole) of the sodium salt IV was treated with potassium chlorate. The precipitate (0.70 g) was dissolved in chloroform and passed through a layer of alumina and the substance was then crystallized repeatedly from acetic acid and benzene. This gave 0.21 g of elongated light yellow prisms with mp 223–223.8° C. Found, %: C 52.49, 52.33; H 1.30, 1.29; Cl 22.35, 22.26; N 8.80, 8.75. Calculated for $C_{14}H_4Cl_2N_2O_3$, %: C 52.67; H 1.25; Cl 22.24; N 8.78.

5-Chloro-4-cyclohexylaminoanthra[1,2-c]-1,2,5-oxadiazole-6,11-dione (VII). a) A solution of 0.50 g (1.6 mmole) of VI in 5 ml of cyclohexylamine was boiled for 1–2 min and was poured into dilute hydrochloric acid, and the reaction product (0.61 g) was crystallized from chlorobenzene and dioxane. Violet brown plates with a golden luster, mp 245–246° C.

b) Over 5 min, a mixture of 0.40 g (0.003 mole) of sulfuryl chloride and 8 ml of chloroform was added to a boiling solution of 0.794 g (0.002 mole) of IIf in 20 ml of chloroform. After cooling, the plates that had deposited (0.405 g) were filtered off. A further 0.16 g of substance was obtained after the evaporation of the filtrate; yield 73%, mp 246–247° C, mp of the mixture with the material obtained in case (a)—245.7–246.5° C. Found, %: C 62.76, 62.72; H 4.19, 4.30; Cl 9.17, 9.05; N 11.00, 10.76. Calculated for $C_{20}H_{16}ClN_3O$, %: C 62.92; H 4.19; Cl 9.30; N 11.00.

Reaction of 4-chloroanthra[1,2-c]-1,2,5-oxadiazole-6,11-dione (V) with pyridine. A mixture of 0.50 g (1.8 mmole) of V and 15 ml of pyridine was boiled for 2–3 min. From the emerald green solution a crystalline precipitate deposited from which extraction with methanol and subsequent treatment with hot pyridine and benzene isolated 0.21 g of the grayish yellow pyridinium chloride **VIII**. The substance gives a red-violet coloration in methanol, and is very sparingly soluble in water forming a yellowish solution, which when made alkaline, deposits a green precipitate. The compound was analyzed in the form of the sparingly water-soluble perchlorate. Found, %: Cl 8.15, 8.22; N 9.63, 9.81. Calculated for $C_{19}H_{16}ClN_3O_7$, %: Cl 8.30; N 9.82.

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