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RESEARCHES ON ANTHRAPYRIDONES

II. Sulfonation of 1-Acetylanthrapyridone and Hydrolysis of 1-Acylanthrapyridones*

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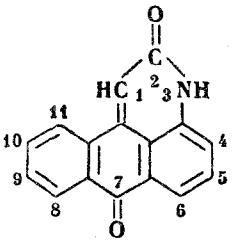
Under mild conditions 1-acetylanthrapyridone sulfonates to 1-ω-sulfoacetylanthrapyridone. It is shown that aqueous alkalies or primary amines in the presence of proton donors split off the acyl group from 1-acylanthrapyridone. Possible reaction mechanisms are considered.

It is known that anthraquinone sulfonates under rather drastic conditions compared with benzene or naphthalene derivatives. The behavior was similar for sulfonating agents and derivatives of anthrapyridone {7H-dibenz [*f*, ij] isoquinoline-2, 7 (3H)-dione} (I). Thus when we attempted to sulfonate N-methylanthrapyridone with 30% oleum at 90°, only traces of sulfonic acid could be isolated.



I

Still, the patent literature [1] indicates a case of sulfonation of anthrapyridones under mild conditions, when they "contain electronegative substituents and aryl groups undergoing sulfonation are absent." In the examples given by the authors, 4, 6-dibromo-1-acetylanthrapyridone, 6-methoxy- and 6-bromo-N-methyl-1-acetylanthrapyridone are sulfonated at room temperature by 5-10% oleum. It is noted that the electronegative substituent itself is unaffected by the sulfonation. The patent does not say anything about the positions of the sulfonic acid groups in the resultant sulfonic acids.

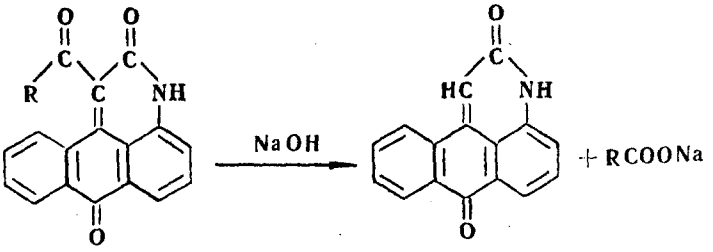
We have sulfonated 1-acetylanthrapyridone (II) under the given conditions, and isolated a monosulfonic acid (III). Attempts to fix the position of the sulfonic acid group in III by comparison with 1-acetylanthrapyridone sulfonic acids with the sulfonic acid group at various positions in the anthraquinone ring system, as prepared by retro-synthesis, were unsuccessful. Condensation of the corresponding 1-aminoanthraquinonesulfonic acids with acetoacetic ester gave the isomeric 4-, 5-, 8-, 9-, and 10-sulfonic acids of 1-acetylanthrapyridone, and their S-benzylthiuronium salts. Not one of the sulfonic acids named was identical with the one under investigation, III. 1, 8-aminoanthraquinonesulfonic acid could not be converted to 1-acetylanthrapyridone-11-sulfonic acid, evidently because of steric hindrance to cyclization.

It was necessary to have recourse to destructive methods of determining structure. Reductive hydrolysis of sulfonic acid III with sodium hydrosulfite in weakly alkaline medium led to the isolation of unchanged anthrapyridone I. Previously it had been shown [2, 3] that under like conditions similar compounds could split off both the acyl group and the mobile sulfonic group (at position 4). We obtained more interesting results by oxidizing III with chromic anhydride in 85% acetic acid, when 1-aminoanthraquinone is formed. When a 1-acetylanthrapyridone sulfonic acid having the sulfonic acid group in the anthraquinone ring system was oxidized under the same conditions, that group was not split off. For example, 1-acetylanthrapyridone-8-sulfonic acid oxidizes to 1-aminoanthraquinone-5-sulfonic acid under those conditions. Thus it emerged that the sulfonic acid group was in the pyridone ring system.

It was discovered that 1-acylanthrapyridones, like derivatives of β-ketocarboxylic acids and β-diketones, can suffer acid decomposition when treated with alkali. For example boiling II or 1-benzoylanthrapyridone (IV) with 5% sodium hydroxide gives unsubstituted I and the corresponding acid.

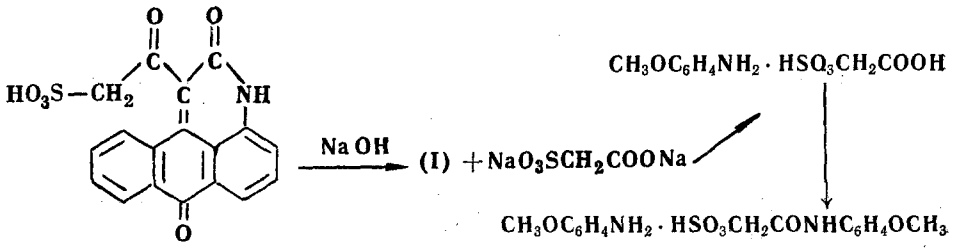
When sulfonic acid III was subjected to alkaline hydrolysis, I was also isolated, but no SO_4^{--} ions were found in the filtrate. So it had to be concluded that on sulfonation the sulfonic acid group enters the acetyl group, and that on hydrolysis sulfoacetic acid is formed. Actually, after removing I, sulfoacetic acid was isolated from the filtrate as its barium salt, and identified as its p-anisidine salt, and as the p-anisidine salt of the C-anisidine of the sulfoacetic acid [4].

*For Part I see [2].



II IV

R = CH_3 (II) or C_6H_5 (IV)



III

It is of interest that splitting off of the acyl group from 1-acylanthrapyridones is found to occur not only in dilute alkali, but under various conditions, and in amine media. The reaction of splitting off the acyl group from 1-acetyl-N-methylanthrapyridone by aniline plus small amounts of aniline hydrochloride at 180° was described in 1959 [5].

We noted that II and IV are unusually readily split in ethanolamine solution. Reaction occurs at appreciable speed

Splitting of 1-Acylanthrapyridones

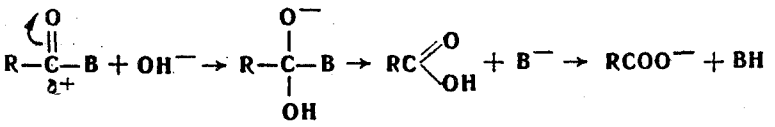
Starting 1-acyl-anthra pyridone	Reagent	Temper-ature, °C	Time, hr	Compound isolated
IV	Hexylamine	140	8	IV
II	Hexylamine	140	8	II
IV	Hexylamine + phenol	150	8	I
IV	Hexylamine + hexanol	150	8	IV
II	Hexylamine + HCl	110	1	I
II	Aniline	160	8	II
II	Aniline + HCl	160	2	I
IV	Aniline + phenol	170	8	IV
IV	Phenol	160	8	IV
IV	Glycol	150	8	IV
IV	Piperidine + glycol	150	8	IV
IV	Cyclohexylamine + glycol	150	8	IV
IV	Pyridine + phenol	130	8	IV
IV	Butylamine + glycol	80	6	IV

even at room temperature, and at 90°complete splitting requires a few minutes. The split-off acid group links up to give β-hydroxyethylamide. It was further shown that when solutions of 1-acylanthrapyridones in various amines, alcohols, or phenol are heated, they do not undergo any change. However, a mixture of primary aliphatic amine plus ethylene glycol or phenol at over 100° hydrolyzates the acyl group, but aromatic amines, used correspondingly, do not. 1-Acylanthrapyridones are vigorously hydrolyzed by both aliphatic and aromatic amines in the presence of small amounts of hydrochloric acid.

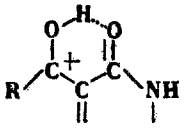
It can be assumed that the hydrolysis of 1-acylanthrapyridones (see table) by alkalies or amines in the presence of proton donors, leading in both cases to the formation of unsubstituted anthrapyridone, proceeds by two different mechan-

isms.

Alkaline hydrolysis involves nucleophilic attack of the OH^- anion on the carbon atom whose positive charge is connected with polarization of the C= O link. A similar reaction mechanism is generally accepted for alkaline hydrolysis of β-diketones [6].



Hydrolysis by amines, which is found only in the presence of proton donors (acids, phenol, glycol) is probably connected with addition of a proton to the carbonyl oxygen of the acyl group, like the initial stage of acid catalyzed formation of Schiff's bases:



Such a coplanar transition state of the 1-acylanthrapyridone can be stabilized by hydrogen bonding leading to formation of a six-membered ring system. Nucleophilic attack by the amine on the positively charged carbon atom subsequently leads to splitting of the C–C bond and formation of the amide of the acid.

Experimental

Starting materials

1-Acetylanthrapyridone (II) was prepared by treating 1-aminoanthraquinone with acetoacetic ester [8]; mp 288-289° (from dimethylformamide).

1-Benzoylanthrapyridone (IV) was prepared by treating 1-aminoanthraquinone with benzoylacetic ester [8]; mp 348.5-349.6° (from trichlorobenzene).

Anthrapyridone (I) was prepared from 1-aminoanthraquinone and acetic anhydride [9], and purified by reprecipitation from sulfuric acid, followed by recrystallization from dimethylformamide; mp 408-410°.

1-ω-Sulfoacetyl-7H dibenz [*f*, ij] isoquinoline-2, 7(3H) dione (III). 5.8 g (0.02 mole) II was dissolved in 50 ml 7% oleum and stirred at 20° for 2-3 hr, until a portion dissolved completely in water. The sulfonated mass was poured onto ice, and the precipitate of sulfonic acid formed filtered off. After squeezing well, the paste of acid was dissolved in 250-300 ml aqueous n-butanol, and the filtrate extracted twice with 75 ml butanol. Butanol solution and extracts were fulked, washed three times with dilute HCl, and the butanol-water azeotrope distilled off. 2.6 g (36%) free sulfonic acid III separated from the dry butanol. Found: C 55.53, 55.24; H 3.45, 3.42; N 3.18, 3.26; S 8.25, 8.44; H_2O 4.75%. Calculated for $C_{18}H_{11}NO_6S \cdot H_2O$: C 55.82; H 3.36; N 3.62; S 8.26; H_2O 4.65%. S-benzylthiuronium salt mp 253.2-255° (from ethanol). Salting out with NaCl the hydrochloric acid washings further gave 2.1 g Na salt of III.

Oxidation of 1-acetylanthrapyridone (II). 1.00 g (3.5 mmole) II, 0.6 g (6 mmole) CrO_3, and 40 ml 85% AcOH were refluxed and stirred for 4 hr, then cooled, poured into 200 ml water, and twice extracted with 100 ml n-butanol each time. The total butanol extracts were washed with dilute HCl till the wash water was no longer green. The extract was evaporated to about 5 ml, the precipitate of 1-aminoanthraquinone which formed filtered off, washed with ether and recrystallized from glacial AcOH. Yield 0.34 g (44%), mp 250-251°, undepressed mixed mp with authentic 1-aminoanthraquinone.

Oxidation of III under the same conditions also led to the isolation of 1-aminoanthraquinone mp 250-251° (ex AcOH).

Hydrolysis of 1-acetylanthrapyridonesulfonic acid (III). 7.8 g (0.02 mole) III was refluxed with 100 ml 5% aqueous NaOH for 5 hr, when a precipitate of anthrapyridone I gradually formed. The suspension was cooled to 20°, neutralized with HCl, the yellow precipitate filtered off, washed with hot water, and dried. Yield of I 4.9 g (98.5%), mp 410° (from dimethylformamide), undepressed mixed mp with a specimen of the compound prepared by an independent method [9]. The filtrate was made alkaline with ammonia, and 10 g $BaCl_2$ added, next day the barium sulfoacetate was

filtered off, yield 4.6 g (82%).

For identification, 2.93 g of the latter (0.01 mole $C_2H_2O_6SBa \cdot H_2O$) was dissolved in hot water, an aqueous solution of 0.01 mole p-anisidine sulfate added, the barium sulfate precipitated filtered off, and the filtrate evaporated to dryness under reduced pressure. The dry residue was dissolved in 50 ml propanol, and the p-anisidine salt of sulfoacetic acid precipitated with 200 ml ether, yield 2.55 g (98%), mp 169.2-170.0° (from absolute ethanol). Found: N 5.22, 5.27; S 12.5, 12.6%. Calculated for $C_9H_{12}O_6NS$: N 5.34; S 12.2%. Undepressed mixed mp with a specimen of the compound prepared by an independent method [4].

1 g (3.8 mmole) p-anisidine salt was heated with 3 ml p-anisidine at 160-170° for 2 hr, the product cooled, diluted with ether, and the resultant p-anisidine salt of C-(p-anisidide) sulfoacetic acid recrystallized from ethanol, yield 0.92 g, mp 225.8-227.0°, the literature [4] gives mp 224-227°. Found: C 52.58, 52.18; H 5.57, 5.47; N 7.53, 7.51%. Calculated for $C_{16}H_{20}N_2O_6S$: C 52.25; H 5.45; N 7.62%.

Hydrolysis of 1-benzoylanthrapyridone (IV). a) 1.5 g (4.3 mmole) IV was refluxed for 5 hr with 15 ml 5% aqueous NaOH, the products cooled, acidified with HCl, filtered, and the solid I washed with hot water, yield 1.02 g (97%), mp 410° (from dimethylformamide). Two extractions of the acid filtrate with ether, followed by distilling off the latter gave 0.39 g (75%) benzoic acid mp 122-122.5° (ex water), undepressed mixed mp with an authentic specimen.

Similarly 0.5 g (1.7 mmole) 1-acetyl-N-methylanthrapyridone (mp 274-276.5°) gave 0.4 g N-methylanthrapyridone, mp 265-267.5°. Mixed mp with authentic pure N-methylanthrapyridone [10] undepressed.

b) 3.0 g (8.5 mmole) IV was treated with 30 ml ethanolamine at 90° for 20 min, the suspension then diluted with water, acidified with HCl, and the anthrapyridone filtered off, yield 2.1 g (99%), mp 408-410°. The filtrate was evaporated to dryness under reduced pressure, the dry residue twice washed with 50 ml $CHCl_3$ each time, the chloroform extracts evaporated to give an oily liquid, which was dissolved in 5 ml ethyl acetate, and then diluted with 40 ml ether. On standing crystals of β-hydroxyethyl-N-benzamide separated, yield 0.83 g (59%), mp 63.3-64.2°; mp of a specimen made from ethyl benzoate [11] and ethanolamine 65-65.8°, the mixed mp was 63.5-65.2°.

c) 4.0 g (11.4 mmole) IV, 10 ml n-hexylamine, and 15 ml ethylene glycol were stirred together for 5 hr at 140°, the products diluted with water, acidified with concentrated HCl, and I filtered off, yield 2.72 g (97%), mp 407-408°. The filtrate was evaporated under reduced pressure, the residue extracted three times with 50 ml ether each time, the bulked extracts twice washed with water, dried over Na_2SO_4, evaporated to 10 ml, and run through an Al_2O_3 column (eluant $CHCl_3$). The $CHCl_3$ eluate was evaporated to 3 ml, and diluted with petrol ether, the precipitate filtered off, and recrystallized from petrol ether. Yield of n-hexyl-N-benzamide 0.92 g, mp 41.0-42.4°. A specimen prepared by the Schotten-Baumann reaction had mp 41.0-42.2°, mixed mp undepressed.

Other experiments on the splitting of 1-acylanthrapyridone are given in the table.

REFERENCES

1. German patent 646 300, 1937; C. A., 31, 3478, 1937.
2. V. A. Puchkov and T. N. Kurdyumova, ZhOKh, 32, 638, 1962.
3. V. A. Puchkov and T. N. Kurdyumova, ZhOKh, 32, 950, 1962.
4. O. Stillich, J. Pr. Chem., 2, 74, 1906; 11, 1001, 1906.
5. Yu Fei-Pai, L. S. Efros, and B. A. Porai-Koshits, Trudy Dal'ninskogo politekhnicheskogo in-ta, 2, 83, 1959; RZhKh 81, 105, 1960.
6. C. R. Hauser, F. W. Swamer, and B. I. Ringler, J. Am. Chem. Soc., 70, 4023, 1948.
7. E. Müller, Neuere Anschaungen der organischen Chemie [Russian translation], IL, Moscow, 297, 1960.
8. German patent 578 995, 1933; C. A., 28, 781, 1934.
9. German patent 209 033, 1907; C. A., 3, 2238, 1909.
10. German patent 192 201, 1906; C. A., 2, 1637, 1908.
11. A. P. Phillips and R. Baltzly, J. Am. Chem. Soc., 69, 200, 1947.

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