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Abstract

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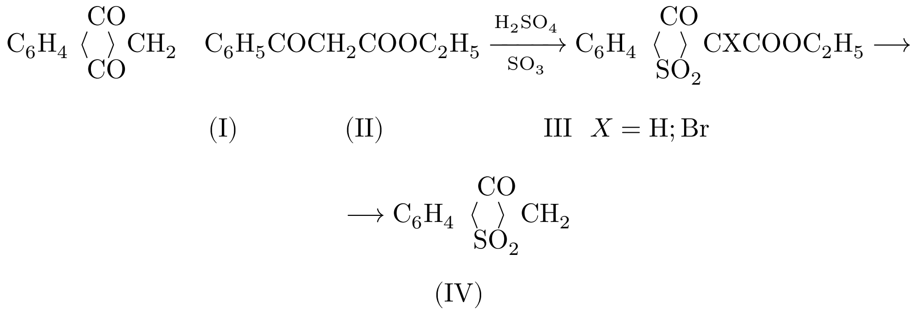
SOME DERIVATIVES OF 1-THIONAPHTHENONE-3-DIOXIDE-1

Many derivatives of indandione-1,3 (I) have found practical application as analytical reagents (2-nitroindandione-1,3, ninhydrin, bindin, 2-nitrosoindandione-1,3, etc.), as blood anticoagulants and rodenticides (2-phenylindandione-1,3, 2-diphenylacetylindandione-1,3, 2-pivalylindandione-1,3, etc.), and have been proposed as narcotics, analgesics, and spasmolytics (many 2-amino-2-arylindandiones) (1–9). It was therefore of interest to study derivatives of analogs of indandione-1,3 as well. As such, we first chose 1-thionaphthenone-3-dioxide-1 (IV), in which one CO group is replaced by an SO_2 group; the latter is frequently encountered in physiologically active substances.

1-Thionaphthenone-3-dioxide-1 is obtained by oxidation of thioindoxyl with hydrogen peroxide (10). By sulfonation of benzoylacetic ester (II), Feist (11) obtained the ester of anhydrobenzoyl-*o*-sulfonic acid (III) and, as a by-product, 1-thionaphthenone-3-dioxide-1 (IV), formed, evidently, by saponification of the ester mentioned. Arndt and co-workers (12), heating the ester for 8 hr with 20% hydrochloric acid, recovered the starting ester; the same was obtained after five hours' boiling in the presence of sulfuric acid in methanol. We carried out saponification with 20% sulfuric acid in ethanol and obtained IV in 83.8% yield.



$$C_6H_4\left\langle\overset{CO}{\underset{CO}{\ }}\right\rangle CH_2 \qquad C_6H_5COCH_2COOC_2H_5 \xrightarrow[SO_3]{H_2SO_4} C_6H_4\left\langle\overset{CO}{\underset{SO_2}{\ }}\right\rangle CXCOOC_2H_5 \longrightarrow$$

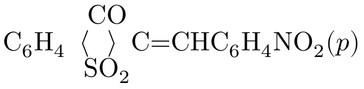
(I) (II) III $X = \mathrm{H}; \mathrm{Br}$

$$\longrightarrow C_6H_4\left\langle\overset{CO}{\underset{SO_2}{\ }}\right\rangle CH_2$$

(IV)

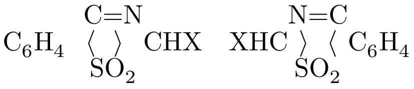
Ester III ($X = H$) possesses acidic properties and readily forms salts; the potassium, ammonium, aniline, and piperidine salts were prepared. An alcoholic solution of the ester gives a red coloration with $FeCl_3$. The ester, like esters of indandionecarboxylic acid, is readily brominated; under mild bromination conditions III ($X = Br$) is formed, while with more vigorous bromination 2,2-dibromo-1-thionaphthenone-3-dioxide-1 is formed.

1-Thionaphthenone-3-dioxide-1 (IV) consists of colorless crystals with m.p. 134-135° (m.p. of indandione-1,3 129-131°). It dissolves in alkalis, forming a colorless solution (indandione gives yellow); on acidification it is precipitated unchanged. It is insoluble in cold water; on boiling, the aqueous solution turns pink, and the reaction of the solution is acidic. In contrast to the starting ester, it does not give a red coloration with $FeCl_3$ in alcoholic solution ([11]). The presence of an active methylene group in IV was demonstrated by obtaining the condensation product (V) with *p*-nitrobenzaldehyde. By bromination of IV both the monobromo and the dibromo derivatives were obtained. The phenylhydrazone and oxime were prepared. Their properties agree with the literature data ([13,14]). From the oxime, its methyl and benzyl ethers were prepared.



$$C_6H_4 \langle \overset{CO}{\underset{SO_2}{\;}} \rangle C{=}CHC_6H_4NO_2(p)$$

(V)

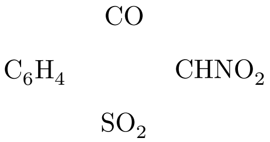


$$C_6H_4 \langle \overset{C=N}{\underset{SO_2}{\;}} \rangle CHX \quad XHC \rangle \overset{N=C}{\underset{SO_2}{\;}} \langle C_6H_4$$

(VI)

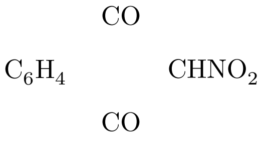
$X = H; Br; NO_2$

By interaction of IV with $NH_2NH_2 \cdot HCl$, azine (VI) was obtained in the form of yellow crystals. Its methylene group remained unaffected; therefore the azine is readily brominated (VI X = Br) and nitrated (VI X = NO_2). By hydrolysis of the latter compound one might have expected to obtain 2-nitro-1-thionaphthenone-3-dioxide-1 (VII), but it proved possible to prepare it more simply—by direct nitration of IV, similarly to the way in which 2-nitroindandione-1,3 (VIII) is obtained. Compound VII, an analogue of VIII, is a very interesting substance; study and comparison of the properties of VII and VIII may provide much information for the solution of a number of theoretical questions. A separate communication on compound VII will follow.



$$C_6H_4 \overset{CO}{\underset{SO_2}{\;}} CHNO_2$$

(VII)



$$C_6H_4 \overset{CO}{\underset{CO}{\;}} CHNO_2$$

(VIII)

Experimental Part

Ethyl ester of 1-thionaphthenone-3-dioxide-1-carboxylic-2 acid (or of benzoic-*o*-sulfonic acid anhydride) (III X = H). To 200 g of 60% oleum, cooled with ice and sodium chloride, 40 g of ethyl phenylacetate are added from a dropping funnel over half an hour with vigorous stirring. The syrup-like reaction product is poured onto five times its amount of ice. The resulting white crystalline precipitate III (X = H) is recrystallized from alcohol. Yield 38 g (82%). M.p. 140°; according to the literature, yield 60% (^{12}), m.p. 140°.

Potassium salt. An alcoholic solution of III (X = H) is neutralized with a saturated aqueous solution of K_2CO_3. On standing, colorless rhombic plates of the potassium salt separate from the filtrate. M.p. 312° (decomp.).

Found %:	C 45.20; H 3.66; K 12.92;
$C_{11}H_9O_5SK$. Calculated %:	C 45.20; H 3.08; K 13.36

Ammonium salt. An alcoholic solution of III (X = H) is saturated with ammonia and left until the next day. Small colorless crystals. M.p. 214° (decomp.).

Found %:	N 5.02
$C_{11}H_9O_5SNH_4$. Calculated %:	N 5.17

Aniline salt. To an alcoholic solution of III (X = H) is added an ethereal solution of aniline; colorless needles separate. M.p. 198°.

Found %:	N 4.43
$C_{17}H_{14}O_5SN$. Calculated %:	N 4.03

Piperidine salt. Analogously to the preceding. Colorless plates. M.p. 161-163° (decomp.).

Found %:	N 4.44
$C_{16}H_{21}O_5SN$. Calculated %:	N 4.13

All these salts crystallize well from alcohol or from alcohol with the addition of ether.

Bromination. To 0.3 g of III (X = H) in 10 ml of chloroform, 10 drops of bromine are added and the mixture is left for several hours in the sun. The chloroform is allowed to evaporate, and the residue is crystallized from dry CCl_4. Colorless crystals of III (X = Br), m.p. 99-100°; according to the literature (^{11}), 98.5°. It dissolves well in acetone and $CHCl_3$, poorly in CCl_4, and does not dissolve in water.

Found %:	Br 24.36
$C_{11}H_9O_5SN$. Calculated %:	Br 24.02

With more vigorous bromination, 2,2-dibromo-1-thionaphthene-3-dioxide-1 is formed (see below).

1-Thionaphthenone-3-dioxide-1 (IV). 5 g of III (X = H) is dissolved in an alcoholic solution of sulfuric acid. The solution is boiled on a water bath until the evolution of CO_2 ceases (~6 hr). On the following day the precipitated colorless needle crystals of IV are separated and washed thoroughly with water. Yield 3 g (83.8%), mp 134–135°, literature mp 132–139° (10–12). The product obtained is sufficiently pure for further processing. By diluting the acidic alcoholic filtrate with a double volume of water, an additional amount of IV can be obtained, separating in the form of oily crystals. These are dissolved in 5% alkali and precipitated with dilute hydrochloric acid. Mp 134° (from alcohol).

Oxime. 0.5 g of IV, 0.5 g of $NH_2OH \cdot HCl$, 1.2 g of anhydrous sodium acetate, and 12 ml of glacial acetic acid are boiled for 3 hours and, after cooling, poured into water. The white precipitate of the oxime is crystallized from dilute acetic acid. Mp 245°, literature (14) 245°. It dissolves in dilute alkali, giving a colorless solution; on acidification it is precipitated unchanged.

Found %: N 6.89
$C_8H_7O_3SN$. Calculated %: N 7.11

Methyl ether of the oxime. 0.1 g of the oxime obtained is dissolved in 5% sodium carbonate, several drops of dimethyl sulfate are added, and the mixture is heated to 90°. Fine white needles precipitate. Mp 148–149° (from dilute alcohol).

Found %: N 6.50
$C_9H_9O_3SN$. Calculated %: N 6.64

Benzoate of the oxime. 0.1 g of the oxime is dissolved in 5 ml of 2% caustic potash, and benzoyl chloride is added dropwise with vigorous shaking. A white crystalline precipitate of the benzoate separates. It is washed first with cold and then with hot water and crystallized from glacial acetic acid. Mp 245–246°; a mixture with the original oxime melts at 225°. It is insoluble in water and ether, and sparingly soluble in alcohol.

Found %: N 4.68
$C_{15}H_{11}O_4SN$. Calculated %: N 4.50

2-*p*-Nitrobenzal-1-thionaphthenone-3-dioxide-1 (V). 0.5 g of IV is fused for 1.5 hours with an equivalent amount of *p*-nitrobenzaldehyde in an oil bath at 160°. The cooled mass is ground, washed with hot benzene, and crystallized from nitrobenzene. Yield 0.3 g of yellow crystals (V). It is insoluble in ordinary organic solvents. In concentrated sulfuric acid it dissolves with an orange coloration. Mp 285–286°.

Found %: N 4.59
$C_{15}H_9O_5SN$. Calculated %: N 4.44

Bromination of 1-thionaphthenone-3-dioxide-1. 0.5 g of IV is dissolved, with heating, in 20 ml of glacial acetic acid, and bromine is added dropwise to the hot solution until the last portion is no longer decolorized. The resulting yellowish solution is diluted with a threefold amount of water, and the precipitated white flocculent precipitate is crystallized from alcohol. White needle crystals of 2-bromo-1-thionaphthenone-3-dioxide-1 melt at 118–120°. They dissolve readily in chloroform, ether, acetone, benzene, and glacial acetic acid.

Found %: Br 29.95
$C_8H_5O_3Br$. Calculated %: Br 30.65

The alcoholic solution is diluted with water, and the precipitate is crystallized from dilute alcohol. White crystals of 2,2-dibromo-1-thionaphthenone-3-dioxide-1, mp 146–147°, dissolve readily in alcohol, chloroform, benzene, and acetone, and with difficulty in ether.

Found %: Br 46.74
$C_8H_4O_3SBr_2$. Calculated %: Br 47.06

The same dibromide is obtained by vigorous action of bromine on ether III ($X = H$). To 0.7 g of III ($X = H$) in 20 ml of glacial acetic acid, 20 drops of bromine are added and the mixture is boiled for 2 hours. HBr is evolved. The cooled solution is poured into water, and the precipitated white solid is crystallized from dilute alcohol. M.p. 146–147°; it gives no depression of the melting point with the dibromide obtained above.

Azine-1-thionaphthenone-3-dioxide-1 VI ($X = H$). To a solution of 0.2 g of IV in 10 ml of alcohol, 0.2 g of $N_2H_4 \cdot HCl$ is added and the mixture is boiled for half an hour; small yellow crystals of VI ($X = H$) precipitate; they are washed with hot water. M.p. 148–149° (decomp.) (from nitrobenzene).

$C_{16}H_{12}O_4S_2N_2$. Found %: N 7.48
Calculated %: N 7.77

It is insoluble in ordinary organic solvents. On heating it dissolves in 5% caustic potash with a more intense coloration, which disappears on acidification. In conc. sulfuric acid it dissolves without color; on dilution with water a white turbidity appears.

Bromination. To a suspension of 0.3 g of VI ($X = H$) in 10 ml of glacial acetic acid, 10 drops of bromine are added and the mixture is boiled until the precipitate dissolves. After several minutes an orange precipitate of VI ($X =$

Br) separates. It is crystallized from glacial acetic acid. M.p. 240° (vigorous decomposition). It is insoluble in ordinary organic solvents and sparingly soluble in glacial acetic acid and ethylene bromide.

$C_{16}H_8O_4S_2N_2$.	Found %:	N 4.11
	Calculated %:	N 4.14

Nitration. To a suspension of VI ($X = H$) in glacial acetic acid, several drops of fuming nitric acid (d 1.5) are added and the mixture is heated to boiling; the azine gradually passes into solution. On cooling, bright-yellow crystals of VI ($X = NO_2$) precipitate. M.p. 168° (with flash).

$C_{16}H_{10}O_8S_2N_4$.	Found %:	N 12.34
	Calculated %:	N 12.44

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Note: Figure translations are in progress. See original paper for figures.

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