# SCIENTIFIC SECTION

## Δ^{1,4}TERPADIENE-DIONE-3,6-SULPHONATE OF POTASSIUM-2 (OR 5). (CARSTANJEN'S COMPOUND.)

BY H. G. HEWITT.

In 1877 Carstanjen[1] recorded some interesting observations concerning the action of potassium sulphite on quinones. He tested the capacity of reaction of the quinone grouping with alkali sulphites presumably in the sense in which the latter react with aldehydes and simple ketones. In other words, he was interested in ascertaining the additive capacity of the carbonyl groups of the quinones, diketones, for alkaline sulphites. While he tried out the quinones of benzene, toluene, xylene and cymene, more correctly the paraquinones of dihydro derivatives of these hydrocarbons, his principal observations were made with the last of these four diketones, the thymoquinone.

Having started out with the thought of the addition of acid sulphites to simple aldehydes and ketones, his first conclusion as to the reaction between thymoquinone and potassium sulphite was that addition of potassium acid sulphite had taken place. However, the behavior of the reaction product was such as to compel a different interpretation. The reaction as interpreted implies, first of all, the hydrolysis of potassium sulphite to potassium acid sulphite and potassium hydroxide, *viz.*

$$K_2SO_3 + H_2O = KHSO_3 + KOH$$
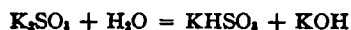
The alkalinity of the reaction mixture readily substantiates this first phase of chemical change. The subsequent reactions are best expressed by means of modern structural formulas.
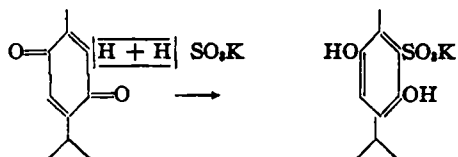
This reaction corresponds to the action of hydrogen chloride on quinone resulting in the formation of chlorhydroquinone

$$C_6H_4O_2 + HCl \longrightarrow C_6H_3Cl(OH)_2$$
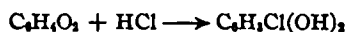
If to a solution of the acid potassium sulphite addition product hydrochloric acid be added, the solution remains clear on standing. Boiling, however, causes it to congeal to a crystalline mass of hydrothymoquinone, whereas the solution contains sulphuric acid.
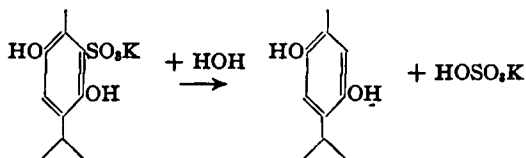
[1] *J. prakt. Chem.*, 123, page 478.

If, however, caustic alkali be used as hydrolizing agent, the solution becomes reddish brown immediately, absorbing oxygen energetically. If, then, hydrogen chloride be added to acidity, hydroxythymoquinone is precipitated.
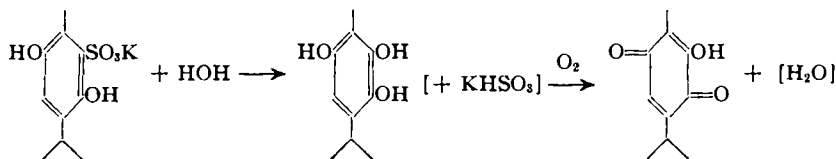
The "purple-violet" color observed by Carstanjen when this oxidation in alkaline solution takes place would seem to indicate the formation of quinhydrone or phenoquinone. The formation of the latter can be accounted for by the addition of two molecules of monohydroxythymoquinone, regarded as monatomic phenol, to one molecule of the same compound, regarded as diketone or quinone. The formation of quinhydrone could be assumed if the initial reaction took place in a somewhat different manner, namely, as indicated by the following formulas:
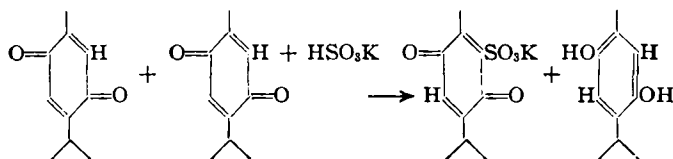
In order to ascertain which of the two sets of reactions takes place, it will be necessary to find out whether hydrothymoquinone is formed or not. This in itself is of sufficient interest when viewed in the light of the reactions between thymoquinone on the one hand and such substances as hydrogen chloride and benzene sulphinic acid on the other hand. Moreover, Carstanjen's compound, whatever the position of the sulphone group—for the sake of simplification only the hydrogen nearest the methyl group has been involved in the structural formulas—ought to prove a convenient stepping stone in the production of at least one of the hydroxythymoquinones. For this reason alone, the reaction should be submitted to a more careful study. Inasmuch as the substitution of sodium sulphite for potassium sulphite some years ago, resulted in the production of tarry masses instead of the handsome crystals of the Carstanjen compound, the investigation called for extension in this direction. Whether this is a matter of individual difference between potassium and sodium or a question of alkalinity, called for an answer. If a question of alkalinity, could not the difficulty be overcome by using a weaker sodium sulphite solution, or by neutralization of the alkali, formed upon hydrolysis of the alkali sulphite in the presence of thymoquinone, with sulphurous acid or acid sulphite?

Given a ready method for the preparation of one of the two hydroxythymoquinones, an entirely new chapter in the investigation of the oxidation products of cymene, from thymol and carvacrol to dihydroxythymoquinone, is made possible. The lability of the one remaining hydrogen in the monohydroxythymoquinone suggests all sorts of possibilities for the further investigation of this group of compounds which plays so important a rôle in the biochemistry of the Monardas and, no doubt, of many another genus of plants, particularly of the *Labiate* family.

As already intimated, Carstanjen gives no specific directions for the preparation of this compound. By way of orientation, therefore, several experiments were made in a rather hit or miss manner using 20 p. c. solutions of both potassium and sodium sulphites. Care was taken to use material from bottles that had been sealed until used, but it was learned later that the sulphites were of poor quality. Nevertheless, the results may, herewith, be recorded if for no other reason than to show how unsatisfactory Carstanjen's directions are.

To the solutions, heated to 60° in an Erlenmeyer flask, thymoquinone was added and the heating continued to 90°. While shaking continually, more thymoquinone was added until an excess of the diketone had been used as became apparent from a red oily layer floating on the surface. Without filtration, the reaction mixtures were transferred to beakers and allowed to cool. From the cooled reaction mixtures the crystals which had formed were separated by filtration and the mother liquids were allowed to evaporate to dryness.

Of the three separate experiments made with potassium sulphite, the reaction mixtures yielded yellowish crystals which burned with a flame, hence appeared to be Carstanjen's compound. However, the presence of white crystals in at least two of the products showed that they were not a uniform product. Ignition yielded 32.7 p. c., 45.7 p. c. and 29.5 p. c., respectively, of residues. Carstanjen's compound should yield 30.5 p. c. of residue computed as sulphite and 36.15 p. c. as sulphate.

From the three separate experiments made with sodium sulphite, colorless crystals separated upon cooling which effloresced upon standing. They contained but traces of organic matter if any. They gave tests for sulphates, hence were presumably $Na_2SO_4 . 10 H_2O$ which lost water of crystallization at room temperature. When heated in a crucible the residue amounted to 108.6 p. c., 109.2 p. c. and 54.5 p. c., respectively. Results one and two may be accounted for by assuming an oxidation of sulphite to sulphate.[1] The third result, however, seems unaccountable, since the substance did not even char.

The filtrates from these compounds, as already stated, were allowed to evaporate. The residues showed but little organic matter to be present. Nevertheless, the crystalline masses were acidulated with dilute sulphuric acid and distilled with water vapor. The distillate showed no traces of thymoquinone, neither did the hot filtrate separate hydrothymoquinone upon cooling.

In order to correct the unsatisfactoriness of quantitative directions in Carstanjen's method of preparation, definite amounts were now taken on a molecular basis.

$$C_{10}H_{12}O_2 \eqsim K_2SO_3 . H_2O$$
$$164 \quad : \quad 194 \ = \ x:35$$
$$x \ = \ 29.38$$
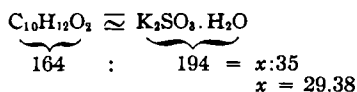
To a solution of 35 Gm. of sulphite in 100 cc. of water, heated to 60°, 5 Gm. of thymoquinone were added and the reaction mixture heated to 90° with constant shaking. Upon cooling masses formed with brown, hard shiny surfaces but soft and tarry under the crust. After 24 hours the reaction product was removed by filtration.

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[1] $Na_2SO_3 : Na_2SO_4 \ = \ 100 : x$
$$126 \quad 142 \qquad x \ = \ 112.69$$

Like experiments were repeated with 7.5, 10.0, 12.5 and 15.0 Gm. of thymo-quinone. In each case the initial yellow color of the reaction mixture increased with the increase in temperature from 60° to 90°. With the increase in the amount of thymoquinone used the final color increased from light yellow to purple. With one exception (10 Gm.), the color remained unchanged upon cooling. In this instance it changed from orange-red to yellow. The yields show no satisfactory regularity, fluctuating from 1.22 Gm. to 6.44 Gm. to 10.45 Gm. to 4.18 Gm. to 16.15 Gm. All of these products burned with a flame showing the phenomenon of intumescence. The first crop consisted of white crystals, the second and third crops of faintly yellowish crystals, and the fourth and fifth crops had a permanga-nate tinge.

These experiments were repeated with smaller amounts of thymoquinone and normal solution of potassium sulphite. The alkalinity of the reaction mixture, after cooling, was titrated with $N/10$ sulphuric acid. The end reaction was more or less interfered with by the color of the reaction mixture. In one instance (2.9 Gm. of thymoquinone) no end reaction was observable, hence the large amount of standard acid added.

Amount thymoquinone.	$N/10\ H_2SO_4$.		Color of solution after titrating.
0.41	a	26.2 cc.	Orange
	b	26.3 cc.	
0.82	a	26.6 cc.	Orange
	b	26.5 cc.	
1.20	a	26.0 cc.	Orange
	b	26.1 cc.	
1.6	a	23.8 cc.	Beautiful pink crystals
	b	23.9 cc.	Hydrothymoquinone?
2.1	a	23.8 cc.	Bright orange-yellow crystals (0.1 Gm.)
	b	23.9 cc.	Thymoquinone?
2.5	a	19.9 cc.	Brown-yellow ppt. (0.1 Gm.). Black
	b	20.0 cc.	Thymoquinone? Quinhydrone?
2.9	a	225.0 cc.	Yellow cryst. in suspension (2.71 Gm.)
	b	18.0 cc.	Thymoquinone? Black cryst. Quinhydrone?
3.2	a	42.1 cc.	Dirty brown-yellow ppt. in susp. (0.04 Gm.)
	b	42.0 cc.	Thymoquinone? Black ppt. on bottom
3.7	a	21.5 cc.	Brownish red quinhyd. residue?
	b	21.7 cc.	(1.35 Gm.)
4.2	a	22.5 cc.	Brownish
	b	22.4 cc.	Black tarry residue. (1.85 Gm.)

The results tabulated above clearly reveal the unsatisfactoriness of these quantitative determinations.

The combined reaction mixtures (a and b) of each titration were subjected to distillation, about one-half of the liquid being distilled over. The residue was filtered while still hot. The tarry portion which remained in the distilling flask was refluxed with fractol, but no crystals could be obtained.

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