## The Chemistry of Hydroxy-quinones. Part III.<sup>1</sup> The Reaction of 2,5-Dihydroxy-benzoquinones with Alkali

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The alkaline degradation of 2,5-dihydroxybenzoquinone yields pyruvic acid and its condensation products as the sole detectable products. The 3-methyl derivative yields a mixture of the corresponding  $\alpha$ -keto-acids together with  $\alpha\beta$ -dimethylsuccinic acid. 3,6-Dialkyl derivatives give only small amounts of  $\alpha$ -keto-acid, the main product being the corresponding succinic acid. Results of a kinetic study are reported, and a mechanism for the reaction is proposed.

FICHTER<sup>2</sup> 3,6-dialkyl-2,5observed that, when dihydroxybenzoquinones (I;  $R^1 = R^2 = alkyl)$  are heated in alkali, the violet colour slowly disappears and a mixture of two stereoisomeric succinic acids (VII) is formed. In contrast to Fichter's results, alkaline degradation of embelin<sup>3</sup> (I;  $R^1 = H$ ,  $R^2 = C_{11}H_{23}$ ) and rapanone<sup>4</sup> (I;  $R^1 = H$ ,  $R^2 = C_{13}H_{27}$ ) has been reported to yield the corresponding  $\alpha$ -keto-acids (R<sup>2</sup>·CH<sub>2</sub>·CO·COH). Kögl and his co-workers<sup>5</sup> have found that similar degradation of polyporic acid (I;  $R^1 = R^2 = Ph$ ) gives a mixture of  $\alpha$ -benzyl- $\beta$ -phenylsuccinic acid (VII;  $R^1 = R^2 = Ph$ ), cis- and trans- $\alpha$ -benzylcinnamic acid (VIII;  $R^1 = R^2 = Ph$ ), and oxalic acid.

These results indicate that the degradation of 2,5dihydroxy-benzoquinones can involve three separate reaction courses, resulting in the formation of (a) isomeric succinic acids and carbon dioxide, (b)  $\alpha$ -keto-acids, and (c)  $\alpha\beta$ -unsaturated acids and oxalic acid. In view of these various modes of degradation it was decided to study the reactions of 2,5-dihydroxybenzoquinone and the 3methyl analogue and to reinvestigate the degradation of 2,5-dihydroxy-3,6-dimethylbenzoquinone and the 3-isopropyl-6-methyl analogue.

In aqueous alkali, the dihydroxy-benzoquinones exhibit two absorption peaks in the region  $250-700 \text{ m}\mu$ . (Table 1). On keeping the solution, both these peaks disappear slowly and it is therefore possible to follow the

<sup>4</sup> M. Asano and K. Yamaguti, J. Pharm. Soc. Japan, 1940, 60, 237.
<sup>5</sup> F. Kögl, A. Detzel, and G. de Voss, Annalen, 1928, 465, 211.

<sup>&</sup>lt;sup>1</sup> Part II, J. F. Corbett, J. Chem. Soc. (C), 1967, 611.

<sup>&</sup>lt;sup>2</sup> F. Fichter, Annalen, 1908, **361**, 363.

<sup>&</sup>lt;sup>3</sup> N. S. Nargund and B. W. Bhide, J. Indian Chem. Soc., 1931, 8, 237.

rate of consumption of the quinone spectrophotometrically. The results for dilute solutions of the quinones, at constant ionic strength, give good first order rate plots up to and beyond 90% reaction. Plots of log [OH<sup>-</sup>]



B.A.R. = Benzilic acid rearrangement

versus log  $k_1$  show the reaction to be first order with respect to hydroxide ion concentration and the temperature dependence indicates an activation energy of about 16.5 kcal. mole<sup>-1</sup>. The rate controlling step for the disappearance of the dihydroxy-benzoquinone is thus a reaction involving one molecule of quinone and a hydroxide ion. The kinetic runs were made by scanning

## TABLE 1

Spectra of dihydroxy-benzoquinones in aqueous alkali

Quinone (1)				
R <sup>1</sup>	$\mathbb{R}^2$	$\lambda_{\max}$ (log $\varepsilon$ )		
н	н	<b>316, 324 (4·47); 497 (2·30)</b>		
$\mathbf{Me}$	$\mathbf{H}$	328(4.48); 536(2.39)		
Me	Me	333(4.37); 538(2.26)		
Me	$Pr^i$	<b>333</b> (4·44); 540 (2·47)		

the complete spectrum at intervals and no strongly absorbing species were detectable as intermediates or products. However it was noted that the optical density in the region 250-290 mµ increased slightly during the decomposition of the methyl derivatives, at low temperatures, but remained near zero in the reaction of the unmethylated compound.

Fichter <sup>2</sup> suggested that the lactone (VI;  $R^1 = R^2 = Me$ ) was an intermediate in the formation of  $\alpha$ -ethyl-

\* For the two consecutive first order reactions it can be shown that the maximum accumulation of the intermediate lactone is given by:

Maximum % = 100 
$$\left(\frac{k_3}{k_1}\right)^{k/(k_1-k_3)}$$
 at time  $t = \frac{\ln k_1/k_3}{(k_1 - k_3)}$ min.

 $\beta$ -methyl-succinic acid from the quinone (I;  $R^1 = R^2 =$ Me). This lactone, in alkaline solution, absorbs at 274 mµ (log  $\varepsilon$  3.91) and its rate of decomposition to the succinic acid can be determined spectrophotometrically. It was found that the decomposition of the un-ionised lactone ( $\lambda_{max}$  241 mµ., log  $\varepsilon$  3.93) was extremely slow, but that the anion of the lactone-acid (VI) decomposed more rapidly and at a rate which is only marginally affected by alkali concentration, the first order rate constant  $(k_3)$ , for the reaction at 98.5°, increasing from 0.0093 min.<sup>-1</sup> for an aqueous solution of the salt (89%) anion) to 0.018 min.<sup>-1</sup> for a solution in 1.0M-alkali. The activation energy, for the reaction in 1.0M-alkali, was found to be 20.5 kcal. mole<sup>-1</sup>. Comparison of these rates with those for the disappearance of the dihydroxybenzoquinone (Table 2) shows that, at high alkali con-

TABLE 2

Rate data for the degradation of 2,5-dihydroxy-benzoquinones in alkali

		1		
Quinone (I)		$k_1$ (l. mole <sup>-1</sup> min. <sup>-1</sup> )		$\Delta E$ (Arrhenius)
$\mathbb{R}^1$	$\mathbb{R}^2$	$98.5^{\circ}$	30°	(kcal. mole <sup>-1</sup> )
н	н	0.0392	$2\cdot 28 imes10^{-4}$	17.0
Me	н	0.0209	$1.07 \times 10^{-4}$	17.2
Me	Me	0.0177	$1.14 \times 10^{-4}$	16.4
Me	$\mathbf{Pr^{i}}$	0.0073	$0.40 imes10^{-4}$	17.0
		* Ionic	strength $= 1.0$	

centration and 98°, the rates are approximately equal, while at low alkali concentration the decomposition of the lactone is the fastest reaction. On the assumption that all other reaction steps are fast relative to these two, the overall reaction can be considered in terms of two consecutive first order reactions:

Quinone 
$$\xrightarrow{k_1}$$
 Lactone  $\xrightarrow{k_1}$  Succinic Acid

and it is evident that the most favourable conditions for accumulation of the lactone intermediate would be high alkali concentration and low temperature. Thus, at  $30^{\circ}$  and in 1.0M-alkali,  $k_1 = 1.14 \times 10^{-4}$  min.<sup>-1</sup> and  $k_3 = 4.4 \times 10^{-5}$  min.<sup>-1</sup>, whence maximum accumulation of the lactone should be 55% at 228 hr.\* Accordingly a reaction was performed under these conditions and stopped at the appropriate time by acidification. On working up, a quantity of a colourless solid, which was not the expected lactone, was isolated. Analysis of the 2,4-dinitrophenylhydrazone of this compound was consistent with its being hydroxy-acid (III;  $R^1 = R^2 =$ Me) or the open chain tautomer (IV;  $R^1 = R^2 = Me$ ). In hot 1.0M-alkali the compound exhibited absorption at 295 m $\mu$ , which was rapidly replaced by a peak at 270 m $\mu$ , which then slowly disappeared at a rate consistent with it being the  $\gamma$ -lactone absorption.

On repeating Fichter's method for the decomposition of the dihydroxydimethylquinone at the boil, we were able to isolate the two stereoisomeric  $\alpha$ -ethyl- $\beta$ -methylsuccinic acids. It is noteworthy that the crude mixture of acids had a strong smell characteristic of the lactone (VI;  $R^1 = R^2 = Me$ ). In addition, treatment of the acidified reaction mixture with 2,4-dinitrophenylhydrazine gave a precipitate of the hydrazone of  $\alpha$ -oxobutyric acid. Control experiments indicated that the hydrazone formation is almost quantitative whence the yield of  $\alpha$ -oxobutyric acid was estimated as 8%, assuming that one mole of quinone gives two moles of  $\alpha$ -keto-acid. That  $\alpha$ -oxobutyric acid is not an intermediate in the formation of the lactone (VI;  $R^1 = R^2 = Me$ ) was shown by its almost quantitative recovery, as its 2,4dinitrophenylhydrazone, after heating in 1.0M-alkali for 4 hr. It was also found that no  $\alpha$ -oxobutyric acid was formed during alkaline degradation of the lactone to the ethylmethylsuccinic acids.

It is thus evident that the divergent formation of the  $\alpha$ -keto acid precedes the formation of the  $\gamma$ -lactone (VI) and it therefore seems reasonable to suggest that the dihydroxy-quinone (I), or its tautomer (II), is converted to the triketo-acid (IV), either by a benzilic acid rearrangement to (III) and subsequent ring opening or by hydrolytic fission (cf. ref. 6). The triketo-acid (IV) can then undergo competing reactions involving (a) benzilic acid rearrangement at the a-diketone system to give the dicarboxylic acid (V) and, subsequently, its lactone (VI), and (b) hydrolytic fission of the  $\beta$ -diketone system to give two molecules, of a-keto-acid. The breaking of the 1,2,4-triketo-system at the 2,3-bond rather than the 3.4-bond is in line with the normal fission of such systems.6

It should be noted here that, in the case of polyporic acid (I;  $R^1 = R^2 = Ph$ ), the formation of the benzylcinnamic acid (VIII;  $R^1 = R^2 = Ph$ ) has been explained 7 by assuming the hydrolytic fission of the triketone system of (IV;  $R^1 = R^2 = Ph$ ) at the 3,4bond with the consequent formation of the  $\alpha$ -diketone PhCH<sub>2</sub>·CO·CO·CH<sub>2</sub>Ph which forms the cinnamic acid by benzilic acid rearrangement and subsequent dehydration of the resulting PhCH<sub>2</sub>·C(OH)(COOH)·CH<sub>2</sub>Ph. However, the intermediate lactone (VI;  $R^1 = R^2 =$ p-HO·C<sub>6</sub>H<sub>4</sub>) has been isolated from the decomposition of atromentin (I;  $R^1 = R^2 = p - HO \cdot C_8 H_4$ ), and has been



shown to give the corresponding cinnamic acid on boiling in 50% aqueous alkali.<sup>5</sup> It thus appears that, when R is aryl, the lactone (VI) decomposes to give a mixture of the succinic acid and  $\alpha\beta$ -unsaturated acid, while only the succinic acid is formed when R is alkyl. The cinnamic acid, together with oxalic acid, could be formed by nucleophilic attack by the hydroxide ion on the ketogroup and subsequent reaction as indicated in (IX), the

<sup>6</sup> M. M. Shemyakin and L. A. Shchukina, Quart. Rev., 1956, **10**, 261.

rate controlling step being the hydroxide ion attack on the keto-group, and this course being favoured by the formation of a fully conjugated system involving the aromatic ring. The formation of the succinic acid also involves a similar reaction course, with collapse as shown in (X), with the collapse of the intermediate being the rate controlling step.

Examination of the alkali degradation products of 2,5-dihydroxybenzoquinone revealed pyruvic acid and its self condensation product 1-methyl-1,2-dihydrotrimesic acid (XI), the structure of which was proved by its conversion to uvitic acid (XII).8 Chromatographic examination of the acidified reaction mixture failed to reveal the presence of any methylsuccinic acid. Quantitative determination of the pyruvic acid, at various times after most of the quinone had decomposed, showed the amount present to decrease as the time increased. It is thus concluded that in the decomposition of (IV;  $R^1 = R^2 = H$ ), the hydrolytic fission of the  $\beta$ -diketone system occurs at the expense of the benzilic acid rearrangement of the  $\alpha$ -diketone system.

The degradation of the dihydroxy-toluquinone (I;  $R^1 = Me$ ,  $R^2 = H$ ) in hot 1.0M-alkali gave a mixture of products which, on distillation under reduced pressure, gave  $\alpha\beta$ -dimethylsuccinic anhydride. Infrared spectral studies of the crude anhydride failed to reveal the presence of any of the possible ethylsuccinic anhydride. The residue from the distillation contained some of the trimesic acid (XI). Treatment of the acidified reaction mixture with 2,4-dinitrophenylhydrazine gave a sample of the hydrazone of  $\alpha$ -oxobutyric acid which was shown, by paper chromatography, to contain some of the hydrazone of pyruvic acid. From the weight of hydrazone obtained it was estimated that the yield of a-oxobutyric acid, and thus of pyruvic acid + the trimesic acid (XI), was 35%.

The absence of any ethylsuccinic acid in the products from the dihydroxytoluquinone is consistent with the non-formation of methylsuccinic acid from the dihydroxybenzoquinone. Thus, when  $R^1 = H$ , the triketo-acid (IV) only undergoes  $\beta$ -diketone fission, while, when  $R^1 =$ alkyl, benzilic acid rearrangement and, to a lesser extent, β-diketone fission occur.

In the case of dihydroxytoluquinone, there is an equilibrium system involving the cyclic diketo-acid (III;  $R^1 = Me$ ,  $R^2 = H$ ) and its two open chain forms A (IV;  $R^7 = Me$ ,  $R^2 = H$ ) and B (IV;  $R^1 = H$ ,  $R^2 =$ Me), the dimethylsuccinic acid evidently being formed solely from A and the a-keto-acids mainly from B (cf. Table 3). Thus the relative yields of the products are dependent on the proportions of A and B in the equilibrium mixture and on their relative rates of decomposition, and will be independent of the position of the initial attack of the hydroxide ion on the quinone.

Alkaline degradation of dihydroxy-thymoguinone (I;  $R^1 = Pr^i$ ,  $R^2 = Me$ ) was found to give a 3% yield of

<sup>&</sup>lt;sup>7</sup> R. H. Thomson, "Naturally Occurring Quinones," Butterworths, London, 1957, p. 28.
<sup>8</sup> L. Wolff, Annalen, 1899, 305, 135.

a mixture of a-oxobutyric acid and 8-methyl-a-oxovaleric acid, isolated in admixture as their 2,4-dinitrophenylhydrazones, together with  $\alpha$ -ethyl- $\beta$ -isopropylsuccinic acid, isolated as its anhydride and reconverted to the higher melting stereoisomeric acid. Like Fichter,<sup>2</sup> we could find no evidence for the presence of the theoretically possible  $\alpha$ -isobutyl- $\beta$ -methylsuccinic acids.

## TABLE 3

Products from the degradation of dihydroxy-benzoquinones

Quinone (I)		Percentage yield		
$\mathbb{R}^1$	$\mathbb{R}^2$	α-Keto-acids	Succinic acid *	
н	н	~100	~0	
Me	н	$\sim 35$	~65 (Di−Me)	
Me	Me	8	92 (Me, Et)	
Me	$\mathbf{Pr^{i}}$	3	97 (Et, Pr <sup>i</sup> )	
		* By difference.		

The formation of only a small amount of  $\alpha$ -keto-acids in the decomposition of the dialkyldihydroxy-benzoquinones would thus appear to be general and it seems likely that the unsymmetrical dialkyl compounds will give the succinic acid containing the more bulky of the original alkyl groups.

## EXPERIMENTAL

Dihydroxy-quinones.— 2,5-Dihydroxybenzoquinone (Light) was recrystallised from acetone as orange rhombs, m. p. 215° (lit., <sup>9</sup> 215°). The monomethyl compound, prepared from toluquinone by the method of Fichter and Glaser,<sup>10</sup> formed orange leaflets, m. p. 185° (lit.,<sup>10</sup> 185°). The dimethyl compound has been described in an earlier Paper.<sup>1</sup> 2,5-Dihydroxy-3-isopropyl-6-methylbenzoquinone, m. p. 230° (lit., 11 220°), was prepared by the method of Flaig and Salfeld.<sup>11</sup>

4-Ethyl-3-methyl-2-oxo-4-butanolide-4-carboxylic Acid.— The lactone was obtained as colourless crystals, m. p. 123- $124^{\circ}$  (decomp.) (lit.,<sup>12</sup> 128°), by the action of 75% sulphuric acid on  $\alpha$ -oxobutyric acid.

Kinetic Experiments.-The reactions were carried out by adding 10 ml. of a fresh 10<sup>-3</sup>M-solution of the dihydroxyquinone in 0.05M-alkali and 0.95M-sodium chloride, or of a  $3.2 \times 10^{-3}$ M-solution of the lactone in 1.0M-aqueous sodium chloride, to 200 ml. of stronger alkali (made up by diluting 1M-alkali with 1M-aqueous sodium chloride) in a stainless steel vessel, at the required temperature. Samples were removed at intervals and the u.v. spectrum was scanned using a Perkin-Elmer 137 recording spectrophotometer. Rate constants were calculated from the change in optical density at  $\lambda_{max}$  of the quinone.

Decomposition of 2,5-Dihydroxybenzoquinone.-The quinone (0.5 g.) in 1.5M-sodium hydroxide (75 ml.) was refluxed in a stainless steel vessel for 4 hr. The cooled solution was acidified and a portion was treated with an equal volume of 2,4-dinitrophenylhydrazine reagent (4 g. in 1.0 l. of 2m-hydrochloric acid). The resulting yellow precipitate was recrystallised from ethanol to give the

- <sup>9</sup> F. Kehrmann, Ber., 1890, 23, 905.
  <sup>10</sup> F. Fichter and H. Glaser, Annalen, 1908, 361, 400.
  <sup>11</sup> W. Flaig and J.-Ch. Salfeld, Annalen, 1958, 618, 117.
- <sup>12</sup> F. Fichter and E. Preiswerk, Annalen, 1902, 35, 1630.

2,4-dinitrophenylhydrazone of pyruvic acid, m. p. 219° (lit.,<sup>13</sup> 218°), identical with an authentic sample (mixed m. p. and i.r. spectrum). The remaining solution was extracted with ether. The dried extract was evaporated to dryness and the residue was recrystallised from ethyl acetate to give 1-methyl-1,2-dihydrotrimesic acid as a white solid, m. p. 215° (decomp.) [lit., 8 195-200° (decomp.)] (Found: C, 53·4; H, 4·7. Calc. for  $C_{10}H_{10}O_6$ : C, 53·1; H, 4·4%). On heating with 90% sulphuric acid at 98° for 2 hr. the acid was converted to uvitic acid, m. p. 298° (lit., 8 298°).

Paper chromatographic analysis of the mother-liquors failed to reveal any methylsuccinic acid.

Decomposition of 3,6-Dihydroxytoluquinone.-The quinone was treated as above (2.5 g. in 150 ml.) for 5 hr. The acidified solution was treated with excess of dinitrophenylhydrazone solution to give 1.71 g. of a yellow solid, m. p. 192-195° which, by paper chromatography (n-butanol-ethanol-0.5M-ammonia 7:1:2), was mainly the 2,4-dinitrophenylhydrazone of  $\alpha$ -oxobutyric acid with a trace of that of pyruvic acid. Recrystallisation from ethanol gave a pure sample of the *a*-oxobutyric acid hydrazone, m. p. 198° (lit.,<sup>14</sup> 201°).

In a further experiment (5 g. quinone in 300 ml. alkali), the acidified reaction mixture was extracted with ether and the residue from the dried extract was distilled under reduced pressure. The initial liquid distillate was a-oxobutyric acid, and this was followed by a liquid which solidified in the condenser. The oily solid was washed with light petroleum and its i.r. spectrum showed it to be  $\alpha\beta$ -dimethylsuccinic anhydride containing a trace of  $\alpha$ -oxobutyric acid but no ethylsuccinic anhydride. The solid (m. p. 70-80°) was boiled in water for 2 hr. to give, on evaporation,  $\alpha\beta$ dimethylsuccinic acid, m. p. 116-118° (lit.,15 anhydride m. p. 87° gives acid m. p. 129°). Comparison of the i.r. spectra with those of authentic samples confirmed the structures.

The residue from the distillation contained mainly 1methyl-1,2-dihydrotrimesic acid.

Decomposition of 2,5-dihydroxy 3,6-dimethylbenzoquinone. —The quinone was treated as above (0.55 g, in 50 ml) for 7 hr., to give the 2,4-dinitrophenylhydrazone of  $\alpha$ -oxobutyric acid (0.15 g., 8%), m. p. 195° (lit., 14 201°).

In a repeat of Fichter's method, the two stereoisomeric  $\alpha\text{-ethyl-}\beta\text{-methylsuccinic acids, m. p. 178 and 100^{\circ} (lit.,^2$ 182 and  $99-100^{\circ}$ ), were obtained.

In a further experiment, the quinone (0.65 g.) in 1.0Malkali (50 ml.) was kept for 9 days at 30°. On acidification, 0.38 g., (58%) of the quinone separated. The motherliquor was subjected to continuous extraction with ether, the dried extract was evaporated, and the residue was recrystallised from benzene to give 108 mg. of off white solid which gave a 2,4-dinitrophenylhydrazone, m. p. 237° (Found: C, 45.3; H, 4.1; N, 15.4. Calc. for C<sub>14</sub>H<sub>14</sub>N<sub>4</sub>O<sub>8</sub>: C, 45.8; H, 3.8; N, 15.3%).

Decomposition of 2,5-dihydroxy-3-isopropyl-6-methylbenzoquinone.-Treatment as for the toluquinone gave a mixture of the 2,4-dinitrophenyhydrazones of  $\alpha$ -oxobutyric acid,  $\gamma$ -methyl- $\alpha$ -oxovaleric acid, and  $\alpha$ -ethyl- $\beta$ -isopropylsuccinic anhydride, m. p. 192-193° (Found: C, 63.2; H, 8.3.  $C_9H_{14}O_3$  requires  $\tilde{C}$ , 63.5; H, 8.2%). On boiling with water the last gave the high melting succinic acid, m. p. 205-208° (lit., 1 210°).

- H. H. Strain, J. Amer. Chem. Soc., 1935, 57, 758.
   K. Felix and K. Zorn, Z. phys. Chem., 1939, 258, 23.
   W. A. Bone and W. H. Perkin, J. Chem. Soc., 1896, 69, 253.

acid.-4-Isobutylidene-2-phenyl- $\gamma$ -Methyl- $\alpha$ -oxovaleric oxazolone 16 (4 g.) was refluxed in conc. hydrochloric acid (40 ml.) for 5 hr. The mixture was cooled and benzoic acid was filtered off. The filtrate (20 ml.) was treated with 2,4-dinitrophenylhydrazine reagent to give the 2,4-dinitrophenylhydrazone of the  $\alpha$ -keto-acid as yellow crystals, m. p. 150° (lit., 14, 17 155, 162°). The remaining 20 ml. of the filtrate was extracted with ether and the dried extract was evaporated. The residue, with phenylhydrazine in acetic acid, gave the phenylhydrazone of the a-keto-acid, m. p. 150° (lit.,<sup>18</sup> 150°).

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