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The Reaction between Acetylacetone and *p*-Benzoquinone

II. Some New Derivatives of Benzofuran

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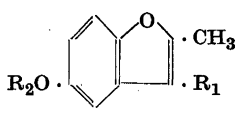
Acetylacetone and *p*-benzoquinone can under certain conditions react to give an intensely red-coloured quinone $C_{16}H_{16}O_6$[1] the constitution of which is being investigated in this laboratory.

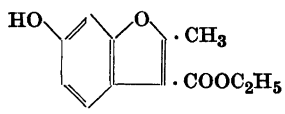
Apart from being one of the reactants acetylacetone also serves as reaction medium and is consequently present in great excess. It became therefore necessary to regenerate the unreacted part of this relatively expensive reagent. During the process of regeneration a new product, a white, crystalline substance with the composition $C_{11}H_{10}O_3$, could be isolated from the reaction mixture. It dissolved in alkali, gave a positive iodoform reaction and could be methylated and acetylated to give the mono derivatives. With 2,4-dinitrophenylhydrazine it formed a monohydrazone and with phenyl isocyanate a monourethan. Combined with the knowledge of the starting materials these results suggested the structure I



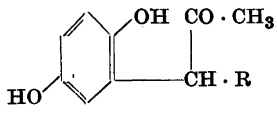
I	$R_1 = COCH_3$	$R_2 = H$
II	$R_1 = COOC_2H_5$	$R_2 = H$
III	$R_1 = COCH_3$	$R_2 = CH_3$
IV	$R_1 = COOH$	$R_2 = CH_3$

A constitutionally similar compound has been prepared by Ikuta [2] by the condensation of *p*-benzoquinone and ethyl acetoacetate in the presence of anhydrous zinc chloride. The structural formula II proposed by Ikuta for his condensation product has, however, been discussed by Graebe and Levy [3] who considered the isomeric structure V as just as probable. The two structures II and V were arrived at by supposing different paths of reaction in the following way: Ikuta presumed that the initial step was the formation of a carbon-carbon bond giving rise to the hydroquinone VI which by loss of one molecule

of water from its tautomeric form will give II. Graebe and Levy gave the structure VIII for the intermediate hydroquinone thus regarding the establishing of the ethereal bond as the first step. Elimination of water from VIII gives of course V.

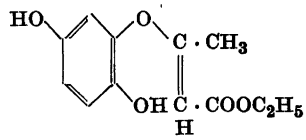


V



VI R = $COOC_2H_5$

VII R = $COCH_3$



VIII

There is good reason to believe that in basic acetylacetone solutions the reaction is initiated by the formation of carbon-carbon bonds [4] and the same seems to be true in the reaction between *p*-benzoquinone and ethyl cyanoacetate in ammoniacal alcoholic solution [5]. In alcoholic solutions of zinc chloride the reaction might or might not take another course. We have, however, been able to isolate the compound I also from the condensation of acetylacetone and *p*-benzoquinone in methanolic zinc chloride solution thus proving the identity of reaction paths in the two different media. Further the methyl ether III could be oxidized by sodium hypobromite to an acid $C_{11}H_{10}O_4$ (IV) which also could be obtained from II by methylating the hydroxyl group and hydrolyzing the ester. Consequently the hydroxyl group has the same position in I and II, and since the structural formula of Ikuta has been corroborated by the above considerations the constitution I for $C_{11}H_{10}O_3$ seems to be established with a good degree of certainty.

The hydroquinone VII which by loss of water would give I has not been isolated but is assumed to be present in the mother liquor from the quinone $C_{16}H_{16}O_6$ for the following reasons: On keeping for a long time the basic solution deposited only very small amounts of the benzofuran but after shaking with dilute sulphuric acid it was obtained readily in about five per cent yield. The fact that I also separated from the acid washings, in which it is almost insoluble, seems to indicate that the condensation product is present as the presumably more soluble hydroquinone VII which is subsequently converted into the benzofuran by action of the sulphuric acid.

The formation of this hydroquinone is obviously a base-catalyzed Michael addition followed by stabilisation through rearrangement to an aromatic structure. Of the two steps which lead from the hydroquinone to the benzofuran *viz.* the enolisation and the elimination of water, one or both must be catalyzed by acids.

EXPERIMENTAL PART

2-Methyl-3-acetyl-5-hydroxybenzofuran (I)

The dark mother liquor from the preparation of the quinone $C_{16}H_{16}O_6$[1] which contained some pyridine was shaken with 2 *N* sulphuric acid in order to remove the basic component from the mixture. Remaining traces of acid were washed out by shaking with pure water. If the reaction mixture after drying for a short time with calcium chloride was left for a couple of days, a crystalline substance separated. Usually, however, this substance was isolated from the residue remaining from the vacuum distillation of the reaction mixture. After washing with ethanol and recrystallisation from the same solvent the reaction product was obtained as greyish needles with m. p. 238°. The discolouration was very difficult to remove by recrystallisation and treatment with charcoal, but the substance could be sublimed *in vacuo* to yield white needles also of m.p. 238°. In all preparations the substance also separated from the sulphuric acid used for the removing of pyridine. The total yield of the benzofuran derivative usually amounted to about five per cent. If the before-mentioned dark mother liquor was kept for some months prior to the acid treatment the benzofuran was deposited only in very small amounts.

$C_{11}H_{10}O_3$	Calc.	C	69.45	H	5.30	
	Found	»	69.25	»	5.12	

Methyl ether of I: The benzofuran (1.0 g) was dissolved in a solution of sodium hydroxide (0.3 g) in water (50 ml). To the clear, somewhat darkish solution was added methyl sulphate (1.0 ml) and the mixture shaken thoroughly. After some time more methyl sulphate (0.4 g) and sodium hydroxide (0.2 g) were added followed by shaking as before, this process was repeated a second time. Precaution had to be taken that the temperature during the methylation did not exceed about 20°. The separated brown solid (0.65 g) was filtered off and recrystallized thrice from dilute ethanol. M.p. 72°.

$C_{12}H_{12}O_3$	Calc.	C	70.58	H	5.93	M	204
	Found	»	70.47	»	5.96	»	192 (in camphor)

Acetate of I: The benzofuran (0.2 g) was dissolved in a mixture of acetic anhydride (5 ml) and pyridine (5 ml) by gentle heating and left for six hours. On pouring on ice an oil separated which rapidly crystallized (0.11 g). After recrystallizing the substance twice from dilute ethanol it had m.p. 88°

$C_{13}H_{12}O_4$	Calc.	C	67.22	H	5.21
	Found	»	67.08	»	5.11

2,4-Dinitrophenylhydrazone of I: To a filtered solution of dinitrophenylhydrazine (1.0 g) in hydrochloric acid (60 ml, 2 *N*) was added a solution of I (0.2 g) in hot ethanol (25 ml). Heated on a water-bath for 20 minutes. Small red needles (0.19 g) separated which after recrystallisation once from ethanol and once from chloroform had m. p. 273°.

$C_{17}H_{14}N_4O_6$	Calc.	C	55.14	H	3.81	N	15.12
	Found	»	55.04	»	4.01	»	14.90

Phenylurethan of I: The benzofuran (0.3 g) dry xylene (5 ml) and phenyl isocyanate (1 ml) were refluxed for one hour. Next day the separated solid was washed with toluene and recrystallized twice from methanol. M.p. 180°

$C_{18}H_{15}NO_4$	Calc.	C	69.90	H	4.88	N	4.53
	Found	»	69.63	»	4.95	»	4.81

Condensation of acetylacetone and *p*-benzoquinone in presence of zinc chloride

p-Benzoquinone (3.0 g) and acetylacetone (3.5 ml) to which anhydrous zinc chloride (10 g) in absolute methanol (12.5 ml) was added were heated on a steam-bath for half an hour. After cooling the separated crystals (1.4 g) were filtered off, washed with dilute methanol and treated with 2*N* sodium hydroxide. The substance went partly in solution (the alkali-insoluble part of the condensation product will be dealt with on another occasion) and on acidifying this a substance separated which after recrystallizing from glacial acetic acid had m. p. 238°. Mixed melting point with I: 238°.

Hypobromite oxidation of the methyl ether III

III (2.6 g), sodium hydroxide solution (20 ml, 2*N*) and sodium hypobromite solution (from 5 g of bromine) were shaken for 10 hours at room temperature. The separated bromoform and some unreacted substance were filtered off. To the filtrate was added a solution of sodium sulphite and the mixture thereafter acidified with 2*N* sulphuric acid. A yellow substance (0.65 g) separated which after two recrystallisations from dilute ethanol was almost white, formed small needles and had m. p. 212°

$C_{11}H_{10}O_4$	Calc.	C	64.06	H	4.89
	Found	»	63.86	»	4.86

Methylation and hydrolysis of II

II (0.95 g) and sodium hydroxide (0.5 g) were dissolved in water (100 ml). Methyl sulphate (0.8 g) was added and the mixture shaken well at room temperature. The addition of methyl sulphate was repeated twice while sodium hydroxide (0.3 g) was added once. The turbid, alkaline solution was extracted twice with 75 ml ether in order to remove the methyl ether of II. The dried ethereal extracts were evaporated to dryness and the crystalline residue (0.15 g) was treated with charcoal and recrystallized twice from dilute ethanol. M. p. 38—40°

$C_{13}H_{14}O_4$	Calc.	C	66.66	H	6.02
	Found	»	66.86	»	6.13

The aqueous phase from the above ether extractions was acidified with concentrated hydrochloric acid and the separated oil extracted with ether (2 × 75 ml). After evaporation of the dried ethereal extract a brownish crystalline residue (0.26 g) was obtained. Treated with charcoal and recrystallised twice from dilute alcohol it yielded almost white needles. M. p. 212—213°. Mixed melting point with $C_{11}H_{10}O_4$ from the foregoing experiment: 212°

$C_{11}H_{10}O_4$	Calc.	C	64.06	H	4.89
	Found	»	64.06	»	4.89

SUMMARY

Acetylacetone and *p*-benzoquinone react in presence of pyridine or methanolic zinc chloride to give 2-methyl-3-acetyl-5-hydroxybenzofuran. Some

derivatives of this compound and of 2-methyl-5-hydroxybenzofuran-3-carboxylic acid are described.

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