

# QUINONE STUDIES

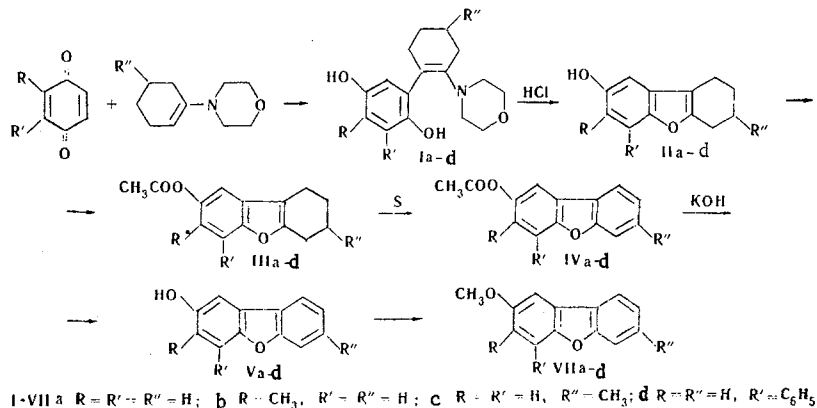
## LI.\* SYNTHESIS AND SOME TRANSFORMATIONS OF ENAMINES OF DIHYDROXYARYLCYCLOHEXANONE

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The morpholine enamines of dihydroxyarylcyclohexanone, which were obtained by the reaction of p-benzoquinone, toluquinone, and phenyl-p-benzoquinone with the morpholine enamine of  $\beta$ -methylcyclohexanone, were converted by hydrochloric acid to hydroxytetrahydrobenzofurans. A method for the synthesis of substituted 2-hydroxydibenzofurans was developed by dehydration of the acetyl derivatives of the latter on heating with sulfur. Some transformations of the 2-hydroxydibenzofuran derivatives were studied.

As was recently shown in [2], the condensation of p-benzoquinone with enamines results in the formation of enamines of dihydroxyarylcycloalkenones and dihydroxyarylalkylacetaldehydes. Continuing our investigation of this reaction, we have studied the reaction of the morpholine enamine of cyclohexanone with toluquinone and phenyl-p-benzoquinone and the reaction of the morpholine enamine of  $\beta$ -methylcyclohexanone [3] with p-benzoquinone. The enamines of the dihydroxyarylcyclohexanone (Ib-d) were converted by hydrochloric acid via the method recently proposed for the synthesis of 2-hydroxy-6,7,8,9-tetrahydrobenzofuran (IIa) [4] to the corresponding hydroxytetrahydrobenzofurans (IIb-d). Acetyl derivatives (IIIa-d) were obtained by the usual method by acetylation of the latter and the known IIa. Dehydrogenation of IIIa-d by heating with sulfur gave 2-acetoxydibenzofurans (IVa-d) in 70-77% yields, and 2-hydroxydibenzofurans (Va-d) were obtained from them after hydrolysis. Compound Va was previously obtained by dehydrogenation of IIa over a palladium catalyst [4]. Methylation of IIa and Va-d leads to the corresponding 2-methoxy derivatives (VI and VIIa-d).

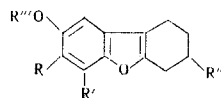


We have found that an orientating group of the primary type, viz., the methyl group of quinone, directs the enamine residue to the 5-position, while a phenyl substituent, which can be considered to be an orientating group of the secondary type, directs the enamine residue to the 6-position of the quinone ring, which

\* See [1] for communication L.

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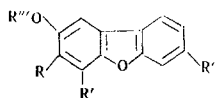
TABLE 1. Tetrahydrodibenzofurans



Comp.	R	R'	R''	R'''	Mp* or bp °C (mm)	Empirical formula	Found, %		Calc., %		Yield, %
							C	H	C	H	
IIb	CH <sub>3</sub>	H	H	H	130—131	C <sub>13</sub> H <sub>14</sub> O <sub>2</sub>	77,0	6,8	77,2	7,0	100
IIc	H	H	CH <sub>3</sub>	H	—	—	—	—	—	—	83
IId	H	C <sub>6</sub> H <sub>5</sub>	H	H	142—143	C <sub>18</sub> H <sub>16</sub> O <sub>2</sub>	81,9	6,5	81,8	6,1	82
IIIa	H	H	H	COCH <sub>3</sub>	64—66	C <sub>14</sub> H <sub>14</sub> O <sub>3</sub>	73,0	6,5	73,0	6,1	82
IIIb	CH <sub>3</sub>	H	H	COCH <sub>3</sub>	185—187(5)	C <sub>15</sub> H <sub>16</sub> O <sub>3</sub>	74,0	6,6	73,8	6,6	88
IIIc	H	H	CH <sub>3</sub>	COCH <sub>3</sub>	187—189(5)	C <sub>15</sub> H <sub>16</sub> O <sub>3</sub>	73,4	6,5	73,8	6,6	89
IIId	H	C <sub>6</sub> H <sub>5</sub>	H	COCH <sub>3</sub>	103—104	C <sub>20</sub> H <sub>18</sub> O <sub>3</sub>	78,6	5,9	78,4	5,9	92

\* From aqueous alcohol.

TABLE 2. Dibenzofurans



Comp.	R	R'	R''	R'''	Mp* or bp °C (mm)	Empirical formula	Found, %		Calc., %		Yield, %
							C	H	C	H	
IVa	H	H	H	COCH <sub>3</sub>	114—115	C <sub>14</sub> H <sub>10</sub> O <sub>3</sub>	74,6	4,5	74,3	4,2	76
IVb	CH <sub>3</sub>	H	H	COCH <sub>3</sub>	157—157,5	C <sub>15</sub> H <sub>12</sub> O <sub>3</sub>	75,1	5,2	75,0	5,0	77 ‡
IVc	H	H	CH <sub>3</sub>	COCH <sub>3</sub>	—	—	—	—	—	—	72 ‡
IVd	H	C <sub>6</sub> H <sub>5</sub>	H	COCH <sub>3</sub>	—	—	—	—	—	—	70 ‡
Vb	CH <sub>3</sub>	H	H	H	154—155	C <sub>13</sub> H <sub>10</sub> O <sub>2</sub>	78,4	5,1	78,8	5,1	97
Vc	H	H	CH <sub>3</sub>	H	127—128 †	C <sub>13</sub> H <sub>10</sub> O <sub>2</sub>	78,5	5,1	78,8	5,1	92 ‡
Vd	H	C <sub>6</sub> H <sub>5</sub>	H	H	—	—	—	—	—	—	84 ‡
VIIa	H	H	H	CH <sub>3</sub>	187—189(13)	C <sub>13</sub> H <sub>10</sub> O <sub>2</sub>	78,5	5,3	78,8	5,1	60
VIIb	CH <sub>3</sub>	H	H	CH <sub>3</sub>	74—75	C <sub>14</sub> H <sub>12</sub> O <sub>2</sub>	79,2	5,9	79,2	5,7	66
VIIc	H	H	CH <sub>3</sub>	CH <sub>3</sub>	198—200(11)	C <sub>14</sub> H <sub>12</sub> O <sub>2</sub>	79,4	5,6	79,2	5,7	78
VIIId	H	C <sub>6</sub> H <sub>5</sub>	H	CH <sub>3</sub>	110—111	C <sub>19</sub> H <sub>14</sub> O <sub>2</sub>	83,1	5,0	83,2	5,1	76

\* From aqueous alcohol.

† From aqueous acetic acid.

‡ The yield of crude product, which was used for the subsequent transformations without additional purification.

is in agreement with the results obtained by Allen [5]. The position of the substituents in enamines I was proved by an investigation of the PMR spectra of dibenzofuran derivatives synthesized from I.

For example, in the spectrum of IIId, for which the protons of the acetyl group of the saturated benzene ring and the benzene ring of the substituent give signals at 2.28, 1.94, 2.65, 7.88, and 7.43 ppm, the peak at  $\delta$  7.19 ppm (AB system,  $J_{\text{meta}}$  2.3 Hz) should be assigned to the protons of the unsaturated dibenzofuran ring, which corresponds to structure IIId. A sharp singlet at  $\delta$  7.76 ppm ( $J_{\text{para}}$  0.5 Hz) and a broad signal at 7.54 ppm because of interaction of the proton with the adjacent methyl group are observed in the PMR spectrum of IVb. The spectra were obtained in deuteroacetone with tetramethylsilane as the internal standard. Condensation of p-benzoquinone with the morpholine enamine of  $\beta$ -methylcyclohexanone yielded 1-(2,5-dihydroxyphenyl)-2-morpholino-4-methyl-1-cyclohexene, which was proved by the PMR spectrum of the dibenzofuran derivative (Vc) obtained from it. The C<sub>(8)</sub> and C<sub>(9)</sub> protons form an AB system ( $J_{\text{ortho}}$  7.5 Hz) with  $\delta$  (9) 8.14 and  $\delta$  (8) 7.30 ppm [broad doublet because of interaction with the C<sub>(6)</sub> proton]. The broad singlet at  $\delta$  7.54 ppm can be assigned to the C<sub>(6)</sub> proton. According to the data of the PMR spectra, there are no isomeric products in the investigated samples. Isomeric compounds could not be isolated from the reaction solution and the mother liquors obtained during recrystallization.

We have studied some transformations of the dibenzofuran derivatives. Nitration of VIIc yielded 2-methoxy-3-nitro-7-methyldibenzofuran (VIII), while formylation with dimethylformamide yielded the 3-formyl derivative (IX). 1-Dimethylaminomethyl-2-hydroxy-3-methyldibenzofuran (Xa) and the previously described [6] 1-dimethylaminomethyl-2-hydroxybenzofuran (Xb) were synthesized by the action of bisdimethylaminomethane on Va and Vb.

The positions of the nitro and dimethylaminomethyl groups were proved by means of PMR spectra. Two sharp singlets which indicate that the protons are in para to one another are clearly seen in the spectrum of VIII. The signal at 8.06 ppm belongs to the proton in the 1-position. The signal of the proton in the 4-position, however, is shifted to weaker field because of proximity to the nitro group. Consequently, the nitro group is in the 3-position of dibenzofuran. The proton in the 4-position gives a doublet at 7.45 ppm in the PMR spectrum of Xb, while the C<sub>(3)</sub> proton forms a similar signal at 7.98 ppm (*J*<sub>ortho</sub> 8.6 Hz). The form of these signals indicates that the dimethylaminomethyl substituent is in the meta and para positions with respect to these protons, i.e., in the 1-position of dibenzofuran. The spectra were obtained in deuterio-dimethyl sulfoxide with a JNM 4 H-100 spectrometer\* with tetramethylsilane as the standard.

Compound Xa was converted to 1-acetoxymethyl-2-acetoxy-3-methyldibenzofuran (XI) by refluxing with acetic anhydride, and the product was deacetylated to 1-hydroxymethyl-2-hydroxy-3-methyldibenzofuran (XII).

## EXPERIMENTAL

The morpholine enamines of dihydroxyphenylcyclohexene (Ib-d) were synthesized via the method described in [4]. 1-(2,5-Dihydroxy-4-methylphenyl)-2-morpholino-1-cyclohexene (Ib) was obtained in 94% yield†; 1-(2,5-dihydroxyphenyl)-2-morpholino-4-methyl-1-cyclohexene (Ic) was obtained in 84% yield.† 1-(3-Phenyl-2,5-dihydroxyphenyl)-2-morpholino-1-cyclohexene (Id) was obtained in 74% yield and had mp 190-191° (from alcohol). Found %: C 74.9; H 7.2; N 3.8. C<sub>22</sub>H<sub>25</sub>NO<sub>3</sub>. Calculated %: C 75.2; H 7.2; N 3.9.

2-Hydroxy-6,7,8,9-tetrahydrobenzofurans (IIb-d, Table 1). These were obtained via the method in [6].

2-Acetoxy-6,7,8,9-tetrahydrodibenzofurans (IIIa-d, Table 1). Compounds IIa-d (5.3 mmole) were refluxed for 1 h in a mixture of 15 ml of acetic anhydride and 15 ml of pyridine, and the reaction solution was then poured into 200 ml of cold water. The resulting precipitates were filtered.

2-Acetoxydibenzofurans (IVa-d, Table 2). A mixture of 9.6 mmole of IIIa-d and 0.0192 g-atom of sulfur was heated at 245° for 4-8 h until hydrogen sulfide evolution ceased, and the reaction mixture was distilled.

2-Hydroxydibenzofurans (Va-d, Table 2). A mixture of 2 mmole of IVa-d and 8 mmole of potassium hydroxide in 5 ml of methanol was refluxed for 1 h, and the reaction solution was poured into 30 ml of water and acidified with 10% acetic acid. The resulting precipitate was filtered.

3-Methoxydibenzofurans (VIIa-d, Table 2). A total of 70 ml of 2 N sodium hydroxide followed by 0.06 mole of dimethyl sulfate was added gradually with stirring at 4-5° to a solution of 0.03 mole of Va-d in a mixture of 10 ml of dioxane and 5 ml of acetone. At the end of the addition, the reaction mass was stirred for another hour, and the substance was extracted with ether.

2-Methoxy-6,7,8,9-tetrahydrobenzofuran (VI). This was similarly obtained in 94% yield and had bp 150-152° (5 mm). Found %: C 77.1; H 6.7. C<sub>13</sub>H<sub>14</sub>O<sub>2</sub>. Calculated %: C 77.2; H 6.9.

2-Methoxy-3-nitro-7-methyldibenzofuran (VIII). A solution of 0.43 ml of nitric acid (sp. gr. 1.5) in 5 ml of glacial acetic acid was added dropwise with ice cooling and vigorous stirring to a solution of 2.15 g (0.01 mole) of VIIc in 7 ml of glacial acetic acid. The stirring was continued for another 2 h. The resulting precipitate was filtered to give 60% of VIII with mp 163-164° (from acetic acid). Found %: C 65.3; H 4.5; N 5.4. C<sub>14</sub>H<sub>11</sub>NO<sub>4</sub>. Calculated %: C 65.4; H 4.3; N 5.4.

2-Methoxy-3-formyl-7-methyldibenzofuran (IX). Phosphorus oxychloride [16.6 ml (0.182 mole)] was added dropwise with stirring at 4-5° to a solution of 4 g (0.0188 mole) of VIIc in 14 ml (0.182 mole) of

\* The spectroscopic investigations were carried out by N. P. Kostyuchenko.

† The yield of the crude liquid product, which was used for the subsequent transformations without additional purification, is given.

dimethylformamide. At the end of the addition, the reaction mass was stirred for another 6 h at 100°, poured over ice, and neutralized with potassium hydroxide solution. The resulting precipitate was filtered to give 58% of IX with mp 173–174° (from acetic acid). Found %: C 74.6; H 5.0.  $C_{15}H_{12}O_3$ . Calculated %: C 74.9; H 5.0.

1-Dimethylaminomethyl-2-hydroxy-3-methyldibenzofuran (Xa). A solution of 1.98 g (0.01 mole) of Vb and 2.05 ml (0.015 mole) of bisdimethylaminomethane in 9 ml of dioxane was refluxed for 2 h. The dioxane and excess amine were removed by distillation, and the residue was recrystallized from alcohol to give 78% of Xa with mp 107–108° (from alcohol). Found %: C 75.4; H 6.5.  $C_{16}H_{17}NO_2$ . Calculated %: C 75.3; H 6.7.

1-Dimethylaminomethyl-2-hydroxydibenzofuran (Xb). This was similarly obtained in 75% yield and had mp 106–107° (from alcohol, mp 114–115° [6]). Found %: C 74.6; H 6.3; N 5.9.  $C_{15}H_{15}NO_2$ . Calculated %: C 74.6; H 6.3; N 5.8.

1-Acetoxymethyl-2-acetoxy-3-methyldibenzofuran (XI). A solution of 0.765 g (3 mmole) of Xa in 2 ml of acetic anhydride was refluxed for 6 h and poured into 10 ml of water. The resulting precipitate was filtered to give a quantitative yield of a product with mp 130–131° (from alcohol). Found %: C 69.3; H 5.2.  $C_{18}H_{16}O_5$ . Calculated %: C 69.2; H 5.2.

1-Hydroxymethyl-2-hydroxy-3-methyldibenzofuran (XII). A solution of 0.77 g (2.47 mmole) of XI and 0.56 g (0.01 mole) of potassium hydroxide in 10 ml of methanol was refluxed for 2.5 h, poured into 100 ml of water, and acidified with acetic acid. The resulting precipitate was filtered to give a quantitative yield of a product with mp 98–99° (from 50% alcohol). Found %: C 74.1; H 5.6.  $C_{14}H_{12}O_3$ . Calculated %: C 73.7; H 5.3.

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