

## Some New Benzodifurans and Naphthofurans from Quinones and $\beta$ -Diketones

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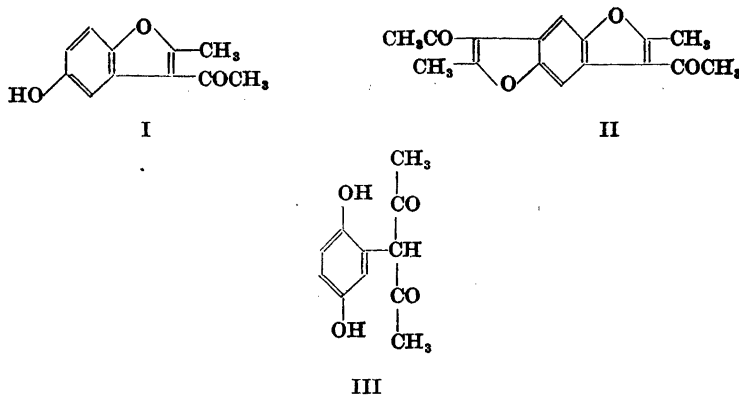
In connection with work on stable ozonides two new benzodifurans and several new naphthofurans have been synthesized from quinones and  $\beta$ -diketones. The reactivity of some substituted naphthoquinones has been tested.

As pointed out by Criegee<sup>1</sup> well-defined ozonides are only rarely encountered in literature. The same author therefore devoted himself to the preparation of stable ozonides as well as to the complete elucidation of their degradative reactions and their rearrangements. He was able to show<sup>2</sup> that in the ozonization of 9,10-octalin no stable ozonide was formed as supposed by Hückel<sup>3</sup>, the reaction product turning out to be a dimeric peroxide of *cyclo*-decanedione-1,6. Likewise the "ozonide" from 2-phenyl-3-ethyl-indenone described by Frank and collaborators<sup>4</sup> could be shown to consist of a mixed anhydride of *o*-propionylbenzoic acid and benzoic acid.

Are thus the stable and well-defined ozonides even more rare than previously supposed, a notable exception is displayed in the ozonides of unsaturated five-membered rings. The reason for this is probably of a steric nature<sup>5</sup>. Such stable ozonides can be prepared from certain steroid derivatives<sup>6,7</sup>, indole derivatives<sup>8,9</sup>, disubstituted maleic imides<sup>10</sup>, *cyclopentene*<sup>11</sup>, cyclic sulphones<sup>12</sup> and 2,3-disubstituted indenones<sup>13</sup>. Recently a new class of compounds has been found to yield stable, monomeric ozonides, *viz.* the benzo [1.2-b, 4.5-b'] difurans<sup>14</sup>. As a preliminary to further work in this field the author has undertaken the synthesis of some new suitably substituted benzodifurans and naphthofurans.

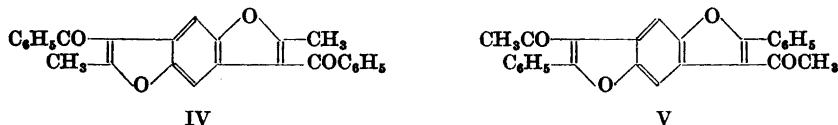
The synthesis of benzofuran and benzodifuran derivatives from quinone and ethyl acetoacetate was established by v. Pechmann<sup>15</sup> and Ikuta<sup>16</sup>. Later Graebe and Levy<sup>17</sup> extended the synthesis to include toluquinone but expressed on the same occasion doubt as to the correctness of some of Ikuta's structural formulae. These, however, seem to have been confirmed by more recent work<sup>18</sup>. Further extensions of the synthesis have been made through the investigation of the reaction between acetylacetone and quinone<sup>18,19</sup>.

The structure of two new furan derivatives from these works are given in the formulae I and II.



These compounds are supposed to be formed by ring closure of intermediate quinols of the type represented by formula III (or its tautomeric form). The determination of the structures I and II was considerably facilitated by the fact that acetylacetone is a symmetrical diketone. Thus the two possible directions of enolization in III are identical and only one product can result from a ring closure. (III will of course give I.)

We now have investigated the reaction between benzoylacetone and quinone in methanolic zinc chloride solution. Only one reaction product could be isolated. Its composition  $C_{26}H_{18}O_4$  corresponded to a benzodifuran derivative and in analogy to our earlier results the structure of this product could be either IV or V.

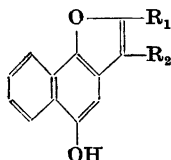


The carbonyls in  $C_{26}H_{18}O_4$  were relatively unreactive. With ordinary carbonyl reagents, *e. g.* 2,4-dinitrophenylhydrazine, it yielded only a mono-hydrazone. The iodoform test was negative. In order to decide between IV and V the presumed benzodifuran was treated with methyl magnesium iodide whereby both carbonyls were converted into tertiary alcohol groups, the resulting compound having the composition  $C_{28}H_{26}O_4$ . The same compound could be prepared by treating II with phenyl magnesium bromide. Consequently the possibility of structure V is ruled out.

Benzoyl acetic ester reacted only very sluggishly with quinone under the conditions tried and gave in extremely low yield a substance  $C_{28}H_{22}O_4$  which probably is a benzodifuran (V,  $COOC_2H_5$  instead of  $COCH_3$ ). This compound was not investigated further.

1,4-Naphthoquinone reacted smoothly with acetylacetone to give a compound  $C_{15}H_{12}O_3$  corresponding to one mole of each of the reactants minus one

mole of water. The reaction medium was as usual methanolic zinc chloride solution and only one reaction product could be isolated. With 2,4-dinitrophenylhydrazine it gave a monohydrazone and with acetyl chloride a monoacetate was obtained. The substance was contrary to expectation not soluble in warm 2 N sodium hydroxide. It is supposed to have the naphthofuran structure VI.



VI	R <sub>1</sub> = CH <sub>3</sub> ,	R <sub>2</sub> = COCH <sub>3</sub>
VII	R <sub>1</sub> = CH <sub>3</sub> ,	R <sub>2</sub> = COOC <sub>2</sub> H <sub>5</sub>
VIII	R <sub>1</sub> = C <sub>6</sub> H <sub>5</sub> ,	R <sub>2</sub> = COOC <sub>2</sub> H <sub>5</sub>
IX	R <sub>1</sub> = CH <sub>3</sub> ,	R <sub>2</sub> = COC <sub>6</sub> H <sub>5</sub>
X	R <sub>1</sub> = CH <sub>3</sub> ,	R <sub>2</sub> = C(OH)(CH <sub>3</sub> )C <sub>6</sub> H <sub>5</sub>

After this part of the investigation was completed it was found in the literature that Ebine<sup>20</sup> also had prepared the substance VI. His findings are in good agreement with ours. In the same paper Ebine reports the synthesis of II and gives the melting point 232—233° which is rather low as compared to our value<sup>19</sup> of 248°. Likewise the found percentage of carbon is by 1.7 smaller than calculated. It is suspected that Ebine has not had the pure compound II in hands but a mixture of II and I. The latter has the melting point 238° and its carbon content is by 1.6 lower than for II<sup>18</sup>. The reason for this contamination is that I and II are always formed together in the condensation of acetylacetone with quinone. Unless I is extracted with alkali (which Ebine has not done) the mixture is very difficult to separate by mere recrystallization. Ebine's dioxime seems to have the correct composition a fact which probably can be explained by different solubilities of the monoxime of the benzofuran and the dioxime of the benzodifuran; the latter most likely being less soluble than the former and therefore separates first from solvents.

In analogy with VI we have prepared VII with ethyl acetoacetate, VIII with benzoylacetate ester, and IX with benzoylacetone. All these compounds could be acetylated to give the monoacetates but were insoluble in 2 N sodium hydroxide. In the case of the benzoyl product there were two structural possibilities, *viz.* one methyl-benzoyl derivative (IX) and one phenyl-acetyl derivative. This question was settled in the same way as for IV by reacting VI with phenyl magnesium bromide and IX with methyl magnesium iodide and obtaining the same tertiary alcohol X in both cases. The identity of the alcohols could not be established by mixed melting point as they readily lost water and melted over a long range. Their infrared spectra were therefore recorded and were found to be absolutely identical.

2-Methyl-1,4-naphthoquinone did not react at all with acetylacetone under the usual reaction conditions while 2-hydroxy-1,4-naphthoquinone gave the corresponding methyl ether and 2-chloro-1,4-naphthoquinone gave bi-1,4-naphthoquinone, C<sub>20</sub>H<sub>10</sub>O<sub>4</sub>.

Naphthazarin and its diacetate were tried as representatives of naphthoquinones with substituents in the benzene ring. In order to avoid alcoholysis the diacetate was treated with acetylacetone in ethereal zinc chloride. Neither the hydroxyquinone nor the diacetate could be induced to react. This is in

agreement with the recent findings of Bruce and Thomson<sup>21</sup> who examined the reactivity of naphthazarin and the diacetate towards several reagents. They conclude that naphthazarin is a relatively unreactive quinone towards nucleophilic and electrophilic reagents (in our reactions we have to deal with the nucleophilic acetylacetonate ion) but reacts normally with substances which add by a radical mechanism (*e. g.* toluene-*p*-thiol) while the diacetate is somewhat, but not markedly, more reactive.

## EXPERIMENTAL

(In part with A. Wulff and S. Steinsvik)

### *p*-Benzoquinone and benzoylacetone

*p*-Benzoquinone (2.0 g) and benzoylacetone (3.0 g) were added to a solution of zinc chloride (10 g) in anhydrous methanol (12.5 ml). The mixture was heated for 7 hours on a water-bath and left overnight at room temperature. Next day a crystalline substance (0.55 g) had separated. Recrystallized twice from glacial acetic acid. M. p. 221°. (Found: C 79.27; H 4.65. Calc. for C<sub>22</sub>H<sub>12</sub>O<sub>4</sub>: C 79.20; H 4.62).

*Dinitrophenylhydrazone*. Dinitrophenylhydrazine (0.3 g) was dissolved in hydrochloric acid (20 ml, 2 N) to which was added ethanol (10 ml) and IV (0.2 g). The mixture was heated for 7 hours on a water-bath with occasional additions of small amounts of ethanol. Next day the separated crystalline substance was isolated and dissolved in a mixture of chloroform and ligroin (1:1). The solution was passed through a column of silica gel where the dissolved substance was adsorbed in different zones, the predominating one being bright red. This zone was separated from the rest of the column and extracted with chloroform. After evaporation of the chloroform the residue was orange-red and weighed 65 mg. M. p. 249–250°. (Found: N 9.71. Calc. for C<sub>22</sub>H<sub>12</sub>N<sub>4</sub>O<sub>7</sub>: N 9.75). The substance seems to be a monohydrazone of the benzodifuran.

*Methyl magnesium iodide and IV*. To a solution of methyl magnesium iodide (from 0.5 g magnesium) in dry ether (20 ml) was added IV (0.5 g). After the vigorous reaction had subsided the reaction mixture was refluxed for 15 minutes and decomposed with water and dilute hydrochloric acid. The ethereal layer was dried and evaporated, the residue weighing 0.44 g. Recrystallized twice from dilute ethanol. M. p. 194–195°. (Found: C 79.89; H 6.14. Calc. for C<sub>22</sub>H<sub>12</sub>O<sub>4</sub>: C 78.86; H 6.15).

### Phenyl magnesium bromide and II

To a solution of phenyl magnesium bromide (from 0.5 g magnesium) in dry ether (20 ml) II (0.5 g) was added. After the moderate reaction had subsided the reaction mixture was refluxed for 25 minutes and decomposed with water and dilute hydrochloric acid. The ethereal layer was dried and evaporated. The residue, which was a yellow plastic mass with a conspicuous smell of biphenyl, was extracted twice with boiling ligroin and recrystallized thrice from dilute ethanol (charcoal). M. p. 197°. Mixed melting point with the substance from the foregoing experiment 197°. (Found: C 80.09; H 6.31. Calc. for C<sub>22</sub>H<sub>12</sub>O<sub>4</sub>: C 78.86; H 6.15).

### *p*-Benzoquinone and benzoylacetic ester

To a solution of zinc chloride (10 g) in anhydrous methanol (15 ml) benzoylacetic ester (3.5 g) was added and thereafter in small portions *p*-benzoquinone (2 g). The mixture was heated on a water-bath for 5.5 hours and placed in a refrigerator. After several days a small amount of a crystalline material had separated. After recrystallization from glacial acetic acid (charcoal) it was yellowish and had m. p. 163°. Due to the very small yield six of the above portions were reacted and worked up. The collected products were

recrystallized five times from glacial acetic acid (charcoal) and then had the constant m. p. of 185–186°. Very small, white needles (45 mg). (Found C 73.66; H 4.82. Calc. for  $C_{22}H_{12}O_4$ : C 74.00; H 4.88).

#### 1,4-Naphthoquinone and acetylacetone

1,4-Naphthoquinone (1.5 g) and acetylacetone (2 ml) were dissolved in a solution of zinc chloride (5 g) in dry methanol (6 ml). The mixture was refluxed for 5 minutes when it solidified into a crystal mass. Isolated by suction and washed with methanol (0.90 g). Recrystallized twice from glacial acetic acid (charcoal) it had m. p. 262°. (Found: C 74.71; H 5.04. Calc. for  $C_{15}H_{10}O_4$ : C 74.98; H 5.03).

*Dinitrophenylhydrazine.* VI (0.2 g) was dissolved in boiling ethanol (25 ml) to which was added a solution of 2,4-dinitrophenylhydrazine (0.2 g) in hydrochloric acid (25 ml, 2 N). Immediately a bright red voluminous precipitate was formed. After 2.5 hours on a water-bath the separated substance was isolated (0.31 g) and recrystallized from glacial acetic acid. M. p. 271–272°. (Found: C 59.82; H 3.94; N 13.22. Calc. for  $C_{21}H_{16}N_4O_6$ : C 60.01; H 3.84; N 13.33).

*Acetate.* VI (0.5 g) and acetyl chloride (50 ml) were refluxed for 1.5 hours and the cooled solution poured into icewater (1 l) when a white substance separated. Recrystallized from dilute alcohol and from benzene. White needles. M. p. 152.5–153.5°. (Found: C 72.21; H 4.92. Calc. for  $C_{17}H_{14}O_4$ : C 72.33; H 5.00).

#### 1,4-Naphthoquinone and ethyl acetoacetate

1,4-Naphthoquinone (5 g) and ethyl acetoacetate (6 ml) were added to a solution of zinc chloride (15 g) in dry methanol (25 ml). The mixture was heated on a steam-bath for 1 hour and cooled to room temperature. The separated crystals (3.5 g) were washed with methanol and recrystallized thrice from glacial acetic acid. White needles. M. p. 208–209° (Kofler bench) (Found: C 70.94; H 5.08. Calc. for  $C_{16}H_{14}O_4$ : C 71.06; H 5.22).

*Acetate.* VII (0.6 g) and acetyl chloride (50 ml) were refluxed for 3 hours and poured into ice-water (1 l). The separated, white substance was recrystallized twice from glacial acetic acid. White needles. M. p. 147–148°. (Found: C 68.89; H 5.22. Calc. for  $C_{13}H_{10}O_5$ : C 69.23; H 5.16).

#### 1,4-Naphthoquinone and benzoyl acetic ester

1,4-Naphthoquinone (4 g) and benzoyl acetic ester (5 ml) were added to a solution of zinc chloride (25 g) in dry methanol (30 ml) and refluxed for 15 minutes when the reaction mixture solidified to a crystal mass. The crystals (4 g) were washed with methanol and recrystallized thrice from glacial acetic acid (charcoal). M. p. 194–195°. (Found: C 75.88; H 4.94. Calc. for  $C_{21}H_{16}O_4$ : C 75.90; H 4.85).

*Acetate.* VIII (0.5 g) and acetyl chloride (20 ml) were refluxed for 2 hours and poured into ice-water (1 l). The separated white substance was recrystallized twice from 80 % ethanol. White needles. M. p. 119.5–120° (Found: C 73.60; H 4.65. Calc. for  $C_{22}H_{16}O_5$ : C 73.79; H 4.84).

#### 1,4-Naphthoquinone and benzoylacetone

1,4-Naphthoquinone (5 g) and benzoylacetone (7 g) were added to a solution of zinc chloride (25 g) in dry methanol (30 ml) and refluxed for 2.5 hours. After cooling the separated crystals (3.5 g) were washed with warm ethanol and recrystallized thrice from glacial acetic acid. Yellow needles. M. p. 240°, decomp. (Kofler-bench). (Found: C 79.36; H 4.68. Calc. for  $C_{20}H_{14}O_3$ : C 79.47; H 4.67).

*Acetate.* IX (0.48 g) and acetyl chloride (50 ml) were refluxed for two hours and poured into ice-water (1 l). The precipitated, white substance was recrystallized thrice from 70 % ethanol. White rhombic crystals. M. p. 144.5–146°. (Found: C 76.38; H 4.70. Calc. for  $C_{22}H_{16}O_4$ : C 76.70; H 4.68).

## VI and phenyl magnesium bromide

The Grignard reagent was prepared from magnesium (1.6 g) and bromobenzene (10 g) in anhydrous ether (25 ml). To a suspension of VI (1 g) in anhydrous toluene (15 ml) were added dropwise 5 ml of the above reagent. The naphthofuran dissolved gradually as the reaction proceeded and to the clear solution an additional amount of dry toluene (35 ml) was added. The solution was heated to 50° for 15 minutes and decomposed with ice and sulphuric acid (20 %). Excess sulphuric acid was neutralized with sodium hydrogen carbonate when a white substance separated on the interface between the aqueous and the toluene layers. This substance was recrystallized twice from dilute alcohol and twice from dilute acetone. No definite melting point. (Found: C 78.70; H 5.79. Calc. for  $C_{21}H_{18}O_3$ : C 79.20; H 5.71).

## IX and methyl magnesium iodide

The Grignard reagent was prepared from magnesium (1 g) and methyl iodide (6 g) in anhydrous ether (10 ml). To a suspension of IX (0.5 g) in dry toluene (15 ml) 6 ml of the reagent were added dropwise. The ensuing reaction led also in this case to a clear solution. From here the procedure was exactly as in the above experiment. The product had no definite melting point. (Found: C 78.83; H 5.81. Calc. for  $C_{21}H_{18}O_3$ : C 79.20; H 5.71).

The author is indebted to *Fridtjof Nansens Fond* for a grant.

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Received November 8, 1955.