

The Hydroxylation of Furan with Osmium Tetroxide

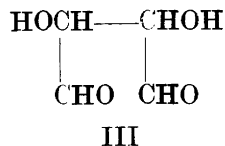
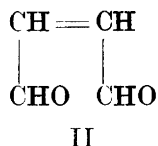
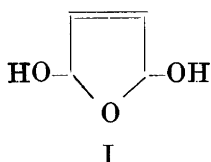
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Hydroxylation of furan should yield 2,5-dihydroxy-2,5-dihydrofuran (I), provided 1,4-addition of the hydroxy groups takes place. In order to ascertain this, furan was oxidized in alcoholic solution with osmium tetroxide and hydrogen peroxide according to Milas and Sussman¹. These authors used an anhydrous solution of hydrogen peroxide in tert. butanol. We have employed a mixture of 30 % aqueous hydrogen peroxide and methanol. This reagent, which is cheaper and easier to prepare than that of Milas and Sussman, proved to be perfectly stable at 0° in the presence of osmium tetroxide.

In aqueous methanol 2,5-dihydroxy-2,5-dihydrofuran is probably easily hydrolyzed to yield hydrates of malealdehyde (II). Consequently no attempt was made to isolate the dihydrofuran but phenylhydrazine added directly to the reaction mixture in order to obtain the bis-phenylhydrazone of malealdehyde.

When equimolar amounts of furan and hydrogen peroxide were allowed to interact at 0° all hydrogen peroxide had disappeared after 40 hours. Addition of phenylhydrazine yielded a precipitate of yellow crystals, which turned out to be a mixture of approximately one part of mesotartaraldehyde bis-phenylhydrazone and two parts of malealdehyde bis-phenylhydrazone. The hydrazones were separated by fractionate crystallization from acetone-benzene and identified by analysis and melting-point determination; the total yield was 38 % proportionate to furan and 47 % proportionate to hydrogen peroxide.



The tartaraldehyde derivative, which has been prepared earlier by Wohl and Mylo², is reported to form yellow crystals just as the corresponding bis-phenylhydrazones of malealdehyde or glyoxal. However in these compounds all double bonds are conjugated. Inasmuch as conjugation is interrupted in tartaraldehyde bis-phenylhydrazone, this compound should be colourless, *e. g.* as succinaldehyde bis-phenylhydrazone. Still our product also had a strong yellow colour, but after three recrystallizations from acetone-benzene perfectly colourless crystals were obtained. The yellow colour of Wohl and Mylo's hydrazone, as well as of our crude product, is undoubtedly due to a small amount of malealdehyde bis-phenylhydrazone. This is in agreement with the fact that the tartaraldehyde tetraethylacetal used by Wohl and Mylo for the preparation of their hydrazone was obtained by hydroxylation of malealdehyde tetraethylacetal.

The hydroxylation of furan had thus taken the expected course, although some of the malealdehyde had been further hydroxylated to mesotartaraldehyde (III).

After standing at room temperature for one week, the reaction mixture furnished exclusively mesotartaraldehyde bis-phenylhydrazone on addition of phenylhydrazine. The yield was exactly the same as that originally obtained of this hydrazone. The malealdehyde had accordingly been completely destroyed by standing, the tartaraldehyde had not been affected. At 0° malealdehyde is somewhat more stable. The stability of the aldehydes, in whatever form they may exist in the reaction mixture, corresponds to that reported by Wohl and Mylo for malealdehyde and tartaraldehyde.

When furan reacts with twice the equimolar amount of hydrogen peroxide, the total yield of the hydrazones isolated from the reaction mixture is increased to 59 % (proportionate to furan). The yield proportionate to hydrogen peroxide is 43 %. The ratio mesotartaraldehyde to malealdehyde bis-phenylhydrazone is now approximately 1 : 1.4.

No attempt was made to examine the other reaction products in order to find out what the rest of the hydrogen peroxide had been used for. Actually there was an evolution of oxygen, but far from enough to account for all the hydrogen peroxide.

In conclusion the effect of different admixtures on the hydroxylation reaction was investigated. Addition of acetic acid in small amounts did neither affect the velocity nor the course of reaction. Small amounts of sulfuric acid caused an almost complete stop of the reaction. Pyridine (*cf.* Crigee³) had a very marked influence; velocity and yield were decreased and the course of reaction was also affected. No appreciable amount of mesotartaraldehyde was formed, and only the bis-phenylhydrazone of malealdehyde could be

isolated. It is possible that the addition of pyridine or similar tertiary amines may find general application for determining the course of hydroxylation reactions with osmium tetroxide.

EXPERIMENTAL

Preparation of reagent

6.00 ml of 30 % (9.7 *M*; determined by titration) hydrogen peroxide, technical grade, were mixed with methanol (18 ml) in a 25 ml volumetric flask and the mixture cooled to 0°. 0.40 ml of a solution of osmium tetroxide in tert.-butanol (0.62 %) were added and the flask filled to the mark with methanol. The molarity was determined by iodometric titration to 2.324. After standing for four days at 0°, *M* was determined to 2.302 which proves the stability of the reagent at this temperature.

The hydrogen peroxide (9.7 *M*) and the osmium tetroxide solution (0.62 %) used here were also employed in all the following experiments.

Hydroxylation of furan (furan:hydrogen peroxide = 1:1.06)

Freshly distilled furan (2.111 g), methanol (18 ml) and hydrogen peroxide (3.36 ml) were mixed in a 25 ml volumetric flask and cooled to 0°. 0.40 ml of osmium tetroxide solution were added and the flask filled to the mark with methanol. After standing for about 40 hours at 0°, all hydrogen peroxide had disappeared. The volume of the reaction mixture had decreased a little, and the flask was anew filled with methanol. 2.00 ml were added to a solution of phenylhydrazine (0.50 ml) in ethanol (1 ml) and glacial acetic acid (0.1 ml). The mixture solidified almost immediately to a mass of orange yellow crystals. After standing for some hours, the crystals were filtered off and washed with ethanol (7 ml) and benzene (6 ml). Yield 243 mg. From the mother liquor another 18 mg were obtained; total yield 261 mg.

The crystals were dissolved in boiling acetone (30 ml). 30 ml of benzene were added, the solution evaporated under atmospheric pressure to 20 ml, cooled rapidly and filtered. The lemon yellow crystals were washed with benzene. Yield 80 mg = 11 %, calculated as tartaraldehyde bis-phenylhydrazone ($C_{16}H_{18}O_2N_4$).

$C_{16}H_{18}O_2N_4$ (298)	Calc. N 18.79	Found N 18.78
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Further evaporation of the mother liquor to about 5 cc. gave another crop of crystals, which was filtered off and washed with a small amount of benzene. Yellow plates, yield 156 mg = 24 %, calculated as malealdehyde bis-phenylhydrazone ($C_{16}H_{16}N_4$).

$C_{16}H_{16}N_4$ (264)	Calc. N 21.21	Found N 21.55
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About twice as much malealdehyde as mesotartaraldehyde has been formed by the reaction. This corresponds to a 38 % yield of the crude mixture of the hydrazones (261 mg) proportionate to furan and a 47 % yield proportionate to hydrogen peroxide.

It is evident that nitrogen determination is not a very fine method to control the purity of the hydrazones. The analyses have been carried out only to get a rough picture

of the proportion in which the two aldehydes are formed by the reaction. The pure bis-phenylhydrazones were obtained by recrystallizing each of the two fractions (80 mg and 156 mg) once or twice more from acetone-benzene. The melting point (Kofler stage, corrected) of the tartaraldehyde fraction hereby rose from 187—189° to 195° (Wohl a. Mylo 197.5²), of the malealdehyde fraction from 162—165° to 172° (171° has earlier been found⁴). Further recrystallizations did not alter the melting points. Both of the two crude fractions had a strong yellow colour but the tartaraldehyde fraction was perfectly colourless after three recrystallizations (N 18.58 %).

Stability of the aldehydes

After standing for a week at 0°, 2.00 ml of the reaction mixture only yielded 188 mg of crude hydrazones. When standing for a week at room temperature, the yield was 78 mg. The melting point (185°) and a nitrogen determination (N 18.90 %) showed that the product consisted mainly of tartaraldehyde derivative. Accordingly, when recrystallized once in a 70 % yield, the melting point was raised to 194°.

Hydroxylation of furan (furan: hydrogen peroxide = 1:1.96)

2.094 g of furan, 6.20 ml of hydrogen peroxide and 0.4 ml of osmium tetroxide solution were mixed with methanol in a 25 ml volumetric flask as described above. The hydrogen peroxide had disappeared after 48 hours. The total yield of crude product from 2.00 ml of the reaction mixture was now 403 mg, consisting of 1 part of tartaraldehyde bis-phenylhydrazone (N 18.84 %) and 1.4 parts of malealdehyde bis-phenylhydrazone (N 21.08 %). This corresponds to a 59 % yield proportionate to furan and a 43 % yield proportionate to hydrogen peroxide.

Effect of admixtures on the reaction

The reaction described above (furan: hydrogen peroxide = 1:1.96) was repeated three times with the addition of 0.5 ml of glacial acetic acid, 0.5 ml of concentrated sulfuric acid and 0.2 ml of pyridine respectively.

Acetic acid had no influence on the reaction and the hydrazones were isolated in exactly the same yields as above.

Addition of sulfuric acid arrested the reaction almost completely. After two days only 10 % of the hydrogen peroxide had been consumed.

Pyridine also markedly decreased the velocity of the reaction. After two, five and twelve days the consumption of hydrogen peroxide was 33 %, 50 % and 75 % respectively. At this time 2.00 ml of the reaction mixture were precipitated with phenylhydrazine. The crude hydrazone melted at 167—170° and contained 21.28 % of nitrogen; it must therefore consist mainly of malealdehyde bis-phenylhydrazone. The yield was only 8 % proportionate to furan.

In another experiment, equimolar amounts of furan and hydrogen peroxide were allowed to react in the presence of osmium tetroxide and pyridine. The hydrazone was precipitated after 24 hours in a 15 % yield (m. p. 168—169°; N 21.16 %). Neither of the two products from these preparations could be divided into different fractions by recrystallization. Hence, no detectable amount of tartaraldehyde is formed by the reaction.

SUMMARY

Furan has been oxidized in methanolic solution with 30 % aqueous hydrogen peroxide in the presence of osmium tetroxide. The bis-phenylhydrazones of malealdehyde and mesotartaraldehyde were isolated by addition of phenylhydrazine to the reaction mixture. The influence of small amounts of acetic acid, sulfuric acid and pyridine on the course of reaction has been studied.

All analyses have been made in the most careful way by our colleague Mr. O. Rosenlund Hansen.

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