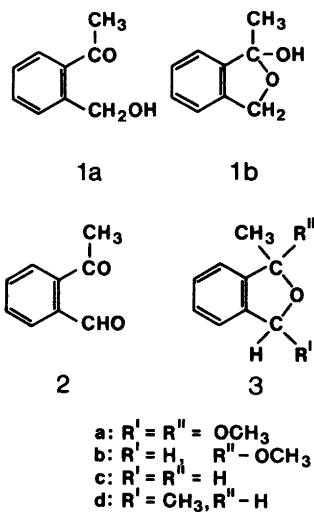


## Some New Orthoderivatives of Benzene

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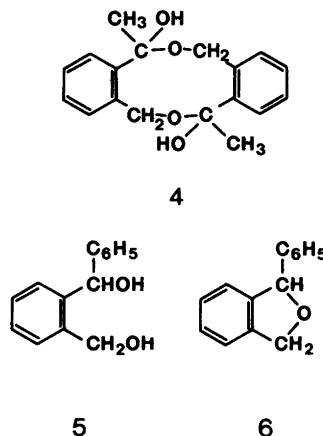
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It has been suggested<sup>1</sup> that the self-condensation of 2-acetylbenzoic acid starts with the formation of a carbonium ion derived from the cyclic form of the acid. It would be interesting to see if another compound with the same constellation of a carbonyl and a hydroxyl group such as 2-acetylbenzylalcohol (*1*) behaves similarly. An attempt to prepare this hitherto unknown alcohol by partial reduction of 2-acetylbenzaldehyde *2* failed. The aldehyde *2* could be prepared by permanganate oxidation of 2-acetylcis-cinnamic acid. On longer standing the crystals of *2* liquefied, gradually taking up oxygen and turning into 2-acetylbenzoic acid.



The useful method for preparation of *1* started with reduction of the ketalized methylester of 2-acetylbenzoic acid with  $\text{LiAlH}_4$ . A direct deketalization of the reduction product by adding HCl to a solution in methanol was unsuccessful. It was necessary to protect the hydroxyl group by forming a *p*-nitrobenzoate. Deketalizing this gave the nitrobenzoate of *1a* which on saponification under strict exclusion of methanol or ethanol led to the pure acetylbenzylalcohol as a colourless liquid from which a semicarbazone was prepared. The  $^1\text{H}$  NMR spectrum of 2-acetylbenzylalcohol shows two singlets ( $\text{CH}_3$ ) near each other about  $\delta$  1.7 and two

AB-quartets partly overlapping at about  $\delta$  5.0. An explanation for this would be that a part of the 2-acetylbenzylalcohol is present as a cyclic dimer (two diastereoisomers) as indicated in *4*. The other lines in the spectrum are then due to the monomer cyclic form *1b*, namely two singlets ( $\text{CH}_3$ ) near each other at  $\delta$  2.4 and a quartet ( $\text{CH}_2$ ) at  $\delta$  4.0.



Reduction of *1* led to a crystalline diol, 1-(2-hydroxymethylphenyl)ethanol (*5*), which on dehydration gave 1,3-dihydro-1-methylisobenzofuran (*3c*). Freshly prepared, this was a very mobile and quite volatile liquid which readily underwent autoxidation.

For comparison, 1,3-dihydro-1,3-dimethylisobenzofuran *3d* was prepared.<sup>3</sup> Also this compound was a volatile liquid which behaved in the same way as *3c*.

The 1,3-dihydroisobenzofuran itself<sup>4</sup> reacted so rapidly with oxygen that it, after being left 2 days in an open vessel, gave a positive reaction on peroxide. The crystalline peroxide obtained after prolonged exposure to air had m.p. 130°C and showed an NMR spectrum in agreement with the formula proposed before.<sup>2</sup>

An attempt to prepare *o*-benzoylbenzyl alcohol following the same procedure as for the methyl derivative failed. Instead of the expected product 3-phenylphthalide and 1-(2-hydroxymethylphenyl)-1-phenylmethanol (*5*) were isolated, of which the latter one was transformed into 1,3-dihydro-1-phenylisobenzofuran (*6*) as described.<sup>5</sup> The NMR spectrum of *6* is quite remarkable, obviously due to coupling of the protons in the CH and  $\text{CH}_2$  groups with the neighbouring aromatic protons: 1 H, triplet at  $\delta$  6.1, 2 H triplet at  $\delta$  5.1 and 9 arom. H. An earlier observation<sup>5</sup> that the crystalline 1,3-dihydro-1-phenylisobenzofuran deteriorated on standing is obviously due to the fact that also this derivative of

1,3-dihydroisobenzofuran reacts with oxygen in the air and gives a positive test for peroxide. It was also found that pure 1,3-dihydroisobenzofuran itself deteriorated on standing.

*Experimental.* 2-Acetyl-cis-cinnamic acid (*A*) was in the present case prepared by oxidizing 1-methyl-2-naphthol with ozone. The naphthol (3.16 g, 20 mmol) prepared according to literature<sup>6</sup> was dissolved in 100 ml methylene chloride and at 20 °C a stream of ozone led through until 20 mmol had been absorbed. Triphenylphosphine (5.2 g 20 mmol) dissolved in methylene chloride was added. The *A* formed was extracted with sodium bicarbonate and finally precipitated by adding acid. Yield 2.90 g (76%) m.p. 142 °C.

2-Acetylbenzaldehyde (*2*). 10 mmol *A* (1.90 g), 0.52 g sodium carbonate and 1.5 g magnesium sulfate were dissolved in 120 ml water and 50 ml benzene placed on top of the solution. Keeping the temperature between 0 and 5 °C and stirring vigorously, 2.5 g potassium permanganate dissolved in 100 ml water was slowly added. After two more portions of benzene had been used for extraction, 0.6 g of *2* was obtained as a liquid which spontaneously crystallized. Recrystallized from pentane; needles, m.p. 44 °C. Anal. C<sub>9</sub>H<sub>8</sub>O<sub>2</sub>: C, H, NMR in CDCl<sub>3</sub> δ 2.63 (3H), 9.0 (1 H), 4 arom. H 7.7.

*Autoxidation of 2.* Crystalline *2* (0.88 g) left on an open dish for 3 weeks had become liquid and the solution of it in ether was shaken with sodium bicarbonate. From the ether was obtained 0.27 g unchanged *2* and from the aqueous solution 2-acetylbenzoic acid, m.p. 114 °C was isolated. The phenylhydrazone of *2* prepared in the usual way after being recrystallized from ethanol m.p. 213 °C. Anal. C<sub>15</sub>H<sub>14</sub>ON<sub>2</sub>: N.

*Dimethylketal of methylester of 2-acetylbenzoic acid (C).* To a mixture of the methylester of 2-acetylbenzoic acid (19 g), methanol (40 ml) methylorthoformate (25 ml) and 5 drops conc. HCl were added and the solution boiled for 5 h. After adding 4 drops of HCl the boiling was continued for 2 h. After removing the volatile material in a vacuum at 50 °C the remaining liquid (24.8 g) showed the NMR expected for C: δ 1.59 (3H), 3.09 (6H), 3.79 (3H) and 4 arom. H.

*Reduction of C.* The liquid from above (24.8 g), dissolved in ether, was added slowly to a suspension of 3.1 g LiAlH<sub>4</sub> in ether. Excess of LiAlH<sub>4</sub> was destroyed by adding ethyl acetate. Finally, water was added and from the ethereal solution the dimethylketal of *1a* was obtained as a colourless liquid (20.6 g). NMR in CDCl<sub>3</sub>: δ 1.58 (3H), 3.26 (6H) (partly overlapping OH), 4.67 (AB q) and 4 arom. H. After distillation in vacuum (145 °C at 12 mmHg) the NMR was unchanged.

*The p-nitrobenzoates.* To a solution of the dimethylketal of *1a* in 8 ml pyridine, *p*-

nitrobenzoylchloride (1.2 g) was added. The temperature rose a little and crystals began to separate. After adding water, solid material (2.2 g) was filtered off. On boiling with ethanol most of it remained unsolved, obviously polymerized material. From the solution was obtained 0.7 g *p*-nitrobenzoate of the dimethylketal, which when recrystallized from ethanol had m.p. 113 °C. Anal. C<sub>16</sub>H<sub>19</sub>O<sub>6</sub>N: C, H, NMR (CDCl<sub>3</sub>) δ 1.59 (3H), 3.16 (6H), 5.63 (2H) and 8 arom. H. On recrystallization from ethanol containing HCl deketalization took place, and the *p*-nitrobenzoate of *1a* was obtained. M.p. 132 °C. Anal. C<sub>16</sub>H<sub>13</sub>O<sub>5</sub>N: C, H, N, NMR (CDCl<sub>3</sub>): δ 2.62 (3H), 5.75 (2H), and 8 arom. H.

Saponification of the *p*-nitrobenzoate in the presence of methanol led to a colourless liquid which, judging from the NMR spectrum, consisted of 50% of the cyclic ketal *3b* and 25% of the open and cyclic forms of 2-acetylbenzylalcohol (*1a* and *1b*). NMR (CDCl<sub>3</sub>) for the cyclic ketal δ 1.71 (3H), 3.00 (3H), 5.11 (2H).

The reaction of 2-acetylbenzylalcohol (*1*) with methanol was demonstrated in an experiment which showed that the reaction product *3b* is very volatile. NMR (CDCl<sub>3</sub>): δ 1.69 (3H), 2.98 (3H), 5.06 (2H) and 4 arom. H at about 7.5.

*Preparation of B.* When either *1* or 2-acetylbenzoic acid was reduced with LiAlH<sub>4</sub> the final product was a colourless liquid which distilled at 180 °C, 15 mmHg. After a few days, crystallization of *B* set in. M.p. 71 °C. Anal. C<sub>9</sub>H<sub>12</sub>O<sub>2</sub>: C, H, NMR (CDCl<sub>3</sub>): δ 1.46 (3H), 3.88 (2H), 4.57 (2H ABq), 5.01 (1 Hq), 4 arom. H at about 7.3. The dinitrobenzoate had m.p. 131 °C. (Found C 60.80, H 3.72; C<sub>23</sub>H<sub>18</sub>O<sub>8</sub>N<sub>2</sub> calc. C 61.33, H 4.03, N 6.22).

*Dehydration of B.* To a few g of *B* an equal quantity of 85% phosphoric acid was added and the mixture heated slightly until an oily substance separated. Dissolved in ether and shaken thoroughly first with water and then with bicarbonate *3c* was obtained as a very mobile liquid which distilled at 85 °C, 10 mmHg. (Found C 80.87, H 7.45; calc. C<sub>9</sub>H<sub>10</sub>O: C 80.56, H 7.51. NMR (CDCl<sub>3</sub>): δ 1.47 (3H), 5.07 (2H ABq), 4 arom. H at 7.2. Leaving *3c* in an open vessel it gradually became viscous and gave a positive reaction on peroxide. After 2 weeks: C 69.69, H 6.17; calc. for a peroxide C<sub>18</sub>H<sub>18</sub>O<sub>4</sub>: C 72.47, H 6.08.

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