303. *Condensation Products of Phenols and Ketones. Part IV.* o-*Cresol with Acetone.*

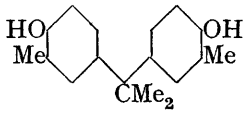
By Wilson Baker and D. M. Besly.

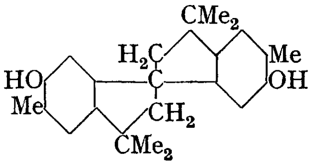
Two molecules of *o*-cresol condense with three molecules of acetone in presence of concentrated sulphuric acid or a mixture of hydrochloric acid and acetic acid to give a dihydric phenol. Analysis of this substance and of a number of derivatives shows that it possesses the formula $C_{23}H_{28}O_2$, and its degradation to phoronic anhydride proves that it is a bis-1 : 1′-*spiro*hydrindene in which the orientation of the hydroxyl and methyl groups in the cresol nuclei are probably as shown in formula (II).

o-Cresol (2 mols.) condenses with acetone (1 mol.) in presence of concentrated hydrochloric acid at room temperature to give di-(4-hydroxy-3-methylphenyl)dimethylmethane (I) (Zincke, *Annalen*, 1913, **400**, 33). More complex products formed from *o*-cresol (2 mols.) and acetone (3 mols.) have been described by Niederl and Casty (*Sitzungsber. Akad. Wiss. Wien*, 1928, **137**, IIb, 1038) and by Sükösd (*Acta Lit. Sci. Univ. Hung. Francisco-Josephinæ*, 1932, **2**, 230). Niederl and Casty condensed *o*-cresol with acetone or phorone in presence of concentrated sulphuric acid and isolated from the reaction products a dihydric phenol (" di-*o*-cresylphorone "), m. p. 245°, believed to possess the molecular formula $C_{23}H_{30}O_3$, and to which was ascribed the structure $HO{\cdot}C_6H_3Me{\cdot}CMe_2{\cdot}CH_2{\cdot}CO{\cdot}CH_2{\cdot}CMe_2{\cdot}C_6H_3Me{\cdot}OH$, the hydroxyl groups being first placed in the ortho-positions and later in the para-positions to the $\cdot CMe_2\cdot$ groups (Niederl, *Sitzungsber. Akad. Wiss. Wien*, 1932, **141**, IIb, 150). The compound failed to react with ketonic reagents and it was suggested that this was due to steric hindrance. These authors further mention a dibenzoyl derivative and a dimethyl ether (neither analysed) and a dibromo-derivative (Br analysis) (see experimental section).

Sükösd heated a mixture of *o*-cresol, acetone, acetic acid and concentrated hydrochloric acid and isolated the condensation product as a diacetyl derivative, $C_{27}H_{32}O_4$, m. p. 263—264°. On the basis of the formula of the diacetate the free phenolic compound should be $C_{23}H_{28}O_2$, containing one molecule of water less than the product described by Niederl and Casty. Sükösd proposed for the substance the stereochemically impossible structure $HO{\cdot}C_6HMe(CMe_2)_3C_6HMe{\cdot}OH$ (cf. a similar structure proposed for the condensation product of catechol with acetone which has been proved to be incorrect; Baker, J., 1934, 1678; Baker and McGowan, J., 1938, 347), but Fisher, Furlong, and Grant (*J. Amer. Chem. Soc.*, 1936, **58**, 820) considered that it was more probably the bis-1 : 1′-*spiro*hydrindene (II), the suggestion being based on the structure of a condensation product of catechol with acetone (Baker, *loc. cit.*). Fisher, Furlong, and Grant further suggested that the product $C_{23}H_{30}O_3$ obtained by Niederl and Casty was an intermediate in the formation of Sükösd's compound $C_{23}H_{28}O_2$.

(I.)





(II).

It has now been found that the condensation products obtained by the methods of Niederl and Casty and of Sükösd are identical, the most convenient method for the preparation of the compound being a modification of Sükösd's process. Both the products themselves and their diacetyl derivatives have been directly compared, and since the condensation products are most easily isolated as acetyl derivatives it has been further established that the compound isolated directly is unchanged after being converted into the acetyl derivative and regenerated by hydrolysis. Analysis of the compound shows that it is $C_{23}H_{28}O_2$, and not $C_{23}H_{30}O_3$, and this formula is supported by the analyses of the diacetate, the *dibenzoate*, the *di*-p-*nitrobenzoate*, the *dimethyl* ether, and the dibromo-compound. The presence of the grouping $C{\cdot}CMe_2{\cdot}CH_2{\cdot}C{\cdot}CH_2{\cdot}CMe_2{\cdot}C$ is proved by the isolation of phoronic anhydride in small quantity from the products of the oxidation of the substance with potassium permanganate, and this directly proves that it is a dihydroxydimethyl-3 : 3 : 3′ : 3′-tetramethylbis-1 : 1′-*spiro*hydrindene as in (II), the reasoning being similar to that employed in previous cases (Baker and McGowan, *loc. cit.*; Baker and Besly, this vol., p. 195). The hydroxyl and methyl groups in the *o*-cresol nuclei probably occupy the positions shown in (II) (see Baker and Besly, *loc. cit.*, p. 197), and this view is strongly supported by the observation that (II) may be easily prepared from the diphenyldimethylmethane derivative (I) by heating with hydrochloric acid and acetic acid, its formation being accompanied by liberation of *o*-cresol.

The action of hot concentrated nitric acid in acetic acid on (II) leads to the production of two *nitro*-compounds, which are probably degradation products.

EXPERIMENTAL.

Preparation of 6 : 6′-*Dihydroxy*-3 : 3 : 5 : 3′ : 3′ : 5′-*hexamethylbis*-1 : 1′-spiro*hydrindene* (II).—(a) *From* o-*cresol and acetone.* A mixture of *o*-cresol (100 g.), acetic acid (250 c.c.), acetone (75 c.c.), and concentrated hydrochloric acid (190 c.c.) was heated under reflux on a boiling water-bath for 60 hours, and then stirred into water. The very thick mass was collected, washed by kneading under water, dried by heating under diminished pressure on the water-bath, and boiled with acetic anhydride (300 c.c.) and pyridine (5 c.c.) for 6 hours. To the hot liquid, water (200 c.c.) was now cautiously added while shaking, and then alcohol (150 c.c.), and the crystalline product collected after cooling. This diacetyl derivative was washed with cold alcohol till quite white, then with water, dried (the yield of the almost pure compound being 32 g.), and hydrolysed by heating on the water-bath for 1 hour with alcohol (100 c.c.) and a solution of sodium hydroxide (16 g.) in water (64 c.c.). The solution was diluted with water (200 c.c.) and acidified with hydrochloric acid, and the white solid collected, washed, dried (yield, 22 g.) and crystallised from xylene (100 c.c.). After several crystallisations 6 : 6′-dihydroxy-3 : 3 : 5 : 3′ : 3′ : 5′-hexamethylbis-1 : 1′-*spiro*hydrindene (II) formed almost 1 cm. long, pointed, four-sided bi-pyramids, m. p. 245—246° (Found : C, 82·0; H, 8·2; *M*, 323. Calc. for $C_{23}H_{28}O_2$:

C, 82·2; H, 8·3%; *M*, 336). The sodium salt is very sparingly soluble in dilute aqueous sodium hydroxide even on heating. Its alcoholic solution develops no characteristic colour with ferric chloride, and it dissolves in concentrated sulphuric acid with an orange colour. It separates from pyridine in long, thin, prismatic needles containing pyridine of crystallisation which is readily lost in contact with organic solvents or on warming, the crystals becoming opaque. Niederl describes the substance as hexagonal plates from alcohol, m. p. 245°.

(b) *From di-*(4-*hydroxy*-3-*methylphenyl*)*dimethylmethane* (I). A solution of (I) (21 g.) in acetic acid (50 c.c.) and concentrated hydrochloric acid (37·5 c.c.) was heated on the water-bath for 48 hours. After standing overnight, the white, crystalline product was collected, washed with 50% acetic acid, then water, and dried (yield, 1·3 g.). It had m. p. 244—245° and was identical with the 6 : 6′-dihydroxy-3 : 3 : 5 : 3′ : 3′ : 5′-hexamethylbis-1 : 1′-*spiro*hydrindene (II) prepared by method (a). The acid liquor from which the product had separated was steam-distilled (*o*-cresol, 9·6 g., being isolated from the distillate by ether extraction), and the non-volatile, red resin was acetylated [see (a)] and yielded 2·75 g. of the diacetate of (II).

Diacetate of (II).—The pure condensation product (II) obtained as above was reacetylated with acetic anhydride and then crystallised three times from acetic acid. As this product contained a little free acetic acid which was lost only with difficulty on heating, it was sublimed over anhydrous potassium carbonate at 20 mm. pressure and obtained in thick, highly refracting, glistening plates, m. p. 266—267° (Found: C, 77·0; H, 7·6; Ac, 20·0. Calc. for $C_{27}H_{32}O_4$: C, 77·2; H, 7·6; Ac, 20·0%). Sükösd records m. p. 263—264° for this compound.

Dibenzoate of (II).—Compound (II) (2 g.), pyridine (8 c.c.), and benzoyl chloride (1·7 g.; 2 mols.) were heated on the water-bath for 20 minutes; the product obtained on the addition of dilute hydrochloric acid crystallised when rubbed with a little alcohol. The *dibenzoyl* derivative was crystallised twice from alcohol and found to be dimorphous; it separated in glistening, highly refracting, transparent rhombs (α-form) and a few larger opaque prisms (β-form). The α-form has m. p. 170—171°, but at or above this temperature it rapidly solidifies as the β-form, which subsequently melts at 201° (Found: C, 81·6; H, 6·7. $C_{37}H_{36}O_4$ requires C, 81·6; H, 6·7%). Niederl and Casty mention a dibenzoate of the *o*-cresol–acetone condensation product, m. p. 130°, but it was not analysed, and it is very doubtful if the compound was really the dibenzoate.

Di-p-*nitrobenzoate of* (II).—This substance was prepared from (II) (2 g.), pyridine (8 c.c.), and *p*-nitrobenzoyl chloride (2·22 g.; 2 mols.) as in the preceding case. After crystallising twice from a large volume of acetic acid it was obtained in very faintly yellow bunches of flattened prisms, m. p. 247—248° (Found in material heated at 200° for ¼ hour over potassium carbonate: C, 70·4; H, 5·5; N, 4·5. $C_{37}H_{34}O_8N_2$ requires C, 70·1; H, 5·4; N, 4·4%).

Dimethyl Ether of (II).—Compound (II) (5 g.), water (75 c.c.), and potassium hydroxide (7·5 g.) were treated with sufficient acetone to cause solution, and then shaken with the gradual addition of methyl sulphate (10 c.c.) and a further quantity of potassium hydroxide (7·5 g.), the mixture being finally heated on the water-bath for ½ hour. The solid product was collected after the addition of water, washed, and crystallised several times from alcohol (yield, 4 g.). It formed highly refracting, almost square, thick tablets resembling crystalline sucrose, m. p. 158—159° (Found: C, 81·9; H, 8·9. $C_{25}H_{32}O_2$ requires C, 82·4; H, 8·8%). This *compound* is dimorphous; during the first crystallisations it separated not only in the form described above, but also in prismatic needles with obliquely truncated, sharp ends, which when recrystallised gave the tablet form. Niederl and Casty give the m. p. of the dimethyl ether as 154°, but no further description of the substance, its preparation or analysis.

7 : 7′-*Dibromo*-6 : 6′-*dihydroxy*-3 : 3 : 5 : 3′ : 3′ : 5′-*hexamethylbis*-1 : 1′-spiro*hydrindene*.—This substance was prepared from (II) according to the directions of Niederl and Casty. It was crystallised twice from alcohol and obtained in thick, colourless, hexagonal plates, m. p. 224° (Found: C, 56·2; H, 4·9; Br, 33·2. Calc. for $C_{23}H_{26}O_2Br_2$: C, 55·8; H, 5·3; Br, 32·3%) (Niederl and Casty record m. p. 220° and found Br, 32·0 and 31·1%).

Oxidation of (II) *and Isolation of Phoronic Anhydride*.—The pure substance (II) (5 g.) was dissolved in warm acetic acid (300 c.c.), and saturated aqueous potassium permanganate solution added with shaking until present in excess after standing 12 hours. After excess of sulphur dioxide had been passed, the solution was extracted with ether, and the product left on removal of the solvent was boiled with water, the filtrate yielding to ether a product which crystallised from light petroleum (b. p. 80—100°) in colourless prismatic needles (few mg.), m. p. 117—121°, which had m. p. 120—122° when mixed with an authentic specimen of phoronic anhydride, m. p. 128—129°.

Action of Nitric Acid on (II).—A mixture of compound (II) (1 g.), acetic acid (7·5 c.c.), and nitric acid (*d* 1·42 ; 2·5 c.c.) was heated on the water-bath for 1 hour and diluted with water, the yellow precipitate (1·1 g.) collected, washed, and dissolved in boiling methyl alcohol, and the solution concentrated to one-half its bulk. The yellow, almost rectangular plates which separated (0·5 g.) were recrystallised several times from methyl alcohol and then had m. p. 233—234° (vigorous decomp.) (Found : C, 54·6, 54·8 ; H, 6·3, 6·2 ; N, 5·7 ; in material heated at 150° for ¼ hour : C, 57·9 ; H, 5·6 ; N, 5·8%). The originally clear crystals of the substance became somewhat opaque when removed from the solvent. It dissolved in warm sodium bicarbonate solution with an orange-yellow colour.

The methyl-alcoholic mother-liquors from the crystallisation of the preceding compound were diluted with water, and the precipitated substance was crystallised several times from dilute ethyl alcohol. It separated in yellow prismatic needles, m. p. about 225° (decomp. ; rapid heating) (Found : C, 56·7 ; H, 5·7 ; N, 5·6%). It dissolved in warm sodium bicarbonate solution with a pale yellow colour, and was much more easily soluble in ethyl alcohol than the previously described nitro-compound.

The authors' thanks are due to the Dyestuffs Group of Imperial Chemical Industries, Ltd., for grants.

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