

STRUCTURE OF CALAMONIC ACID

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Calamonic acid has been shown to be 2, 4, 5-trimethoxybenzoic acid.

Khuda, Mukherjee and Ghosh¹ described the reactions of an essential oil, calamol, isolated from the rhizomes of *Acorus calamus* Linn. On oxidation of calamol, they obtained an acid, m. p. 143°, which they called calamonic acid. At that time, it was not clear which one of the six possible isomers of trimethoxy benzoic acid was identical with calamonic acid, though it was conceived that it would probably be identical with any of the three isomeric acids, i.e. 2,3,5-, 2,3,6- or 2,4,5-trimethoxybenzoic acids.

It was felt by the author that calamonic acid could very probably be 2,4,5-trimethoxybenzoic acid which is known to have been obtained by the degradation of some naturally occurring substances.^{2,3} So, for comparison, 2,4,5-trimethoxybenzoic acid was prepared. The method adopted for this is described below:

o-Toluidine was oxidised to toluquinone with potassium dichromate and sulphuric acid. Thiele acetylation of toluquinone gave 2,4,5-triacetoxytoluene which, after deacetylation, was oxidised with ferric chloride to 4-hydroxy-2,5-toluquinone. The latter, on methylation with methanol and sulphuric acid, and subsequent reduction with SO₂, was converted into 2,5-dihydroxy-4-methoxytoluene. This, on further methylation with dimethyl sulphate and alkali, yielded 2,4,5-trimethoxytoluene which, on oxidation with alkaline potassium permanganate, gave 2,4,5-trimethoxybenzoic acid, C₁₀H₁₂O₅, m.p. 141°. The reaction sequence is shown below:

Calamonic acid that the author obtained by oxidation of calamol, had m. p. 141°; a mixed melting point of this acid with the synthetic 2,4,5-trimethoxybenzoic acid showed no depression.

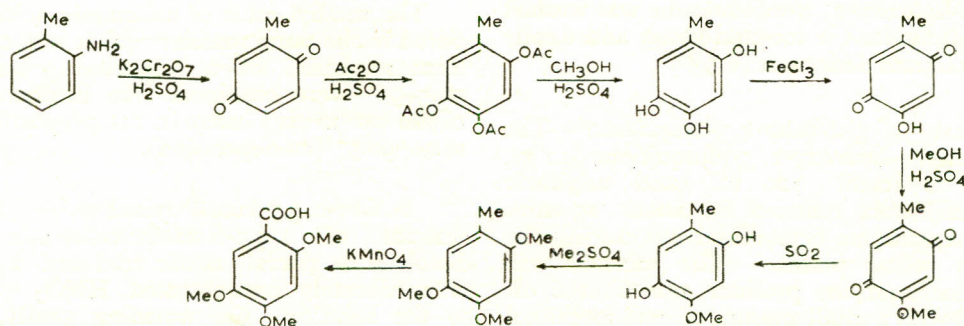
The methyl esters of calamonic acid and 2,4,5-trimethoxybenzoic acid were prepared and they were found to melt at 90.5–91° and 90° respectively. A mixture melting point of the two esters did not show any depression. Similarly, the nitro-compounds obtained on nitration of calamonic acid and 2,4,5-trimethoxybenzoic acid, were found to have m. ps 127–127.5° and 127° respectively and their mixture melting points also showed no depression. Moreover, the infra-red spectra of calamonic acid and 2,4,5-trimethoxybenzoic acid were found to be identical.

All these proved that calamonic acid is 2,4,5-trimethoxybenzoic acid and, hence, calamol (*loc. cit.*) should be 2,4,5-trimethoxyallylbenzene.

Experimental

Analyses were done by Dr. Alfred Bernhardt, 433 Mulheim, Ruhr, West Germany. M. ps are uncorrected.

Calamonic Acid.—Calamol was oxidised with 10% alkaline potassium permanganate solution and the resulting acid recrystallised 2–3 times from benzene–light petroleum when white,



glistening needles of calamonic acid, m. p. 141°, were obtained.

*Preparation of Toluquinone.*⁴—*o*-Toluidine (30 g) was carefully added to a well-cooled mixture of conc. H₂SO₄ (240 g) and water (900 ml). While stirring the mixture vigorously, finely powdered potassium dichromate (78 g) was added in portions of about 1 g. The stirring was continued for about 1/2 hr after all the dichromate had been added, and the mixture left overnight. The black solid that separated was filtered off by suction and steam-distilled in small portions at a time. Golden-yellow leaflets of toluquinone were collected in the receiver. They were filtered off by suction and dried. The crystals melted at 69°.

*Preparation of 2,4,5-triacetoxytoluene.*⁵—Toluquinone (25 g) was dissolved in freshly distilled acetic anhydride (40 ml) and the solution slowly added to an ice-cooled solution of conc. H₂SO₄ (ca. 3 ml) in acetic anhydride (40 ml) and the mixture allowed to stand overnight at room temperature. Next day, it was poured into excess of cold water and the oil that separated was stirred with a glass rod until it solidified. The solid was filtered off, dissolved in hot ethanol, charcoaled, filtered and allowed to cool. The crystals that separated were filtered and dried (yield 20 g; m. p. 110–12°).

*Preparation of 4-hydroxy-2,5-toluquinone.*⁵—The triacetoxytoluene (20 g), conc. H₂SO₄ (ca. 8 ml) and methanol (25 ml) were refluxed for 1 hr. Most of the solvent was carefully removed by distilling in an atmosphere of nitrogen under reduced pressure. The residual 2,4,5-trihydroxytoluene was dissolved in water (ca. 60 ml) and added to a rapidly stirred solution of FeCl₃·6H₂O (50 g) in water (ca. 20 ml) at room temperature. The reaction mixture was cooled in ice for a short time and the separated solid filtered off. The solid was suspended in a saturated salt solution and again filtered. The resulting 4-hydroxy-2,5-toluquinone was washed with a small amount of ice-cold water and finally dried in a vacuum desiccator (6.5 g).

*Preparation of 4-methoxy-2,5-toluquinone.*⁶—The carefully dried 4-hydroxy-2,5-toluquinone (12 g), anhydrous methanol (120 ml) and sulphuric acid (2.5 ml) were refluxed for about 15 min. The methoxyquinone crystallised out during the reaction as yellow plates. The mixture was cooled in ice, and the product was filtered off and washed with a small amount of cold methanol (yield ca. 8 g; m. p. 170°).

Preparation of 2,4,5-trimethoxytoluene.—4-Methoxy-2,5-toluquinone (8 g) was suspended in hot water (ca. 100 ml) and SO₂ gas was passed through it when all the solid gradually went into solution. The solution, on cooling, yielded colourless needles of 4-methoxy-2,5-dihydroxytoluene, m. p. 124°, which was dissolved in methanol (ca. 25 ml). To this solution pure dimethyl sulphate (25 g) was added, and the mixture cooled in ice and ca. 40 ml of 10N aqueous KOH added to this when a vigorous reaction set in. The product was extracted with ether and the ethereal solution was washed, dried (Na₂SO₄) and freed from solvent. The residue was a syrupy mass which crystallised from dilute methanol (m. p. 54°).

Oxidation of 2,4,5-trimethoxytoluene to 2,4,5-trimethoxybenzoic acid.—About 1 g of 2,4,5-trimethoxytoluene was suspended in water and boiled. To this, a 5% alkaline permanganate solution was gradually added until the pink colour persisted even after boiling. The excess of permanganate was destroyed by adding a little ethanol. The precipitated MnO₂ was removed by filtration and the clear filtrate was concentrated and acidified when crystalline needles of 2,4,5-trimethoxybenzoic acid separated. The acid was collected, dried and recrystallised from benzene-light petroleum in the form of white, glistening needles, m. p. 141° (Found: C, 57.34; H, 5.77; O, 37.08; OCH₃, 44.57%. Calc. for C₁₀H₁₂O₅: C, 56.60; H, 5.70; O, 37.70; 3 × OCH₃, 43.86%). An intimate mixture of this acid with calamonic acid in 1:1 proportion melted at 141° (no depression).

Methyl ester of 2,4,5-trimethoxybenzoic acid.—A solution of 2,4,5-trimethoxybenzoic acid in methanol was treated with ethereal diazomethane and the mixture left overnight. The solvent was then completely removed and the residue crystallised from methanol in the form of colourless prisms, m. p. 90° (Found: C, 58.17; H, 5.85%. Calc. for C₁₁H₁₄O₅: C, 58.40; H, 6.24%).

The methyl ester of calamonic acid was prepared in the same manner and it was crystallised from methanol when colourless prisms, m. p. 90.5–91° were obtained. An intimate mixture of the two methyl esters in 1:1 proportion melted at 90–90.5° (no depression).

*1-Nitro-2,4,5-trimethoxybenzene.*²—A small amount of 2,4,5-trimethoxybenzoic acid was dissolved in glacial acetic acid and a few drops of moderately concentrated HNO₃ were added to the solution. On warming gently, effervescence set in due to the evolution of CO₂ and

then, on cooling, pale yellow needles separated out (m. p. 127°).

Calamonic acid was similarly nitrated and a solid was obtained from it in the form of pale yellow needles (m. p. 127-127.5°).

An intimate mixture of the nitro-compounds, obtained from 2,4,5-trimethoxybenzoic acid and calamonic acid, melted at 127-127.5° (no depression).

References

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