

Physical Sciences Section

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CHLORINATION OF *o*-HYDROXYPROPIOPHENONES

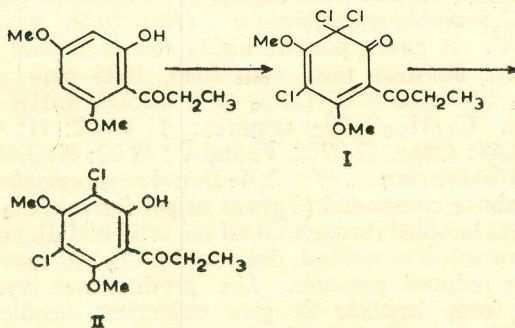
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Abstract. Chlorination of *o*-hydroxypropiophenones gave the expected nuclear chlorinated compounds along with trichlorocyclohexa-3,5-dien-1-ones. This led us to investigate the structural and chemical behaviour of the unusual reaction products. The structures of these compounds have been established from their elemental analyses and spectral data.

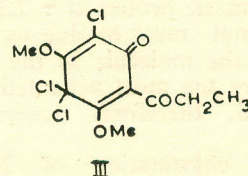
It has been reported that 2-hydroxy-4,6-dimethoxyacetophenone on bromination in CCl_4 gave only 2-hydroxy-4,6-dimethoxy-3-bromoacetophenone.¹ We required 2-hydroxy-4,6-dimethoxy-3-chloropropiophenone as an intermediate towards the synthesis of potentially antibacterial agents. We, therefore, chlorinated 2-hydroxy-4,6-dimethoxypropiophenone in CCl_4 at room temperature and obtained exclusively 6-propionyl-3,5-dimethoxy-2,2,4-trichlorocyclohexa-3,5-dien-1-one (I).



The system of this unusual reaction product I suggests a parallel with 4,6-dimethoxy-2,4-ditertiarybutylcyclohexa-2,4-dien-1-one which has been patented for its herbicidal and parasiticidal properties.² This prompted us to investigate the structure, chemical behaviour and antibacterial properties of I and to compare it with model compounds.

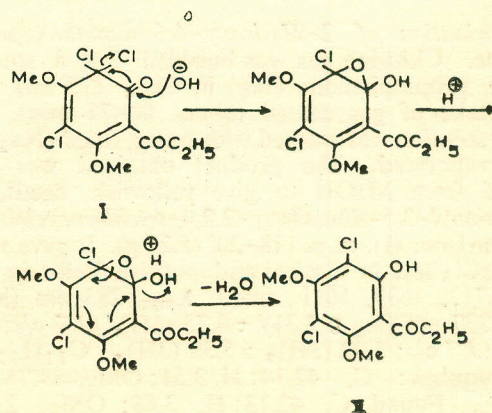
The proposed structure I follows from its elemental analysis and spectral data. The analysis of the compound indicated the presence of three chlorine atoms in the molecule. A triplet centered at τ 8.75 (J 7 c/s) and a quartet centered at τ 7.07 (J 7 c/s) ruled out the possibility of chlorination in the side chain. There were no signals in the aromatic region. The compound gave negative FeCl_3 test in alcohol and it was insoluble in alkali. This clearly indicated that the compound has lost its aromaticity. The IR of I in nujol mull showed peaks at 1712, 1639

and 1611 cm^{-1} . The shift of the carbonyl peak to higher frequency at 1712 cm^{-1} of the cyclohexadienone system is due to the two halogen atoms at the carbon atom adjacent to the carbonyl group.³ The peak at 1639 cm^{-1} is designated to the carbonyl group of the side chain. The evidence presented so far could also accommodate the alternative structure III.



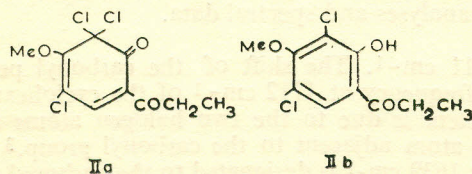
The UV spectrum of the compound in methanol showed λ_{max} at 283 and 337 nm which showed the presence of an ortho dienonoid configuration for which structure I alone is possible.^{4,5}

The treatment of I in aqueous NaOH at water bath temperature gave a compound, m.p. 85° . It gave positive FeCl_3 test in alcohol. IR of the compound showed peaks at $1625\text{--}1630\text{ cm}^{-1}$ (broad peak *o*-hydroxyketone), 1595 cm^{-1} (benzene), and 3540 cm^{-1} (OH). The compound was readily soluble in cold alkali. Elemental analysis and NMR spectrum of the compound were found in accordance with the proposed structure II. A possible conversion of dienone I into phenol II is shown below.



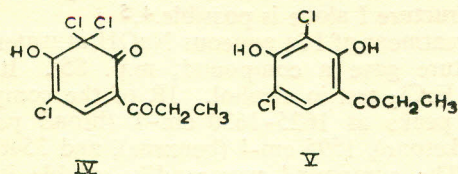
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A similar reaction on 2-hydroxy-4-methoxypropionophenone gave two compounds, IIa and IIb, m.p. 180° and 80° respectively. IIa was insoluble in alkali and gave negative FeCl₃ test in alcohol. Its NMR indicated the presence of an olefinic proton at τ 5.75. A triplet centered at τ 8.70 and a quartet centered at τ 6.71 clearly showed no substitution in the side chain. UV of the compound showed λ_{\max} at 284 and 340 nm. Analysis indicated the presence of three chlorine atoms in the molecule. UV showed the presence of *o*-dienonoid configuration. The only *o*-dienonoid structure which is consistent with the spectral data is IIA.



IIb was an alkali-soluble phenol and the presence of an aromatic proton at τ 2.20 clearly suggested that the signal must be due to aromatic proton at position 5 in the molecule as the other two positions 3 and 5 are the most activated for electrophilic substitution and, therefore, occupied by chlorine atoms.

Similarly the chlorination of 2,4-dihydroxypropionophenone gave the corresponding 6-propionyl-3-hydroxy-2,2,4-trichlorocyclohexa-3,5-dien-1-one (IV) and 2,4-dihydroxy-3,5-dichloropropionophenone (V).



A study of antibacterial properties of the compounds is in progress and will be published later.

Experimental

Chlorination of 2-Hydroxy-4,6-dimethoxypropionophenone. Chlorine gas was bubbled into a solution of the propionophenone (10g) in CCl₄ (75 ml) until the uptake of gas ceased (about 60-75 min). The yellow solution was washed with water, dried (Na₂SO₄) and evaporated. The product obtained was crystallized from MeOH to give yellowish needles of 6-propionyl-3,5-dimethoxy-2,2,4-trichlorocyclohexa-3,5-dien-1-one (I), m.p. 118-20° (5.27 g). It gave negative FeCl₃ test in alcohol and positive Beilstein test. ν_{\max} 1712, 1639, 1611 cm⁻¹ λ_{\max} 283 nm (log ϵ 4.13), 337 nm (log ϵ 3.31). τ 8.75 (3H)_t (*J* 7 c/s; 7.0⁷ (2H)_q (*J* 7 c/s; 5.92 (3H)_s; 5.58 (3H)_s. C₁₁H₁₂O₄-Cl₃ requires: C, 42.14; H, 3.51; OMe, 19.78; Cl, 33.90%. Found: C, 42.13; H, 3.88; OMe, 21.99; Cl, 32.18%.

The cyclohexadienone I (1 g) was suspended in 5% aqueous NaOH (50 ml) and heated on water bath for about 2 hr. The solution was allowed to cool and 5% ice-cold HCl added and the white precipitate obtained was collected, washed and crystallized with MeOH to give colourless needles (0.48 g, m.p. 85°) of 2-hydroxy-4,6-dimethoxy-3,5-dichloropropionophenone II. It gave positive FeCl₃ test in alcohol and also gave positive Beilstein test. ν_{\max} 1625-1630 (broad peak) 1595, 3540 cm⁻¹. τ 8.75 (3H)_t (*J* 7 c/s); 6.69 (2H)_q (*J* 7c/s; 5.82 (3H)_s 5.87 (3H)_s. (C₁₁H₁₂O₄Cl₂ requires: C 47.35; H, 4.34; OMe, 22.26; Cl, 25.48%. Found: C, 3, 47.88; H, 3.92; OMe, 23.28; Cl, 24.63%.)

Chlorination of 2-Hydroxy-4-methoxypropionophenone. As in the previous reaction similar treatment of this propionophenone (1g) with Cl₂ in CCl₄ gave a reaction product which crystallized from CCl₄ to give pale needles of 6-propionyl-3-methoxy-2,2,4-trichlorocyclohexa-3,5-dien-1-one (II a) m.p. 181-86° (0.3 g). It gave negative FeCl₃ test in alcohol and positive Beilstein test ν_{\max} 1713, 1660 cm⁻¹ λ_{\max} 284 nm (log ϵ 3.86), 340 nm (log ϵ) 3.0). τ 8.76 (3H)_t (*J* 7 c/s; 6.62 (5H)_q (*J* 7 c/s; 5.90 (3H)_s; 5.75 (1H)_s. (C₁₀H₉O₃Cl₃ requires: C, 42.35; H, 31.7; Cl, 37.53; OMe, 10.93%. Found C, 42.01; H, 3.25; Cl, 38.21; OMe, 10.87%.)

The mother liquor of the above reaction gave colourless needles from MeOH of 2-hydroxy-4-methoxy-3,5-dichloropropionophenone (IIb) (0.28 g), m.p. 82-84°. It gave positive FeCl₃ test in alcohol and positive Beilstein test. ν_{\max} 1640, 1605 cm⁻¹ 8.66 (3H)_t (*J* 7 c/s; 6.92 (2H)_q (*J* 7 c/s; 5.93 (3H)_s 2.20 (1H)_s. C₁₀H₉O₃Cl₂ requires: C 48.22; H; 4.01; Cl 28.47; OMe, 12.97%. Found C: 48.02; H: 3.85%.

Chlorination of 2,4-Dihydroxypropionophenone The above compound (2 g) was suspended in CCl₄ and Cl₂ gas bubbled through till all the solid had dissolved. Yellow solution washed, dried and CCl₄ was removed under reduced pressure. The product was crystallized from benzene to give colourless needles of 2,4-dihydroxy-3,5-dichloropropionophenone (V), m.p. 142-45° (0.32 g). It gave positive FeCl₃ test in alcohol and positive Beilstein test. ν_{\max} 1615-1630 (broad peak), 3540 cm⁻¹. (C₉H₈O₃Cl₂ requires: C, 45.97; H, 3.40; Cl, 30.18%. Found: C, 45.50; H, 3.27; Cl, 29.59%.)

From the mother liquor of the above reactions were obtained light brown rhomboids, m.p. 201-15° of 6-propionyl-3-hydroxy-2,2,4-trichlorocyclohexa-3,5-dien-1-one (IV) (0.110 g). It gave negative FeCl₃ test in alcohol and positive Beilstein test. λ_{\max} 1625, 1735, 3460 cm⁻¹. (C₉H₇O₃Cl₃ requires C, 40.11; H 2.60; Cl, 39.48%. Found: C, 39.87; H, 2.51; Cl, 38.02%.)

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