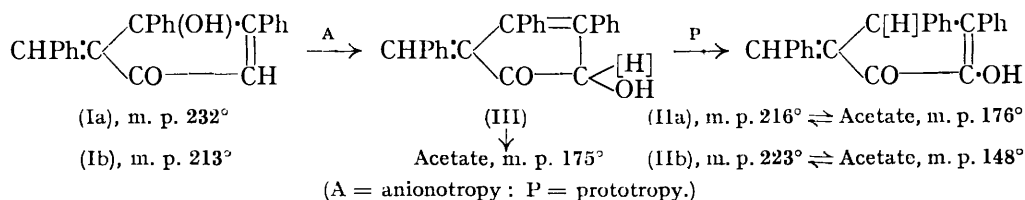


52. Anionotropic and Prototropic Changes in Cyclic Systems. Part II. The Hydroxy-3 : 4-diphenyl-5-benzylidenecyclopentenones.

By HAROLD BURTON and CHARLES W. SHOPPEE.

WE have shown recently (J., 1933, 720) that the conversion of 4-hydroxy-3 : 4-diphenyl-5 : 5-dimethyl- Δ^2 -cyclopentenone ($\beta\beta$ -dimethylanhydroacetonebenzil) into the 2-hydroxy-isomeride involves successive anionotropic and prototropic changes. Gray, who originally described the foregoing transformation (J., 1909, 95, 2138), also dealt with the series of compounds derived from the stereoisomeric 5-benzylideneanhydroacetonebenzils (Ia, Ib). Condensation of anhydroacetonebenzil with benzaldehyde affords the stereoisomerides (Ia, Ib), either of which gives by acetylation with acetic anhydride and a trace of sulphuric acid the same acetate, m. p. 175°, formulated by Gray as the acetate of (Ia or Ib). Hydrolysis of this acetate with alcoholic potassium hydroxide yields a 2-hydroxy-ketone (IIa), possessing the properties typical of a keto-enol; the substance (IIa) furnishes its own acetate, m. p. 176°, and is converted by alcoholic hydrogen chloride into the stereoisomeric 2-hydroxy-ketone (IIb), which also forms a characteristic acetate, m. p. 148°.

Analogy suggests that the conversion (Ia, Ib) \longrightarrow (IIa) takes place by consecutive anionotropic and prototropic changes, and that the acetate, m. p. 175°, is actually that derived from one of the two unknown stereoisomeric Δ^3 -unsaturated intermediates (III). We have endeavoured to obtain an acetate corresponding to (Ia), but under all conditions leading to acetylation, (III) is the sole isolable product.

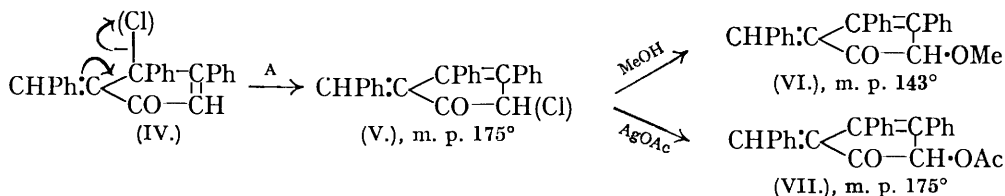


Such a scheme, (Ia, Ib) \longrightarrow (III) \longrightarrow (IIa), necessitates the existence of three pairs of stereoisomeric alcohols and we have prepared five of the six possible methyl ethers. The missing ether is one of the pair derived from the two stereoisomerides (III).

Methylation of (Ia) with activated silver oxide and methyl iodide furnishes 4-methoxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone, m. p. 158°, whilst under the same conditions (Ib) gives the stereoisomeric 4-methoxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone, m. p. 122°. Treatment of the 2-hydroxy-ketone (IIa) with sodium methoxide and methyl iodide yields 2-methoxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone, m. p. 110°, and (IIb) similarly affords the stereoisomeric 2-methoxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone, m. p. 124°.

When (Ia) is treated with thionyl chloride at 78°, a chloride is obtained, the chlorine atom of which is potentially ionic and reacts with methyl alcohol in the presence of silver acetate to give a single methyl ether, m. p. 143°, which differs from the four methyl ethers described above. We consider, therefore, that the chloro-compound is 2-chloro-3 : 4-diphenyl-5-benzylidene- Δ^3 -cyclopentenone (V), formed from the precursor (IV) by anionotropic change, and that the methyl ether is 2-methoxy-3 : 4-diphenyl-5-benzylidene- Δ^3 -cyclopentenone (VI). This view is confirmed by treatment of the chloride (V) with glacial

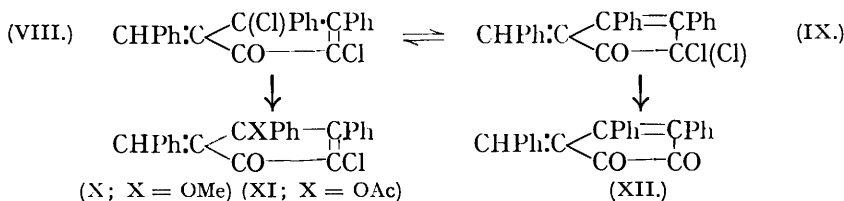
acetic acid and silver acetate, whereby Gray's acetate, m. p. 175°, which must be formulated as (VII), is obtained.



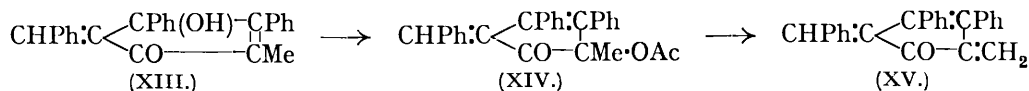
The chloride (V) should be obtained by chlorination of 3 : 4-diphenyl-5-benzylidene- Δ^3 -cyclopentenone, but we have been unable to prepare this ketone; under all the conditions tried, the 2 : 5-dibenzylidene derivative was formed.

We were unable to prepare (Ib) in sufficient amount to examine whether it is converted by thionyl chloride into the same chloride (m. p. 175°) or a geometrical isomeride. Since Gray (*loc. cit.*) showed that both (Ia) and (Ib) gave the same acetate (III), it appears likely that reactions involving anionotropy will lead to a single product, the less stable spatial configuration disappearing in the tautomeric change.

The action of thionyl chloride on (Ia) gives in addition to (V), a dichloride, $\text{C}_{24}\text{H}_{16}\text{OCl}_2$. This substance appears to contain one potentially ionic chlorine atom, since treatment with absolute methyl alcohol and silver acetate gives a single chloromethoxy-compound; with boiling glacial acetic acid and silver acetate, however, two products are obtained: a yellow chloro-acetate (75%) and a red chlorine-free diketone (25%). In the formation of the latter, both chlorine atoms have become labile, and we suggest that the dichloride must be represented by two interconvertible structures which may be (VIII) and (IX). From (VIII), in which the 4-chlorine atom only would be reactive, are derived the chloromethoxy-compound (X) and the chloro-acetate (XI), whilst from (IX), which is an $\alpha\alpha$ -dichloro-ketone and might therefore be expected to possess two labile chlorine atoms, is derived the highly coloured 3 : 4-diphenyl-5-benzylidene- Δ^3 -cyclopentenedione (XII), possibly *via* the intermediate 2 : 2-diacetate.



We have also examined 4-hydroxy-3 : 4-diphenyl-5-benzylidene-2-methyl- Δ^2 -cyclopentenone (XIII), which, according to our view, should be capable of anionotropy but not of prototropy. Gray (*loc. cit.*), by treatment of (XIII) with acetic anhydride and a trace of sulphuric acid at 15°, obtained a red compound which he considered to be 3 : 4-diphenyl-5-benzylidene-2-methylene- Δ^3 -cyclopentenone (XV). This substance possesses an extra-cyclic methylene group, since it gives formaldehyde by ozonolysis, and results by loss of acetic acid from the intermediate tertiary acetate (XIV), which is formed from (XIII) by anionotropic change of the corresponding acetate.



EXPERIMENTAL.

4-Hydroxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenones (Ia, Ib).—Anhydroacetonebenzil was condensed with benzaldehyde in the presence of sodium hydroxide (Gray, *loc. cit.*); only a trace of the isomeride, m. p. 213.5°, was obtained, the isomeride, m. p. 232°, constituting the bulk of the condensation product. Use of piperidine as condensing agent was ineffective.

4-Methoxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenones.—(a) Benzylideneanhydroacetonebenzil, m. p. 232° (3.4 g.), silver oxide (10 g.), powdered sodium hydroxide (0.1 g.), and methyl iodide were refluxed for 10.5 days. After evaporation of the excess of methyl iodide, the product was extracted with hot acetone (5 × 20 c.c.), and the combined extracts evaporated. The residual oil crystallised when rubbed with methyl alcohol, and was repeatedly crystallised from this solvent, from which **4-methoxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone** separated in pale yellow prisms (2.5 g.), m. p. 158° (Found : C, 85.25; H, 5.8; OMe, 8.8. C₂₅H₂₀O₂ requires C, 85.2; H, 5.75; OMe, 8.8%).

4-Ethoxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone, similarly prepared, formed pale yellow prisms (1.5 g.), m. p. 159°, from alcohol (Found : C, 84.7; H, 6.1; OEt, 11.9. C₂₆H₂₂O₂ requires C, 85.2; H, 6.05; OEt, 12.3%).

(b) Similar treatment of benzylideneanhydroacetonebenzil, m. p. 213.5° (0.7 g.), yielded **4-methoxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone** (0.4 g.), m. p. 122°, after crystallisation from ethyl acetate–ligroin (b. p. 60–80°) (Found : OMe, 8.8%).

2-Acetoxy-3 : 4-diphenyl-5-benzylidene- Δ^3 -cyclopentenone.—This was prepared according to Gray (*loc. cit.*) and had m. p. 175°; benzylideneanhydroacetonebenzil (Ia) could not be acetylated by any of the usual methods, and was unchanged after prolonged treatment in acetone solution with keten.

2-Hydroxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone (IIa).—Hydrolysis of the above acetate with 5% alcoholic potassium hydroxide (compare Gray, *loc. cit.*) or with hydrochloric acid in acetone yielded the 2-hydroxy-ketone, m. p. 216°; it gave a brown-violet colour with ferric chloride and on acetylation furnished the acetate, m. p. 176°, described by Gray [Found : C, 82.1; H, 5.35; M (Rast), 394, 405. Calc. for C₂₆H₂₀O₃ : C, 82.1; H, 5.35%; M, 380], which depressed the m. p. of (VII).

2-Methoxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone.—The hydroxy-ketone (IIa) (1.1 g.) was converted into the scarlet sodio-derivative by treatment with 3 c.c. of sodium methoxide solution (0.25 g. of sodium in 9 c.c. of methyl alcohol), and refluxed with excess of methyl iodide for 4 hours. After removal of methyl iodide, water was added, and the product extracted with ether. The ethereal extract was washed twice with 5% sodium hydroxide solution, dried (calcium chloride), and evaporated. The residual oil solidified when rubbed with methyl alcohol; **2-methoxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone** crystallised from methyl alcohol or ethyl acetate–ligroin (b. p. 60–80°) in yellow needles, m. p. 112° (Found : C, 85.0; H, 5.7; OMe, 8.8. C₂₅H₂₀O₂ requires C, 85.2; H, 5.75; OMe, 8.8%).

2-Hydroxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone (IIb).—Gray (*loc. cit.*) states that concentrated alcoholic hydrogen chloride converts the 2-hydroxy-ketone (IIa), m. p. 216°, into the isomeride (IIb), m. p. 223°; in our hands this treatment leads to ethylation. The 2-hydroxy-ketone, m. p. 216°, was suspended in ethyl alcohol saturated with hydrogen chloride at 0°, and mechanically shaken over-night at 15°, and the clear yellow solution kept for 4 days. The solution was poured into a large volume of ice-water with stirring, and the precipitate filtered off. The low-melting product separated from ethyl alcohol as an oil, but crystallised when rubbed with a little ether. Repeated crystallisation from ethyl acetate–ligroin (b. p. 60–80°) gave **2-ethoxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone** as yellow needles, m. p. 122–123° (Found : C, 85.35; H, 6.05; OEt, 12.3. C₂₆H₂₂O₂ requires C, 85.2; H, 6.05; OEt, 12.3%). Similar treatment of the 2-hydroxy-ketone, m. p. 216°, but using methyl-alcoholic hydrogen chloride, did not lead to methylation, but gave the isomeric 2-hydroxy-ketone, m. p. 223°.

2-Methoxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone.—The procedure and quantities given for the methylation of (IIa) were used for the 2-hydroxy-ketone, m. p. 223° (IIb). **2-Methoxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone** separated from methyl alcohol in pale yellow prisms, m. p. 124° (Found : C, 85.3; H, 5.8; OMe, 9.5. C₂₅H₂₀O₂ requires C, 85.2; H, 5.75; OMe, 8.8%). It depressed the m. p. 122° of the methoxy-derivative of (Ib).

Action of Thionyl Chloride on Benzylideneanhydroacetonebenzil (Ia).—Benzylideneanhydroacetonebenzil, m. p. 232°, (Ia) (10 g.) was refluxed with thionyl chloride (30 c.c.) on the steam-bath; hydrogen chloride was evolved, and after completion of the reaction ($\frac{1}{2}$ hour), the product was poured into ice-water. The yellow solid obtained was dried, and fractionally crystallised from di-*n*-propyl ether. From the head fractions there was ultimately obtained **2-chloro-3 : 4-diphenyl-5-benzylidene- Δ^3 -cyclopentenone** (V), crystallising in bright yellow nodules, m. p. 175° (Found : C, 80.7; H, 4.9; Cl, 10.3. C₂₄H₁₇OCl requires C, 80.7; H, 4.8; Cl, 10.0%). From the tail fractions there was obtained a dichloride, probably **2 : 4-dichloro-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone** [Found : C, 73.4; H, 3.9; Cl, 17.7; M (Rast), 338, 326.

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$C_{24}H_{16}OCl_2$ requires C, 73.6; H, 4.1; Cl, 18.1%; *M*, 391]. The substance is dimorphous, and separates from di-*n*-propyl ether in pale yellow, felted needles, or in well-formed prisms, *m. p.* 173°; the latter represent the stable modification, since the needles become converted into the prismatic form when kept at 15° in the solvent.

Reactions of the Chloride (V).—(i) *With methyl alcohol and silver acetate.* The chloride (0.2 g.) and an equal weight of silver acetate were refluxed with absolute methyl alcohol (2.5 c.c.) for $\frac{1}{4}$ hour, and the filtered solution diluted. The yellow solid product was crystallised from methyl alcohol, giving 2-methoxy-3 : 4-diphenyl-5-benzylidene- Δ^3 -cyclopentenone in yellow prisms, *m. p.* 143° (Found : C, 84.8; H, 5.8; OMe, 8.8. $C_{25}H_{20}O_2$ requires C, 85.2; H, 5.75; OMe, 8.8%). A mixture of this methyl ether with the methyl ether of (Ia), *m. p.* 158°, had *m. p.* 123°.

(ii) *With acetic acid and silver acetate.* The chloride (0.2 g.), an equal weight of silver acetate, and A.R. acetic acid (5 c.c.) were refluxed for $\frac{1}{4}$ hour, and the hot solution filtered into water. The product, a yellow solid (*m. p.* 70—100°), was very soluble in all organic solvents except ligroin; it could not be crystallised satisfactorily, but was obtained solid by allowing a solution in ether-ligroin (*b. p.* 40—60°) to evaporate spontaneously (Found : C, 81.5; H, 5.5. $C_{26}H_{20}O_3$ requires C, 82.1; H, 5.3%). The solid appears to be a mixture of isomeric acetates, for by treatment with warm alcohol it melts and gradually gives a solid, which dissolves on boiling and crystallises in clusters of yellow needles, *m. p.* 168—169°. Recrystallisation from alcohol affords 2-acetoxy-3 : 4-diphenyl-5-benzylidene- Δ^3 -cyclopentenone, *m. p.* 174—175° [alone or mixed with a specimen prepared directly from benzylideneanhydroacetonebenzil (Ia) by acetylation] (Found : C, 81.8; H, 5.45; OEt, 0. Calc. for $C_{26}H_{20}O_3$: C, 82.1; H, 5.3%). This acetate was the sole isolable product.

Reactions of the Dichloride (VIII or IX).—(i) *With methyl alcohol and silver acetate.* The dichloride (0.1 g.), silver acetate (0.1 g.), and absolute methyl alcohol (2.5 c.c.) were refluxed for $\frac{1}{2}$ hour, and the filtered liquid diluted. The solid product was crystallised from methyl alcohol; not quite pure 2-chloro-4-methoxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone separated in pale yellow plates, *m. p.* 155°, which appear to contain methyl alcohol of crystallisation (Found : C, 75.8; H, 5.2; Cl, 10.4; OMe, 10.8. $C_{25}H_{19}O_2Cl, \frac{1}{2}MeOH$ requires C, 76.0; H, 5.2; Cl, 8.8; OMe, 11.5%).

(ii) *With acetic acid and silver acetate.* The dichloride (0.2 g.), silver acetate (0.4 g.), and A.R. acetic acid (5 c.c.) were refluxed for $\frac{1}{2}$ hour, and the hot solution filtered into water. The product was a low-melting yellow solid, which on hydrolysis with 50% sulphuric acid gave acetic acid [Found : C, 77.9; H, 4.55; Cl, 7.0%; *M* (Rast), 355, 347], which by dissolution in 95% alcohol gave two substances, one yellow and the other red, which crystallised side by side. After separation by hand-picking, 2-chloro-4-acetoxy-3 : 4-diphenyl-5-benzylidene- Δ^2 -cyclopentenone separated from alcohol in yellow prisms, *m. p.* 160° [Found : C, 75.1; H, 4.7; Cl, 9.4; *M* (Rast), 391, 375. $C_{26}H_{19}O_3Cl$ requires C, 75.3; H, 4.6; Cl, 8.6%; *M*, 414.5]. 3 : 4-Diphenyl-5-benzylidene- Δ^3 -cyclopentene-1 : 2-dione crystallised from alcohol in bright red rosettes of needles, *m. p.* 198—199° [Found : C, 85.8; H, 4.9; *M* (Rast), 343, 338. $C_{24}H_{16}O_2$ requires C, 85.7; H, 4.8%; *M*, 336]. With 2 : 4-dinitrophenylhydrazine sulphate the diketone gives an *osazone*, *m. p.* 279—280° (decomp.), which could not be recrystallised owing to its sparing solubility in all the common solvents (Found : N, 15.4. $C_{36}H_{24}O_8N_8$ requires N, 16.1%).

3 : 4-Diphenyl- Δ^3 -cyclopentenone.—This was prepared by the improved method of Japp and Lander (J., 1897, 71, 131); it was found advantageous to crystallise the product from benzene, from which the ketone separates with benzene of crystallisation, *m. p.* 92—93°. The crystals effloresce on standing, and after repeated crystallisation from alcohol the ketone has *m. p.* 110°. Condensation with benzaldehyde did not occur in the presence of piperidine, and the use of 1 mol. of benzaldehyde in the presence of sodium ethoxide led to the formation of the 2 : 5-dibenzylidene derivative only; this separated from benzene in orange needles, *m. p.* 202° [Found : C, 90.6; H, 5.6; *M* (Rast), 387, 391. $C_{31}H_{22}O$ requires C, 90.7; H, 5.4%; *M*, 410].

4-Hydroxy-3 : 4-diphenyl-5-benzylidene-2-methyl- Δ^2 -cyclopentenone (XIII).— α -Methylanhydroacetonebenzil, prepared from benzil and methyl ethyl ketone (Japp and Meldrum, J., 1901, 79, 1029; compare Japp and Knox, J., 1905, 87, 679), by condensation with benzaldehyde gave 4-hydroxy-3 : 4-diphenyl-5-benzylidene-2-methyl- Δ^2 -cyclopentenone, *m. p.* 227° (compare Japp and Meldrum, *loc. cit.*).

3 : 4-Diphenyl-5-benzylidene-2-methylene- Δ^3 -cyclopentenone (XV).—Following the procedure of Gray (*loc. cit.*), this compound was obtained as orange-red clusters of needles, *m. p.* 253°, after crystallisation from acetic anhydride (Found : C, 88.8; H, 5.3. Calc. for $C_{25}H_{16}O$: C, 89.8; H, 5.4%). By dissolution in chloroform and treatment with ozonised oxygen, and

decomposition of the ozonide with hot water, formaldehyde was obtained (resorcinol test) together with benzoic acid and unidentified substances.

A second *substance*, $C_{50}H_{36}O_2$, accompanied (XV); it was present only in minute amount and separated from ethyl acetate-ethyl alcohol in yellow needles, m. p. 225° [Found: C, 89.7; H, 5.4; *M* (Rast), 569, 589. $C_{50}H_{36}O_2$ requires C, 89.8; H, 5.4%; *M*, 668]. It appears to be a dimeride of (XV).

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