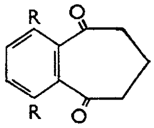
SECTION C
Organic Chemistry

The Reduction of 3′,6′-Dihydroxy-1,2-benzocycloheptene-3,7-dione

By N. M. D. Brown, A. M. Khan, and G. R. Proctor

Hydrogenation of the title compound and its diacetate over various catalysts has been studied and the products identified. Clemmensen reduction gave several substances but none of these corresponded to a novel compound, $C_{11}H_{12}O_4$, reported in the literature from this reaction and formulated as a dihydroxydiketone: this was obtained by zinc dust reduction of the title compound, and its structure was confirmed by n.m.r. spectroscopy and by chemical studies.

In connection with other studies on benzosuberones,[1] we became interested in the readily available [2] 3′,6′-dihydroxy-1,2-benzocycloheptene-3,7-dione (I; R = OH) and the possibility of converting it by reduction and dehydration into the corresponding dihydroxybenzotropylidine (II). Unlike the parent compound (I; R = H),[1] reduction of compound (I; R = OH) with sodium borohydride gave no recognisable products; borohydride reduction of the diacetate (I; R = OAc) unexpectedly gave (after working up in air) a golden yellow material ($C_{11}H_{12}O_2$) which we can only formulate as the quinone (III).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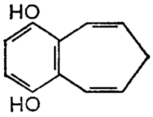
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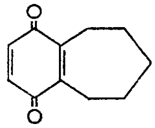
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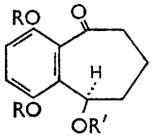
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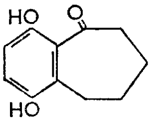
We then studied the catalytic reduction of the diketone (I; R = OH) and found that apparently only one of the carbonyl groups was hydrogenated at atmospheric pressure. When Adams catalyst was used in very low concentrations (~1% by weight), the only new product was a colourless trihydroxymonoketone ($C_{11}H_{12}O_4$) of m. p. 174—175°. The n.m.r. spectrum was obtained in deuteropyridine and, although poorly resolved, showed *inter alia* (see Experimental section) a bonded hydroxyl proton at τ −1·2 and an aliphatic hydroxyl proton at τ 4·1. Under mild conditions this substance formed a triacetate (m. p. 132°), the n.m.r. spectrum of which showed 3 singlets at τ 7·65, 7·80, and 8·10 attributable to acetyl protons. The same triacetate could be obtained by acetylation of the monohydroxy-compound (IV; R = Ac, R′ = H) isolated during hydrogenation of the diacetate (I; R = OAc). It seems beyond doubt, then, that the structure of the trihydroxymonoketone and its triacetate are (IV; R = R′ = H) and (IV; R = R′ = Ac), respectively.

Models show that in the original diketone (I; R = OH) only one carbonyl group can be hydrogen-bonded and coplanar with the benzene ring at one time: it is presumably this carbonyl group that resists hydrogenation. But in the diacetate (I; R = OAc) and the ether (I; R = OMe), which is reported to be only partly reduced by potassium borohydride,[3] there is no hydrogen-bonding and one must conclude that these phenomena are not fully understood.

Hydrogenation of the diketone (I; R = OH) over palladium catalysts or Adams catalyst (3% by weight or greater), led to the production of a dihydroxymonoketone (V), presumably by dehydration and further reduction of the ketone (IV; R = R′ = H). The m. p. of the substance (V) and of its diacetate correspond with those reported in the literature.[4]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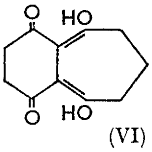
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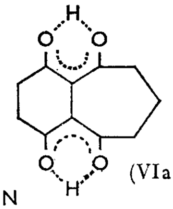
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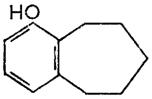
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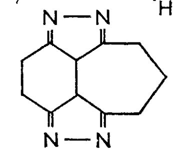
(VIII)

While this work was in progress, Hahn and Madeja-Kotkowska reported [5] without experimental details that Clemmensen reduction of the title compound (I; R = H) gave a substance ($C_{11}H_{12}O_4$, m. p. 179°) which they formulated as a dihydroxydiketone (VI). We felt that this structure was sufficiently unusual to merit further investigation. In our hands, Clemmensen reduction of the diketone (I; R = OH) gave only a monobasic

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[1] A. M. Khan, G. R. Proctor, and L. Rees, *J. Chem. Soc.* (*C*), 1966, 990.

[2] A. J. S. Sorrie and R. H. Thomson, *J. Chem. Soc.*, 1955, 2233.

[3] W. E. Hahn and Z. Madeja-Kotkowska, *Roczniki Chem.*, 1964, **38**, 963.

[4] N. F. Hayes and R. H. Thomson, *J. Chem. Soc.*, 1956, 1585.

[5] W. E. Hahn and Z. Madeja-Kotkowska, *Roczniki Chem.*, 1963, **37**, 915.

phenol ($C_{11}H_{14}O$) presumably (VII) and a hydrocarbon fraction (of approximate composition $C_{11}H_{18}$) which was shown by v.p.c. to consist of three substances. However, reduction of the title compound with zinc dust in acetic acid gave a substance (m. p. 180°) in good yield as claimed by Hahn and Madeja-Kotkowska.[1] We have confirmed their observations on the behaviour of this substance ($C_{11}H_{12}O_4$) and can suggest no alternative structure, except that we prefer to regard it as (VIa). The n.m.r. spectrum contained a broad peak at τ −5·1 due to the two chelated hydrogens of the enolic β-diketone systems: this signal disappeared when the sample was treated with deuterium oxide. The remainder of the spectrum consisted of a sharp line (area 4) at τ 7·4 (which we assign to the saturated protons of the 6-membered ring) and a complex pattern having a tallest peak at τ 7·55 (area 6; hydrogens on the 7-membered ring).

It is attractive to explain the formation of the compound (VIa) by assuming that a zinc chelate is formed, thus making the benzene ring unusually vulnerable to reduction, but although we have made what is presumably a zinc chelate[6] from the hydroxyketone (I; R = OH), we find that it is unstable in acetic acid and is so insoluble (one would expect it to be polymeric) in other solvents that we could not reduce it catalytically. One of the only types of chelated structure that one can visualise occurring as a monomer in this system is that from boron trifluoride;[7] the product from the title material (I; R = OH) was rather unstable and gave unrecognisable products on catalytic reduction, but the chelate from the compound (VIa) was fairly stable, and its formation and analysis helps to confirm the structure of (VIa).

Hahn and Madeja-Kotkowska[5] stated that the hydroxy-ketone (VIa) formed a bis-2,4-dinitrophenylhydrazone but they gave no analytical data. We expected that reactions involving hydrazines should give derivatives of pyrazole and have found that when compound (VIa) and hydrazine react together the product is best represented by structure (VIII). The possibility of using this substance (VIII) as the basis of new aromatic systems is being investigated.

EXPERIMENTAL

3′,6′,7-Trihydroxy-1,2-benzocyclohept-1-en-3-one (IV; R = R′ = H).— 3′,6′-Dihydroxy-1,2-benzocycloheptene-3,7-dione[2] (2 g.) in ethanol (200 ml.) was hydrogenated in presence of platinum oxide (25 mg.) at atmospheric pressure. When no more gas was absorbed (300 ml.), the filtered solution was evaporated *in vacuo* leaving the desired *product*, which was washed with benzene and crystallised from ether giving a colourless material (m. p. 174—175°) (Found: C, 63·4; H, 5·95. $C_{11}H_{12}O_4$ requires C, 63·45; H, 5·8%); $\nu_{max.}$ (Nujol) 3344, 3226 (OH), and 1640 (>C=O) cm.$^{-1}$. The n.m.r. spectrum (in deuteropyridine) showed signals as follows: τ 1·3 (singlet), τ 2·4 (broad singlet), τ 2·6—3·1 (multiplet), τ 3·8 (triplet), τ 6·5—8·2 (multiplet). The integral areas were approximately correct for the proposed structure; the deuteropyridine was apparently not pure.

The *triacetate* (IV; R = R′ = Ac) was obtained in the usual way with acetic anhydride in cold pyridine and crystallised from light petroleum (b. p. 60—80°) and had m. p. 132—133° (Found: C, 61·0; H, 5·9. $C_{17}H_{18}O_7$ requires C, 61·05; H, 5·4%); $\nu_{max.}$ (Nujol) 1761, 1748 (ester), and 1724 (>C=O) cm.$^{-1}$. The n.m.r. spectrum (in $CDCl_3$) showed the following signals: τ 2·7—3·0 (multiplet area 2), τ 3·8 (triplet, area 1), τ 7·65 (singlet area 3), τ 7·80 (singlet area 3), τ 8·1 (singlet area 3), τ 7·2—8·4 (multiplet area 6).

3′,6′-Diacetoxy-1,2-benzocycloheptene-3,7-dione[8] (I; R = OAc).— 3′,6′-Dihydroxy-1,2-benzocycloheptene-3,7-dione (4·2 g.) in dry pyridine (25 ml.) was cooled on ice while acetic anhydride (5 ml.) was added dropwise with mechanical stirring for 6 hr. The reaction mixture was poured on to ice and dilute hydrochloric acid (excess) and the required product (6·0 g.) was obtained after recrystallisation from ethanol in needles, m. p. 175° (Found: C, 62·35; H, 5·05. Calc. for $C_{15}H_{14}O_6$: C, 62·05; H, 4·85%); $\nu_{max.}$ (Nujol) 1779 (ester), 1692 (>C=O) cm.$^{-1}$.

3′,6′-Diacetoxy-7-hydroxy-1,2-benzocyclohepten-3-one.— The foregoing diacetate (5 g.) in ethanol (200 ml.) was hydrogenated in presence of platinum oxide (150 mg.) at atmospheric pressure; when gas uptake was complete (450 ml.), the filtered solution was evaporated *in vacuo*, leaving a gum (5 g.) which was chromatographed on silica gel M.F.C. giving a small quantity of starting material. The main fraction (chloroform elution) proved to be the desired product, which was crystallised from light petroleum (b. p. 60—80°) as a colourless solid, m. p. 143—147° (Found: C, 61·8; H, 5·55. $C_{15}H_{16}O_6$ requires C, 61·5; H, 5·15%); $\nu_{max.}$ (Nujol) 3344 (OH), 1751, 1706 (ester), 1687 (>C=O) cm.$^{-1}$. The *triacetate* was obtained using acetic anhydride in pyridine at 20° and was identical with the material already described, m. p. and mixed m. p. 132°.

3′,6′-Dihydroxy-1,2-benzocyclohepten-3-one (V).—3′,6′-Dihydroxy-1,2-benzocyclohepten-3,7-dione (3 g.) in ethanol (200 ml.) was hydrogenated at atmospheric pressure in presence of palladised charcoal (20%, 150 mg.). The uptake was 370 ml. of 34 hr. After filtration and dilution with water, the product was extracted with methylene chloride and, after removal of solvent *in vacuo*, was obtained as a gum (2·8 g.). Crystallisation from light petroleum (b. p. 80—100°) gave a yellow material, m. p. 124—125° (lit.,[4] 121°) (Found: C, 68·6; H, 6·05. Calc. for $C_{11}H_{12}O_3$: C, 68·75; H, 6·3%); $\nu_{max.}$ (Nujol) 3326 (OH), 1613 (>C=O) cm.$^{-1}$. The n.m.r. spectrum (in $CDCl_3$) showed signals as follows: τ −1·3 (singlet area 1), τ 3·12 (multiplet area 2), τ 4·26 (singlet area 1), τ 7·1 (multiplet area 4), and τ 8·1 (multiplet area 4).

The *acetate* was obtained as in previous examples and had m. p. 113—114° (lit.,[4] 112°) (Found: C, 65·45; H, 5·85. Calc. for $C_{15}H_{16}O_5$: C, 65·2; H, 5·85%). The n.m.r. spectrum (in CCl_4) showed signals as follows: τ 3·025 (doublet area 2), τ 7·72 (singlet area 3), τ 7·82 (singlet area 3), the latter superimposed on broad absorption from τ 7·35—8·5 (area 8).

Reduction of 3′,6′-Dihydroxy-1,2-benzocycloheptene-3,7-dione with Sodium Borohydride.—The dione (1·04 g.) in ethanol (200 ml.) was treated with sodium borohydride (2 g.)

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[6] H. D. Murdoch and D. C. Nonhebel, *J. Chem. Soc.*, 1962, 2153.

[7] H. Musso and K. Figge, *Annalen*, 1963, **668**, 1; N. M. D. Brown, unpublished data.

[8] D. B. Bruce, A. J. S. Sorrie, and R. H. Thomson, *J. Chem. Soc.*, 1953, 2403.

and left at room temperature for 5 hr., when methanol was added and the reaction mixture diluted with water, acidified with dilute hydrochloric acid, and extracted with chloroform. After drying, the solvent was evaporated *in vacuo* leaving a solid (600 mg.) which, when crystallised from ether, had m. p. 290—295° (Found: C, 50·5; H, 4·75%); $\nu_{max.}$ (Nujol) 3448 (OH), 826 (tetrasubstituted benzene?) cm.$^{-1}$. The identity of this material could not be deduced.

2,3-Cyclohepteno-1,4-benzoquinone (III).—3′,6′-Diacetoxy-1,2-benzocycloheptene-3,7-dione (1 g.) in ethanol (100 ml.) was treated with sodium borohydride (1 g.) and left at room temperature overnight. After addition of methanol, the solution was diluted with water, acidified with dilute hydrochloric acid, and extracted with methylene chloride; the extract was dried and evaporated in a stream of air, leaving a dark brown product (0·66 g.). The latter was purified by distillation at 120°/0·5 mm. and by crystallisation from light petroleum (b. p. 60—80°) in golden yellow prisms, m. p. 82° (Found: C, 74·45; H, 7·35. $C_{11}H_{12}O_2$ requires C, 74·4; H, 6·85%); $\nu_{max.}$ (Nujol) 1640 ($>$C=O) cm.$^{-1}$ (no hydroxyl absorption). The n.m.r. spectrum (in CCl_4) showed the following signals: τ 3·35 (singlet area 2), τ 7·1—7·5 (multiplet area 4), τ 8·1—8·5 (multiplet area 6).

Clemmensen Reduction of 3′,6′-Dihydroxy-1,2-benzocycloheptene-3,7-dione.—The dione (3 g.) was heated under reflux in toluene with amalgamated zinc (8 g.) and conc. hydrochloric acid for 20 hr. The organic layer was separated and evaporated *in vacuo* leaving a liquid (2·14 g.) which was chromatographed on silica gel M.F.C.: elution with benzene–light petroleum (b. p. 60—80°) (1 : 3) gave two main fractions. (a) Liquid (1·3 g.), b. p. 60—65°/0·03 mm.; infrared spectroscopy failed to detect any functional groups (*e.g.*, OH, $>$C=O, etc.) (Found: C, 87·75; H, 11·45. Calc. for $C_{11}H_{18}$: C, 87·95; H, 12·05%). It was shown by g.l.c. that this product consisted of at least 3 constituents. (b) 3′-Hydroxy-1,2-benzocycloheptene (0·6 g.) (VII), which crystallised from light petroleum (b. p. 40—60°) in needles, m. p. 111—112° (sublim.) (Found: C, 81·15; H, 8·25. $C_{11}H_{14}O$ requires C, 81·45; H, 8·7%); $\nu_{max.}$ (Nujol) 3290 (OH), 1370, 1247 (–C–O–H) cm.$^{-1}$. The n.m.r. spectrum showed the following signals: τ 2·7—3·4 (multiplet area 3), τ 5·25 (broad singlet area 1), τ 7·0—7·3 (multiplet area 4), τ 8·1—8·6 (multiplet area 6).

Zinc Dust[5] *Reduction of 3′,6′-Dihydroxy-1,2-benzocycloheptene-3,7-dione* (I; R = OH).—The hydroxyketone (I; R = OH, 3 g.), glacial acetic acid (120 ml.), water (2 ml.), and zinc dust (10 g.) were mechanically stirred together at from 20—35° for 3 hr. After 24 hr. at room temperature, the mixture was filtered and diluted with water and chloroform. After separation, the organic layer was dried and evaporated leaving the crude bluish-grey product (2·5 g.) which was purified by crystallisation from ethanol and sublimation *in vacuo* (160°/0·3 mm.) to yield the product, m. p. 180—181° (Found: C, 63·5; H, 5·8%; *M* (osmometer, benzene), 196. Calc. for $C_{11}H_{12}O_4$: C, 63·5; H, 5·8%; *M*, 208). The *dipyrazole* derivative was formed by refluxing with hydrazine hydrate (excess of 99%) and was crystallised from ethanol in colourless flakes, m. p. 320° (Found: C, 65·75; H, 6·2; N, 27·6. $C_{11}H_{12}N_4$ requires C, 66·0; H, 6·05; N, 28·0%). The *boron fluoride chelate*[7] was obtained from dry ether with boron fluoride etherate (2 molar quantity) and was purified by recrystallisation from chloroform–light petroleum (b. p. 40—60°) to give a pale yellow solid, m. p. >320° (Found: C, 44·35; H, 3·4. $C_{11}H_{10}O_4B_2F_4$ requires C, 43·8; H, 2·7%); $\nu_{max.}$ 1570 (chelated $C\cdots O$), 1510 (chelated $C\cdots C$), 1300 (B–O str.), 1140—1220 (B–F def.), 1020—1090 (O–B–O def.) cm.$^{-1}$.

Zinc Chelate of 3′,6′-Dihydroxy-1,2-benzocycloheptene-3,7-dione.—The hydroxy-ketone (1·25 g.), zinc acetate dihydrate[6] (2·55 g.), water (20 ml.), and ethanol (150 ml.) were mechanically stirred together while dilute ammonium hydroxide (50 ml., 2N) was slowly added at 60—80°; after 2 hr. the mixture was cooled with stirring and the orange product (m. p. >320°) was removed, washed successively with dilute ammonium hydroxide solution, water, and ethanol, and then dried *in vacuo* at 100°.

The i.r. spectrum showed that the original carbonyl absorption was absent and that there were no absorptions in this region above a strong peak at 1675 cm.$^{-1}$ (chelated $C\cdots O$).

When the zinc chelate (0·5 g.) was shaken in ethanol with palladised charcoal (100 mg., 10%) in an atmosphere of hydrogen, an uptake of gas (170 ml.) over 16 hr. was noted, but after acidification with acetic acid and working up in the usual way, the product (400 mg.) proved to be the hydroxy-ketone (I; R = OH), m. p. and mixed m. p. 146—148°.

Reaction of 3′,6′-Dihydroxy-1,2-benzocycloheptene-3,7-dione with Boron Trifluoride.—The hydroxy-ketone (1 g.) in dry ether (25 ml.) was treated with boron trifluoride etherate containing methanol (0·1 ml.) as before. The yellow product (300 mg.) was purified as before and had m. p. 184—186°. It gave unsatisfactory analytical results, but the i.r. spectrum showed $\nu_{max.}$ 1585 (chelated $C\cdots O$), 1510 (chelated C=C), 1400 (B–O str.), 1140—1220 (B–F def.), and 1020—1090 (O–B–O def.) cm.$^{-1}$. This product (600 mg.) in tetrahydrofuran (150 ml.) (orange solution with green fluorescence) was shaken in an atmosphere of hydrogen with palladised charcoal (100 mg. 10%); the gas uptake was 140 ml. in 15 hr. After filtration, acid treatment, and working up in the usual way, thin-layer chromatography showed that the crude product contained no recognisable materials, and chromatography on silica gel M.F.C. yielded only traces of white solid, m. p. >220°.

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DEPARTMENT OF PURE AND APPLIED CHEMISTRY,
UNIVERSITY OF STRATHCLYDE,
GLASGOW C.1.

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