216. *The Condensation of Benzoin with 3-Chloropropane-1,2-diol and 2,3-Epoxypropyl Chloride.*

By Vladimir Petrow and Oliver Stephenson.

Condensation of benzoin with 3-chloropropane-1,2-diol and 2,3-epoxypropyl chlorides under a variety of experimental conditions has been examined and some of the products have been identified.

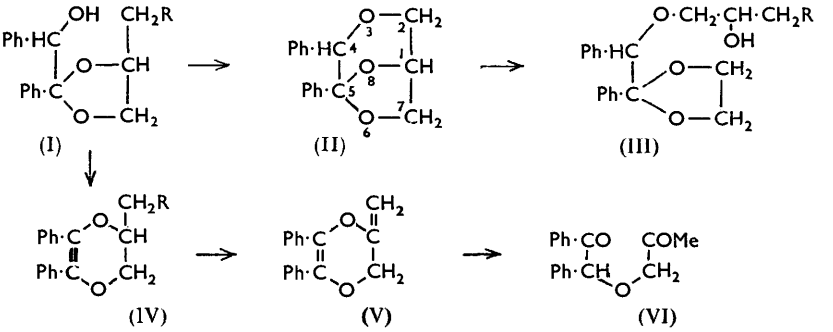
Extending our earlier studies on aryloxyhydroxypropylamines [1,2] we have examined the condensation of benzoin with 3-chloropropane-1,2-diol and 2,3-epoxypropyl chloride, hoping thereby to obtain 1-chloro-3-(2-oxo-1,2-diphenylethoxy)propan-2-ol and thence derived amines, which were required for pharmacological study.

Benzoin with the chloro-diol in the presence of toluene-*p*-sulphonic acid [3] gave a mixture of ketals (I; R = Cl) from which only the higher-melting isomer (A) was obtained pure, albeit with some difficulty. A mixture of lower-melting isomeric ketals (B), free from isomer (A), was also isolated, but for our study of the general reactions the original mixed ketals (C), which contained (A), (B), and other isomers, were used. Their structures followed from (i) their infrared absorption spectra which revealed the presence of ether and hydroxyl-oxygen and the absence of carbonyl and ethylenic groups, and (ii) their ready hydrolysis to benzoin by mineral acid. Attempts at inter-conversion of the isomers were

[1] Beasley, Petrow, and Stephenson, *J. Pharm. Pharmacol.*, 1958, **10**, 47.
[2] Boggiano, Petrow, Stephenson, and Wild, *J.*, 1959, 1143.
[3] Cf. Petrow, Stephenson, and Thomas, *J. Pharm. Pharmacol.*, 1956, **8**, 666.

not successful. Long heating of the mixture (C) with a trace of iodine in benzene led to dehydration and molecular rearrangement with formation of, *inter alia*, 2-chloromethyl-2,3-dihydro-5,6-diphenyl-1,4-dioxin (IV; R = Cl) (see below). Simple refluxing of the isomers (C) with ethanediol led to trans-ketalisation with formation of 2,3-dihydro-5,6-diphenyl-1,4-dioxin in over 80% yield.

Reaction of the ketals (C) with sodium ethoxide led to dehydrohalogenation with formation of isomers of 4,5-diphenyl-3,6,8-trioxabicyclo[3,2,1]octane (II). The higher-melting



form of the ketal (A) passed largely into a labile isomer (II) (m. p. 129°) which was converted by hydrochloric acid into a stable isomer (m. p. 134°). The lower-melting fraction (B) of the ketals, in contrast, reacted more slowly with the alkaline reagent to give the stable isomer (II) (m. p. 134°) together with a mixture of ethoxy-ketals (I; R = OEt).

Treatment of the mixture (C) with *p*-nitrobenzoyl chloride in pyridine yielded mixed esters from which the least soluble [corresponding to isomer (A)] was readily isolated and likewise was converted into the labile form of the bicyclo-compound (II) on reaction with alkali. The stable isomer (II) was also obtained, in moderate yield, by condensing benzoin with glycerol at 150° in the presence of hydrogen chloride, the reaction probably involving intermediate formation of the ketal (I; R = OH).

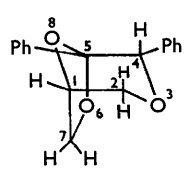
Formulation of these products as isomeric trioxabicyclo-octanes (II) is supported by their stability to hydrolysis by hot mineral acid and their infrared absorption spectra which reveal the presence of only ether-linked oxygen groups.

Examination of atomic models permits tentative conclusions regarding the stereochemistry of the isomers (II). It seems likely that the stable isomer is represented by structure (VII) in which both phenyl groups are equatorial and the 6-membered ring has the chair conformation. The labile isomer may then be represented by structure (VIII) in which the 4-phenyl group has the axial configuration whilst the 6-membered ring retains the chair conformation. The alternative formulation of the labile isomer as the boat structure (IX) is considered less likely as in this case the phenyl groups are eclipsed. Conversion of the labile isomer (VIII) into the stable form (VII) would then proceed by a mechanism involving hydride transfer with initial formation of the oxonium ion (X) (cf. ref. 4), which may be expected to pass into the more stable form (XIV) by way of (XI) and (XIII) with consequent inversion at $C_{(4)}$.

The isomeric ketals (C) (I; R = Cl) with ammonia at 150° in an autoclave gave *ca.* 8% of the corresponding amine hydrochloride (I; R = NH_2,HCl), together with larger quantities of the stable isomer (II) and of benzoin. When morpholine was employed, all forms of the ketal (I; R = Cl) were converted into the same morpholino-derivative (I; R = N<[CH_2·CH_2]$_2$>O), presumably by inversion of the isomers when in the cationic form. The structure of this product was established by its acid hydrolysis to benzoin and 4-(2,3-dihydroxypropyl)morpholine. With boiling aniline the isomers (C) (I; R = Cl) yielded 2,3-diphenylindole, also obtained from benzoin and aniline hydrochloride.[5]

[4] Woodward, *J. Amer. Chem. Soc.*, 1958, **80**, 6693.
[5] Japp and Murray, *Ber.*, 1893, **26**, 2638.

Condensation of benzoin and 3-chloropropane-1,2-diol at 120—140° with hydrogen chloride as catalyst was next examined. The main product proved to be 2-chloromethyl-2,3-dihydro-5,6-diphenyl-1,4-dioxin (IV; R = Cl), accompanied by smaller quantities of the dioxolans (I; R = Cl) and tetraphenylfuran.[6] The reaction probably proceeds through the ketals (I; R = Cl), as these form the main product under less vigorous conditions and are themselves converted into the dioxin (IV; R = Cl) by the chloro-diol at 140°. The dioxin (IV; R = Cl), which was isolated in labile and stable crystalline forms, reacted metathetically with morpholine and with 1,2,3,6-tetrahydropyridine.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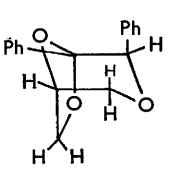
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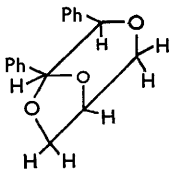
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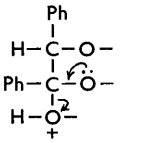
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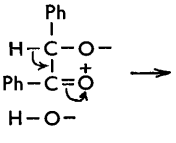
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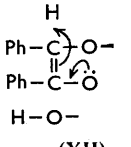
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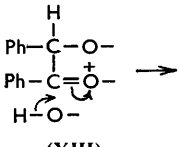
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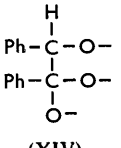
(XIV)

The dioxin (IV; R = Cl) surprisingly proved stable to boiling aqueous ethanolic sodium carbonate, but was converted by methanolic potassium hydroxide into 2,3-dihydro-2-methylene-5,6-diphenyl-1,4-dioxin (V), which on mild acid hydrolysis furnished benzoin acetonyl ether (VI) and smaller amounts of hydroxyacetone and benzoin.

Finally, we examined the condensation of benzoin with 2,3-epoxypropyl chloride in the presence of catalysts, but again failed to obtain the required 1-chloro-3-(2-oxo-1,2-diphenylethoxy)propan-2-ol. We ascribed this lack of success to the effect of the carbonyl group in benzoin upon the normal reactivity of the hydroxyl group with epoxypropyl chloride. To overcome this difficulty, we converted benzoin into the ethylene ketal [7] and condensed the latter with 2,3-epoxypropyl chloride in the presence of stannic chloride as catalyst: [8] the required normal condensation product (III; R = Cl) was obtained. Metathesis with morpholine gave the expected morpholino-derivative, but cautious deketalisation of this was accompanied by loss of the elements of water and formation of the dioxin (IV; R = N<[CH_2·CH_2]$_2$>O). Attempted hydrolysis of the chlorohydrin (III; R = Cl) with sodium formate in ethanediol [9] gave a gum [presumably (III; R = OH)], smoothly converted into the trioxabicyclo-octane (II) on acid hydrolysis. Hydrolysis of the chlorohydrin (III; R = Cl) with hot mineral acid yielded the dioxin (IV; R = Cl).

Experimental

Infrared spectra were kindly determined by Mr. M. T. Davies, B.Sc., and Miss D. F. Dobson, B.Sc.

4-Chloromethyl-2-α-hydroxybenzyl-2-phenyl-1,3-dioxolan (I; R = Cl).—A solution of benzoin (159 g.) in 3-chloropropane-1,2-diol (300 ml.) containing toluene-*p*-sulphonic acid (1 g.) was heated at 120° for 1 hr., slight vacuum being applied at intervals to remove the water formed. Excess of chlorohydrin was removed at 0·5 mm., the viscous residue dissolved in chloroform and

[6] Zinin, *J. prakt. Chem.*, 1921, **101**, 160.
[7] Salmi, Tamminen, and Louhenkuru, *Suomen Kem.*, 1947, **20, B**, 1.
[8] Van Zyl, Zuidema, Zack, and Kromann, *J. Amer. Chem. Soc.*, 1953, **75**, 5002.
[9] Beasley, Petrow, Stephenson, and Wild, *J. Pharm. Pharmacol.*, 1959, **11**, 36.

washed with dilute sodium carbonate solution, then with water, and the extract concentrated. Dilution of the residual oil with light petroleum (b. p. 60—80°) furnished the product (C) (169 g.) in feathery needles, m. p. 80—90°. Repeated crystallisation from light petroleum (b. p. 60—80°), then from methanol, furnished *isomer A*, m. p. 118—119° (Found: C, 66·8; H, 5·6; Cl, 11·9. $C_{17}H_{17}O_3Cl$ requires C, 67·0; H, 5·6; Cl, 11·7%). The most soluble fraction gave mixture B, m. p. 85—89° (Found: C, 67·0; H, 5·4; Cl, 12·1%).

The infrared spectra of the isomers (A) and (B) in carbon disulphide and carbon tetrachloride were indistinguishable with strong hydroxyl bands at 3582 (3590), strong ether bands at 1233, 1193, 1178, and 1154 (1235, 1194, 1178, and 1152) and strong bands due to C–O(H) stretching at 1059, 1045, 1025, and 1004 cm.$^{-1}$ (1062, 1046, 1027, and 1005 cm.$^{-1}$) [figures for isomers (B) are in parentheses]. In addition the spectra confirmed the absence of carbonyl and stilbene groups.

Concentration of the reaction mother-liquors gave a gum which was distilled at 0·3 mm., to yield fractions, (*a*) b. p. 130—160° (11·8 g.), mainly benzoin, and (*b*) b. p. 160—172° (33·3 g.); the latter on treatment with light petroleum (b. p. 60—80°) yielded the dioxolan (17·8 g., m. p. 76—95°). Concentration of the light petroleum furnished 2-chloromethyl-2,3-dihydro-5,6-diphenyl-1,4-dioxin (2·8 g.), m. p. 71—73°, not depressed on admixture with an authentic specimen (see below).

Reactions of the Mixed Isomers (*C*).—(*a*) Hydrolysis with aqueous-ethanolic 2N-hydrochloric acid on the steam-bath for 1·5 hr. yielded benzoin (94%), m. p. 135—137°.

(*b*) The dioxolans (5·0 g.) in ethanediol (25 ml.) were heated at reflux temperature for 2·5 hr., yielding 2,3-dihydro-5,6-diphenyl-1,4-dioxin (3·05 g., 78%), plates m. p. 93—95° (from aqueous ethanol). The m. p. was not depressed on admixture with an authentic specimen.

(*c*) The dioxolans (15 g.) in benzene (50 ml.) containing iodine (100 mg.) were heated at the b. p. for 50 hr. and the product was distilled at 0·1 mm., to yield fractions, (i) b. p. 130° (3·0 g.), m. p. 94—95° (from methanol) not depressed on admixture with benzil, (ii) b. p. 148—160° (6·8 g.), yielding 2-chloromethyl-2,3-dihydro-5,6-diphenyl-1,4-dioxin (3·6 g.), m. p. 72—74°, in colourless prisms from methanol.

(*d*) The dioxolans (5 g.) were heated in morpholine (15 ml.) on the steam-bath for 16 hr. Excess of base was removed under reduced pressure, the residue treated with water, and the base isolated with chloroform. 2-α-Hydroxybenzyl-4-morpholinomethyl-2-phenyl-1,3-dioxolan formed a thick amber gum (5 g.), b. p. 198—200°/0·2 mm., which yielded a *hydrochloride*, colourless prisms (from ethanol), m. p. 231—233° (Found: C, 64·1; H, 6·4; N, 3·7; Cl, 9·4. $C_{21}H_{26}O_4NCl$ requires C, 64·3; H, 6·7; N, 3·6; Cl, 9·1%).

The foregoing hydrochloride (4·0 g.) was heated in N-hydrochloric acid (50 ml.) on the steam-bath for 6 hr. Benzoin (2·03 g., 94%), m. p. 136—137°, separated on cooling. The aqueous filtrate, evaporated to dryness under reduced pressure, yielded 3-*morpholinopropane*-1,2-*diol hydrochloride*, prisms, m. p. 99—100° (Found: C, 42·1; H, 8·0; N, 6·9. $C_7H_{16}O_3NCl$ requires C, 42·5; H, 8·2; N, 7·1%).

(*e*) The dioxolans (20 g.) were heated in aniline (50 ml.) for 5 hr., then the excess of aniline was removed under reduced pressure, yielding 2,3-diphenylindole (6·4 g.), m. p. and mixed m. p. 124—125° (Found: C, 89·0; H, 5·6; N, 5·4. Calc. for $C_{20}H_{15}N$: C, 89·2; H, 5·6; N, 5·2%) after crystallisation from methanol and then from light petroleum (b. p. 80—100°).

Action of Alkali on 4-*Chloromethyl*-2-α-*hydroxybenzyl*-2-*phenyl*-1,3-*dioxolan.*—(*a*) A solution of the dioxolans (C) (60·9 g.) in ethanol (200 ml.) was heated with sodium ethoxide solution (2 equiv.) [from sodium (9·2 g.) and ethanol (250 ml.)] for 8 hr., with concentration to half-bulk during the last hour. Dilution with water followed by extraction with chloroform furnished the stable isomer of 4,5-*diphenyl*-3,6,8-*trioxabicyclo*[3,2,1]*octane* (18·5 g.), needles, m. p. 132—134° (from methanol) (Found: C, 75·8; H, 5·9. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%). Concentration of the methanolic filtrate yielded a smaller quantity of the labile *isomer* (6·1 g.), m. p. 128—129° (from methanol) (Found: C, 76·6; H, 6·3%). Dilution of the reaction mother-liquors furnished an oil (19·6 g.), b. p. 160°/0·1 mm. Analysis (Found: C, 71·0; H, 5·8; Cl, 8·4%) showed that hydrolysis was incomplete. A portion of the oil (4 g.) in ethanol (20 ml.) containing concentrated hydrochloric acid (3 ml.) was heated for 30 min. on the steam-bath, giving benzoin (2·48 g., 92%), m. p. 135—137°. The rest of the oil (15 g.) was heated with sodium ethoxide solution [prepared from sodium (3·45 g.) in ethanol (50 ml.)] at the b. p. for 12 hr., yielding a small quantity of the labile bicyclo-compound (II) and viscous fractions, (*a*) b. p. 130—150°/0·1 mm. (3·5 g.) (Found: C, 75·5; H, 6·0; Cl, 0·9%), and (*b*) b. p. 160°/0·1 mm. (1·5 g.) (Found: C, 72·6; H, 6·1; Cl, 1·0%). Fraction (*a*) crystallised slowly and

was presumably crude bicyclo-compound (II). Fraction (*b*) (1·0 g.), hydrolysed by aqueous-alcoholic hydrochloric acid, gave benzoin (0·57 g.), m. p. 134°, and was therefore presumably a ketal of type (I; R = OEt).

(*b*) The high-melting isomer (A) (3·04 g.) of the dioxolan was heated under reflux with sodium ethoxide (4 equiv.) in ethanol (55 ml.) for 6 hr. Separation of sodium chloride was rapid. Dilution with water furnished solids (2·4 g.) which on crystallisation from methanol gave the labile isomer (II) (1·7 g.), m. p. 126—128°.

Conversion of the Labile Isomer (II) *into the Stable Isomer.*—A solution of the labile isomer (0·4 g.) in ethanol (10 ml.) containing concentrated hydrochloric acid (0·5 ml.) was heated on the steam-bath for 1 hr. Dilution with water furnished solids (0·35 g.), m. p. 131—133°. The m. p. was unchanged on admixture with the stable isomer (II), but was strongly depressed on admixture with the labile isomer (II).

The infrared spectra of the stable isomer of 4,5-diphenyl-3,6,8-trioxabicyclo[3,2,1]octane in carbon disulphide and carbon tetrachloride showed strong or medium bands at: m 3057, 3028; s 2941, 2891, 2862; m 1498, 1478; s 1454; m 1376, 1354; s 1324, 1300, 1289, 1228, 1122, 1100; m 1039; s 1021, 995, 963; m 908, 876; s 763; m 746; s 690 cm.$^{-1}$. For the labile isomer bands were at: m 3060, 3036; s 2961; m 2887, 1494; s 1452; m 1355, 1329; s 1308; m 1287; s 1232; m 1193; s 1125, 1101; m 1091, 1081, 1053, 1039; s 1010, 982, 928; m 909, 854, 830; s 753, 670 cm.$^{-1}$. Weak bands for the two isomers showed similar discrepancies.

Condensation of Benzoin with Glycerol.—A suspension of benzoin (53 g.) in glycerol (92 g.) was saturated with hydrogen chloride and heated with stirring at 150° for 2 hr. The hot mixture was poured with stirring into water, and the thick oil isolated with chloroform. Distillation at 0·4 mm. yielded fractions, (*a*) b. p. 140° (19 g.) (unchanged benzoin), (*b*) b. p. 160—180° (26·4 g.), and (*c*) 15 g., high-boiling residue. Fraction (*b*) yielded the stable isomer of 4,5-diphenyl-3,6,8-trioxabicyclo[3,2,1]octane (II) (12·9 g.), m. p. 132—134° (from methanol).

Stability of the Stable Isomer (II).—(*a*) A solution of the compound (2·5 g.) in ethanol (50 ml.), saturated with hydrogen chloride, was heated under reflux for 8 hr. Unchanged material (1·6 g.) separated on cooling. The filtrate contained ethyl benzoate and gave a precipitate with 2,4-dinitrophenylhydrazine. (*b*) The compound (6·7 g.) was heated in benzylamine (18 g.) at 170—180° for 6·5 hr. After removal of the benzylamine at reduced pressure crystallisation of the residual solids from methanol gave unchanged material (6·1 g.), m. p. 130—132°.

Action of Ammonia on 4-Chloromethyl-2-α-hydroxybenzyl-2-phenyl-1,3-dioxolan.—The isomers (C) (20 g.) were heated in ethanol (300 ml.) with ammonia solution (200 ml.; *d* 0·880) under pressure at 140—150° for 5·5 hr. Concentration under reduced pressure yielded the stable isomer (4·65 g.) of 4,5-diphenyl-3,6,8-trioxabicyclo[3,2,1]octane (II), m. p. 130—132° (from methanol). The methanolic mother-liquors deposited *4-aminomethyl-2-α-hydroxybenzyl-2-phenyl-1,3-dioxolan hydrochloride* (1·45 g.) (Found: C, 63·5; H, 6·4; N, 4·6; Cl, 11·0. $C_{17}H_{20}O_3NCl$ requires C, 63·4; H, 6·3; N, 4·4; Cl, 11·0%), feathery needles, m. p. 208—209° (from ethanol). Further concentration yielded benzoin (6·9 g.), m. p. 132—135°.

p-*Nitrobenzoate of 4-Chloromethyl-2-α-hydroxybenzyl-2-phenyl-1,3-dioxolan.*—A solution of the isomers (C) (16·4 g.) in pyridine (50 ml.) was treated with *p*-nitrobenzoyl chlorides (10 g.) added in portions with shaking and cooling. The mixture was heated on the steam-bath for 20 min., cooled, and poured on ice, and the product was isolated with chloroform. Concentration and dilution with light petroleum (b. p. 60—80°) furnished solids (20·5 g.) which yielded a sparingly soluble isomer (4·45 g.), m. p. 168—169° (from ethanol) (Found: C, 63·8; H, 4·2; N, 3·1; Cl, 7·9. $C_{24}H_{20}O_6NCl$ requires C, 63·5; H, 4·4; N, 3·1; Cl, 7·8%). The mother-liquors furnished a solid (12 g.), m. p. 104—110°, which gave a small amount of a second *isomer*, m. p. 122—125° (Found: C, 63·6; H, 4·5; N, 3·3; Cl, 8·2%) after repeated crystallisation from light petroleum (b. p. 60—80°) and then from methanol.

Action of Alkali on the p-*Nitrobenzoates.*—(*a*) The isomer of m. p. 168—169° (2·7 g.), suspended in ethanol (30 ml.), was treated with potassium hydroxide (1·7 g.) in methanol (20 ml.) on the steam-bath for 3 hr., yielding the labile isomer (1·28 g., 80%) of 4,5-diphenyl-3,6,8-trioxabicyclo[3,2,1]octane (II), m. p. 126—128°. (*b*) The isomers of m. p. 104—110° (4·54 g.) similarly yielded the stable form (0·65 g., 25%), m. p. 131—133°. Dilution of the filtrate gave crude solids (1·45 g.), m. p. 80—96°. Heating these (0·2 g.) in ethanol (6 ml.) containing concentrated hydrochloric acid (1 ml.) on the steam-bath for a short period gave benzoin (0·1 g.), m. p. 131—133° (from methanol).

2-Chloromethyl-2,3-dihydro-5,6-diphenyl-1,4-dioxin (IV; R = Cl).—A solution of benzoin

(40 g.) in 3-chloropropane-1,2-diol (75 ml.) containing a trace of hydrogen chloride was heated to 140—150°, then distilled slowly under reduced pressure during 1 hr. to remove about half of the chlorohydrin. The hot residue was poured into water, and the product isolated with chloroform. Distillation at 0·15 mm. yielded fractions, (*a*) b. p. 142° (11·5 g.) (unchanged benzoin) and (*b*) b. p. 152—158° (34·8 g.) which gave 2-*chloromethyl*-2,3-*dihydro*-5,6-*diphenyl*-1,4-*dioxin* (27·0 g.) as short colourless prisms, m. p. 72—74° (Found: C, 71·3; H, 5·3; Cl, 12·5. $C_{17}H_{15}O_2Cl$ requires C, 71·2; H, 5·3; Cl, 12·4%), from methanol. In an early experiment the compound was obtained with m. p. 61—63° (Found: C, 71·2; H, 5·2; Cl, 12·6%) in the white feathery needles of a labile polymorphic *form*. The infrared spectra of the two forms in carbon disulphide and carbon tetrachloride were indistinguishable, showing a strong stilbene band at 1638 and strong bands at 1273, 1247, 1146, 1137, 1113, 1099, 972, 910, 760, and 694 cm.$^{-1}$, confirming additionally the absence of carbonyl and hydroxyl groups.

Excess of hydrogen chloride in the foregoing condensation led to increased yields of higher-boiling products including tetraphenylfuran,[5] plates, m. p. 174—175° [from light petroleum (b. p. 60—80°)] (Found: C, 90·4; H, 5·2. Calc. for $C_{28}H_{20}O$: C, 90·3; H, 5·4%).

2,3-*Dihydro*-2-*morpholinomethyl*-5,6-*diphenyl*-1,4-*dioxin* (IV; R = $N<[CH_2\cdot CH_2]_2>O$).—2-Chloromethyl-2,3-dihydro-5,6-diphenyl-1,4-dioxin (2 g.) and morpholine (5 ml.) were heated on the steam-bath for 20 hr. After addition of water the base was isolated with chloroform. Treatment with ethanolic hydrogen chloride furnished the *hydrochloride*, needles, m. p. 220—222° (from ethanol–ether) (Found: C, 67·7; H, 6·5; N, 3·8; Cl, 9·7. $C_{21}H_{24}O_3NCl$ requires C, 67·4; H, 6·5; N, 3·8; Cl, 9·5%). The *picrate* (Found: N, 9·8. $C_{27}H_{26}O_{10}N_4$ requires N, 9·9%) separated from ethanol in light yellow needles, m. p. 215—216° (decomp.).

2,3-*Dihydro*-5,6-*diphenyl*-2-(1,2,3,6-*tetrahydropyridino*)-1,4-*dioxin hydrochloride*, m. p. 235—236° (decomp.) (Found: C, 71·0; H, 6·8; N, 3·6; Cl, 9·5. $C_{22}H_{24}O_2NCl$ requires C, 71·4; H, 6·5; N, 3·8; Cl, 9·6%), separated from ethanol in needles.

2,3-*Dihydro*-2-*methylene*-5,6-*diphenyl*-1,4-*dioxin* (V).—2-Chloromethyl-2,3-dihydro-5,6-diphenyl-1,4-dioxin (28·7 g.) in ethanol (100 ml.) was heated with sodium ethoxide (2 equiv.) [from sodium (4·6 g.) in ethanol (70 ml.)] for 8 hr. The whole was filtered hot and the precipitate washed with a little hot ethanol. The *product* (17 g.) formed needles, m. p. 89—90° (Found: C, 81·6; H, 5·4. $C_{17}H_{14}O_2$ requires C, 81·6; H, 5·6%), from methanol. It (1·0 g.) in acetic acid was treated with cooling with a slight excess of bromine in acetic acid. Dilution with aqueous sodium acetate gave benzil (0·41 g.), m. p. 96—98°. The infrared spectrum of the methylene compound (V) in carbon tetrachloride showed a strong band (1665 cm.$^{-1}$) due to the combined stilbene–methylene groups. Absence of hydroxyl and carbonyl groups was confirmed. Strong ether bands (1129 and 1077 cm.$^{-1}$) were shown in carbon disulphide solution. In the related 2,3-dihydro-5,6-diphenyl-1,4-dioxin the infrared spectrum showed a strong stilbene band at a lower wavelength (1636 cm.$^{-1}$).

Acid-hydrolysis of 2,3-*Dihydro*-2-*methylene*-5,6-*diphenyl*-1,4-*dioxin*.—The compound (1·0 g.) in ethanol (20 ml.) containing concentrated hydrochloric acid (2 ml.) was heated on the steam-bath for 1 hr., then the whole was concentrated and diluted with water and the oil was isolated with chloroform. The aqueous extract heated with 2,4-dinitrophenylhydrazine reagent gave pyruvaldehyde bis-2,4-dinitrophenylhydrazone, red needles, m. p. 301° (decomp.) (from anisole) (Found: C, 41·8; H, 2·9. Calc. for $C_{15}H_{12}O_8N_8$: C, 41·7; H, 2·8%). Evaporation of the chloroform extract left a gum which crystallised from methanol to yield *benzoin acetonyl ether* (VI) (0·4 g.) (Found: C, 76·1; H, 6·2. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%), having m. p. 85—86° after further crystallisation from light petroleum (b. p. 60—80°) [*disemicarbazone*, m. p. 221—222° (decomp.) (Found: C, 59·8; H, 5·8; N, 22·0. $C_{19}H_{22}O_3N_6$ requires C, 59·7; H, 5·8; N, 22·0%)]. Concentration of the alcoholic washings from the disemicarbazone yielded a small amount of benzoin semicarbazone, m. p. and mixed m. p. 202—204° (decomp.). The infrared spectrum of the dione in chloroform showed strong bands at 1722 and 1690 cm.$^{-1}$ in agreement with the diketonic structure, whilst in carbon disulphide the spectrum showed strong ether bands at 1180 and 1123 cm.$^{-1}$. Absence of hydroxyl and stilbene groups was confirmed.

Reaction of Benzoin with Ethanediol (cf. ref. 10).—(*a*) Benzoin (53 g.) was heated in hot ethanediol (150 ml.) with toluene-*p*-sulphonic acid (1 g.) at 120—130° for about 1 hr., slight vacuum being applied at intervals to remove water. Excess of diol was removed under reduced pressure and the residue diluted with water. 2-α-*Hydroxybenzyl*-2-*phenyl*-1,3-*dioxolan* formed needles, m. p. 146—147° (from benzene) (Found: C, 75·3; H, 6·3. $C_{16}H_{16}O_3$ requires C, 75·0;

[10] Summerbell and Berger, *J. Amer. Chem. Soc.*, 1959, **81**, 633.

H, 6·3%). (*b*) A solution of benzoin (53 g.) in ethanediol (350 ml.) containing hydrogen chloride (6 g.) was heated to 120° for 1 hr., water being removed at intervals by the application of a slight vacuum. Excess of diol was removed at 40 mm., the residue was diluted with water, and the solids were extracted with chloroform. Concentration of the chloroform and dilution with light petroleum (b. p. 60—80°) yielded the aforementioned dioxolan (25 g.), m. p. 146—147°. Concentration of the mother-liquors afforded solids (27·9 g.), m. p. *ca.* 90°, which yielded 2,3-*dihydro*-5,6-*diphenyl*-1,4-*dioxin*, having m. p. 95—97° (Found: C, 80·1; H, 6·0. $C_{16}H_{14}O_2$ requires C, 80·6; H, 5·9%) after crystallisation from methanol and light petroleum (b. p. 60—80°). (*c*) The dioxolan (12 g.), when heated under reflux in ethanediol (100 ml.) containing hydrogen chloride (3 g.), yielded the 1,4-dioxin, m. p. 95—97°.

A solution of the 1,4-dioxin (1·0 g.) in acetic acid (20 ml.) was treated with a slight excess of bromine in the same solvent with cooling. Dilution with aqueous sodium acetate yielded benzil (0·65 g., 74%), m. p. 95—97°.

A solution of the 1,4-dioxin (5·95 g.) in acetic acid (15 ml.) was added in portions with cooling to a solution of peracetic acid prepared from 30% hydrogen peroxide (5·7 g.) in acetic acid (25 ml.). The mixture was heated at 70—75° for 5 hr. Dilution with water yielded benzoic acid (2·5 g.), m. p. and mixed m. p. 120—122°.

The infrared spectrum of the 1,4-dioxin in carbon disulphide showed a strong stilbene band (1636 cm.$^{-1}$) and ether bands (1135 and 1106 cm.$^{-1}$), and confirmed the absence of hydroxyl and carbonyl groups.

Condensation of 2-α-*Hydroxybenzyl*-2-*phenyl*-1,3-*dioxolan with* 2,3-*Epoxypropyl Chloride*.—A solution of the dioxolan (25·6 g.) in dry benzene (100 ml.) was treated with stannic chloride (0·5 ml.), then heated to the b. p., and 2,3-epoxypropyl chloride (9·3 g.) was added dropwise during 5 min. The mixture was then heated for 5 hr. Unchanged dioxolan (5 g.) separated on cooling and was removed. The benzene solution was just basified with ammonia, washed with water, and concentrated, and the residual oil distilled at 0·2 mm. to yield fractions, (*a*) b. p. 140—160° (3·9 g.), (*b*) b. p. 166—200° (12·8 g.), and (*c*) b. p. 200—230° (5 g.). Fraction (*a*) was mainly unchanged dioxolan. Fraction (*b*), on refractionation, yielded α-(3-*chloro*-2-*hydroxypropoxy*)*benzyl*-2-*phenyl*-1,3-*dioxolan* (III; R = Cl), b. p. 185°/0·5 mm. (Found: C, 65·0; H, 5·9. $C_{19}H_{21}O_4Cl$ requires C, 65·4; H, 6·1%). This chlorohydrin was heated with a slight excess of morpholine on the steam-bath for 20 hr. The resultant base yielded 2-α-(2-*hydroxy*-3-*morpholinopropoxy*)*benzyl*-2-*phenyl*-1,3-*dioxolan hydrochloride* (Found: C, 63·2; H, 7·1; N, 3·4; Cl, 8·3. $C_{23}H_{30}O_5NCl$ requires C, 63·4; H, 6·9; N, 3·2; Cl, 8·2%), plates, m. p. 193—194° (from ethanol–ether).

This hydrochloride (1·3 g.) in ethanol (20 ml.) containing concentrated hydrochloric acid (2 ml.) was heated at the b. p. for 1 hr. After removal of solvents, the gummy residue crystallised from ethanol–ether, yielding 2,3-dihydro-2-morpholinomethyl-5,6-diphenyl-1,4-dioxin hydrochloride (0·88 g., 79%), m. p. and mixed m. p. 220—222°.

The chlorohydrin (III; R = Cl) (4·5 g.) was heated in ethanol (30 ml.) containing 6N-hydrochloric acid (10 ml.) on the steam-bath for 1 hr. The solution was diluted, and the oil isolated with chloroform. Crystallisation from aqueous methanol yielded 2-chloromethyl-2,3-dihydro-5,6-diphenyl-1,4-dioxin (1·5 g., 40%), m. p. and mixed m. p. 70—72°.

The chlorohydrin (III; R = Cl) (2·3 g.) was heated in ethanediol (15 ml.) containing sodium formate (0·68 g.) under reflux for 2 hr.[9] Excess of solvent was removed under reduced pressure, the residue diluted with water, and the oil isolated with chloroform and heated in ethanol (8 ml.) containing concentrated hydrochloric acid (5 ml.) on the steam-bath for 1 hr. The solids which separated on cooling yielded the stable isomer of 4,5-diphenyl-3,6,8-trioxabicyclo[3,2,1]-octane (II) (0·85 g.), m. p. and mixed m. p. 132—134° (from methanol).

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