

297. Arylglycerols. Part I. The Preparation of Two New Forms of $\alpha\gamma$ -Diphenylglycerol.

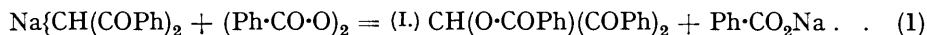
By WILLIAM BRADLEY and JOHN K. EATON.

Two new forms of $\alpha\gamma$ -diphenylglycerol have been encountered in the course of experiments on the preparation of hydroxyarylglycerols. They are regarded as diastereoisomerides. According to Robinson, hydroxyarylglycerols are probably intermediates in natural syntheses of plant products.

AMONGST recent developments in the chemistry of natural products, the views of Robinson (*Brit. Assoc. Rep.*, 1921, 417; *Proc. Univ. Durham Phil. Soc.*, 1928, 8, 1, 15; *Cong. Internat. Union Pure and Appl. Chem.*, 1934, 9, V, 17) on the course of the natural synthesis of plant products are of particular interest. Reviewing the wide variety of structural types which have been recognised, he indicated the prevalence of forms based on the groupings C_6-C_3 and $C_6-C_3-C_6$. Typical examples of the simpler grouping are the propylbenzene derivatives safrole, coniferyl alcohol, and *p*-coumaric acid. The more complex diphenylpropane type is represented by both open-chain and cyclic forms as in butein and quercetin. The groupings were regarded as derived by interaction and modification of hexose and triose units, and consideration of the state of oxidation of the several parts of a naturally occurring compound enabled Robinson to discern the manner in which the union of the parts had been effected. Thus, the C_6 of the first C_6-C_3 group formed was recognised as the origin of the substituted phenyl group of the flavones, anthocyanins, etc. A circumstance, remarkable in view of the importance of carbohydrates in plant metabolism, is the absence of arylglycerols from the list of isolated natural products. The most probable reason is that the hydroxylated arylglycerols are very easily changed. Robinson (*Nature*, 1936, 137, 172) has, in fact, suggested that oxidation of 2 : 4 : 6 : 3' : 4'-pentahydroxy- $\alpha\gamma$ -diphenylglycerol affords a ketone which is dehydrated to a cyanidin salt in presence of acid. No hydroxylated arylglycerol has yet been described, and it was of interest, therefore, to study the properties of typical members of the class.

$\alpha\gamma$ -Diphenylglycerol, the simplest member of the series related to the natural flavones, flavonols, and anthocyanidins, was prepared by Bigelow, Rule, and Black (J., 1935, 83) by catalytic reduction of diphenyl triketone, and obtained as colourless needles or prisms, m. p. 84.5—85°, which readily formed a monohydrate, m. p. 97—99°. A benzene solution of the glycerol, shaken with concentrated sulphuric acid, gave a characteristic bright red coloration, and the solid compound dissolved in sulphuric acid to a brilliant purple solution. The triacetate formed plates, m. p. 85—86°. Two other forms of this glycerol have now been obtained by the methods described below.

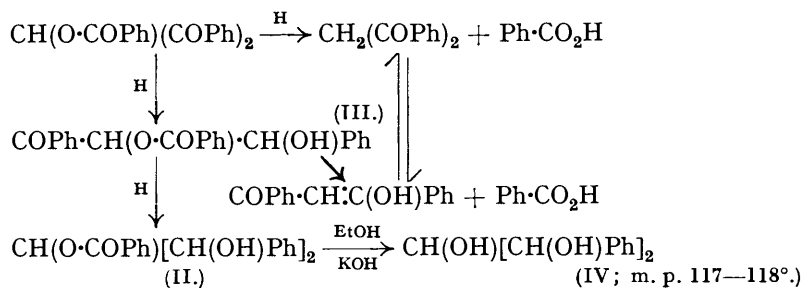
(a) Benzoyl peroxide (1 mol.) reacted with a cold benzene suspension of the sodium salt of dibenzoylmethane (1 mol.) to form ω -benzoyloxy- ω -benzoylacetophenone (I) and benzoic acid (1.1 mols.) (cf. Bradley and Robinson, J., 1928, 1543) :



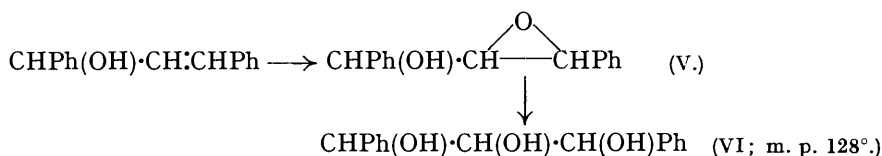
Catalytic reduction of (I) afforded β -O-benzoyl- $\alpha\gamma$ -diphenylglycerol (II) in poor yield, together with dibenzoylmethane, benzoic acid, and other products. The highest yields of (II) were obtained when 5 mols. of hydrogen had been absorbed, a circumstance which indicates the occurrence of side reactions. A monoketone (III) could be isolated when 2 mols. of hydrogen had been taken up. The formation of dibenzoylmethane and benzoic acid is probably to be regarded as an instance of ester "hydrogenolysis" (cf. Covert, Connor, and Adkins, *J. Amer. Chem. Soc.*, 1932, 54, 1651). Alternatively, the monoketone (III) may lose the elements of benzoic acid.

Hydrolysis of the benzoyl derivative (II) with alcoholic potassium hydroxide gave a form of $\alpha\gamma$ -diphenylglycerol, m. p. 117—118° (IV). Unlike Bigelow, Rule, and Black's compound (*loc. cit.*), this second form shows no tendency to hydration, and the colour of its sulphuric acid solution is brown.

(b) Phenylstyrylcarbinol and perbenzoic acid afforded an *oxide* (V), from which a third form of $\alpha\gamma$ -diphenylglycerol (VI), m. p. 128°, was obtained by hydrolysis with dilute

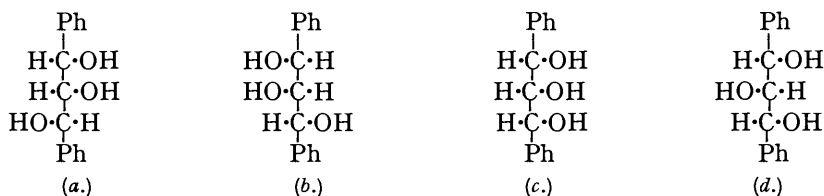


sulphuric acid. This resembled the form of m. p. 117—118° in showing no tendency to hydration, and in the brown colour of its solution in sulphuric acid. A mixture of these two forms melted at 98°. The higher-melting form affords a *triacetate*, m. p. 129—130°

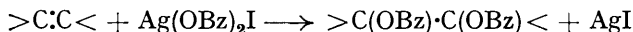


Configurations of the Diastereoisomeric $\alpha\gamma$ -Diphenylglycerols.—As indicated by Rule *et al.* (*loc. cit.*), $\alpha\gamma$ -diphenylglycerol must be capable of existing in a racemic form, and in two internally compensated forms. In the absence of sufficient data it is not possible to assign irrefutable configurations to the three isolated forms, but analogies exist which strongly suggest the structures of two.

In its low m. p., and in its ability to form a hydrate, Bigelow, Rule, and Black's form of m. p. 84.5—85° resembles the closely related *isohydrobenzoin*, which has a lower m. p. than hydrobenzoin, and, unlike the latter, exists in a hydrated form [hydrobenzoin : m. p. 134°, Forst and Zincke, *Annalen*, 1876, **182**, 286; m. p. 137—138°, Ciamician and Silber, *Ber.*, 1910, **43**, 948; *isohydrobenzoin* : m. p. 121°, *idem*, *Ber.*, 1901, **34**, 1539; m. p. 119—120° (anhydrous), m. p. 95—96° (hydrated), Forst and Zincke, *ibid.*, p. 279]. This $\alpha\gamma$ -diphenylglycerol may therefore be regarded as the racemic form (*a*, *b*).

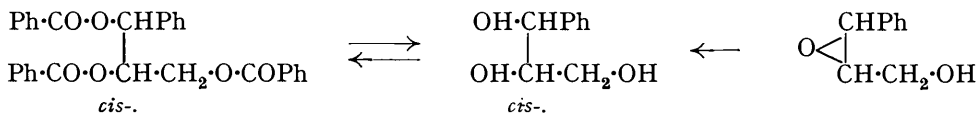


Of the two remaining configurations, (*c*) probably represents the $\alpha\gamma$ -diphenylglycerol, m. p. 128°, since this is obtained by hydrolysing an α -oxide. Instances are available of the production of a *trans*-1 : 2-diol by acid hydrolysis of an α -oxide. For example, Kuhn and Ebel (*Ber.*, 1925, **58**, 919) obtained both *dl*- and *meso*-tartaric acid from *cis*-dicarboxyethylene oxide. In the present case, however, the product is likely to be a *cis*-1 : 2-diol for the following reason. Prévost (*Compt. rend.*, 1934, **197**, 1661) found that the complex, Ag(OBz)₂I, obtained by treating silver benzoate with iodine, would react with ethylenic compounds to form the related ethylene dibenzoates :

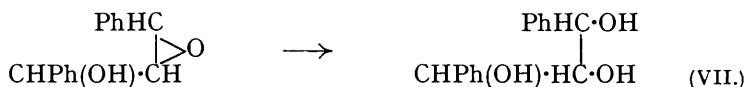


The main product was the *trans*-isomeride. When the reaction was applied to cinnamyl benzoate (Prévost and Lossen, *ibid.*, **198**, 659), the main product (yield, 85%) was an

α -phenylglyceryl tribenzoate, m. p. 116.5°, which was therefore regarded as the *trans*-compound. An isomeride (*cis*-) was formed simultaneously in much smaller amount (15%). The latter melted at 152° and gave on hydrolysis the *cis*-form of α -phenylglycerol, m. p. 99.5°. The same α -phenylglycerol, m. p. 98—99°, has also been obtained by hydrolysing α -phenylglycidol (Platt and Hibbert, *Canadian J. Res.*, 1932, 7, 629). In this instance, therefore, hydrolysis of an α -oxide affords the *cis*-form of the derived 1 : 2-diol. We have confirmed the identity of the α -phenylglycerol obtained from phenylglycidol with the *cis*-form described by Prévost and Lossen (*loc. cit.*), since the former, too, affords a tribenzoate, m. p. 151—152°.



The $\alpha\gamma$ -diphenylglycerol, m. p. 128°, was obtained analogously by hydrolysing the oxide of phenylstyrylcarbinol, and is therefore to be regarded as a *cis*-1 : 2-diol (VII).



Configuration (*d*) remains to represent the $\alpha\gamma$ -diphenylglycerol, m. p. 117—118°.

EXPERIMENTAL.

ω -Benzoyloxy- ω -benzoylacetophenone (I).—Dibenzoylmethane (45 g.) was converted into the sodium derivative by heating it in dry benzene (150 c.c.) with powdered sodium (4.5 g.). The suspension was stirred while a solution of benzoyl peroxide (48.4 g.) in benzene (550 c.c.) was added slowly during 2.5 hours, the temperature being kept below 10°, and access of moisture being prevented. After being stirred for a further 6 hours and then kept overnight, the suspension was neutral to phenolphthalein. It was shaken with water (100 c.c., 40 c.c., 40 c.c.), and the aqueous solutions united, washed with benzene, and acidified. The yield of benzoic acid was 22.0 g. [Calc. for equation (1), 19.9 g.]. The benzene solution contained 8.9 g. of unreacted benzoyl peroxide, and this was decomposed by adding sodium iodide (23 g.) dissolved in a mixture of acetone (130 c.c.) and glacial acetic acid (20 c.c.). The liberated iodine was removed by shaking with aqueous sodium thiosulphate. The benzene layer was washed with sodium carbonate solution, then with water, and finally dried over calcium chloride. Evaporation of the solvent afforded successive crops of crystals, m. p. 92—94°, which were further purified from alcohol; yield 38 g., m. p. 96—97°. ω -Benzoyloxy- ω -benzoylacetophenone crystallises from alcohol in colourless needles, m. p. 97° (Found: * C, 76.5; * H, 4.6; *M*, 338. $\text{C}_{22}\text{H}_{16}\text{O}_4$ requires C, 76.7; H, 4.7%; *M*, 344). It dissolved in concentrated sulphuric acid to a golden-yellow solution. It neither gave a coloration with ferric chloride, nor formed a copper derivative, but it reduced Fehling's solution on warming.

β -Hydroxy- α -benzoyloxy- β -phenylpropiophenone (III).—A suspension of platinum oxide (Adams; 0.2 g.) in ethyl acetate (100 c.c.) containing ω -benzoyloxy- ω -benzoylacetophenone (12 g.) was stirred in hydrogen for 6 hours, during which 2000 c.c. of the gas were absorbed at 20°/748 mm. Evaporation of the filtered solution gave crystals (6 g.), m. p. 118—123°, and finally a viscous oil from which benzoic acid separated. The oil gave a red coloration with ferric chloride, and a green copper derivative separated when an ethereal solution was shaken with aqueous copper acetate. Recrystallised from benzene, the copper derivative had m. p. 293—294°, not depressed by that of dibenzoylmethane, m. p. 295—297°. The material, m. p. 118—123°, gave small colourless prisms, m. p. 137°, after several crystallisations from benzene (Found: * C, 76.7; * H, 5.4. $\text{C}_{22}\text{H}_{18}\text{O}_4$ requires C, 76.3; H, 5.2%). β -Hydroxy- α -benzoyloxy- β -phenylpropiophenone was moderately soluble in alcohol and in benzene, very sparingly in water and in light petroleum. It gave a pale yellow precipitate with an aqueous solution of 2 : 4-dinitrophenylhydrazine hydrochloride. In the cold it was stable to Fehling's solution, but on warming, the reagent was slightly reduced, benzaldehyde being formed.

β -O-Benzoyl- $\alpha\gamma$ -diphenylglycerol (II).— ω -Benzoyloxy- ω -benzoylacetophenone (12 g.) was reduced in ethyl acetate solution (100 c.c.) in contact with platinum oxide (0.22 g.), 4065 c.c. of hydrogen being absorbed at 20°/748 mm. When the filtered solution was allowed to evapor-

ate, crystals (3.5 g.) separated. Recrystallisation from benzene gave material, m. p. 154—155°. The mother-liquor deposited crystals, m. p. 165—166°. The m. p. of the first fraction remained almost unchanged after several crystallisations from alcohol; colourless, stout prisms, m. p. 154.5—155.5°, were obtained (Found: † C, 75.8; † H, 6.0; *M*, 347. $C_{22}H_{20}O_4$ requires C, 75.9; H, 5.8%; *M*, 348). The compound was moderately soluble in benzene, more easily in alcohol, sparingly in ether, water, or light petroleum. It was stable to hot Fehling's solution. There was no reaction with an aqueous acid solution of 2:4-dinitrophenylhydrazine. It dissolved in concentrated sulphuric acid to a colourless solution.

α -Diphenylglycerol, m. p. 117—118° (IV).—0.15 G. of the *O*-benzoyl derivative (II) was dissolved in alcohol (2 c.c.) and boiled for 3 hours with 30% alcoholic potassium hydroxide (1 c.c.). Estimation of the amount of potassium hydroxide consumed indicated that hydrolysis was then complete. The solution was neutralised with hydrochloric acid and evaporated to dryness. The residue was extracted with benzene and the solution evaporated. An oil remained and this was extracted with hot water. The colourless, filtered solution gave crystals, m. p. 113—116°, on cooling. Recrystallisation from acetone–light petroleum gave material, m. p. 114—117°, and this was twice crystallised from water; colourless prisms, m. p. 117—118°, were obtained (Found: * C, 73.7; * H, 6.6. $C_{15}H_{16}O_3$ requires C, 73.8; H, 6.6%). This form of α -diphenylglycerol shows no tendency to hydration. It is sparingly soluble in light petroleum, more readily soluble in acetone and in water. It dissolves in concentrated sulphuric acid with a brown colour. It is unaffected by boiling Fehling's solution.

α -Diphenylglycerol, m. p. 128°.—Phenylstyrylcarbinol was prepared by adding freshly distilled cinnamaldehyde (12.5 g.) to the Grignard reagent prepared from bromobenzene (23.5 g.) (cf. Kohler, *Amer. Chem. J.*, 1904, **31**, 660; Nomura, *Bull. Soc. chim.*, 1925, **37**, 1245). The reaction product was decomposed with ice and dilute sulphuric acid, and the carbinol extracted with ether. The extract was washed with aqueous sodium bisulphite, then with sodium bicarbonate, and finally with water until neutral. If the solvent was removed without delay, the residue crystallised. If, however, the solution was kept for a few hours before evaporation, only syrupy material could be obtained. The crystalline carbinol was washed with light petroleum, and dried on porous tile. Recrystallisation from the same solvent gave slender prisms, m. p. 56—57°, as described by Nomura (*loc. cit.*); yield, 10.6 g.

Perbenzoic acid (7 g.), dissolved in chloroform (150 c.c.), was added during 1 hour to a solution of phenylstyrylcarbinol (10.5 g.) in chloroform (50 c.c.), which was stirred at 0°. Only a trace of perbenzoic acid remained after the reactants had been kept for 24 hours. The solution was washed with 10% sodium hydroxide, then with water, and finally dried over sodium sulphate. When the solvent was evaporated at 40°, a colourless oil remained, and this was dissolved in alcohol (10 c.c.) and added through a capillary tube to 0.02*N*-hydrochloric acid (80 c.c.), which was stirred at 0°. The addition required 2 hours, and stirring was continued for 40 hours longer. The product consisted of colourless crystals, and an oil which contained benzaldehyde. The crystalline material was collected and washed with a little benzene; yield, 4.4 g., m. p. 115—120°. A further quantity (0.2 g., m. p. 122—124°) separated when the neutralised aqueous solution was kept. Crystallisation from benzene and then from water gave colourless prisms, m. p. 128° (Found: C, 73.7; H, 6.4; *M*, 253. $C_{15}H_{16}O_3$ requires C, 73.8; H, 6.6%; *M*, 244). This form of α -diphenylglycerol is very sparingly soluble in light petroleum, moderately soluble in acetone and in benzene, readily in alcohol and in ether. It dissolves in water to give a 1% solution at the ordinary temperature. It is stable to boiling Fehling's solution, and, like the form of m. p. 117—118°, it dissolves in concentrated sulphuric acid with a brown colour and shows no tendency to form a hydrate. A mixture of the two forms melted at 98°. Benzaldehyde, which was encountered in the preparation of the glycerol, did not appear to have been formed at the oxidation stage, but during the subsequent treatment with acid. It resulted no doubt by fission of α -diphenylglycerol, which with dilute mineral acids yields benzaldehyde and a crystalline solid, probably benzoylcarbinol.

O-Triacetyl- α -diphenylglycerol, m. p. 129—130°.— α -Diphenylglycerol (0.5 g.), m. p. 128°, was boiled for 30 minutes with acetic anhydride (10 c.c.) and fused sodium acetate (1 g.). The product (0.74 g.), which separated when water was added to the cooled solution, was recrystallised from alcohol, affording colourless plates, m. p. 129—130° (Found: * C, 68.1; * H, 6.0; CH_3CO , 35.6. $C_{21}H_{22}O_6$ requires C, 68.1; H, 6.0; CH_3CO , 34.9%).

O-Tribenzoyl- α -phenylglycerol, m. p. 154°.— α -Phenylglycerol, obtained by hydrolysing α -phenylglycidol (Platt and Hibbert, *loc. cit.*), is most easily purified by crystallisation from acetone. Benzoyl chloride (8.5 g.) was added in successive small amounts to an agitated

* Analyses by Dr. Ing. A. Schoeller.

† Analysis by Dr. G. Weiler.

suspension of α -phenylglycerol (3.4 g.) in 10% aqueous sodium hydroxide (15 c.c.). The slight excess of benzoyl chloride was removed by adding more dilute sodium hydroxide. The crystalline product (m. p. 145—146°), further purified from alcohol, was obtained as colourless prisms, m. p. 151—152° (Found: * C, 74.9; * H, 5.1. Calc. for $C_{30}H_{24}O_6$: C, 75.0; H, 5.0%).

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