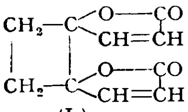
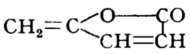
169. *Experiments in the* cyclo*Butane Series. Part I.*

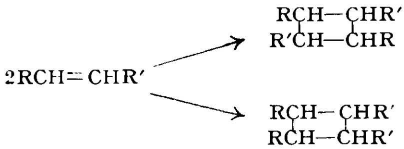
By K. B. Alberman and F. B. Kipping.

The carbinols are described which result from the action of phenylmagnesium bromide and methylmagnesium iodide on the diethyl esters of *cis-* and *trans-cyclo*butane-1 : 2-dicarboxylic acids. Complete dehydration to a diolefin was achieved in only one case, and experiments on the ozonolysis of this compound are reported.

Anemonin has been assigned the structure (I) (Asahina and Fujita, *Acta Phytochim.*, 1922, **1**, 1; *Chem. Zentr.*, 1922, **3**, 712) on the basis of degradation experiments, but no *cyclo*butane derivative has been obtained from it nor has it been synthesised; it is formed by the dimerisation of protoanemonin (II), the structure of which is firmly based on degradation and synthesis (Kipping, *J.*, 1935, 1145; Shaw, *J. Amer. Chem. Soc.*, 1946, **68**, 2510). It seems very probable that a *cyclo*butane ring is indeed produced in the dimerisation and numerous examples of this phenomenon are known. In most recorded cases of the dimerisation of ethylenic compounds, however, the reaction proceeds in such a way that the product is of type (III) rather than of type (IV).

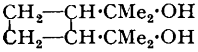

(I.)

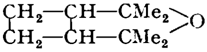

(II.)

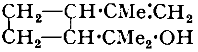

(III.)
(IV.)

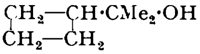
Examples of this are the dimerisation of cinnamic acid to truxillic acid and of ethyl methylenemalonate to tetraethyl *cyclo*butane-1 : 1 : 3 : 3-tetracarboxylate: such a mode of reaction would be expected on general grounds. On the other hand, Lebedeff (*J. Russ. Phys. Chem. Soc.*, 1911, **43**, 820) obtained 1 : 2-di*iso*propylidene*cyclo*butane by the dimerisation of 1 : 1-dimethylallene. By ozonolysis, 2-*iso*propylidene*cyclo*butanone was formed and this on further oxidation gave succinic anhydride. Nevertheless, it seemed of interest to re-examine this diolefin and others of a similar type since they seemed to be possible intermediates for the synthesis of anemonin from a derivative of *cyclo*butane. The preparation of 1 : 1-dimethylallene is, however, unsuited to large-scale operation and the subsequent yield of dimeride is only 5%. The comparatively ready availability of the *cyclo*butane-1 : 2-dicarboxylic acids (Buchman, Reims, Skei, and Schlatter, *J. Amer. Chem. Soc.*, 1942, **64**, 2996) suggested that 1 : 2-di*iso*propylidene*cyclo*butane and other similar compounds could be easily made by the dehydration of the ditertiary alcohols resulting from the reaction of Grignard reagents on the diesters of these acids. *cis-cyclo*Butane-1 : 2-dicarboxylic anhydride was therefore prepared by the above-mentioned method and thence the *trans*-acid by Perkin's method (*J.*, 1894, **65**, 572); the *cis-* and *trans*-diethyl esters were then prepared in the usual way.

Both esters readily gave the respective carbinols (V) with methylmagnesium iodide, but neither could be dehydrated to a diolefin. The *cis*-carbinol gave the tetrahydrofuran (VI), whilst the *trans*-form, from which the formation of a furan would be impossible, also lost only


$$\begin{array}{l} CH_2-CH\cdot CMe_2\cdot OH \\ CH_2-CH\cdot CMe_2\cdot OH \end{array}$$
(V.)


$$\begin{array}{l} CH_2-CH-CMe_2 \\ CH_2-CH-CMe_2 \end{array}\!\!>O$$
(VI.)


$$\begin{array}{l} CH_2-CH\cdot CMe{:}CH_2 \\ CH_2-CH\cdot CMe_2\cdot OH \end{array}$$
(VII.)

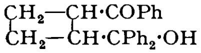

$$\begin{array}{l} CH_2-CH\cdot CMe_2\cdot OH \\ CH_2-CH_2 \end{array}$$
(VIII.)

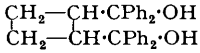
one molecule of water giving probably (VII). The infra-red spectra and the chemical properties support the structures (VI) and (VII), but it is possible that, in the case of the *trans*-isomeride, changes in the ring system have occurred [cf. Chavanne and Chiurdoglu, *Bull. Soc. chim. Belg.*, 1942, **51**, 11, who studied the dehydration of (VIII)].

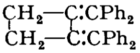
As the methylcarbinols were therefore unsuited to the object in view, attention was directed to the corresponding phenyl compounds since the dehydration of *cyclo*butyldiphenylcarbinol was known to proceed normally (Kishner, *Chem. Zentr.*, 1911, I, 544) : in this case, the *cis*-ester reacted with only three molecules of phenylmagnesium bromide to give (IX) in poor yield, but the *trans*-isomeride reacted in the usual way giving (X) in good yield.

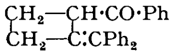
The difference in behaviour between the two esters towards phenylmagnesium bromide, both with regard to the products formed and to the yields obtained, can be ascribed to the considerable steric hindrance associated with the *cis*-configuration. 1 : 2-*trans*-di(hydroxydiphenylmethyl)*cyclo*butane (X) was readily dehydrated by iodine in boiling xylene (Hibbert, *J. Amer. Chem. Soc.*, 1915, **37**, 1748) or, better, by heating it with concentrated hydrochloric acid in glacial acetic acid (Wittig and von Lupin, *Ber.*, 1928, **61**, 1627), and yielded the desired hydrocarbon (XI); and similarly the *cis*-carbinol (IX) gave (XII). The hydrocarbon (XI) formed clusters of fine yellow needles which exhibited an intense green fluorescence under ultra-violet light.

The ultra-violet absorption spectra of these compounds have been examined, and a discussion of the results and their bearing on the configuration and degree of conjugation present in the compounds involved will be communicated elsewhere.

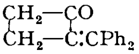

$$\begin{array}{l} CH_2-CH\cdot COPh \\ CH_2-CH\cdot CPh_2\cdot OH \end{array}$$
(IX.)

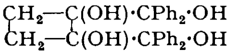

$$\begin{array}{l} CH_2-CH\cdot CPh_2\cdot OH \\ CH_2-CH\cdot CPh_2\cdot OH \end{array}$$
(X.)


$$\begin{array}{l} CH_2-C{:}CPh_2 \\ CH_2-C{:}CPh_2 \end{array}$$
(XI.)


$$\begin{array}{l} CH_2-CH\cdot CO\cdot Ph \\ CH_2-C{:}CPh_2 \end{array}$$
(XII.)

Ozonolysis of (XI) yielded different products according to the conditions employed. With a short ozonolysis at −15°, it was possible to isolate the ketone (XIII) in small yield, in addition to benzophenone. With complete ozonolysis at −5°, the only products which could be isolated were benzophenone and succinic acid, as well as a small amount of crystalline material which


$$\begin{array}{l} CH_2-CO \\ CH_2-C{:}CPh_2 \end{array}$$
(XIII.)


$$\begin{array}{l} CH_2-C(OH)\cdot CPh_2\cdot OH \\ CH_2-C(OH)\cdot CPh_2\cdot OH \end{array}$$
(XIV.)

was apparently the tetrol (XIV). These findings agree substantially with those of Lebedeff for the ozonolysis of 1 : 2-di*iso*propylidene*cyclo*butane. As it seemed that *cyclo*butane-1 : 2-dione could not be prepared by ozonolysis or otherwise from such starting materials, other methods for the synthesis of anemonin are being investigated.

EXPERIMENTAL.

(M. p.s are corrected; b. p.s are uncorrected.)

cis-cyclo*Butane*-1 : 2-*dicarboxylic Anhydride*.—A mixture of dimethyl (±)- and *meso*dibromoadipates (2150 g.) gave the anhydride (220 g.; overall yield, 26%) (Buchman, Reims, Skei, and Schlatter, *loc. cit.*).

trans-cyclo*Butane*-1 : 2-*dicarboxylic Acid*.—The *cis*-anhydride (10 g.) and concentrated hydrochloric acid (15 c.c.) were heated at 190° overnight (Perkin, *J.*, 1894, **65**, 572). The crude *trans*-acid was recrystallised from concentrated hydrochloric acid with the addition of charcoal, giving acid (6 g.) of m. p. 130—131°.

Diethyl cis-cyclo*Butane*-1 : 2-*dicarboxylate*.—Dry hydrogen chloride was passed through a solution of the *cis*-anhydride (50 g.) in absolute ethanol (200 c.c.) during 3½ hours, the mixture being allowed to reflux gently. It was then poured into water (500 c.c.). A little carbon tetrachloride was added, the ester layer separated, and the aqueous layer extracted twice with carbon tetrachloride. The combined extracts were washed with sodium carbonate solution and with water and dried ($CaCl_2$). After removal of the solvent, the ester was distilled *in vacuo*, having b. p. 85°/0·5 mm. (47 g., 59%).

Diethyl trans-cyclo*Butane*-1 : 2-*dicarboxylate*.—This was prepared from the *trans*-acid in the usual way : 88 g. of acid yielded 99 g. of ester (91%), b. p. 100°/4 mm. The unused acid from the aqueous solution and washings was recovered by acidification, evaporation to dryness, and extraction with acetone.

cis-1 : 2-*Di* (*2-hydroxy-2-propyl*)cyclo*butane* (V).—An ethereal solution of *cis*-ester (20 g., 0·1 mole) was added dropwise to a Grignard solution (from methyl iodide, 70 g.; 0·5 mole) during thirty minutes, the heat of the reaction causing the ether to reflux vigorously. After a further hour's refluxing, the mixture was added to crushed ice (500 g.) and ammonium chloride (150 g.). The ethereal layer was separated and the aqueous layer extracted with two 150-c.c. portions of ether. The combined ethereal solutions were washed once with 20% sodium carbonate solution, twice with water, and dried overnight (Na_2SO_4); evaporation of the solvent left a viscous yellow oil which crystallised as clusters of needles (16 g., 93%). The *carbinol* was recrystallised from light petroleum (b. p. 40—60°) from which it was obtained as colourless needles, m. p. 62·5° (Found : C, 69·6; H, 11·75. $C_{10}H_{20}O_2$ requires C, 69·8; H, 11·6%).

(±)-trans-1 : 2-*Di*-(*2-hydroxy-2-propyl*)cyclo*butane* was prepared from the *trans*-ester in the same manner (yield, 80%). It crystallised from light petroleum (b. p. 40—60°) as colourless blades, m. p. 94° (Found : C, 69·35; H, 11·5. $C_{10}H_{20}O_2$ requires C, 69·8; H, 11·6%).

Dehydration of the cis-*Carbinol* (V).—The carbinol (3 g.) was refluxed with aqueous oxalic acid (100 c.c.; 6%) during 6 hours. The mixture had now separated into an oily deep-yellow upper layer and a turbid aqueous lower layer. The whole was twice extracted with ether, and the combined extracts were washed successively with sodium carbonate solution and water, then dried ($CaCl_2$), and the ether was removed. The residual yellow oil (3 g.) was distilled under oxygen-free nitrogen and obtained as a colourless mobile liquid with a camphor-like odour, b. p. 57°/20 mm., 67—68°/25 mm. (Found : C, 78·0; H, 11·7. $C_{10}H_{18}O$ requires C, 77·9; H, 11·7%). *Tetrahydro*-2 : 2 : 5 : 5-*tetramethyl*-3 : 4-cyclo*butanofuran* (VI) decolourised bromine and permanganate but was not reduced when shaken with hydrogen and palladium at atmospheric pressure.

Dehydration of the trans-*Carbinol* (V).—To the carbinol (17·5 g.), in a 50-c.c. Claisen flask fitted with an 8-cm. Vigreux column and connected to a water-condenser and a cooled receiver, iodine (85 mg.) was added and the temperature slowly raised. Water began to be evolved at 140° and a yellow mobile liquid distilled at 200°. A small amount of dark residue remained, although the distillation had been carried out under nitrogen. The dried distillate [? 1-(*2-hydroxy-2-propyl*)-2-iso*propenyl*cyclo*butane*] had b. p. 83—85°/14 mm. and was a colourless liquid with an odour similar to that of the product obtained by the dehydration of the *cis*-isomeride. It decolourised bromine and permanganate (Found : C, 76·6; H, 11·5. $C_{10}H_{18}O$ requires C, 77·9; H, 11·7%). The infra-red absorption spectrum of this compound showed bands at 890 and 1645 cm.$^{-1}$, characteristic of the grouping $>C{=}CH_2$. The dehydration product of the *cis*-carbinol did not show these bands but possessed two absorption bands of equal strength at *ca.* 1375 cm.$^{-1}$, indicative of the presence of two $>CMe_2$ groupings, and not one $\gg CMe$ and one $>CMe_2$.

(±)-2-*Benzoyl*-1-(*a-hydroxydiphenylmethyl*)cyclo*butane* (IX).—A solution of *cis*-ester (5 g., 0·025 mole) in anhydrous ether (20 c.c.) was added dropwise during 30 minutes to a Grignard solution prepared from bromobenzene (19·6 g., 0·125 mole) and magnesium (3·1 g.) in ether (75 c.c.). The yellow solution was refluxed for a further hour and then poured on ice and ammonium chloride as previously described. After removal of the ether, the crude *carbinol* was steam-distilled to remove diphenyl and then recrystallised from alcohol, forming clusters of colourless needles, m. p. 162·5° (1 g., 12%) (Found : C, 84·0; H, 6·4. $C_{24}H_{22}O_2$ requires C, 84·2; H, 6·4%).

(±)-2-*Benzoyl*-1-*diphenylmethylene*cyclo*butane* (XII).—The carbinol (IX) (1 g.) was dissolved in glacial acetic acid (12 c.c.), and concentrated hydrochloric acid (2 c.c.) was added. The mixture was boiled under reflux during 10 minutes, becoming greenish and turbid. The *ketone* was precipitated on cooling as fine colourless needles which, recrystallised from alcohol, had m. p. 94—95° (0·7 g., 78%) (Found : C, 89·05; H, 6·45. $C_{24}H_{20}O$ requires C, 88·9; H, 6·1%). Absorption in ethanol : Max., 2510—2520 and 3220—3250 A.; ε = 25,000 and 400, respectively.

The *oxime* crystallised from alcohol as small colourless prisms m. p. 149° (decomp.) (Found : C, 84·6; H, 6·5; N, 4·5. $C_{24}H_{21}ON$ requires C, 85·0; H, 6·2; N, 4·1%).

(±)-trans-1 : 2-*Di*-(*a-hydroxydiphenylmethyl*)cyclo*butane* (X) was prepared, in the same way as (IX), from the *trans*-ester (10 g., 0·05 mole), bromobenzene (39·25 g., 0·25 mole), and magnesium (6·2 g.). It crystallised from alcohol in stout hexagonal prisms, m. p. 180—181° (19·6 g., 93·5%) (Found : C, 85·9; H, 6·9. $C_{30}H_{28}O_2$ requires C, 85·7; H, 6·7%).

1 : 2-*Bisdiphenylmethylene*cyclo*butane* (XI).—A mixture of the carbinol (X) (15 g.), glacial acetic acid (250 c.c.), and concentrated hydrochloric acid (25 c.c.) was boiled under reflux during 1 hour. The mixture first became yellow, and then yellow needles were precipitated which after recrystallisation from alcohol–benzene (charcoal) gave the *diolefin* as fine pale yellow needles, m. p. 183—184° (9·2 g., 70%) (Found : C, 93·5; H, 6·6. $C_{30}H_{24}$ requires C, 93·75; H, 6·25%). Absorption in ethanol : Max., 2580 and 3510 A.; ε = 23,000 and 21,400, respectively.

Ozonolysis of (XI).—(i) The diolefin (5 g.), dissolved in pure anhydrous chloroform (30 c.c.), was cooled in ice–salt to −15° and ozonized oxygen (3% by wt.) was passed through during 5 hours : the colour, originally orange, had become pale yellow but no solid ozonide separated. The solution was then treated with water (5 c.c.), zinc dust (0·5 g.), and traces of silver nitrate and quinol (cf. Clark, Whitmore, and McGrew, *J. Amer. Chem. Soc.*, 1934, **56**, 177). After removal of the chloroform, the residual oil was separated from the aqueous layer and washed with water which was added to the aqueous layer.

The aqueous layer was neutral to litmus and gave no precipitate on being treated with semicarbazide hydrochloride and sodium acetate.

The non-aqueous layer was again taken up in chloroform, the solution filtered, and the solvent evaporated, giving a red oil which partly crystallised when kept. The crystals gave a green fluorescence under ultra-violet light, indicating the presence of unchanged starting material. The mixture of oil and crystals was then extracted with light petroleum (b. p. 60—80°), and a little of the solution poured on a small alumina column. Five fractions were taken, the column being developed with benzene for the first three and with ethyl acetate for the others.

Fraction	1	2	3	4	5
Volume (c.c.)	20	50	40	50	100
Colour	yellowish green	pale green	colourless	yellow	pale yellow

Fraction (1), after evaporation of the solvent, left a yellow oil which partly crystallised when kept. The crystals, after being pressed on a porous tile, gave the intense green fluorescence characteristic of the starting material. Removal of solvent from fraction (2) left only a trace of material which was combined with the first fraction. The residue from fraction (3) was a minute quantity of a pale yellow oil. This crystallised on being seeded with a small crystal of benzophenone and gave almost colourless needles, m. p. 46—48°. Fraction (4) also consisted of benzophenone, m. p. 43—47°. A sample of benzophenone oxime prepared from fractions (3) and (4) gave a m. p. and mixed m. p. of 144° with an authentic specimen. Fraction (5) left a yellow oil which did not crystallise when seeded with the previous fraction. It was insoluble in water but soluble in alcohol, the yellow solution becoming orange on the addition of alkali.

The remainder of the ozonolysis products originating from the non-aqueous layer were dissolved in chloroform and run on to an alumina column 20 × 30 mm. Most of the material travelled down the column as a deep yellow band which yielded an orange oil after removal of the solvent. This was again taken up in chloroform and run down a small column. The first fraction collected was an orange, partly crystalline syrup. This was washed with alcohol, leaving a fine pale yellow powder, m. p. 132—136° (sintered at 122°). The washings deposited more material which melted at about 100° and possessed the appearance and green fluorescence characteristic of the starting material. The material melting at 132—136° was recrystallised from alcohol, giving 2-*diphenylmethylene*cyclo*butanone* (XIII) as glistening yellow blades, m. p. 140·5° (Found: C, 87·2; H, 6·2. $C_{17}H_{14}O$ requires C, 87·2; H, 6·0%). Absorption in ethanol: Max., 2310 and 3110—3140 A.; ε = 14,600 and 11,200, respectively. The oxime crystallised from alcohol as colourless prisms, m. p. 182—183°.

(ii) The diolefin (5 g.) in anhydrous chloroform (50 c.c.) was ozonised at 0° until titration of the effluent gas showed that an amount of ozone corresponding to two moles had been absorbed: this process required about 10 hours for an initial ozone concentration of about 3%. The originally orange solution had become almost colourless and a crystalline ozonide separated. This was decomposed as previously described and the products separated into aqueous and non-aqueous fractions as before. The aqueous fraction was reddish-brown and was slightly acid. It was extracted with ether which upon evaporation left a pale brown crystalline solid, m. p. 185—186°, mixed m. p. with succinic acid 185—186°. The non-aqueous fraction was a partly crystalline deep-red syrup (4·8 g.) which was washed with alcohol; a colourless residue (0·42 g.) obtained on recrystallisation from chloroform gave 1 : 2-*di*-(*α-hydroxydiphenylmethyl*)cyclo*butane*-1 : 2-*diol* (XIV) as monoclinic prisms, m. p. 192—193° (decomp.) (Found: C, 79·4; H, 5·75. $C_{30}H_{28}O_4$ requires C, 79·7; H, 6·2%).

The remainder of the non-aqueous layer, in alcoholic solution, was poured on an alumina column and eluted with methanol. The first fraction yielded benzophenone (2·8 g., 76% of the theoretical yield allowing for the formation of the tetrol).

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