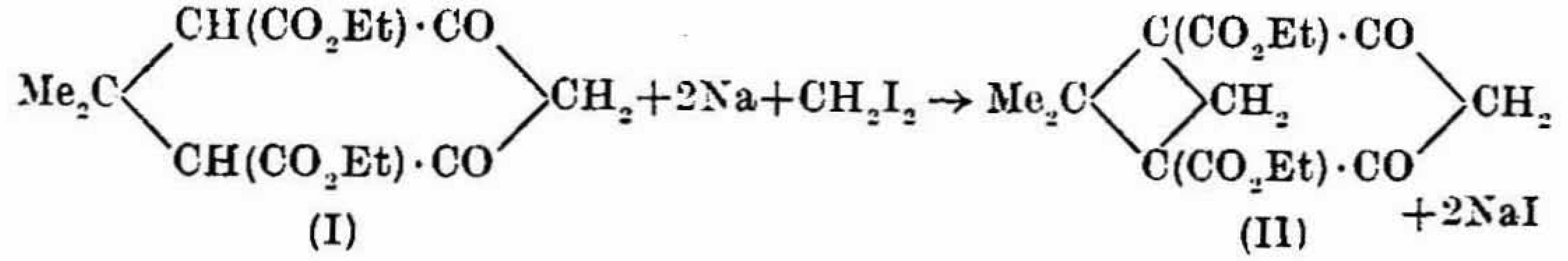
STUDIES IN BRIDGE FORMATION.

PART II. FORMATION AND STABILITY OF A BRIDGED *CYCLO*HEXENONE, 1-DIMETHYLETHANE-$^{1:2:2}$-III-$^{1:4:4}$-*CYCLO*BUTANE-2-ONE.*

By P. S. Mayuranathan and P. C. Guha.

Although the synthesis of carone, fenchone and camphor has long been realised, only one attempted synthesis of nopinone has been recorded (Simonsen and Perkin, *J.C.S.*, 1907, **91**, 1736). Analogous with the synthesis of carone by Baeyer (*Ber.*, 1894, **27**, 1919; 1896, **29**, 6) from dihydrocarvone hydrobromide by treatment with potash, Simonsen and Perkin tried to effect the synthesis of nopinone with the hydrobromide of 4-*iso*propylidene*cyclo*hexanone.

Kerr discovered recently (*J. Amer. Chem. Soc.*, 1929, **51**, 615) the formation of a synthetic bridged ring from the Gaureschi imide and methylene iodide. A similar study was contemplated with Scheiber and Miesel's ester (*Ber.*, 1915, **48**, 238), *viz.*, ethyl *cyclo*hexane-1 : 1-dimethyl-3 : 5-diketo-2 : 6-dicarboxylate (I) expecting a synthetic bridged carbon ring of the type (II), which was to provide an easy step to the synthesis of the dicyclic ketone, nopinone.



$$Me_2C\begin{cases}CH(CO_2Et)\cdot CO\\ CH(CO_2Et)\cdot CO\end{cases}CH_2+2Na+CH_2I_2 \rightarrow Me_2C\begin{cases}C(CO_2Et)\cdot CO\\ C(CO_2Et)\cdot CO\end{cases}CH_2 \quad +2NaI$$

(I) (II)

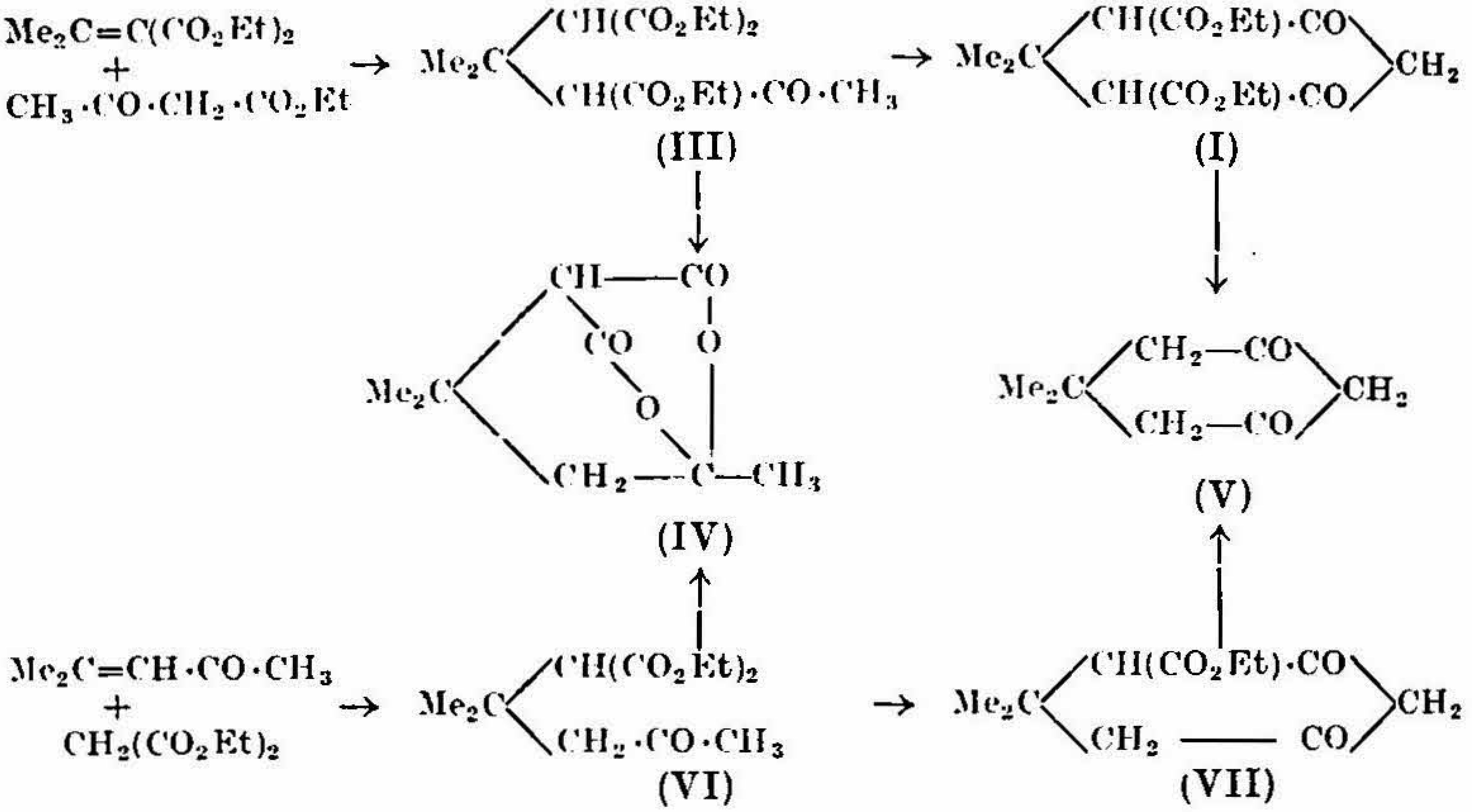
Although the di-ester does not react with methylene iodide to yield the desired bridged product (II), study of the constitution of the starting material by hydrolysis has led to the discovery of a new dicyclic ketone, $C_8H_{10}O$. Applying the nomenclature of Beesley and Thorpe (*J.C.S.*, 1920, **117**, 591) it may be distinguished as 1-dimethylethane $^{1:2:2}$-III-$^{1:4:4}$-*cyclo*butane-2-one. In future, for simplicity, this ketone will be referred to as the bridged *cyclo*hexenone (X).

Scheiber and Miesel (*loc. cit.*) state that *iso*propylidenemalonic ester and acetoacetic ester condense to give ethyl *cyclo*hexane-1 : 1-dimethyl-3 : 5-diketo-2 : 6-dicarboxylate (I), in presence of atomic proportion of sodium. Proof of ring structure was afforded by its conversion on hydrolysis into dimethyldihydroresorcin (V). We find that in presence of traces of sodium ethylate simple addition takes place producing a substituted malonic ester (III), which gives on hydrolysis a dilactone (IV), previously obtained by Vorländer

---

* Preliminary reports on this work were published in the Proceedings of the Indian Science Congress (Chemistry Section, 1931, 159; 1932, 117) and were communicated before 15th October, 1930 and 1931, respectively.

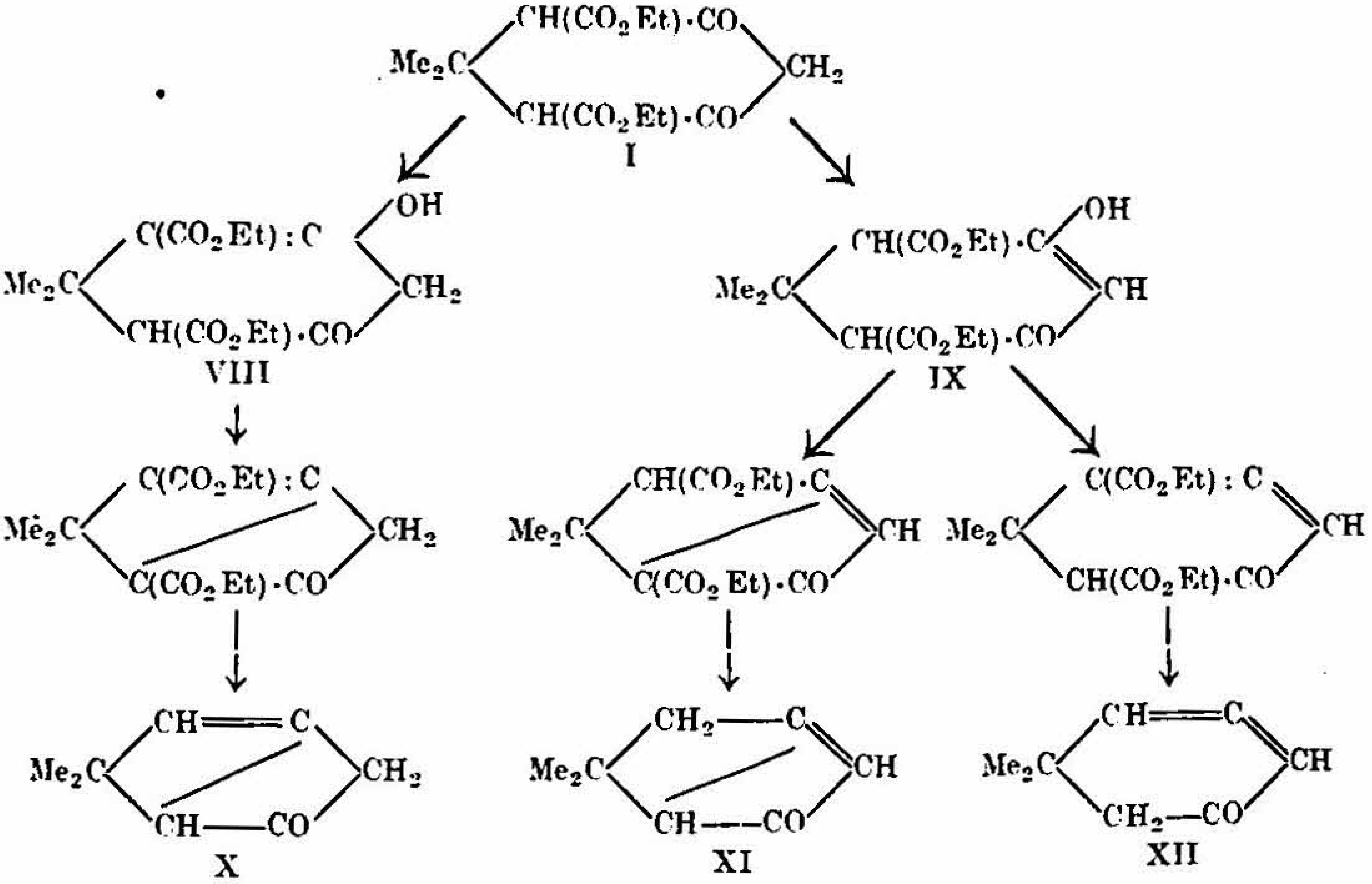
(*Annalen*, 1896, 194, 257) and recently by Khuda (*J.C.S.*, 1929, 201) from the addition product (VI) of mesityl oxide and malonic ester.



Although the open-chain ester (III) was not actually isolated by Scheiber and Miesel they assumed its intermediate formation and conversion on distillation or on treatment with semicarbazide acetate into the ring-closed ester (I). It has now been found that the open-chain ester is not transformed into the ring-closed ester under any of the conditions mentioned above. Conversion of (III) into (I) and (IV), which are compounds of established constitution, supports the structure ascribed to (III).

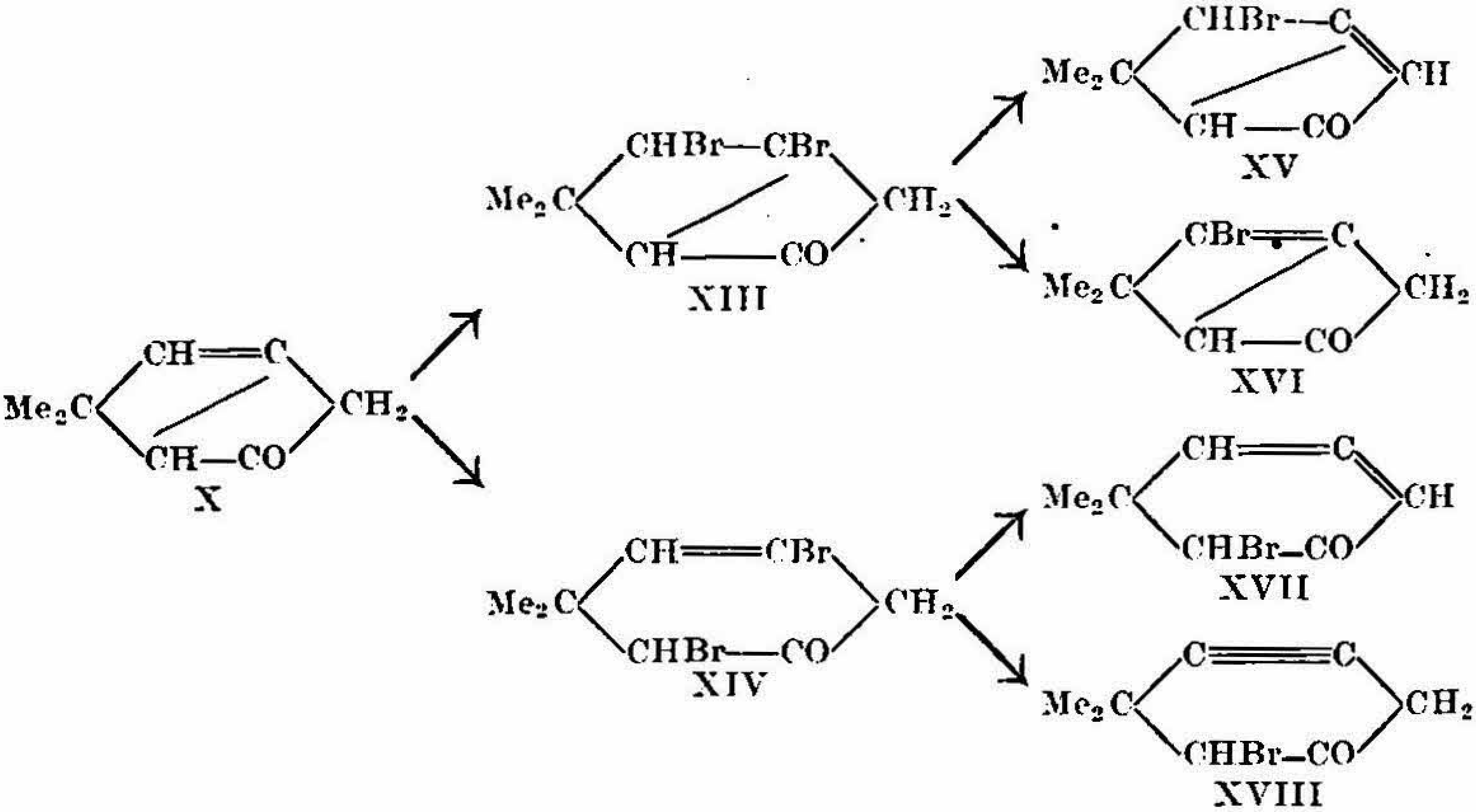
As mentioned before, the ring-closed ester (I) on hydrolysis gives besides dimethyldihydroresorcin the bridged *cyclo*hexenone (X). The condition controlling the exclusive production of the bridged *cyclo*hexenone has now been found to depend on the quantity rather than on the quality of the hydrolysing agent. The bridged *cyclo*hexenone is not acidic. Unlike dimethyldihydroresorcin (V) and its carboxylic esters (I and VII) it does not give colour with ferric chloride, proving its incapacity to enolise. It decolourises an acetic acid solution of bromine and an acetone solution of permanganate, manifesting unsaturation. It corresponds with an empirical formula $C_8H_{10}O$ and gives a semicarbazone. It has a molecular weight of 126 in glacial acetic acid solution thus agreeing with the monomolecular formula (calc. 122) : in benzene, however, the value is almost double (246) showing that the molecules are associated in this solvent. Scheiber and Miesel failed to isolate this interesting ketone, as they hydrolysed the ester to the resorcin with excess of strong baryta, which we find converts the ketone into dimethyldihydroresorcin. The fact that neither Vorländer's mono-ester (VII) (*loc. cit.*) nor dimethyldihydroresorcin gives the bridged *cyclo*hexenone on dehydration proves definitely that the two ester groups in propinquity with the *gem*dimethyl group are responsible for this interesting reaction. The process can be explained by assuming an initial enolisation, followed by loss of one molecule of water from the hydroxyl with a reactive hydrogen atom in the *para*-position. Moreover, enolisation and subsequent dehydration must be assumed to have preceded decarboxylation, as otherwise the entire formation of the bridged *cyclo*hexenone to the exclusion of dimethyldihydroresorcin cannot be explained. If decarboxylation had preceded dehydration, dimethyldihydroresorcin should have been the intermediary, but as mentioned before this cannot be converted into the bridged *cyclo*hexenone. The presence of the two ester groups alone, without the *gem*dialkyl group in the resorcin residue, is insufficient for bridge formation as evidenced by the failure of the phenyl analogue of ester (I), *viz.*, ethyl *cyclo*hexane-1-phenyl-3: 5-diketo-2: 6-dicarboxylate, to give a corresponding bridged *cyclo*hexenone.

At this stage the following three possible formulæ (X, XI and XII) for the bridged *cyclo*hexenone may be considered :

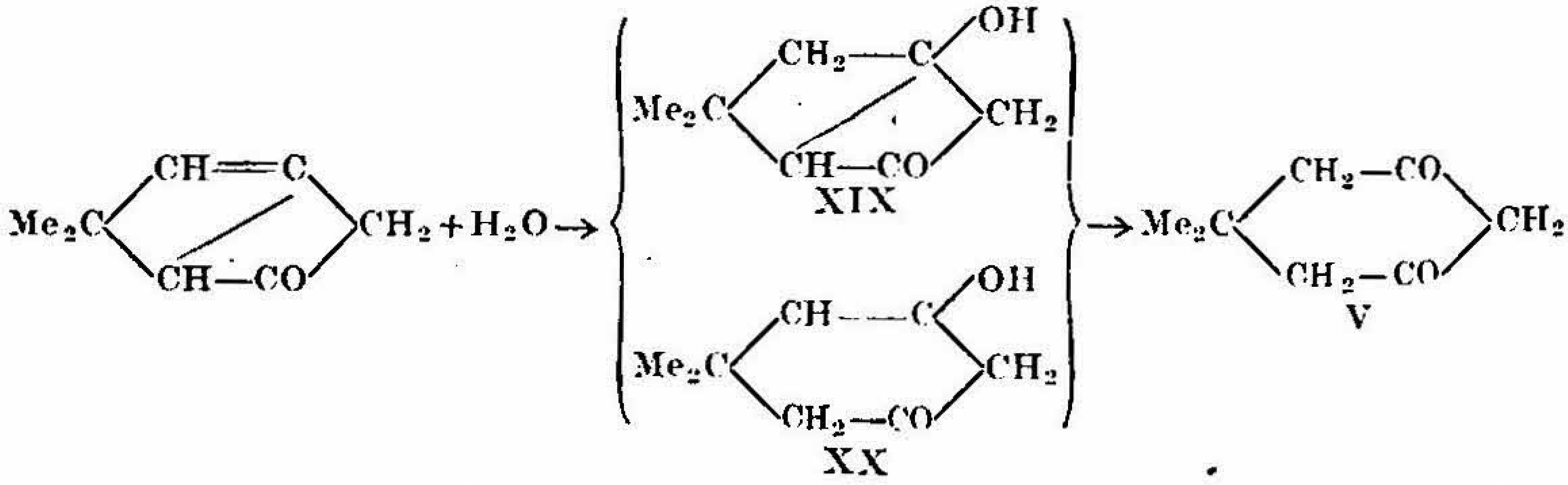


Structure (XII) can be rejected as its existence is contrary to the fundamental conceptions of strain hypothesis. The fact that Vorländer's ester (VII), which to give the bridged *cyclo*hexenone must enolise only as in the phase (IX), does not undergo this type of dehydration indicates the phase (VIII) as more probable: presence of two ester groups in the position adjacent to the dimethylmethylene group thus appears to be indispensable for the reaction. Also the ketonic property of the compound excludes internal ether formation in dimethyldihydroresorcin. Nevertheless, before finally accepting structure (X) it should be stated that there are circumstances in pinene and camphor chemistry to question its stability, though they bear no direct analogy with the present case. It may be mentioned that Ingold succeeded in effecting the synthesis of a similar bridged ring (*J.C.S.*, 1921, 121, 1143) in his attempt to establish the presence of a Dewar phase for orcinol, but he discovered that as soon as formed the compound was rearranged to the Kekulé phase. It is remarkable that the new bridged *cyclo*hexenone does not undergo a similar transformation, and its stability must be ascribed to the influence of the *gem*dimethyl group.

The bridged *cyclo*hexenone takes up two atoms of bromine to give a dibromo-compound which remains unchanged with excess of the halogen. If it is assumed that the bromine is added at the bridged bond instead of the double bond, two more atoms of bromine might readily have been added to yield a tetrabromo-compound. Moreover, removal of hydrogen bromide leads to a monobromo-compound (XV or XVI), either formula for which is more acceptable than the alternative structures (XVII and XVIII):



Probably also addition of water to the bridged *cyclo*hexenone must occur at the double bond giving an unstable intermediate compound (XIX) which later would rearrange itself to dimethyldihydroresorcin (V).



The bridged *cyclo*hexenone resists mild oxidation, and with a boiling solution of alkaline permanganate or cold hypochlorite gives ββ-dimethylglutaric acid besides other acids not isolated. In this connection the oxidation of Perkin and Thorpe's di*cyclo*pentane acid (*J.C.S.*, 1901, **79**, 729) by Farmer and Ingold (*J.C.S.*, 1922, **121**, 128) may be mentioned in which an initial breakdown of the bridged bond by addition of water was supposed, though subsequently rejected. Probably, the bridged *cyclo*hexenone is first transformed into the resorcin which then undergoes oxidation to ββ-dimethylglutaric acid.

Experimental.

Addition of acetoacetic ester to iso*propylidenemalonic ester: Formation of the ester* (III).—*iso*Propylidenemalonic ester (200 g.) and acetoacetic ester (130 g.) were added to a one per cent. solution of sodium ethoxide (300 c.c.). The mixture was heated in a sealed bottle under pressure at 105-110° for 60 hours, and after removing excess of alcohol was acidified with 5 per cent. sulphuric acid and extracted with ether; this was dehydrated by anhydrous magnesium sulphate and removed, when the ester distilled under 5 mm. pressure at 155-158° as a light yellow oil. Yield 30 per cent. (Found: C, 57·8; H, 8·5. $C_{16}H_{26}O_7$ requires C, 58·2; H, 8·0 per cent.).

Hydrolysis of the ester (III) : *Formation of the dilactone* (IV).—The ester (5 g.) was mixed with concentrated hydrochloric acid (25 c.c.) and heated under reflux for 12 hours, the resulting white solid being crystallised from benzene (m.p. 136°; yield. 0·8 g.). Its identity with Vorländer's dilactone was established by mixed melting point (Found: C, 58·5; H. 6·8. $C_9H_{12}O_4$ requires C. 58·7; H. 6·5 per cent.).

Ethyl cyclo*hexane*-1 : 1-*dimethyl*-3 : 5-*diketo*-2 : 6-*dicarboxylate* (I).—A mixture of *iso*propylidenemalonic ester (200 g.), acetoacetic ester (130 g.) and sodium (23 g.) in alcohol (300 c.c.) was boiled for 24 hours on the water-bath. Excess of alcohol was removed, the yellow sodium derivative decomposed with 5 per cent. sulphuric acid and the oil that separated extracted with ether. The crude ester was dissolved in 5 per cent. sodium carbonate, ether extracted and the aqueous layer acidified with 2*N* sulphuric acid. The ester was taken up in ether, dried and the ether removed, the residual brown oil distilling at 190–195° under 4–5 mm. as a thick yellow oil. Yield, 85 per cent. (Found: C, 59·3; H, 7·5. $C_{14}H_{20}O_6$ requires C, 59·2; H. 7·1 per cent.).

Ring-closure of the additive ester (III) *to compound* (I).—The ester (15 g.) was added to alcohol (25 c.c.) containing sodium (1 g.) and the mixture heated on a water-bath for about 12 hours, 10 grams of the ester (I) being obtained. The semicarbazone was a white powder from alcohol, m.p. 205° (decomp.) (Found: C, 48; H, 6·6; N, 21·1. $C_{16}H_{26}O_6N_6$ requires C, 48·2; H, 6·5; N, 21·1.).

Hydrolysis of the ester (I) *with baryta: Formation of dimethyldihydroresorcin* (V).—The ester (10 g.) was hydrolysed with concentrated baryta (100 c.c.) for a day. The liquid was concentrated, and the dried ether extract on being freed from ether left a solid residue (3 g.) which crystallised from benzene in shining yellow needles, m.p. 148°, identical with Vorländer's dimethyldihydroresorcin.

1–*Dimethylethane*–$^{1:2:2}$ III $^{1:4:4}$–cyclo*butane-2-one.*

Hydrolysis of ester (I) *with* (a) *hot and cold ethyl alcoholic potash: Formation of the bridged* cyclo*hexenone* (X).—The ester (10 g.) was mixed with 25 per cent.

ethyl alcoholic potash (25 c.c.) and kept for 2 days at room-temperature or heated under reflux for 6 hours. After removing excess of alcohol under suction the residue was acidified with 5*N* hydrochloric acid, effervescence being due to decomposition of the sodium carbonate formed on hydrolysis. The solution was saturated with ammonium sulphate and extracted half a dozen times with ether, which when washed and evaporated left a crystalline white solid separating from ordinary alcohol as long rhombic plates m.p. 176° (corr.); yield, 3 grams. The same product was obtained using methyl alcoholic potash.

Hydrolysis with (b) *75 per cent. sulphuric acid or concentrated hydrochloric acid.*—The ester (20 g.) was mixed with 75 per cent. sulphuric acid (50 c.c.) or with concentrated hydrochloric acid (50 c.c.), and both heated for 6 hours on a water-bath. The mixtures were diluted with 50 c.c. of water, saturated with ammonium sulphate and ether extracted. On purification the compound as in (*a*) was obtained. Yield, 6 and 8 grams respectively (Micro, Found: C, 78·5, 78·2; H, 8·1, 8·5. $C_8H_{10}O$ requires C, 78·7; H, 8·2 per cent. Mol. wt. in benzene, 246; camphor, 264; formic acid, 286; acetic acid, 126. $C_8H_{10}O$ requires 122.).

The semicarbazone of (X) was obtained from alcohol as a white powder m.p. 220° (decomp.) (Found: C, 60·1: H, 7·5; N, 23·4. $C_9H_{13}ON_3$ requires C, 60·4; H, 7·3; N, 23·4 per cent.).

Hydrolysis of Vorländer's ester (VII) *to dimethyldihydroresorcin by* (a) *cold alcoholic potash.*—The ester (5 g.) was added to ethyl alcoholic potash (12 c.c. of 25 per cent.) and kept for 2 days at room temperature; excess of alcohol was removed under diminished pressure and the residue acidified with 5*N* sulphuric acid which liberated carbon dioxide. The acid solution was saturated with ammonium sulphate, ether extracted half a dozen times, dried and freed from ether, the residual yellow solid crystallising from benzene in yellow needles, m.p. 148°.

Hydrolysis with (b) *baryta.*—The ester (5 g.) was boiled under reflux with a strong solution of baryta (200 c.c.), the solution concentrated, acidified with strong hydrochloric acid and ether extracted. The extract dried with anhydrous magnesium sulphate left a solid which crystallised from benzene in yellow needles m.p. 148°, identical with the product from (*a*) and with dimethyldihydroresorcin.

Addition of water to the bridged cyclo*hexenone* (X) *with baryta.*—The compound (5 g.) was heated with concentrated baryta (100 c.c.) under reflux for 6 hours, when the solution was evaporated, acidified with concentrated hydrochloric acid and extracted with ether; the residual solid on crystallisation from benzene was obtained as fine yellow needles m.p. 148°, identified with dimethyldihydroresorcin.

The *dibromide* of the bridged *cyclo*hexenone (XIII).—The ketone (10 g.) was dissolved in glacial acetic acid (50 c.c.) and treated with bromine (4·5 c.c.) the colour fading gradually. Excess of acid was evaporated and the brown solid crystallised from a large quantity of absolute alcohol, which deposited a brown powder m.p. 196°. Yield, 10·6 grams (Found: C, 34·0; H, 3·72; Br, 56·3. $C_8H_{10}OBr_2$ requires C, 34·0; H, 3·51: Br, 56·7 per cent.).

The *monobromo*-derivative of the bridged *cyclo*hexenone (XV or XVI).—The dibromo-compound (2 g.) was added to methyl alcohol (20 c.c.) containing (0·8 g.) potassium hydroxide and heated under reflux during 6 hours: after evaporating alcohol the product was crystallised from alcohol in pale brown needles m.p. 142°. Yield, 0·8 g. (Found: C, 47·5: H, 4·6; Br, 39·5. C_8H_9OBr requires C, 47·7: H, 4·5: Br, 39·8).

Oxidation of the bridged cyclo*hexenone* (X) *with* (a) *permanganate.*—The ketone (5 g.) was suspended in boiling 2*N* sodium carbonate (1 *l.*) and treated with potassium permanganate (10 g.) during 6 hours. Manganese dioxide was filtered, the solution decolorised with sulphur dioxide, evaporated to small bulk, acidified with 10 per cent. sulphuric acid and ether extracted half a dozen times. The residue was redissolved in 2*N* sodium hydroxide, filtered from unchanged di*cyclo*hexenone, acidified and again ether extracted. The thick oil (3 g.) thus obtained became a crystalline mass on standing for a month, recrystallising from benzene in plates, m.p. 101°.

Oxidation with (b) *hypochlorite.*—Into a 30 per cent. ice-cooled solution of sodium hydroxide (100 c.c.) was passed chlorine generated from potassium permanganate (2 g.) and concentrated hydrochloric acid (20 c.c.) and the ketone (5 g.) was added. The mixture was shaken constantly for 12 hours and then treated with sodium bisulphite till a sample of it liberated no more chlorine with hydrochloric acid. The solution was evaporated to small bulk and ether extracted several times. The unchanged product was removed as in the previous case and the residual oil partially solidified after a fortnight. The separated solid crystallised from benzene m.p. 101° and was identified along with the acid obtained in (*a*) as ββ-dimethylglutaric acid (Found: C, 52·1: H, 8; Equiv., 80. $C_7H_{12}O_4$ requires C, 52·5; H, 7·5: Equiv., 80).

Attempt to bridge ester (I) *with methylene iodide.*—The ester (35 g.) was added to alcohol (80 c.c.) in which sodium (6 g.) had been dissolved, methylene iodide (40 g.) was added and after 12 hours the mixture was heated under reflux in an oil-bath at 105-110° for 12 hours. Excess of alcohol was removed under reduced pressure and the residue acidified with 2*N* sulphuric acid and the separated oil extracted with ether: this was dried by anhydrous magnesium sulphate and removed, when a thick brown oil remained. On distillation under 2 mm. a solid began to deposit in the condenser at about 170–180°; it crystallised readily from benzene, m.p. 148° and was identified as dimethyldihydroresorcin.

In conclusion, the authors wish to acknowledge their indebtedness to Dr. M. O. Forster, F.R.S., for his kind interest and helpful suggestions in this investigation.

Department of Organic Chemistry,
Indian Institute of Science,
Bangalore.

[Accepted, 21-11-32.]

CONTENTS

ABBREVIATIONS OF TITLES

ABBREVIATION	NAME OF PERIODICAL
Bell System Tec. J.	Bell System Technical Journal.
Bur. Standards Bull.	Bureau of Standards Bulletin.
Bur. Stand. J. Research	Bureau of Standards Journal of Research.
Elec. Jour.	Electric Journal.
E.T.Z.	Elektrotechnische Zeitschrift.
J.I.E.E.	Journal of the Institution of Electrical Engineers.
J. Inst. Elec. Eng.	Journal of the Institution of Electrical Engineers.
Phys. Rev.	Physical Review.
Proc. I.R.E.	Proceedings of the Institute of Radio Engineers.

AUTHOR INDEX