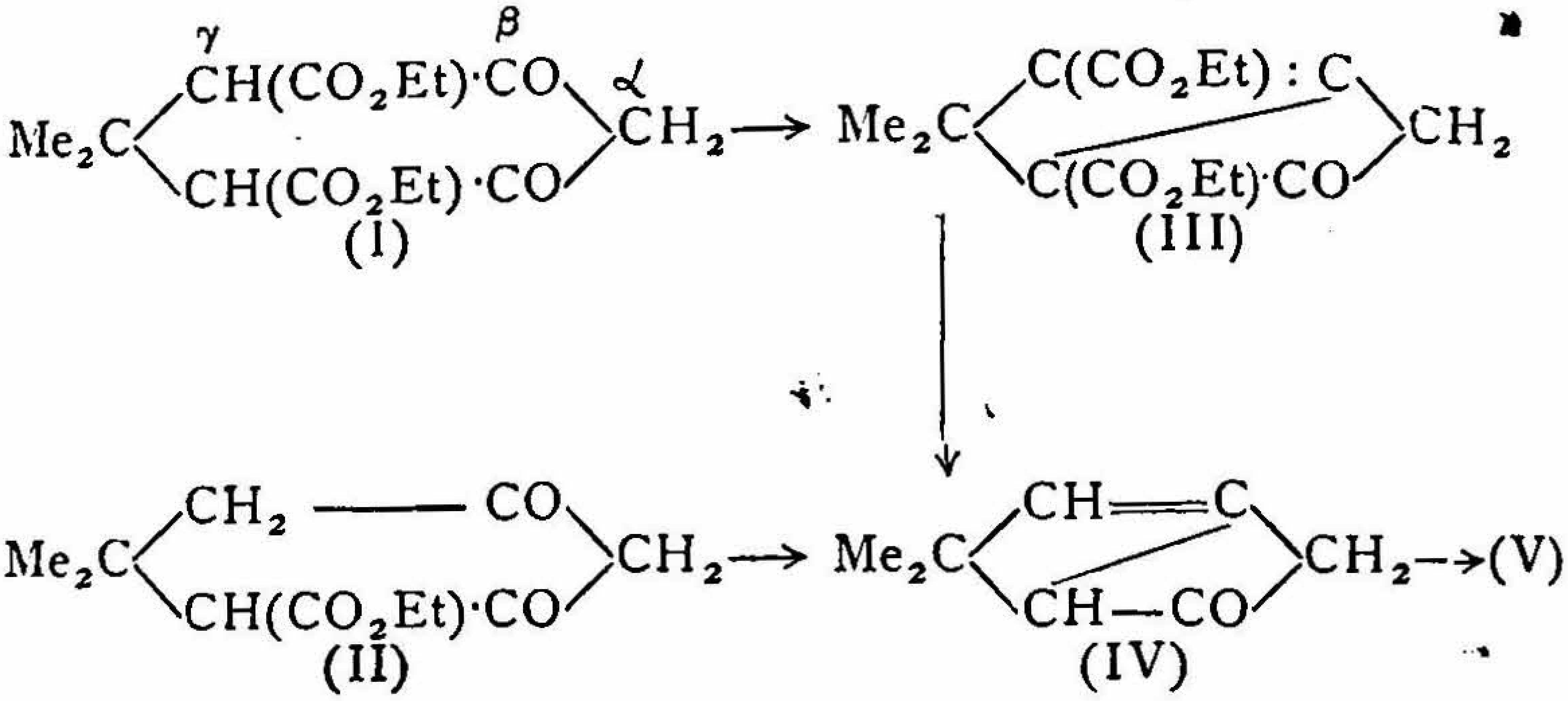
STUDIES IN BRIDGE FORMATION

PART III. THE INFLUENCE OF THE METHYL AND CARBETHOXY-GROUPS IN THE INTERNAL DEHYDRATION OF *gem*-DISUBSTITUTED DIHYDRORESORCINOL ESTERS

BY P. S. MAYURANATHAN.

Since the classical researches of Crossley and his co-workers on the conversion of dimethyldihydroresorcinol to chloro-*ortho*xylenes with phosphorus pentachloride (*J. C. S.*, 1903, **83**, 110, 494), no attempt has been made to explain this phenomenon as a process of internal dehydration and subsequent redistribution of the valencies to the aromatic complex. It is the endeavour of the author to elucidate this phenomenon by the application of a method discovered in an earlier paper (Mayuranathan and Guha, *J. Indian Inst. Sci.*, 1932, **15**A, 131) wherein a dehydrated form of the resorcinol, $C_8H_{10}O$ (IV), was isolated during hydrolysis of Scheiber and Miesel's ester (I) (*Ber.*, 1915, **48**, 238), which has now been utilised in determining the characteristics of other substituted dihydroresorcinol esters.

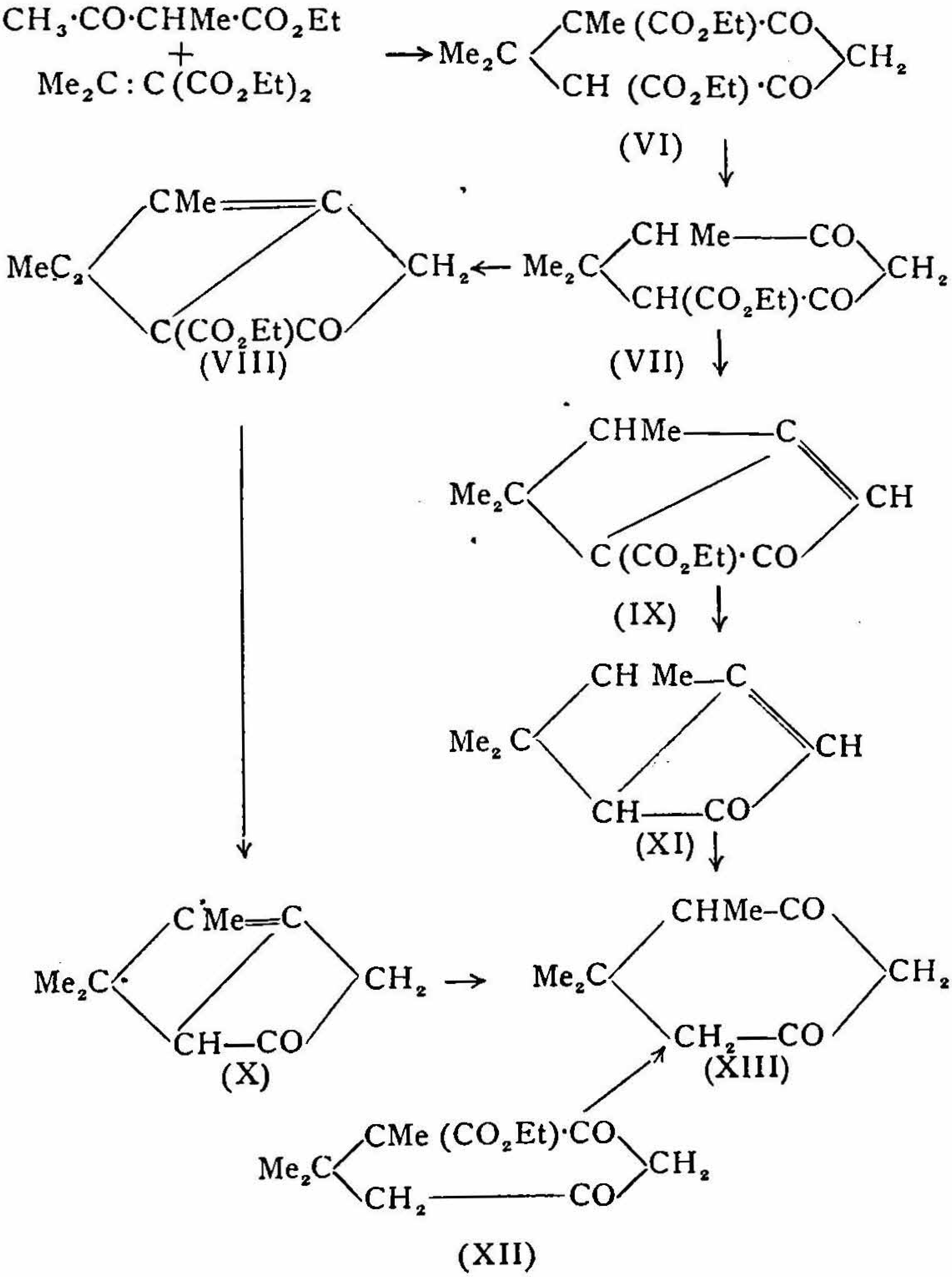
Scheiber and Miesel state that strong baryta hydrolyses the ester (I) to the corresponding dihydroresorcinol, $C_8H_{12}O_2$ (V). This transformation has been shown in the preceding paper (*loc. cit.*) to be only a sequel to the formation of a bridged *cyclo*hexenone, $C_8H_{10}O$ (IV), formed by dehydration of the ester during hydrolysis which is later transformed into dimethyldihydroresorcinol. A constitution was tentatively proposed to the bridged *cyclo*hexenone based on its ease of formation from Scheiber and Miesel's ester in contrast with its non-formation from Vorländer's ester (II) (*Annalen*, 1896, **194**, 257). As mentioned therein, in differentiating the characteristics of Scheiber and Miesel's ester from that of Vorländer's, enolisation in the $\beta\gamma$ position was assumed in the former; still this cannot leave out of account the possibility of the latter behaving similarly, at any rate in a lesser degree of magnitude. In justification, it can be stated that, concurrently with the formation of dimethyldihydroresorcinol during hydrolysis of (II), the ketone (IV) is also formed. The same product has been obtained with extreme difficulty and only in traces from dimethyldihydroresorcinol by the action of phosphorus pentoxide. These observations appear to warrant the statement that some unique characteristics have to be attributed to the *gem*-disubstituted dihydroresorcinol residue.



The chief difficulty lies, however, in precisely explaining the mechanism of dehydration, since a hydroxyl group can be formed by enolisation in two different ways, although the one presumed is more probable from a comparison of properties of (I) and (II). Furthermore, in illustration of the hypothesis that dehydration precedes decarboxylation in the formation of the new ketone two dehydrated esters (III) and (VIII) have been isolated from (I) and (VII) respectively, which in their turn have been converted to the corresponding ketones (IV) and (X). Thus the constitution of the bridged *cylo*hexenone having gained some support, it seemed desirable to extend the work to similar esters (VII) and (XIV) having additional methyl groups to further facilitate dehydration in analogy with Rothstein and Shoppee's observation (*J. C. S.*, 1927, 531) regarding the influence of the methyl groups on the lactolone formation in the α-ketoglutaric acids.

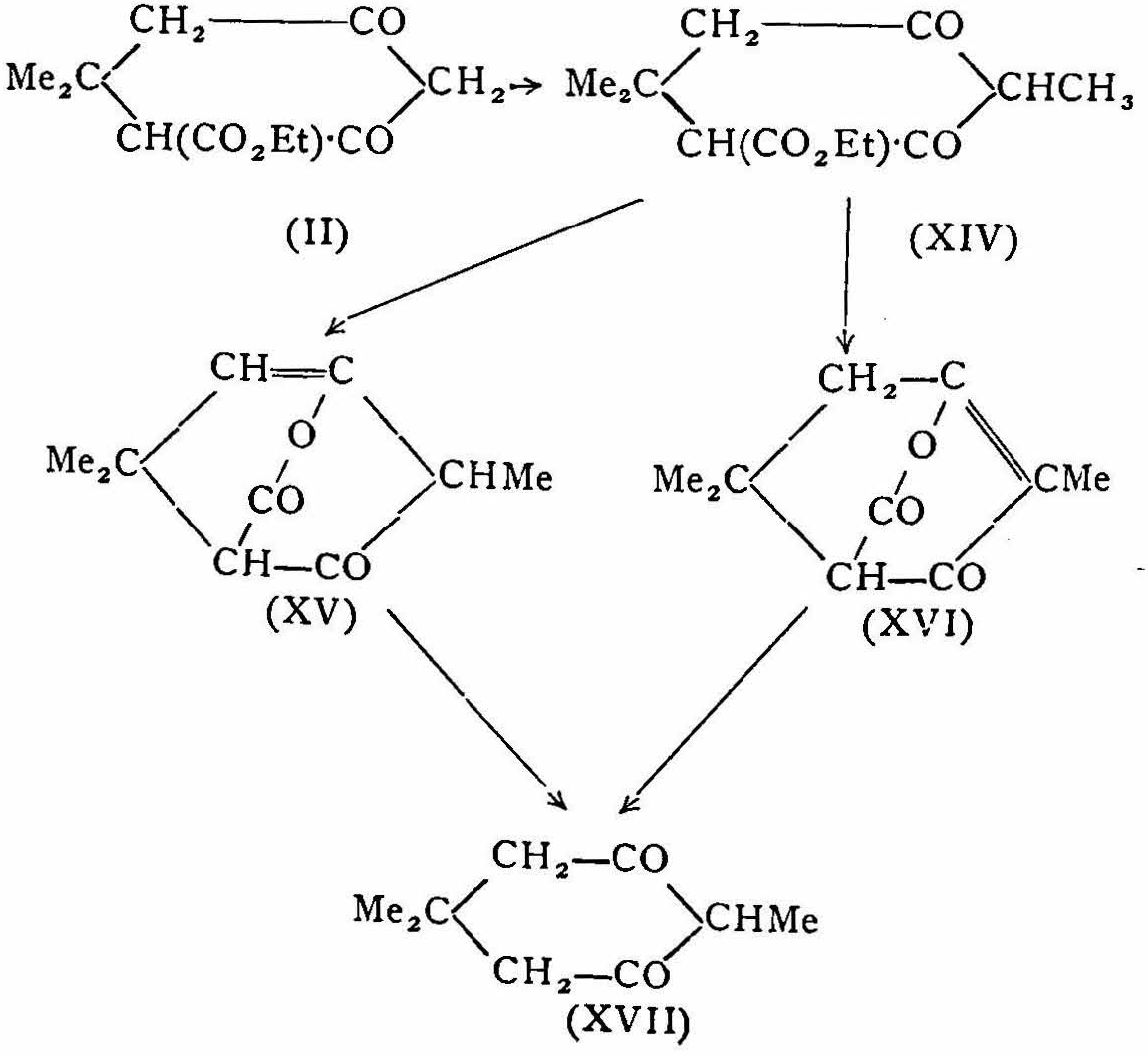
The principal product obtained from *iso*propylidene malonic ester and methyl acetoacetic ester is ethyl *cyclo*hexane-1 :1 :2-trimethyl-3 :5-diketo-6-carboxylate (VII). The diester (VI) as soon as it is formed loses one carbethoxy-group and in analogy with the observations of Crossley (*J.C.S.*, 1909, **95**, 19; 1910, **97**, 520) the elimination is likely to take place from the carbon atom carrying the methyl group. Moreover, as this dihydroresorcinol ester is different from its isomer (XII) obtained by Crossley (*ibid*, 1901, **79**, 138) from mesityl oxide and methyl malonic ester, the constitution (VII) assigned to the ester seems to be quite probable. The structure gets further support from the identity of (VII) with the product obtained from methyl mesityl oxide and malonic ester (cf. Bardhan, *J. C. S.*, 1928, 2608).

Unlike Vorländer's ester the present one is converted comparatively easily to its dehydrated ester (VIII) or (IX) which is finally hydrolysed to a methylated ketone $C_9H_{12}O$ (X) or (XI). Formulae (VIII) and (X) for the dehydrated ester and the ketone have been preferred (the



closely assembled methyl groups being undoubtedly the controlling factors) in analogy with the formation of the ketone, $C_8H_{10}O$; any comparison with (VI) and (I) being impossible as the activity of the former has been greatly impaired by the substitution of an active hydrogen with a methyl situated propinquous with *gem*-dimethyl group. On boiling with baryta or keeping with strong alkali, the ketone (X) is converted into the trimethyldihydroresorcinol (XIII) (Crossley, *loc. cit.*).

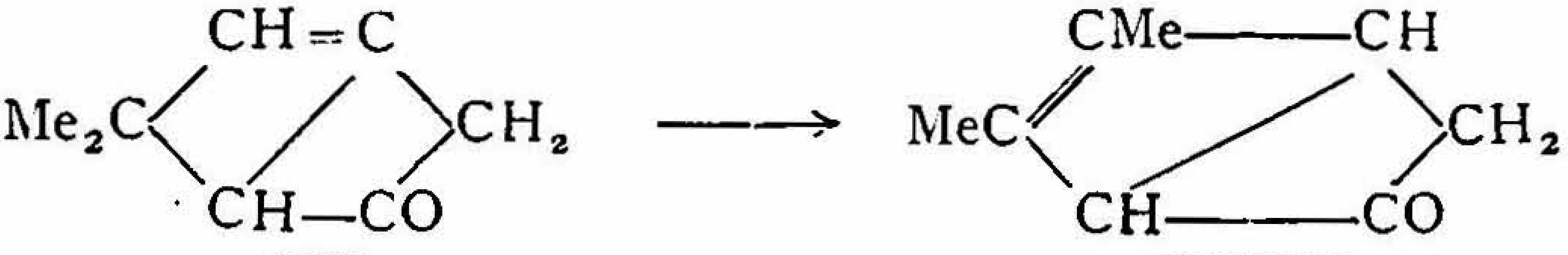
Methylation of Vorländer's ester or Scheiber and Miesel's ester gives ethyl *cyclo*hexane-1 : 1 : 4-trimethyl-3 : 5-diketo-6-carboxylate (XIV), proof for constitution being its conversion on hydrolysis into the trimethyldihydroresorcinol (XVII) (Desai, *J. C. S.*, 1932, 1079). On hydrolysing with sulphuric acid an appreciable quantity of a stable, crystalline solid, $C_{10}H_{12}O_3$, m.p. 79°, is obtained along with the corresponding dihydroresorcinol (XVII). With hot alkali it titrates as a dibasic acid and so it is an internal lactone (XV) or (XVI) formed evidently by dehydration in the enolic form of the acid corresponding to the ester (XIV). This reaction seems to be remarkable and is



perhaps a new example of bridged-lactone formation and indicates a fulfilment of Vorländer's expectation (*loc. cit.*) with his ester.

A noteworthy feature of these reactions is the influence exercised by the third methyl group besides the two already present in ester (II) in giving an appreciable yield of the lactone (XV or XVI) and the bridged ketone (X) from the esters (XIV) and (VII) respectively.

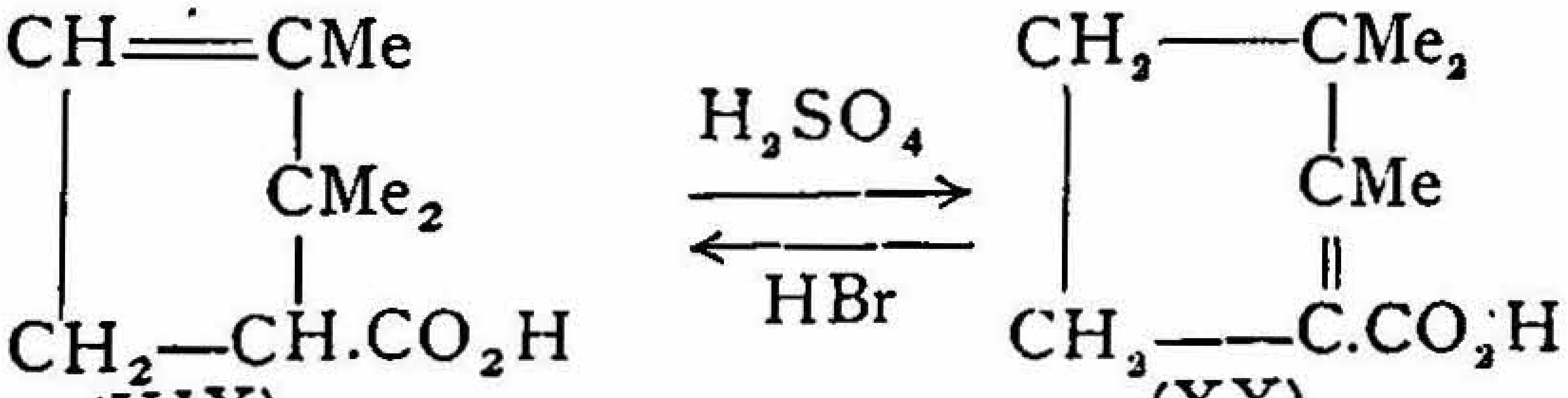
It will be observed that compounds (IV), (VIII), (IX), (X), (XI), (XV) and (XVI) do not conform with Bredt's hypothesis, which postulates that a double bond cannot be stable adjacent to the bridged head of a bridged six-membered ring (Bredt, Thuoet, and Schmitz, *Annalen*, 1924, **437**, 1; Windaus and Bohne, *ibid.*, 1925, **442**, 7) and it is possible that a wandering of the methyl group occurs, thus :—



(IV) (XVIII)

A similar example is the conversion of camphenilol to santene by Ruzicka and Leibl (*Helv. Chim. Acta*, 1923, **6**, 271).

This assumption, however, appears improbable because of the conversion of the bridged *cyclo*hexenone to dimethyldihydroresorcinol which requires a reversal of (XVIII) to the phase (IV). Although Wagner-Meerwein rearrangement of a reversible type has been established in the conversion of α-campholytic acid (XIX) to *iso*lauronolic acid (XX) and *vice versa* (Noyes, *Ber.*, 1895, **28**, 548; *Amer. Chem. J.*, 1895, **17**, 428; Perkin, *J. C. S.*, 1903, **83**, 854; Walker and Cormack, *J. C. S.*, 1900, **77**, 378)



(XIX) (XX)

the mechanism cannot readily be applied in the case of the bridged ketones or lactone. The possibility of a rearrangement taking place must therefore be left undecided until the constitution of the bridged products is definitely established in attainment of which work is in progress.

EXPERIMENTAL

Hydrolysis of Vorländer's ester (II) *to bridged* cyclo*hexenone* (IV), with (*a*) *cold alcoholic potash*.—The ester (100 g.) was mixed with 25 per cent. alcoholic potash (250 c.c.) and left for 2 days. 2 *N* potash (100 c.c.) was added later and the alkaline solution extracted with ether several times. The ethereal solution gave after drying and distilling the solvent an oil (nearly 2 g.). From 10 g. of this oil a fraction (2 g.) boiling at 145-147°/24 mm. was obtained. This has not been further investigated, but was found to contain C, 67.8; H, 7.5 per cent. The flask contained after distilling all oily products till 180° a thick residue which set to a semi-solid mass on cooling. On filtering the crystalline solid and purifying it from alcohol it melted at 176° (sublimes in vacuum at 100°) and was identified with the bridged *cyclo*hexenone (Found: C, 78.4; H, 8.5; *M*, 245. $C_8H_{10}O$ requires C, 78.2; H, 8.2 per cent. *M*, 122).

Hydrolysis of ester (II) *with* (*b*) 60 *per cent. sulphuric acid*.—The ester (100 g.) was mixed with 60 per cent. sulphuric acid (100 c.c.) and kept aside for 2 days. After diluting with water, it was made alkaline and extracted with ether; this gave an oil as before (2.5 g.) which on being treated as above gave the ketone m.p. 176°. Yield (1 g.)

Dehydration of dimethyldihydroresorcinol (V) *with phosphorus pentoxide: Formation of the bridged* cylo*hexenone* (IV).—Dimethyldihydroresorcinol (12 g.) was dissolved in anhydrous xylene (200 c.c.) and phosphorus pentoxide (12 g.) added. It was warmed on the water bath for 8 hours and then heated in an oil bath at 120° for a couple of hours. Xylene was distilled and the brown residue decomposed with water and extracted with ether. The ethereal solution after being washed with 2 *N* sodium hydroxide gave a resinous mass (o. 8 g.) from which was obtained only a trace of IV after repeated crystallisation from benzene alcohol mixture.

Ethyl cyclo*hexane*-1 : 1 : 2-*trimethyl*-3 : 5-*diketo*-6-*carboxylate* (VII).—To a solution of sodium (12 g.) in alcohol (150 c.c.) were added methyl acetoacetic ester (72 g.) and *iso*propylidene malonic ester (100 g.) and the mixture boiled under reflux for 12 hours. Alcohol was distilled and the residue on acidification evolved carbon dioxide. The ether extract gave an oil (122 g.) from which was collected a fraction distilling at 187°/21 mm., yield (35 g.); d^{23° 1.3151, $n_d^{23^\circ}$ 1.4838, $[R_L]_D$ 56.99 (calc.: 57.09) (Found: C, 63.4; H, 9.3; *M*, 232. $C_{12}H_{18}O_4$ requires C, 63.7; H, 8.0 per cent. *M*, 226).

The *disemicarbazone* melted at 225° (decomp.) (Found: N, 14.6. $C_{13}H_{21}O_4N_3$ requires N, 14.8 per cent.).

Condensation of methyl mesityl oxide with malonic ester. Synthesis of ester (VII).—Methyl mesityl oxide prepared by Blaise-Maire reaction on Perkin and Thorpe's trimethyl acrylyl chloride (*J.C.S.*, 1896, **69**, 1080), b.p. 142-144°/684 mm. was condensed according to Bardhan (*J.C.S.*, 1928, 2608) with malonic ester. The oil obtained from the reaction product distilled at the same temperature as the previously mentioned ester (X), and had the same constants.

Hydrolysis of ester (VII) to 1: 1: 2-*trimethyl*-3: 5-*diketo*cyclo*hexane*, (XIII).—Ester (VII) (10 g.) was mixed with concentrated baryta (150 c.c.) and boiled under reflux for 12 hours. The solution was evaporated to dryness, acidified with concentrated hydrochloric acid and extracted with ether, when it gave a thick brown liquid (2.5 g.) which solidified in a vacuum desiccator. The solid crystallised from dilute alcohol in needles, m.p. 100° (Found: C, 69.8; H, 9.6. $C_9H_{14}O_2$ requires C, 70.1; H, 9.2 per cent.) and was identified with Crossley's (*J. C. S.*, 1901, **79**, 138) trimethyldihydroresorcinol obtained by hydrolysing the condensation product of mesityl oxide with methyl malonic ester. Alcoholic potash was found to be a better hydrolysing agent.

Dehydration of (VII). *Formation of the bridged dehydrated ester* (VIII).—A mixture of trimethyldihydroresorcinol ester (VII) (20 g.) and 20 per cent. alcoholic potash (30 c.c.) was kept at room temperature for 48 hours. The alcohol-free reaction mixture was neutralised and ether extracted and washed with sodium carbonate to remove all the resorcinols and other soluble products, yield (12 g.). The main product distilled at 145-147°/20 mm., yield (4 g.). d^{24} 1.0582, $n_{d}^{24°}$ 1.4830, $[^{R}{}_{L}]_{D}$ 56.18 (calc.: 54.41) (Found: C,69.0; H, 7.9; *M*, 205. $C_{12}H_{16}O_3$ requires C, 69.2; H, 7.7 per cent.; *M*, 208). The *semicarbazone* had m.p 205° (decomp.) (Found: N, 15.5. $C_{13}H_{19}O_3N_3$ requires N, 15.1 per cent.).

50 per cent. sulphuric acid also effects dehydration.

Hydrolysis of the bridged ester (VIII) *to the resorcinol* (XIII).—The ester (1 g.) was boiled under reflux with concentrated baryta (25 c.c.) The solution was evaporated to small bulk, acidified with hydrochloric acid, extracted with ether and the solid obtained therefrom crystallised from dilute alcohol, m.p. 100°.

Formation of the bridged ester (III) *from Scheiber and Miesel's ester* (I).—A mixture of Scheiber and Miesel's ester (40 g.) and 20 per cent. alcoholic potash (25 c.c.) was kept at room temperature for 2 days. Similarly another portion of the ester (40 g.) was kept with 50 per cent. sulphuric acid (25 c.c.) for the same period. Afterwards the products were worked up in the same way the yield being (12 g.) and (15 g.) respectively. It distilled as a colourless oil at 195°/20 mm.; $d^{23.5°}$ 1.1386, $n_d^{23.2°}$ 1.4812, $[R_L]_D$ 66.49 (calc.: 65.30) (Found: C, 62.9; H, 8.3; *M*, 272. $C_{14}H_{18}O_5$ requires C, 63.2; H, 8 per cent.; M, 266). The *semicarbazone* had m.p. 232° (decomp.) (Found: N, 12.8. $C_{15}H_{21}O_5N_3$ requires N, 13.0 per cent.).

Hydrolysis of the ester (III) *to the bridged* cyclo*hexenone* (IV).—A mixture of the ester (5 g.) and 60 per cent. sulphuric acid (20 c.c.) was warmed on the water bath for 4 hours. The resulting solution after dilution was extracted with ether from which a solid m.p. 176° (2 g.) was obtained, identified with the bridged *cyclo*hexenone.

Hydrolysis of ester (VII) *to the bridged* cyclo*hexenone* (X).—The ester (XI) (20 g.) was mixed with 20 per cent. alcoholic potash (40 c.c.) and kept aside for nearly a week. The same quantity of the ester was separately warmed on the water bath for 4 hours with 60 per cent. sulphuric acid (50 c.c.). The ether extract after sodium carbonate treatment gave a light yellow pleasant smelling liquid (5 g. and 6 g. respectively) distilling at 105/20 mm. d^{25} 0.9508, $n_d^{25°}$ 1.4743, $[R_L]_D$ 40.24 (calc.: 38.91) (Found: C, 79.0; H, 9.3; *M*, 142. $C_9H_{12}O$ requires C, 79.4; H, 8.8 per cent.; *M*, 136).

The *semicarbazone* crystallised from alcohol in flaky needles, m.p. 186° (Found: N, 21.5. $C_{10}H_{15}ON_3$ requires N, 21.7 per cent.).

Conversion of (X) *to the dihydroresorcinol* (XVII).—The bridged *cyclo*hexenone (2 g.) was boiled under reflux with 10 per cent. alcoholic potash (20 c.c.) for 5 hours and the alcohol distilled. The ether extract gave a semi-solid crystallising from dilute alcohol, m.p. 100°; identified with Crossley's trimethyldihydroresorcinol (*loc. cit.*).

*Methylation of Vorländer's ester to ethyl*cyclo*hexane*-1 : 1 : 4-*trimethyl*-3 : 5-*diketo*-6-*carboxylate* (XIV).—Vorländer's ester (106 g.) was slowly added to a solution of sodium (12 g.) in alcohol (150 c.c.) and the mixture boiled under reflux for 12 hours with methyl iodide (75 g.). The alcohol-free residue on acidification and extraction with ether gave a semi-solid. The oily products were filtered, and the solid crystallised from a mixture of ethyl acetate-petroleum ether in fine clusters of needles, m.p. 108°, yield (70 g.) (Found: C, 63.3; H, 8.5; *M*, 218. $C_{12}H_{18}O_4$ requires C, 63.7; H, 8 per cent.; *M*, 226.)

The *disemicarbazone* crystallised from alcohol; m.p. 236° (decomp.) (Found: N, 14.5. $C_{13}H_{21}O_4N_3$ requires N, 14.8 per cent.).

Formation of (XIV) *from Scheiber and Miesel's ester* (I).—Scheiber and Miesel's ester (140 g.) was added to a solution of sodium (12 g.) in alcohol (150 c.c.) to which was added methyl iodide (75 g.) and the mixture boiled under reflux for 12 hours. After the usual process of purification a crude product (200 g.) was obtained which on distilling under diminished pressure gave a thick oil (10 g.) distilling at 165°/5 mm. and solidifying on cooling. It melted at 106°. The residue charred on distillation.

Hydrolysis of (XIV) *to the resorcinol* (XVII).—The ester (10 g.) was mixed with 20 per cent. alcoholic potash (50 c.c.) and kept for a week. After removing alcohol and acidifying, the ether extract gave a solid (5 g.) which crystallised from benzene-petroleum ether as rhombic needles m.p. 161°, identified with Desai's (*loc. cit.*) methylated dimethyldihydroresorcinol (Found: C, 69.9; H. 10.2. $C_9H_{14}O_2$ requires C, 70.1; H, 9.9 per cent.).

Action of 60 per cent. sulphuric acid on the ester (XVIII). *Formation of the lactone* (XV) *or* (XVI).—To the ester (50 g.) was added 60 per cent. sulphuric acid (100 c.c.) when it became warm; the mixture was kept at room temperature for 3 days. Heating on the water bath finished the reaction sooner without any loss in yield. After dilution the mixture was ether extracted and washed with sodium carbonate to remove all the resorcinols. The ethereal solution gave a thick oil (6 g.) which in a vacuum desiccator at low temperature sets to a crystalline mass. This freed from the oily impurities, crystallised from alcohol as beautiful cubical plates, m.p. 79° (Found: C, 63.4; H. 7.4; *M*, 190. $C_{10}H_{12}O_3$, $\frac{1}{2}H_2O$ requires C, 63.5; H, 6.9 per cent.; *M*, 189). The product was dehydrated by keeping over phosphorus pentoxide at 100° (Found: C, 66.1; H, 7.1. $C_{10}H_{12}O_3$ requires C, 66.6; H. 6.7 per cent.). It was neutral to sodium carbonate or cold alkali. With hot alkali it titrated as a dibasic acid, and was estimated by back titration. (Equiv. 100; Calc. 95).

The *semicarbazone* crystallised from alcohol in plates m.p. 188° (decomp.) (Found: N, 17.5. $C_{11}H_{15}O_3N_3$ requires N, 17.7 per cent.).

Hydrolysis of the lactone (XV) *or* (XVI) *to the resorcinol* (XVII). —The lactone (2 g.) was boiled under reflux with 10 per cent. alcoholic potash (25 c.c.) for 4 hours. After the usual ether extraction it gave a thick oil (1 g.) which solidified and was crystallised from benzene-petroleum ether, m.p. 161°; identified with Desai's (*loc. cit.*) methylated dimethyldihydroresorcinol (Equiv. 156; Calc.: 154).

The author has great pleasure in acknowledging his gratitude to Dr. P. C. Guha, D.Sc., and Sir Martin Forster, F.R.S., for their continued interest and helpful suggestions during the progress of this investigation.

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