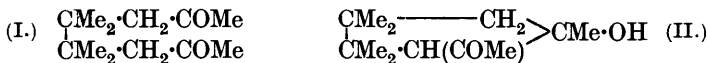## XC.—*Ring-chain Tautomerism. Part XVI. The Effect of Two Adjacent* gem-*Dimethyl Groups on the Ease of Formation of the* cyclo*Pentane Ring.*

### By ISRAEL VOGEL.

THE effect of the *gem*-dimethyl and other groups on the ease of formation of *cyclo*propane, *cyclo*butane, and *cyclo*pentane rings has formed the subject of numerous communications from these laboratories, but the influence of two adjacent *gem*-groups on ring formation does not appear to have been studied. The present communication deals with the effect of two adjacent *gem*-dimethyl groups on the formation of the *cyclo*pentane ring. This case is of especial interest from the point of view of the modified strain theory of Thorpe and Ingold, since the angle between the remaining two valencies of a carbon atom attached to a *gem*-dimethyl group is 109·5° (Ingold, J., 1921, **119**, 305), which differs only slightly from the angle of the normal *cyclo*pentane ring. On theoretical grounds, it would therefore be expected that in a system containing two adjacent *gem*-dimethyl groups and capable of exhibiting the phenomenon of ring-chain tautomerism, the ring isomeride would predominate; consequently the tautomerism of the substituted 1 : 6-diketone, $\alpha\delta$-diacetyl-$\beta\beta\gamma\gamma$-tetramethylbutane (I), has been investigated.

$$(\text{I.}) \quad \begin{array}{l} \text{CMe}_2\cdot\text{CH}_2\cdot\text{COMe} \\ \text{CMe}_2\cdot\text{CH}_2\cdot\text{COMe} \end{array} \qquad \begin{array}{l} \text{CMe}_2\text{------CH}_2 \\ \text{CMe}_2\cdot\text{CH(COMe)} \end{array} \!\!\!\!>\!\!\text{CMe}\cdot\text{OH} \quad (\text{II.})$$

This would be expected to exist mainly in the form of the ring isomeride (II). It may be said at once that, although the mode of preparation of the compound left no doubt as to its having the open-chain formula (I) at the moment of formation, yet its properties

indicated that it reacted exclusively in the form of the ring isomeride (II). No evidence could be obtained of the existence of the open-chain compound. It is noteworthy that neither αδ-diacetylbutane, $COMe \cdot [CH_2]_4 \cdot COMe$ (III) (Marshall and Perkin, J., 1890, **57**, 241) nor αδ-dibenzoylbutane, $COPh \cdot [CH_2]_4 \cdot COPh$ (IV) (Wollemann, Diss., Göttingen, 1913), the simplest 1 : 6-diketones, shows any tendency to react in the ring form as would be expected from theory. Both react exclusively as diketones, although, in common with all 1 : 6-diketones, they possess a great tendency to pass into a five-membered ring by the elimination of water (compare Kipping and Perkin, J., 1889, **55**, 330; 1890, **57**, 1, 29; 1891, **59**, 214; Kipping and Mackenzie, J., 1891, **59**, 571).

The requisite 1 : 6-diketone was prepared by the reduction of mesityl oxide by moist aluminium amalgam, the reaction following the equation

$$2C_6H_{10}O + 2H = C_{12}H_{22}O_2.$$

This reduction had been previously studied by other investigators, whose results can now be readily interpreted if (II) be taken as the formula of the reduction product. Harries and Hübner (*Annalen*, 1897, **296**, 295; compare Harries and Eschenbach, *Ber.*, 1896, **29**, 380) studied the reduction of mesityl oxide by sodium and by aluminium amalgam and assigned the constitution (V) ($C_{12}H_{20}O$) to the product, although this was not in strict accordance with

(V.) $\begin{array}{l}CMe_2\text{-----}CH_2\\CMe_2 \cdot C(COMe)\end{array}\!\!>\!\!CMe$ $\qquad$ $\begin{array}{l}CMe_2\text{-----------}CH_2\\CMe_2 \cdot C(CMe\colon NOH,H_2O)\end{array}\!\!>\!\!CMe$ (VI.)

the analytical results, as was first pointed out by Law (J., 1912, **101**, 1016). They prepared two isomeric *mono*-oximes of the formula $C_{12}H_{20}N \cdot OH, H_2O$ to which the constitution (VI) was given. Law (*loc. cit.*) effected the reduction by an electrolytic process and obtained the same products. He was, however, able to isolate a solid which he regarded as the pure reduction product ($C_{12}H_{22}O_2$), yielding a *mono*-semicarbazone, m. p. 185—186°, and a *mono*-oxime, identical with one of the oximes prepared by Harries and Hübner. Law does not assign any definite constitution to the reduction product, but merely gives the following possible constitutional formulæ :

(*a*) $COMe \cdot CH_2 \cdot CMe_2 \cdot CMe_2 \cdot CH_2 \cdot COMe.$
(*b*) $CMe_2 \colon CH \cdot CMe(OH) \cdot CMe(OH) \cdot CH \colon CMe_2.$
(*c*) $COMe \cdot CH_2 \cdot CMe_2 \cdot CMe(OH) \cdot CH \colon CMe_2.$

and remarks that the most probable constitution is (*c*).

The results of the author, however, are in agreement neither with the formula of Harries and Hübner nor with those of Law,

but can be readily interpreted in terms of the constitution (II). Indeed, all the apparently divergent results of previous investigators can be simply explained by the new formula.

The reduction of mesityl oxide by moist aluminium amalgam resulted in the formation of a solid (α) and a liquid (β) form of the reduction product; the former passed into the latter on exposure to the atmosphere unless the oily liquid adhering to the solid was removed by recrystallisation. The solid form yielded a *mono*-semicarbazone, m. p. 185°, identical with that obtained by Law (*loc. cit.*), whilst the liquid also yielded a *mono*-semicarbazone, m. p. 165°. Further, the α-form yielded a *mono*-benzoyl derivative, m. p. 115°, the β-form a *mono*-benzoyl derivative, m. p. 42°, whilst tetramethylsuccinic acid resulted from both forms on oxidation with chromic acid. There appears to be little doubt that the solid and liquid forms are *cis*- and *trans*-modifications (VII) and (VIII), the α-form probably having the configuration (VII). The
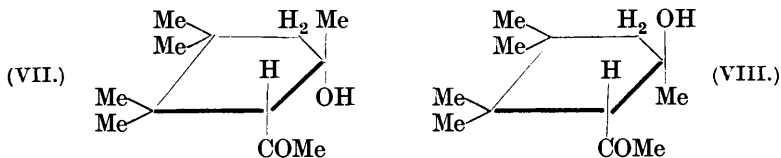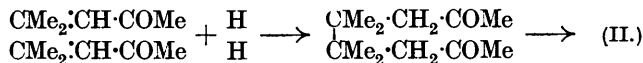


existence of two isomeric *mono*-oximes discovered by Harries and Hübner (*loc. cit.*) is in complete harmony with the above formulæ, but the constitution (VI) assigned to them by these authors must be regarded as erroneous, the correct constitutions being those represented by the oximes of the two stereoisomerides (VII) and (VIII).

The ring compound (II) is very stable towards oxidising agents. Sodium hypochlorite and potassium permanganate do not appear to have any marked effect, although with sodium hypobromite a quantitative yield of bromoform corresponding to one acetyl group was obtained, but unfortunately no other product could be isolated in sufficient quantity to admit of its complete identification. Fission of the ring took place with chromic acid and tetramethylsuccinic acid was formed.
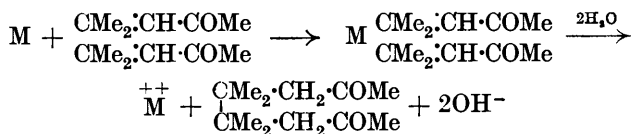
The remarkable influence which two adjacent *gem*-dimethyl groups exert on the formation of a five-membered ring is further illustrated by the fact that all attempts to prepare the anilic acid and acid chloride of tetramethylsuccinic acid have failed, the ring anil and anhydride being invariably formed (Auwers and Gardner, *Ber.*, 1890, **23**, 3622). It is apparent that experiment fully confirms the predictions made from the modified strain theory of Thorpe and Ingold and one may assert, with some confidence, that

the production of an open-chain compound containing two adjacent *gem*-dimethyl groups will be practically if not entirely impossible should there be a possibility of the formation of a five-membered ring.

The scheme for the formation of the reduction product of mesityl oxide may be represented as follows (compare Law, J., 1912, **101**, 1016) :

$$\begin{array}{c} CMe_2{:}CH{\cdot}COMe \\ CMe_2{:}CH{\cdot}COMe \end{array} + \begin{array}{c} H \\ H \end{array} \longrightarrow \begin{array}{c} CMe_2{\cdot}CH_2{\cdot}COMe \\ CMe_2{\cdot}CH_2{\cdot}COMe \end{array} \longrightarrow \quad \text{(II.)}$$

The coupling at the β-position of reduced residues has been previously observed in the reaction between moist sodium or aluminium amalgam and benzylideneacetone (Harries and Eschenbach, *Ber.*, 1896, **29**, 380), benzylideneacetophenone, phorone (Harries and Hübner, *Annalen*, 1897, **296**, 295), and other compounds (*Ber.*, 1898, **31**, 1806; *Annalen*, 1904, **330**, 235; Möller, Diss., Rostock, 1905) and more recently by Higginbotham and Lapworth (J., 1923, **123**, 1618) in the reduction of ethyl ethylidenemalonate by moist sodium amalgam. If mesityl oxide be written $Me_2\overset{+}{C}{=}\overset{-}{CH}{-}\overset{+}{C}Me{=}\overset{-}{O}$ in accordance with the theory of alternate latent polarities, it is evident that coupling takes place between carbon atoms denoted by + signs (compare Higginbotham and Lapworth, *loc. cit.*). The author is inclined to accept the mechanism (*b*) of Higginbotham and Lapworth as that which most probably represents the course of the reaction in the reduction of mesityl oxide by moist aluminium amalgam. The modified method of reduction employed results in the presentation of a very large surface to the reacting compound and one may assume that the molecules are adsorbed on the surface of the metal and actual reaction takes place in the surface, where chemical forces are known to be very powerful, according to the scheme :

$$M + \begin{array}{c} CMe_2{:}CH{\cdot}COMe \\ CMe_2{:}CH{\cdot}COMe \end{array} \longrightarrow M \begin{array}{c} CMe_2{:}CH{\cdot}COMe \\ CMe_2{:}CH{\cdot}COMe \end{array} \xrightarrow{2H_2O}$$

$$\overset{++}{M} + \begin{array}{c} CMe_2{\cdot}CH_2{\cdot}COMe \\ CMe_2{\cdot}CH_2{\cdot}COMe \end{array} + 2OH^-$$

## EXPERIMENTAL.

*Preparation of Aluminium Amalgam.*—200 G. of thin aluminium foil in strips about 6 inches long and 1 inch wide, loosely folded, are covered with a 10% solution of sodium hydroxide and warmed until a vigorous evolution of hydrogen has taken place for several minutes. The foil is then washed with water and with rectified

spirit, the latter operation producing an exceptionally clean surface for amalgamation.    Sufficient of a 2% solution of mercuric chloride is added to cover the aluminium completely and is allowed to act for 2 minutes; it is then poured off and the amalgam is washed with water, with rectified spirit, and finally with moist ether. The amalgam is covered with about 3 litres of moist ether and is ready for immediate use.    Repetition of the process is unnecessary, as it does not materially affect the yield of the reduction product.

*Reduction of Mesityl Oxide.    Formation of 5-Acetyl-*1 : 3 : 3 : 4 : 4-*pentamethylcyclopentan-*1-*ol*    (II).—Mesityl    oxide    (200 g.), pre-pared in 65% yield by the method described by Roger Adams (" Organic Syntheses," 1921, Vol. 1, p. 53), is added to the aluminium amalgam covered with moist ether in a flask fitted with two double-surface condensers.    The evolution of hydrogen ceases almost immediately after the addition of the mesityl oxide and after about 20 minutes the ether boils; too vigorous ebullition must be checked by cooling the flask with running water.    The reduction is usually complete after about 3 hours, and the whole is kept over-night. The ethereal solution is then filtered, and the aluminium hydroxide sludge washed with ether.    The ethereal solution is dried with calcium chloride, and the ether evaporated.    The crude reduction product (about 200 g.), which has an odour which can best be described as that of a mixture of camphor and peppermint, is frac-tionated as rapidly as possible, since prolonged heating tends to cause the partial elimination of water from the primary reduction product.    Further, it is advisable to carry out the fractionation as soon as possible after the completion of the reduction, as standing in contact with even a small quantity of dry ether produces a con-siderable quantity of high-boiling material, which was not investig-ated.    The bulk of the liquid distils at 119—126°/20 mm., and a small quantity at 138—140°/20 mm.    The main fraction, on long standing and strong cooling, deposits a crystalline solid soluble in most organic solvents.    Law (J., 1912, **101**, 1016) was unable to find a medium for recrystallisation and records the m. p. of the crude solid as 53—55°.    It can, however, be readily crystallised from a mixture of light petroleum (b. p. 40—60°) and ether and has, after one recrystallisation, m. p. 45°, which remains constant even after five recrystallisations.    The solid, if not quickly re-crystallised, passes into the liquid form on exposure to the atmo-sphere for several days (Found for solid, m. p. 45°: C, 72·7; H, 11·0.    Found for the liquid, b. p. 122—124°/20 mm.: C, 72·6; H, 11·2.    $C_{12}H_{22}O_2$ requires C, 72·7; H, 11·0%).

The *semicarbazone* of the solid form is formed after some standing and crystallises from alcohol in hard prisms, m. p. 185° (Found :

C, 60·0; H, 9·3; N, 18·7. $C_{13}H_{25}O_2N_3$ requires C, 59·8; H, 9·6; N, 18·4%). No disemicarbazone could be detected.

The *semicarbazone* of the liquid form, prepared in the usual manner, after several recrystallisations from methyl alcohol, melts constantly at 165° (Found : N, 18·6%). No trace of a disemicarbazone could be detected.

The *benzoyl* derivative of the solid form is prepared by dissolving 1 g. of the solid in 4 g. of pure pyridine and slowly adding 1·5 g. of freshly-distilled benzoyl chloride. The colour of the solution gradually darkens and after ½ hour the whole is poured into excess of dilute hydrochloric acid (1 : 1). The yellowish-brown oil produced is isolated by means of ether (the ethereal solution being washed with dilute sodium bicarbonate solution and with water and dried with sodium sulphate) and solidifies after being kept in a vacuum desiccator for 2 months. It crystallises from methyl alcohol in lustrous plates, m. p. 115° (Found : C, 75·3; H, 8·5. $C_{19}H_{26}O_3$ requires C, 75·5; H, 8·6%).

The *benzoyl* derivative of the liquid form is prepared in a similar manner, except that the benzoyl chloride is added to the pyridine solution cooled to − 5° and the whole is kept for 2 days. The yellowish-brown oil thus obtained solidifies when a small quantity of the oil is removed by distillation in a vacuum. The monobenzoyl derivative separates from a mixture of light petroleum (b. p. 40—60°) and sodium-dried ether in thick needles, m. p. 42° (Found : C, 75·4; H, 8·4. $C_{19}H_{26}O_3$ requires C, 75·5; H, 8·6%).

*Oxidation with Sodium Hypobromite.*—The procedure of Baeyer (*Ber.*, 1896, **29**, 25) is followed for the oxidation of the liquid fraction, b. p. 120—125°/20 mm. A quantitative yield of bromoform corresponding to one acetyl group is obtained, but the only oxidation product which can be isolated consists of a small quantity of viscid gum. A portion crystallises after several months and melts at 122—123°. The acid yields sparingly soluble silver and barium salts, but sufficient could not be isolated to admit of its full characterisation.

*Oxidation with Nitric Acid.*—The only product which can be isolated by the oxidation of the liquid, b. p. 120—125°/20 mm., by concentrated nitric acid is oxalic acid.

*Oxidation with Potassium Permanganate.*—The substance is scarcely affected by permanganate.

*Oxidation with Chromic Acid.*—10 G. of the liquid, b. p. 120—126°/20 mm., are dissolved in 160 c.c. of glacial acetic acid, and a solution of 100 g. of chromic acid in 160 c.c. of 50% acetic acid is added. After the initial vigorous reaction has subsided, the mixture is refluxed for 1 hour. The product is distilled in steam until the

distillate is no longer acid; the distillate is extracted six times with ether, and the ethereal extract dried with anhydrous sodium sulphate. The residue, after removal of the ether, consists of a solution of the oxidation product in acetic acid. The latter is almost completely removed by distillation in a vacuum ; a crystalline acid, m. p. 198° (rapid heating), is then obtained. Its identity with tetramethylsuccinic acid was established by analysis (Found : C, 55·1; H, 8·0. Calc. : C, 55·2; H, 8·0%) and by conversion into the anil.

The anil of tetramethylsuccinic acid is obtained by heating 0·4 g. of the acid (m. p. 198°) with 0·4 g. (2 mols.) of freshly distilled aniline to the boiling point for a few moments ; the whole solidifies on cooling in ice. The excess of aniline is removed by washing with dilute hydrochloric acid. The anil (0·5 g.) separates from dilute alcohol in colourless needles, m. p. 87—88° (compare Auwers and Gardner, *Ber.*, 1890, **23**, 3622: Auwers, *Annalen*, 1896, **292**, 176, who give m. p. 88°) (Found : N, 6·2. Calc. : N, 6·1%).

Identical results are obtained on oxidation of the solid form of the reduction product with chromic acid under similar conditions.