CCCXLIV.—*The Chemistry of the Three-carbon System. Part XVI. The Effect of some Bridged and Unsaturated Rings on Tautomerism.*

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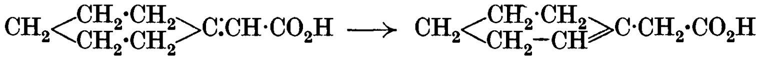
In several previous papers of this series (J., 1926, 1792, 2727; 1923, **123**, 1361, 2440) it has been suggested that the tendency of the double bond to enter a *cyclo*pentane or *cyclo*hexane ring in a compound such as (I) could be correlated with the internal strain in the ring. Particularly striking examples of this correlation were



$$CH_2{<}\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}{>}C{:}CH\cdot CO_2H \longrightarrow CH_2{<}\begin{matrix}CH_2\cdot CH_2\\ CH_2-CH\end{matrix}{\geqslant}C\cdot CH_2\cdot CO_2H$$

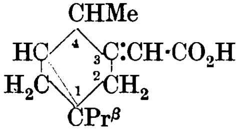
(I.) (II.)

found in ethyl *cyclo*pentylidenemalonate and the *cyclo*hexane compound, the former having the αβ-, and the latter the βγ-unsaturated structure.

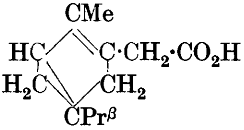
In *cyclo*hexane rings which occur in nature the strain is generally relieved either by a double bond (limonene, carvone, piperitone) or by a bridge (thujone, pinene). Such rings, if introduced in place of the simple *cyclo*hexane ring in a compound such as (I), should exhibit less tendency to acquire a double bond and consequently the stability of the βγ-form (II) of the new compounds should be diminished as compared with the acids (I) and (II). The same should be true of compounds in which the *cyclo*pentane or *cyclo*hexane ring already contains a double bond, but the issue here is complicated by the tendency to form a conjugated system with two double bonds in the ring; the βγ-form in these cases should be actually much more stable than in (I) and (II).

In order to test these conclusions, we selected a number of pairs of unsaturated acids containing suitable bridged rings and derived from the corresponding ketones such as β-thujone, pinocamphone, sabinaketone, nopinone, and fenchocamphorone, whilst a variety of acids derived from *cyclo*hexenones had already been prepared by Wallach and were easily available.

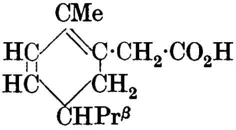
β-Thujone was readily converted into the αβ-unsaturated acid (III), but all attempts to prepare the pure βγ-isomeride (IV) * were fruitless, the bridge being attacked to a greater or less extent by



(III.)



(IV.)



(V.)

the dehydrating agents employed. The high-melting solid acid so produced evidently contains two double bonds and probably has the structure (V). The αβ-acid, on treatment with alkali, was partly converted into the liquid βγ-isomeride; the equilibrium, estimated by Bougault's method, was 75 : 25 in favour of the βγ-form, as compared with 88 : 12 for the acids (I) and (II) (the method em-

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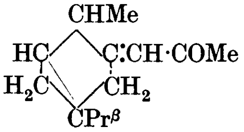
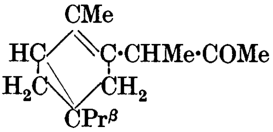
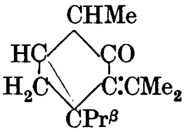
* No attempt has been made to decide between this formula and one with the double bond in the position 2 : 3; the same applies to the compounds (V) and (VII).

ployed gives a *minimum* value for the αβ-acid). The acid (III) can be converted into the corresponding ketone, which, unlike *cyclo*hexenylacetone, has the αβ-structure (VI); it is, however, readily methylated, the new ketone having the βγ-structure (VII). The


(VI.)


(VII.)


(VIII.)

methylated ketone shows an exaltation of the molecular refraction (0·43 unit), which is, however, less than that of the parent ketone (1·08 units). This is doubtless due to the " conjugation " of the double bond with the three-membered ring in the βγ-formula (VII); the low density of the ketone also supports this formula. β-Thujone readily condenses with acetone, but the product is quite different from the ketone (VI), being a solid of the formula (VIII), having evidently been formed in the same way as the condensation product of acetone and *cyclo*pentanone (Wallach, *Annalen*, 1912, **394**, 376).

These reactions suffice to show that the αβ-form is much more favoured in the compounds derived from thujone than in those derived from *cyclo*hexanone. The reaction with acetone can be taken to indicate that the acidity of the ketone group in thujone is less than that of the ketone group in *cyclo*hexanone, the relatively high acidity of which can in turn be correlated with a tendency to enolisation and thus to the production of a double bond in the ring.

The effect of a bridge containing a carbon atom on the stability of compounds derived from pinocamphone could not be studied, because this ketone, like camphor, could not be condensed either with ethyl cyanoacetate or with ethyl bromoacetate, and we have not yet obtained a sufficient quantity of nopinone or fenchocamphorone to serve as a starting point for further work. In the meantime, it appeared of interest to examine the acid (IX) and the ketone (X) derived from 3-methyl*cyclo*hexenone in which one double bond is already present in the ring.


$$CH_2{<}\begin{matrix}CMe{:}CH\\CH_2{\cdot}CH\end{matrix}{>}C{\cdot}CH_2{\cdot}CO_2H$$
(IX.)


$$CH_2{<}\begin{matrix}CMe{:}CH\\CH_2{\cdot}CH\end{matrix}{>}C{\cdot}CH_2{\cdot}COMe$$
(X.)

The ester of this acid does not undergo the Michael reaction (Dr. E. H. Farmer, private communication), so evidently it does not possess an αβ-phase. It is now found that the acid itself is unaffected by prolonged boiling with alkali and shows no tendency whatever to pass into its αβ-isomeride. All attempts to synthesise the latter, and to prepare the ketone from the chloride of the acid, failed.

This behaviour of the acid as a static $\beta\gamma$-form, whilst confirming our view on the probable effect of a double bond in the ring on the stability, is in contrast with that of the cyano-esters prepared by Farmer and Ross (J., 1926, 1570). The reason for the difference appears to be that there are two activating groups in the latter, both favouring the $\alpha\beta$-form and competing with the double bond in the ring, a condition enabling tautomeric equilibrium to be established. In the acid now examined, the stability of one form ($\beta\gamma$) is so much greater than that of the other ($\alpha\beta$) that mobility is completely suppressed. Ethyl α-cyano*cyclo*hexylideneacetate exists apparently only in the $\alpha\beta$-form, whereas Farmer's cyano-esters can be isolated in three forms, of which one is the $\beta\gamma$; the existence of this is evidently due to the additional stabilising effect of the double bond already present in the ring on the $\beta\gamma$-phase.

EXPERIMENTAL.

β-*Thujolacetic Acid.*—β-Thujone was isolated from oil of tansy (Semmler, *Ber.*, 1892, **25**, 3343) and had b. p. 81—82°/12 mm., $d_4^{17\cdot7^\circ}$ 0·91773, $n_D^{17\cdot7^\circ}$ 1·45143, $[\alpha]_D^{17\cdot7^\circ} + 75\cdot64^\circ$. The semicarbazone crystallised from alcohol in needles, m. p. 174°. The ketone did not condense with ethyl bromoacetate in the presence of magnesium, but the reaction proceeded well with zinc, ethyl thujolacetate, b. p. 136—142°/10 mm., being obtained in 54% yield; much of the ketone was recovered. The acid, m. p. 90—91°, was obtained from it on hydrolysis with sodium ethoxide (Wallach, *Annalen*, 1900, **314**, 166.).

β-*Thujylideneacetic Acid* (III).—The hydroxy-acid was boiled with acetic anhydride for 3 hours and the product was diluted with water and distilled in steam for a long time; the *unsaturated acid*, which separated from the distillate as a solid (yield, 64%), crystallised from light petroleum in needles, m. p. 103—104° (Found: C, 74·2; H, 9·2. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·3%). On oxidation with alkaline potassium permanganate in a current of steam the acid gave oxalic acid and β-thujone (which was identified by its semicarbazone, m. p. 174°), the structure (III) assigned to the acid thus being confirmed. The *acid chloride*, prepared with the aid of thionyl chloride, had b. p. 136—138°/14 mm.; the *ethyl* ester, prepared by pouring the chloride into ethyl alcohol, had b. p. 136—137°/10 mm., $d_4^{17\cdot8^\circ}$ 0·95995, $n_D^{17\cdot8^\circ}$ 1·47800, $[R_L]_D$ 65·61 (calc., 64·40).* The *anilide* crystallised from petroleum (b. p. 60—80°) in prisms, m. p. 118·5°

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* This and subsequent values take into account the exaltation due to the three-membered ring.

(Found: C, 79·9; H, 8·5; N, 5·4. $C_{18}H_{23}ON$ requires C, 80·3; H, 8·6; N, 5·2%).

Dehydration of Ethyl Thujolacetate.—The hydroxy-ester was heated with potassium hydrogen sulphate at 160° for 3 hours, and the resulting ester was isolated by means of steam and distilled. The fraction, b. p. 138—148°/14 mm., was hydrolysed with 30% aqueous potassium hydroxide and alcohol, and the acid formed was liberated and isolated by means of ether. This acid was a mixture of a solid (main product) and an oil. The solid *acid* (V) separated from benzene–petroleum in plates, m. p. 169° (Found: C, 74·2; H, 9·3. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·3%). The oily acid could not be purified and decomposed on distillation, and solid derivatives could not be obtained from it. The same mixture of acids was also produced when the hydroxy-ester was dehydrated with phosphorus oxychloride or pentoxide.

The acid, m. p. 169°, could not be characterised by the formation of derivatives because the acid chloride, although evidently formed, decomposed violently on attempted distillation. The *sodium* salt is characteristic, being sparingly soluble in water and forming fine, silvery plates. The *silver* salt was prepared from it (Found: Ag, 35·9. $C_{12}H_{17}O_2Ag$ requires Ag, 35·9%).

Equilibration Experiments.—β-Thujylideneacetic acid in 1·94 g. lots was heated with 18 c.c. of 25% aqueous potassium hydroxide in sealed tubes at 100° for 24, 32, 40 and 48 hours. The products were worked up under the standard conditions of Linstead and May (this vol., p. 2565) and the iodine values of the equilibrated acids and of the original αβ-acid were then determined as described by them:

Time (hrs.)	0	24	32	40	48
% Absorption	8·4	33·9	52·0	49·6	56·8

The last three values, although not very concordant, suffice to show that equilibration was complete after 32 hours. As the iodine value of the pure βγ-acid was not known, it was necessary to estimate the proportion of the two acids present in the equilibrium mixture by isolating the αβ-acid by Bougault's method (*Ann. Chim. Phys.*, 1908, **14**, 145); this gives the minimum amount of αβ-acid present. For this purpose, 10 g. of pure αβ-acid were heated with potassium hydroxide for 45 hours; the semi-liquid product was isolated as before and treated with iodine under Linstead and May's standard conditions. The excess of iodine was removed with sodium thiosulphate after 10 minutes and the unchanged αβ-acid contained in the aqueous layer was liberated, extracted with ether, and recovered from the extract by evaporation, 2·50 g. being obtained.

This represents a minimum of 25% of αβ-acid in the equilibrium mixture.

The acid (V) was similarly treated with both 25% and 50% potassium hydroxide solution, but in every case it was isolated completely unchanged. The acid was treated with iodine before and after treatment with alkali, and the absorptions were identical within the limits of experimental error (96·1 and 96·3%). The high iodine value and the high melting point (169°) of the acid and its general similarity to dihydro-*m*-tolylacetic acid (see below) point to a formula with two double bonds in the ring. The true βγ-acid (IV) appears to be a liquid.

β-*Thujylideneacetone* (VI).—The chloride of β-thujylideneacetic acid, on treatment with zinc methyl iodide (Blaise and Maire, *Ann. Chim. Phys.*, 1908, **15**, 556), gave a 30% yield of the ketone. The sparingly soluble *semicarbazone* crystallised from methyl alcohol in plates, m. p. 191° (Found : C, 67·2; H, 9·2; N, 17·1. $C_{14}H_{23}ON_3$ requires C, 67·5; H, 9·2; N, 16·9%). The *ketone* regenerated from it had b. p. 120°/10 mm., $d_{4°}^{17·4°}$ 0·93111, $n_{D}^{17·4°}$ 1·48464, $[R_L]_D$ 59·15 (calc., 58·07), its physical properties agreeing with the αβ-structure (VI). The ketone was readily methylated with sodium and methyl iodide (Kon, J., 1926, 1792), a 30% yield of an oil, b. p. 122—124°/14 mm., being obtained. This was converted into the *semicarbazone*, which crystallised from methyl alcohol in plates, m. p. 194° (Found: C, 68·3; H, 9·6; N, 16·1. $C_{15}H_{25}ON_3$ requires C, 68·4; H, 9·6; N, 16·0%), and was less soluble than the semicarbazone of the parent ketone; a mixture of the two melted at about 176°. The *ketone* (VII) regenerated from the semicarbazone had b. p. 122°/14 mm., $d_{4°}^{17·8°}$ 0·91690, $n_{D}^{17·8°}$ 1·47339, $[R_L]_D$ 63·12 (calc., 62·69).

Condensation of β-*Thujone with Acetone.*—Dry sodium methoxide, prepared from 12 g. of sodium by Komppa's method (*Annalen*, 1909, **368**, 137), was cooled in ice, an ice-cold mixture of β-thujone and acetone (½ g.-mol. of each) added, and the whole kept in the ice-chest for 4 days. Water and dilute sulphuric acid were then added and the mixture was distilled in steam for a short time. From the residue in the flask a considerable quantity of solid, accompanied by an oil, separated on cooling. The solid consisted of 2-iso*propylidene*-β-*thujone* (VIII) and crystallised from methyl alcohol in needles, m. p. 78·5° (Found : C, 81·2; H, 10·2; *M*, cryoscopic in benzene, 194·6, 186·3. $C_{13}H_{20}O$ requires C, 81·3; H, 10·4%; *M*, 192). Further small quantities of the ketone could be isolated from the oily by-product in the form of its sparingly soluble *semicarbazone*, which crystallised from methyl alcohol in leaflets, m. p. 208° (Found : C, 67·3; H, 9·2; N, 17·0. $C_{14}H_{23}ON_3$ requires C, 67·5; H, 9·2;

N, 16·9%). The ketone, on oxidation with ozone, gave acetone and a substance (giving a purple colour with ferric chloride), which was not further investigated.

Pinocamphone.—This ketone was obtained from oil of hyssop by fractionation under reduced pressure; the fraction, b. p. 84—86°/11 mm., had $d_{4^\circ}^{16\cdot5^\circ}$ 0·95676, $n_{D}^{16\cdot5^\circ}$ 1·47522, $[R_L]_D$ 44·74, and gave a semicarbazone, m. p. 228°. All attempts to condense the ketone with ethyl bromoacetate, ethyl malonate, ethyl acetoacetate, and ethyl cyanoacetate were fruitless.

*Dihydro-*m*-tolylacetic Acid* (IX).—This acid was prepared from 3-methyl*cyclo*hexenone as described by Wallach (*Annalen*, 1902, **323**, 138). The pure acid was treated with potassium hydroxide as described on p. 2598, but was recovered completely unchanged. Specimens of the acid before and after treatment with alkali were treated with iodine, but no difference in iodine absorption could be detected (95·6% in both cases).

Attempts to prepare the corresponding ketone (X) by the Blaise–Maire reaction failed because the chloride of the acid, like that of the acid (V), could not be distilled. The crude acid chloride did not give a satisfactory product.

Attempts were also made to obtain the ketone by condensing 3-methyl*cyclo*hexenone with acetone, but a pure substance could not be isolated from the complex mixture formed.

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