CCV.—*The Chemistry of the Three-carbon System. Part XIII. The Effect of Bulky Substituents and of the* cyclo*Heptane Group on the Tautomerism.*

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The effect of a positive substituent in the α-position on the tautomerism of a three-carbon system has been discussed (this vol., p. 1536); that of bulky substituents in the β-position is now described.

To obtain a strictly comparable series it would be necessary to work with β-substituted pentenoic acids, because it has already been shown that the βγ-phase does not become stable until the γ-carbon atom carries at least a methyl group, as in the acid $CHMe{:}CMe{\cdot}CH_2{\cdot}CO_2H$ (Kon and Linstead, J., 1925, **127**, 616). The next member of the series is diethylacrylic acid; this and its βγ-isomeride were studied by Kon and Linstead. Other β-substituted pentenoic acids are, however, difficult to prepare owing to lack of accessible initial materials, and a further difficulty is that there are in every case two possible βγ-acids, according as the double bond is in the shorter or the longer chain. We have therefore limited the present experiments to two compounds, namely, ββ-dipropyl- and ββ-di*iso*butyl-acrylic acids (I; R = Et and Pr^β^, respectively) and their βγ-isomerides (II), to which these objections do not apply.

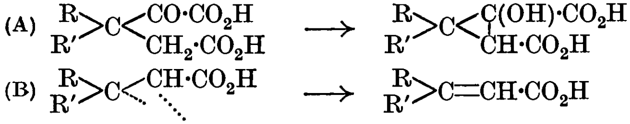
(I.)

$$\begin{matrix}CH_2R\\CH_2R\end{matrix}\!>\!C{:}CH\cdot CO_2H$$

$$\begin{matrix}CH_2R\\CHR\end{matrix}\!\geqslant\!C\cdot CH_2\cdot CO_2H$$

(II.)

The γ-substituent in these acids may be expected to have some effect on the stabilities of the αβ- and βγ-forms. From considerations based on the electronic theory (compare Allan, Oxford, Robinson, and Smith, J., 1926, 401; Ingold, Shoppee, and Thorpe, *ibid.*, p. 1477), it is deduced that the presence of a positive substituent in the γ-position would favour the βγ-phase, whilst in the β-position this substituent would have little effect. These effects will be comparatively insignificant if it is merely a question of substituting a larger for a smaller group. Should, however, steric factors have any considerable influence on the equilibrium, then it might be expected that such a substitution would produce a very definite effect; and this will be shown to be the case. The tendency of a double bond to migrate from the αβ- to the βγ-position appears to be connected with the alteration of the normal tetrahedral angle about the β-carbon atom (J., 1926, 2727); the case may be compared with the formation of a three-membered ring by ring-chain tautomerism (Bains and Thorpe, J., 1923, **123**, 1206; Deshapande and Thorpe, J., 1922, **121**, 1430).



(A) $$\begin{matrix}R\\R'\end{matrix}\!>\!C\!<\!\begin{matrix}CO\cdot CO_2H\\CH_2\cdot CO_2H\end{matrix}\longrightarrow\begin{matrix}R\\R'\end{matrix}\!>\!C\!<\!\begin{matrix}C(OH)\cdot CO_2H\\|\\CH\cdot CO_2H\end{matrix}$$

(B) $$\begin{matrix}R\\R'\end{matrix}\!>\!C\!<\!\begin{matrix}CH\cdot CO_2H\\\end{matrix}\longrightarrow\begin{matrix}R\\R'\end{matrix}\!>\!C{=}CH\cdot CO_2H$$

The formation of an αβ-double bond in (B) will be analogous to the formation of a three-membered ring from (A), an increase in bulk of the groups R and R′ in each case facilitating the formation of the " ring " system. In (B) there are three possible positions for the double bond; the four valencies of the central carbon atom must be regarded as asymmetrically directed, the angle between any two of them being determined by the resultant of two opposing steric factors. The double bond should therefore be most readily produced in the direction of the smallest group (this does not apply to the methyl group owing to the comparative instability of a terminal methylene group, unless specially stabilised as in itaconic acid). In straight-chain acids where R = H (*e.g.*, the pentenoic acids), the steric effect is negligible and the αβ-phase is the more stable; as the bulk of R increases, the βγ-form is stabilised. When, however, both R and R′ increase to such an extent that the group

$-CH\cdot CO_2H$ becomes relatively small, the equilibrium again tends towards the αβ-form. It is doubtless for this reason that Johnson and Kon (J., 1926, 2748) found the equilibrium in the β-ethylcinnamic acids to be on the side of the βγ-form (76 : 24), whilst in the next higher acids the equilibrium was already of the order 50 : 50. Again, in the *gem*-diethyl series, the equilibrium is strongly on the side of the βγ-form (95 : 5, according to Linstead; this vol., p. 355). The two pairs of acids now studied fall well into line, for the equilibrium in the dipropyl series is 67 : 33 in favour of the βγ-form, whilst in the di*iso*butyl series it is already 51 : 49, thus illustrating the effect of bulky groups.

In the behaviour of the cyclic acids, other factors come into play. The tendency of a ring to acquire a double bond—which is a measure of the stability of the βγ-phase—is difficult to correlate with the distortion of the normal tetrahedral angle in these rings; *e.g.*, the stability of the βγ-phase increases but slightly from the *cyclo*pentane (85 : 15; Linstead, private communication) to the *cyclo*hexane series (88 : 12; Linstead, *loc. cit.*), although the difference in the distortion of the normal tetrahedral angle is considerable; it decreases appreciably in the *cyclo*heptane series, the equilibrium being about 75 : 25 in favour of the βγ-phase. In other words, the *cyclo*heptane ring shows less tendency to acquire a double bond than either of the smaller rings.

ββ-Dipropylacrylic acid (I; R = Et) has been described by Albitzki (*J. pr. Chem.*, 1884, **30**, 209) as a solid, m. p. 80—82°; this was analysed only in the form of variously hydrated salts. Reformatski (*J. Russ. Phys. Chem. Soc.*, 1890, **22**, 44) obtained the acid only as a liquid; the dibromide he prepared from it differed from Albitzki's dibromide. We have prepared the acid, which melts at 9°, by dehydrating ββ-dipropylhydracrylic acid with acetic anhydride and have characterised it by the formation of an amide, m. p. 72°; its structure was confirmed by oxidation. Albitzki's method of dehydrating the hydroxy-acid could lead only to the βγ-acid, and did so in our hands. The βγ-acid obtained thus and in other ways was always contaminated with αβ-acid; all the preparations were liquid (all the βγ-acids studied up to the present melt at lower temperatures than the αβ-acids; the converse holds for the amides), and the acid itself has not yet been obtained pure, although a pure ester and an amide (m. p. 120—121°) have been prepared. The di*iso*butyl compound proved even more discouraging in this respect, as inseparable mixtures of the two acids were obtained by all the available methods.

cyclo*Heptylideneacetic acid*, on the other hand, was readily obtained as a solid, m. p. 54°, giving a dibromide, m. p. 125°.

Baker and Ingold isolated a small quantity of a liquid which they described as the αβ-acid and characterised by the formation of a dibromide, m. p. 125°; this must have been the αβ-dibromide. This is surprising, because, under the experimental conditions used by Baker and Ingold, the αβ-acid is rapidly isomerised to the extent of 75% into the liquid βγ-isomeride, previously described by Wallach as the αβ-form (*Annalen*, 1902, **314**, 157) and yielding a dibromide, m. p. 103—104°. It must be assumed that Baker and Ingold's hydrolysis was carried out so rapidly that complete equilibration of the αβ-acid first produced could not take place and the mixture contained enough αβ-acid to give its dibromide.

EXPERIMENTAL.

ββ-*Dipropylacrylic Acid* (I; R = Et).—The reaction between dipropyl ketone and ethyl bromoacetate with magnesium proceeded well in benzene solution, the yield of ethyl ββ-dipropylhydracrylate, b. p. 139°/15 mm., being 50%. The acid was obtained from the ester, on hydrolysis in the usual manner, as a thick oil which could not be distilled even at 2 mm.

On dehydration with acetic anhydride (Wallach, *Annalen*, 1907, **353**, 288), it yielded ββ-dipropylacrylic acid (I), which is a colourless, practically odourless oil, b. p. 144°/17 mm.; this set, on freezing, to a mass of crystals which melted at 9°. It had $d_4^{20\cdot0^\circ}$ 0·93624, $n_D^{20\cdot0^\circ}$ 1·46350, $[R_L]_D$ 45·97 (calc. 44·84) (Found: C, 68·9; H, 10·4. Calc. for $C_9H_{14}O_2$: C, 69·1; H, 10·3%. Found in the silver salt: Ag, 41·1. Calc.: Ag, 41·1%). The *chloride* had b. p. 128°/25 mm. and gave with ammonia in ethereal solution the *amide*, which separated from light petroleum in long, flattened needles, m. p. 72°. The p-*toluidide* crystallised from dilute methyl alcohol in needles, m. p. 82·5°. The *ethyl* ester, prepared through the acid chloride, had b. p. 108—109°/14 mm., $d_4^{18\cdot0^\circ}$ 0·89284, $n_D^{18\cdot4^\circ}$ 1·44923, $[R_L]_D$ 55·35 (calc., 54·19). Both the ester on treatment with ozone and the acid on oxidation with permanganate gave good yields of dipropyl ketone, which was identified by means of its semicarbazone, m. p. 133°.

β-*Propyl*-Δ^{β}-*hexenoic Acid* (II; R = Et).—The ethyl ester was readily obtained pure by heating ethyl ββ-dipropylhydracrylate with a 20% excess of phosphorus pentoxide under reduced pressure; it gradually distilled and was purified by redistillation (yield 75%); b. p. 116—118°/25 mm., $d_4^{25\cdot0^\circ}$ 0·89264, $n_D^{25\cdot0^\circ}$ 1·43778, $[R_L]_D$ 54·13. It gave no trace of dipropyl ketone on oxidation. The acid was prepared by the hydrolysis of this ester, also by dehydrating the hydroxy-acid by means of 20% sulphuric acid (compare Farrow and Kon, J., 1926, 2138; Albitzki, *loc. cit.*; Reformatski, *loc. cit.*), 50% sulphuric acid, or phosphorus trichloride. In the last case, the acid (3 mols.) in ether was gradually added to rather more than 2 mols. of the chloride with cooling, and the mixture was kept for 24 hours and finally warmed on the steam-bath until no more hydrogen chloride was evolved. The acid obtained by these processes had b. p. 138—140°/22 mm. and 126—128°/11 mm., and the following properties :

(1 ; 20% H_2SO_4) $d_{4^\circ}^{22^\circ}$ 0·93400, n_D 1·45593, $[R_L]_D$ 45·43.
(2 ; 50% H_2SO_4) $d_{4^\circ}^{16^\circ}$ 0·93813, n_D 1·45833, $[R_L]_D$ 45·42.
(3 ; PCl_3) $d_{4^\circ}^{19^\circ}$ 0·93692, n_D 1·45753, $[R_L]_D$ 45·42.

All the samples thus showed a slight exaltation, and gave on oxidation small quantities of dipropyl ketone. Many methods of purification were tried without success. The *chloride* boiled at 107°/30 mm. and gave a mixture of amides on treatment with ammonia. This was resolved into its constituents by repeatedly washing it with petroleum, in which only the αβ-amide was freely soluble. The residue, after several crystallisations from benzene–petroleum, consisted of the pure βγ-*amide*, m. p. 120—121° ; it could be sublimed (Found : C, 69·5 ; H, 11·2. $C_9H_{15}ON$ requires C, 69·6 ; H, 11·1%).

Equilibration of the Acids.—The αβ- and the βγ-acid (in the latter case, the purest sample available) were each refluxed with ten times the calculated quantity of potassium hydroxide (20 or 60% solution) for 24 hours ; the acid mixture was then isolated by Linstead's method (*loc. cit.*). The percentage of αβ-acid in the mixture was determined by Bougault's method (*Ann. Chim. Phys.*, 1908, **14**, 145) with the following results :

Equilibrium mixture from the αβ-acid : (a) 35·7%, (b) 33·0%.
„ „ βγ-acid : (a) 31·4%,

from which the mean figure is 33%. A discussion of the details of procedure is reserved for a future communication.

Attempts to Prepare the Acids by Other Methods.—An attempt to prepare the αβ-acid by elimination of hydrogen bromide from α-bromo-β-propylhexoic acid was abandoned because the bromo-acid could not be obtained free from unbrominated material. The preparation was carried out as follows : Dipropylcarbinol (100 g.), prepared in 50% yield by the method followed by Grignard (*Compt. rend.*, 1901, **132**, 336) for preparing di*iso*butylcarbinol and in 75% yield by reducing dipropyl ketone with sodium wire in wet ether (Kurtz, *Annalen*, 1876, **181**, 205), was refluxed for 4—5 hours with 600 g. of hydrobromic acid (*d* 1·5) free from sulphuric acid. The bromide, b. p. 161—165°/749 mm. (slight decomp.), 88°/64 mm., thus obtained in 50% yield, was condensed with ethyl sodiomalonate in alcohol in the usual manner, a good yield of *ethyl hydrogen* iso*heptylmalonate*, b. p. 168°/35 mm., being obtained in the place of the diethyl ester (Found: C, 62·9; H, 9·4. $C_{12}H_{22}O_4$ requires C, 62·6; H, 9·6%). The acid was readily obtained on alkaline hydrolysis; it refused to solidify and therefore was distilled, a good yield of β-*propylhexoic acid* being collected as a colourless liquid with a not unpleasant odour, b. p. 144°/30 mm. (Found: C, 68·2; H, 11·3. $C_9H_{16}O_2$ requires C, 68·3; H, 11·5%). The acid was converted into its chloride and brominated, crystals of an unstable bromo-acid chloride being obtained; these could not be freed from unbrominated material and rapidly decomposed on distillation or on exposure to the air.

Attempts to obtain the corresponding β-bromo-acid (hydrobromide of dipropylacrylic acid) were also unsuccessful.

ββ-*Di*iso*butylacrylic Acid.*—Di*iso*butyl ketone (*iso*valerone) was condensed with ethyl bromoacetate; the yield of ethyl β-hydroxy-ββ-di*iso*butylpropionate was always poor, the best (35%) being obtained by carrying out the condensation in ether and warming the reaction product over-night; 30% of the ketone was recovered. The ester boiled at 138—140°/20 mm. and yielded a viscous liquid acid on hydrolysis. The hydroxy-acid could not be purified by distillation. It was dehydrated both with acetic anhydride and with dilute sulphuric acid, mixtures of unsaturated acids being obtained in every case; b. p. 144—149°/20 mm. (Found: C, 71·5; H, 10·6. $C_{11}H_{18}O_2$ requires C, 71·7; H, 10·9%). The properties of different preparations were as follows ($[R_L]_D$ calc., 54·06):

Source of acid.	*t.*	*d.*	n_D.	$[R_L]_D$ obs.
(1) Dehydr. by Ac_2O	21°	0·92530	1·46091	54·60
(2) ,, ,, ,, ...	21	0·92488	1·46111	54·65
(3) ,, ,, ,, ...	26	0·91885	1·46982	54·88
(4) ,, ,, dil. H_2SO_4	19	0·92141	1·46723	54·46
(5) KOH on (1)	18·5	0·92609	1·46131	54·56
(6) ,, (4)	20	0·91660	1·46603	54·51
(7) Regen. from acid chloride...	17·5	0·92782	1·46144	54·54

Equilibration. This was carried out as described on p. 1553, and the percentage of αβ-acid in the mixture determined as before; the mean value was 49% of αβ-acid.

cyclo*Heptylideneacetic Acid.*—Suberone, obtained in 40% yield from thorium suberate by Ruzicka's method (*Helv. Chim. Acta*, 1926, **9**, 515), was converted into ethyl *cyclo*heptanolacetate (Wallach, *loc. cit.*) as before, 30 g. being obtained from 56 g. of suberone, 16 g. of which were recovered. This quantity of ester gave 20 g. of hydroxy-acid which did not solidify.

The acid (20 g.) was boiled with 35 c.c. of acetic anhydride for

3—4 hours, and the unsaturated acid isolated by distillation in steam, 5 g. of solid being obtained in addition to a small amount extracted from the head and tail fractions; it formed colourless needles, m. p. 54° (Found: C, 69·6; H, 9·2. $C_9H_{14}O_2$ requires C, 70·1; H, 9·2%).

A small quantity of the acid was treated with dry ozone in chloroform solution; the ozonide on decomposition gave an 80% yield of suberone (weighed as semicarbazone).

αβ-*Dibromo*cyclo*heptylacetic Acid.*—The αβ-acid (0·5 g.) was dissolved in 2 c.c. of acetic acid, 0·5 g. of bromine in acetic acid added, and the mixture left in an exhausted desiccator; crystals of the dibromide slowly separated. On recrystallisation from chloroform–petroleum colourless crystals, m. p. 125°, were obtained.

Δ^1-cyclo*Heptenylacetic Acid.*—The hydroxy-acid (15 g.) was refluxed for 3 hours with an excess of 10% sulphuric acid, and the unsaturated acid was distilled in steam and isolated by means of ether, the yield being 2·5 g. Its properties corresponded closely with those of Wallach's acid: b. p. 158—160°/18 mm., $d_{4°}^{22°}$ 1·0382, $n_D^{22°}$ 1·49232, $[R_L]_D$ 43·09. When examined by Bougault's method, this acid was proved to contain 24% of αβ-acid.

βγ-*Dibromo*cyclo*heptylacetic Acid.*—The crude βγ-acid was converted into a dibromide under the same conditions as the αβ-acid; it crystallised only partly, the solid being the new dibromo-acid, which on crystallisation formed hard, colourless prisms, m. p. 103—104°. A mixture of this with the αβ-dibromide melted at about 79°. On standing, the βγ-dibromide gradually darkened and appeared to be converted into a bromo-lactone.

Equilibration. Experiments were carried out starting both with the αβ- and with the βγ-acid; the mean of several determinations gave the percentage of the αβ-acid in the mixture as 25·6.

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