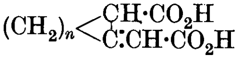
357. *The Structure of the Glutaconic Acids and Esters. Part IV. Some Cyclic Glutaconic Derivatives.*

By G. A. R. KON and H. R. NANJI.

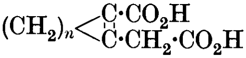
PREVIOUS experiments (J., 1931, 560; this vol., pp. 1, 1027) lead to the conclusion that the chemistry of glutaconic acid derivatives is satisfactorily accounted for by the simultaneous occurrence of tautomerism and stereoisomerism. It is of importance to determine the part played by each of these forms of isomerism in the development of what may be termed " glutaconic character " and therefore some glutaconic acid derivatives in which stereoisomerism is precluded by ring formation have been studied.

Such compounds are the reduced *iso*phthalic acids (Farmer and Richardson, J., 1926, 2127) and 3-methyl*cyclo*propenedicarboxylic acid (Goss, Ingold, and Thorpe, J., 1923, **123**, 327). In the compounds now to be described, two of the carbon atoms of the propene chain are part of a five- or a six-membered ring and they are therefore comparable with an αβ-disubstituted glutaconic acid derivative :

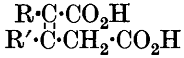


$(CH_2)_n<\begin{matrix}CH\cdot CO_2H\\ C{:}CH\cdot CO_2H\end{matrix}$

$\begin{matrix}R\cdot CH\cdot CO_2H\\ R'\cdot C{:}CH\cdot CO_2H\end{matrix}$

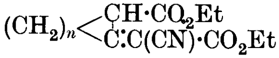


$(CH_2)_n<\begin{matrix}C\cdot CO_2H\\ \|\\ C\cdot CH_2\cdot CO_2H\end{matrix}$

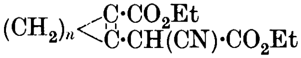


$\begin{matrix}R\cdot C\cdot CO_2H\\ \|\\ R'\cdot C\cdot CH_2\cdot CO_2H\end{matrix}$

The compounds themselves are obtained by an extension of Rogerson and Thorpe's synthesis of cyanoglutaconic esters (J., 1905, **87**, 1669) to cyclic acetoacetic esters. Ethyl *cyclo*pentanone-2-carboxylate condenses with ethyl cyanoacetate in presence of piperidine or potassium ethoxide, giving a good yield of an *ester* the

(I.) 

$(CH_2)_n<\begin{matrix}CH\cdot CO_2Et\\ C{:}C(CN)\cdot CO_2Et\end{matrix}$

 (II.)

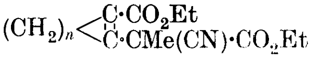
$(CH_2)_n<\begin{matrix}C\cdot CO_2Et\\ \|\\ C\cdot CH(CN)\cdot CO_2Et\end{matrix}$

reactions of which show that, unlike the analogous ethyl α-cyano-βγ-dimethylglutaconate similarly obtained from ethyl methylacetoacetate, it is not an equilibrium mixture of (I) and (II) ($n = 3$) but consists solely of the latter. For instance, it gives on oxidation with ozone a diketonic ester, $CO_2Et\cdot CO\cdot (CH_2)_3\cdot CO\cdot CH(CN)\cdot CO_2Et$, no trace of the easily recognisable ethyl *cyclo*pentanone-2-carboxylate being formed.

Like the corresponding open-chain ester, the ester (II; $n = 3$) readily forms a potassio-derivative, even with 10% aqueous alkali, and is therefore more acidic than ethyl α-cyano-βγ-dimethylglutaconate and is comparable with ethyl α-cyano-β-methylglutaconate. The potassio-derivative has the metal attached to the cyanoacetic residue, since on treatment with methyl iodide it gives the α-*methyl* derivative (III) and this on treatment with sodium ethoxide loses a carbethoxyl group and passes into the *nitrile* (IV); the nitrile, unlike the majority of unsaturated nitriles studied (compare Kandiah and Linstead, J., 1929, 2139; Letch and Linstead, this vol., p. 443), appears to be a pure βγ-unsaturated compound :

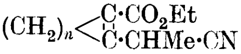
(II) ⟶ 

$(CH_2)_n{<}\begin{array}{l}C\cdot CO_2Et\\ C\cdot C(CN)\cdot CO_2Et\}K\end{array}$

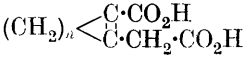


$(CH_2)_n{<}\begin{array}{l}C\cdot CO_2Et\\ C\cdot CMe(CN)\cdot CO_2Et\end{array}$

(III.)

(IV.) 

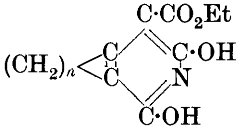
$(CH_2)_n{<}\begin{array}{l}C\cdot CO_2Et\\ C\cdot CHMe\cdot CN\end{array}$

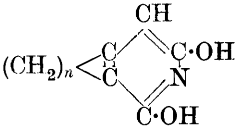
 (V.)

$(CH_2)_n{<}\begin{array}{l}C\cdot CO_2H\\ C\cdot CH_2\cdot CO_2H\end{array}$

On acidification with benzoic acid in presence of a neutral solvent or with mineral acid in presence of water the potassio-derivative regenerates the pure ester (II), which evidently has no tendency to pass into the modification (I).

The hydrolysis of the ester (II) has been carried out with acid and with alkaline reagents. The former produce a mixture of the non-nitrogenous *acid* (V; $n = 3$) and a substituted *pyridine* derivative, to which the formula (VI; $n = 3$) has been assigned; hydrolysis with alkali leads to the production of a pyridine derivative (VII; $n = 3$) probably formed from (VI) by decarboxylation; the acid (V) is not formed in this case.

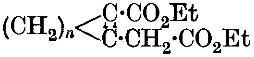
(VI.) 

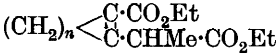
 (VII.)

Both the methylated ester (III) and the nitrile (IV) give pyridine derivatives on hydrolysis, no nitrogen-free acid having been obtained up to the present.

The cyclic glutaconic acid (V) is a definite individual compound, unaccompanied by any trace of an isomeride; it is unaffected by prolonged boiling with alkalis or acids. The ester, whether prepared through the silver salt or merely by boiling the acid with alcoholic sulphuric acid, is also an individual compound of the structure (VIII; $n = 3$), as shown by the nature of the product obtained on oxidation with ozone. The ester is completely unaffected by prolonged treatment with sodium ethoxide, the recovered ester having the same physical properties and giving the same individual oxidation product as the initial material; addition of the elements of ethyl alcohol does not occur in 24 hours, no trace of a high-boiling fraction being formed.

The ester forms a potassio-derivative which can be converted into the *methylated* ester (IX; $n = 3$) by means of methyl iodide; methylation in alcoholic solution is not quite complete.

(VIII.)

$$(CH_2)_n{<}\begin{matrix}C\cdot CO_2Et\\ \| \\ C\cdot CH_2\cdot CO_2Et\end{matrix}$$


$$(CH_2)_n{<}\begin{matrix}C\cdot CO_2Et\\ \| \\ C\cdot CHMe\cdot CO_2Et\end{matrix}$$
(IX.)

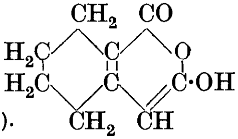
The ester thus behaves like a typical disubstituted glutaconic ester.

The acid (V) does not react with acetyl chloride, but is converted by boiling acetic anhydride into an acidic *anhydride* which gives an intense colour with ferric chloride in the manner characteristic of the hydroxy-anhydrides of typical glutaconic acids. The structure of this compound is, however, abnormal: it has the formula $C_{10}H_{10}O_4$, not $C_8H_8O_3$, agreeing with the composition of an acetyl anhydride, but on treatment with aniline it gives a *compound* which appears to be $C_{16}H_{15}O_3N$. The anhydride $C_{10}H_{10}O_4$ is accompanied by one of the ordinary type, because a small amount of the corresponding *semianilide* has been isolated from the liquid portion of the dehydration product on treatment with aniline.

Little need be said of the analogous *cyclo*hexane derivatives, which are very similar to the lower homologues. The original *cyano*-ester, the non-nitrogenous acid and its ester (II, V, and VIII; $n = 4$) are pure individual compounds, static in the $\beta\gamma$-form. The cyano-ester is acidic and is readily methylated on the α-carbon, the new *ester* (III; $n = 4$) losing the carbethoxyl group to form the *nitrile* (IV; $n = 4$), which also has the $\beta\gamma$-structure. The non-nitrogenous ester forms a potassio-derivative and can be alkylated.

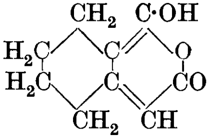
The nitrogenous *compound* (VII; $n = 4$) formed in the hydrolysis of the cyano-ester is less stable than the lower homologue and the acid is consequently obtained in much better yield. The preparation of the compound (VII) constitutes a new synthesis of an *iso*quinoline derivative.

The cyclic *glutaconic acid* (V; $n = 4$) differs from its lower homologue in melting with decomposition and in forming a hydroxy-anhydride which has the expected structure (X):



(X).

or, less probably,



This compound has not been obtained pure, but it is sufficiently characterised by the crystalline semianilide obtained from it; on treatment with strong alkali, followed by acidification, the anhydride reverts to the acid (V).

The cyclic glutaconic acid derivatives now described, although incapable of stereoisomerism, nevertheless exhibit the characteristics usually associated with true glutaconic acids and esters. They do not appear to occur in two forms differing in the position of the double bond, all the compounds examined being $\beta\gamma$-unsaturated.

In this connexion it is clear—and was only to be expected *a priori*—that the existence of $\alpha\beta$- and $\beta\gamma$-unsaturated modifications in the glutaconic acid series is a question of the relative stability of these forms; the probability of their occurrence must increase with the increasing symmetry of the molecule. As an example of this may be cited the failure of Gidvani, Kon, and Wright (this vol., p. 1027) to obtain an individual ester from α-methyl-γ-ethylglutaconic acid in spite of all precautions and the employment of a technique which had proved successful with the less symmetrical α-benzyl-β-methylglutaconic esters. The compounds now studied provide an example of the opposite state of affairs, although it is not obvious why the inclusion of the β- and the γ-atom of the propene chain in a ring should stabilise the $\beta\gamma$-form to the complete exclusion of the $\alpha\beta$. The same phenomenon has previously been observed to a less degree in simpler unsaturated compounds and still awaits a satisfactory theoretical explanation.

EXPERIMENTAL.

Ethyl 2-Carbethoxy-Δ^1*-*cyclo*pentenylcyanoacetate* (II; $n = 3$).—A mixture of ethyl *cyclo*pentanonecarboxylate (56 g.) (Dobson, Ferns, and Perkin, J., 1909, **93**, 2015), ethyl cyanoacetate (38 g.), and a few drops of piperidine was kept for 2 days and then warmed on the steam-bath for 4—5 hrs. The oil produced was washed (dil. HCl) and dried in Et_2O and fractionated; the new ester (50% yield) boiled at 188°/16 mm. A somewhat better yield (59%) was obtained by adding to an ice-cold solution of K (13 g.) in 90 c.c. of dry EtOH first the ethyl cyanoacetate and then, slowly, the ketonic ester. The mixture was kept in ice and then at room temp. for 2 days, treated with dil. acid, and worked up as before. The pure *ester* had $d_{4^\circ}^{20\cdot0^\circ}$ 1·129, $n_D^{20\cdot0^\circ}$ 1·4838, $[R_L]_D$ 64·53 (Found: C, 61·9; H, 6·9. $C_{13}H_{17}O_4N$ requires C, 63·1; H, 6·8%), and was readily converted into a cryst. yellow K compound by 10% KOH aq. or by KOEt.

Ozonisation. Treatment with ozonised oxygen in dry AcOEt at 0°, removal of the solvent, and shaking with H_2O over-night gave a product, which was washed in Et_2O with $NaHCO_3$ aq. and distilled; b. p. 150—190°/30 mm., no low fraction corresponding to ethyl *cyclo*pentanonecarboxylate being obtained. The oil gave a deep purple colour with $FeCl_3$ and formed a sparingly sol. *diphenylhydrazone*, scales, m. p. 256° (decomp.), from much EtOH (Found: C, 64·3; H, 6·1. $C_{25}H_{29}O_4N_5$ requires C, 64·7; H, 6·2%). The ester was therefore *ethyl α-cyano-βε-diketosuberate.*

Regeneration of the Cyano-ester from the Potassio-derivative.—The ester was added to a suspension of KOEt, freed from EtOH, in dry Et_2O (compare Kon and Nanji, J., 1931, 560) and the gelatinous potassio-derivative was filtered off, suspended in dry Et_2O, and shaken with a slight deficiency of dry $Ph\cdot CO_2H$ for 3 days. After removal of $Ph\cdot CO_2K$ the Et_2O was evaporated off; the residue, b. p. 190—191°/18 mm., had $d_{4^\circ}^{20\cdot0^\circ}$ 1·123, $n_D^{20\cdot0^\circ}$ 1·4839, $[R_L]_D$ 64·57 and therefore consisted of unchanged initial material; it gave the same product on ozonisation.

Ethyl α-Cyano-α-2-carbethoxy-Δ^1-cyclo*pentenylpropionate* (III; $n = 3$).—The potassio-derivative of the cyano-ester, prepared as described above but not isolated, was refluxed with MeI, a 90% yield of the methylated *ester* being obtained, b. p. 177—178°/17 mm., $d_{4°}^{20\cdot0°}$ 1·0704, $n_{D}^{20\cdot0°}$ 1·4737, $[R_L]_D$ 69·57 (Found: C, 63·2; H, 7·3. $C_{14}H_{19}O_4N$ requires C, 63·4; H, 7·2%).

Ozonisation. The methylated ester was treated as described on p. 2429. The neutral oxidation product boiled entirely between 140° and 170°/16 mm., except for a small high fraction of unoxidised initial material; it gave with $FeCl_3$ a faint colour due to a trace of the parent ester (II). The main fraction gave a *diphenylhydrazone*, small plates, m. p. 217—218°, from EtOH (Found: C, 64·9; H, 6·4; N, 14·4. $C_{26}H_{31}O_4N_5$ requires C, 65·3; H, 6·3; N, 14·8%), and was evidently *ethyl α-cyano-βε-diketo-α-methylsuberate.*

α-2-Carbethoxy-Δ^1-cyclo*pentenylpropionitrile* (IV; $n = 3$).—The methylated ester, dissolved in a little EtOH, was added to the calc. quantity of Na dissolved in 12 parts of EtOH; after 24 hrs. the mixture was poured into dil. HCl and extracted with Et_2O. From the washed and dried extract, Et_2CO_3 was obtained by distillation, and then the *nitrile*, b. p. 151°/20 mm., $d_{4°}^{20\cdot0°}$ 1·0477, $n_{D}^{20\cdot0°}$ 1·4729, $[R_L]_D$ 51·70 (calc., 51·57) (Found: C, 68·4; H, 7·7. $C_{11}H_{15}O_2N$ requires C, 68·4; H, 7·8%).

Ozonisation. The sole product was an oil, b. p. 150—160°/19 mm.; this gave a violet colour with $FeCl_3$ and was characterised by the formation of a *diphenylhydrazone*, small plates, m. p. 210—211°, from EtOH (Found: C, 68·0; H, 6·6. $C_{23}H_{27}O_2N_5$ requires C, 68·1; H, 6·7%), and a semicarbazone, m. p. 242° (decomp.); it was evidently *ethyl ξ-cyano-βε-diketo-octoate.* No trace of ethyl *cyclo*pentanonecarboxylate could be detected.

Hydrolysis of the Cyano-ester (II).—(i) *With potassium hydroxide.* The ester (7 g.) was refluxed with 4·7 g. of KOH in MeOH for 24 hrs., the solution evaporated to dryness, and the residue treated with dil. HCl. The solid obtained, recryst. from AcOH, had m. p. 258° (darkening) and appeared to be (VII; $n = 3$) (Found: C, 63·5; H, 5·9. $C_8H_9O_2N$ requires C, 63·6; H, 5·9%); it formed a hydrochloride (unstable in moist air), dissolved in alkalis and alkali carbonates, forming blue solutions, and gave with $FeCl_3$ a violet colour which gradually faded.

(ii) *With hydrochloric acid.* The ester was boiled with conc. HCl (4 vols.) until it had dissolved (2·5 hrs.). On cooling, a solid separated: from this, the acid (V; $n = 3$) was extracted with dil. Na_2CO_3 aq., leaving the pyridine derivative, which constituted the greater part of the solid. A further small quantity of the acid was obtained by extracting the acid mother-liquor with Et_2O. The *pyridine* derivative, which was almost insol. in the usual solvents, was recrystallised from AcOH; m. p. 241° (decomp.); a solution of it in much boiling EtOH gave a bluish-violet colour with $FeCl_3$ and reduced ammoniacal $AgNO_3$. It appears to be (VI; $n = 3$) (Found: C, 58·9; H, 5·9. $C_{11}H_{13}O_4N$ requires C, 59·2; H, 5·8%); the benzoyl derivative had m. p. 80—100°.

(iii) *With sulphuric acid.* The ester was mixed with conc. H_2SO_4 (1 vol.) and kept over-night. After addition of H_2O, an amorphous solid separated from the hot solution, and silky needles on cooling. The insol. compound was the pyridine derivative, m. p. 241°, already described. The second compound, m. p. 89°, which was readily extracted by hot H_2O, was probably *ethyl 2-carboxy-*Δ^1-cyclo*pentenylmalonamate,* since it was further hydrolysed to the acid

(V) by HCl aq. (Found : C, 58·1; H, 7·2. $C_{13}H_{19}O_5N$ requires C, 58·0; H, 7·1%).

2-*Carboxy*-Δ^1-cyclo*pentenylacetic acid* (V; $n = 3$), obtained from the cyano-ester as described above, crystallised from H_2O in long needles, m. p. 187° (Found : C, 56·0; H, 5·9. $C_8H_{10}O_4$ requires C, 56·4; H, 5·9%). The ethyl ester (VIII; $n = 3$), prepared through the Ag salt, had b. p. 155°/20 mm., $d_{4°}^{20·0°}$ 1·0662, $n_D^{20·0°}$ 1·4694, $[R_L]_D$ 59·10 (calc., 58·02).

Ozonisation. The above ester gave as sole product an oil boiling almost completely between 130° and 140° and giving a deep purple colour with $FeCl_3$; this was evidently ethyl $\beta\varepsilon$-diketosuberate, which was characterised by its phenylhydrazine *derivative*, plates, m. p. 126°, apparently a phenylhydrazido pyrazolone (Found : C, 67·1; H, 6·4. $C_{22}H_{24}O_3N_4$ requires C, 67·3; H, 6·1%); it also gave a semicarbazone, m. p. 254°. No trace of ethyl *cyclo*pentanone-carboxylate, ethyl glyoxylate, or oxalic acid was isolated.

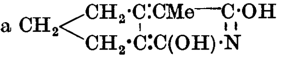
Action of sodium ethoxide. The ester was added to Na (1 equiv.) dissolved in 12 parts of dry EtOH and kept at 25° for 24 hrs. The ester was then recovered by addition of H_2O and dil. AcOH and extraction with Et_2O; it boiled at 160°/25 mm. to the last drop, had $d_{4°}^{20·0°}$ 1·0667, $n_D^{20·0°}$ 1·4696, and on ozonisation gave the same individual product as the initial material, no trace of ethyl *cyclo*pentanonecarboxylate being formed.

Methylation. The ester reacted vigorously with the theo. amount of " molecular " K suspended in C_6H_6, an orange potassio-derivative being formed; after 12 hrs., this was refluxed with an excess of MeI for 3 hrs. The ester isolated was *ethyl* 2-*carbethoxy*-Δ^1-cyclo*pentenylpropionate* (IX; $n = 3$), b. p. 149—150°/13 mm., $d_{4°}^{20·0°}$ 1·0486, $n_D^{20·0°}$ 1·4692, $[R_L]_D$ 63·80 (calc., 62·64) (Found : C, 65·2; H, 8·4. $C_{13}H_{20}O_4$ requires C, 65·0; H, 8·3%). This was also prepared by refluxing the parent ester with alc. NaOEt (1 equiv.) with an excess of MeI until neutral (3 hrs.). The action was not quite complete in either case, because the *acid* obtained by alkaline hydrolysis contained a small amount of the parent acid (V); after repeated crystn. from C_6H_6 and finally from H_2O, it formed thick prisms, m. p. 151° (Found : C, 68·2; H, 6·5. $C_9H_{12}O_4$ requires C, 68·7; H, 6·5%).

Hydroxy-anhydride. The acid was boiled with Ac_2O (3 parts) for 3 hrs., and the reagent distilled from the dark red product under reduced press. The residue was repeatedly crystallised from C_6H_6–petroleum, but could not be freed from a purplish-blue tinge; it formed flattened needles, m. p. 150° (Found : C, 61·8, 61·8; H, 5·1, 5·0. $C_{10}H_{10}O_4$ requires C, 61·8; H, 5·2%). The compound gave a fine violet colour with $FeCl_3$ and immediately dissolved in alkalis; on titration it behaved approximately as a monobasic acid, but the end-point was unsatisfactory. It was not reconverted into the original acid on more prolonged treatment with alkalis. On treatment with NH_2Ph in C_6H_6 it formed a sparingly sol. *anilic acid*, small prisms (from EtOH), blackening at about 240° but not melting below 300° (Found : C, 71·0; H, 5·5. $C_{16}H_{15}O_3N$ requires C, 71·4; H, 5·6%). If the mother-liquors from the purification of the *anhydride* were used for the preparation of the anilic acid, the latter was accompanied by a much more sol. compound, forming fine flattened needles (from dil. EtOH), m. p. 172°, which appeared to be the true *semianilide* of the acid (V) (Found : C, 68·8; H, 6·3. $C_{14}H_{15}O_3N$ requires C, 68·6; H, 6·1%).

Hydrolysis of the Ester (III; $n = 3$).—Hydrolysis with KOH, H_2SO_4, or HCl gave as the sole product a *pyridine* derivative, m. p. 252° after cryst. from

AcOH (Found: C, 65·2; H, 6·8. $C_9H_{11}O_2N$ requires C, 65·5; H, 6·6%). This gave a red colour with $FeCl_3$, reduced ammoniacal $AgNO_3$, dissolved in alkalis with a blue colour, and formed a hydrochloride, needles, m. p. 200°, which was decomposed by H_2O with formation of the base. The latter is evidently represented by the formula



$$CH_2<\begin{array}{l}CH_2\cdot C\!:\!CMe\text{—}C\cdot OH \\ CH_2\cdot C\!:\!C(OH)\cdot N\end{array}$$

Attempts to prepare an Isomeric Methylated Ester.—Ethyl 2-methyl*cyclo*pentanonecarboxylate was treated with ethyl cyanoacetate and piperidine or KOEt, but no condensation took place either in the cold or on heating.

Ethyl 2-Carbethoxy-Δ^1-cyclo*hexenylcyanoacetate* (II; $n = 4$).—Ethyl *cyclo*hexanonecarboxylate (Kötz and Michels, *Annalen*, 1906, **350**, 210) was condensed with ethyl cyanoacetate as described on p. 2429; the yields were poor, 18% with piperidine and 38% with KOEt. The *ester* had b. p. 190—191°/19 mm., $d_{4°}^{20·0°}$ 1·0889, $n_D^{20·0°}$ 1·4897, $[R_L]_D$ 70·36 (Found: C, 63·3; H, 7·2. $C_{14}H_{19}O_4N$ requires C, 63·4; H, 7·2%).

Ozonisation (see p. 2429). The sole product, b. p. 160—180°/16 mm., gave a violet colour with $FeCl_3$ and formed a *diphenylhydrazone*, sparingly sol. plates, m. p. 246°, from EtOH (Found: C, 65·1; H, 6·1. $C_{26}H_{31}O_4N_5$ requires C, 65·4; H, 6·4%); it was evidently *ethyl α-cyano-βζ-diketoazelate.* No trace of ethyl *cyclo*hexanonecarboxylate could be isolated.

Ethyl α-Cyano-α-2-carbethoxy-Δ^1-cyclo*hexenylpropionate* (III; $n = 4$).—The cyano-ester forms a sodio-derivative, from which it is recovered unchanged by acidification as described on p. 2429, and treatment of which with MeI (p. 2430) gives a 90% yield of the methylated *ester*, b. p. 186°/17 mm., $d_{4°}^{20·0°}$ 1·0531, $n_D^{20·0°}$ 1·4774, $[R_L]_D$ 74·69 (Found: C, 64·2; H, 7·3. $C_{15}H_{21}O_4N$ requires C, 64·5; H, 7·5%).

Ozonisation. The sole product, b. p. 150—170°, gave no colour with $FeCl_3$; it formed a *diphenylhydrazone*, small plates, m. p. 206°, from EtOH (Found: C, 65·5; H, 6·5. $C_{27}H_{33}O_4N_5$ requires C, 65·9; H, 6·9%). It was evidently derived from ethyl α-cyano-βζ-diketo-α-methylazelate.

α-2-Carbethoxy-Δ^1-cyclo*hexenylpropionitrile* (IV; $n = 4$), prepared from the methylated cyano-ester as described on p. 2430, had b. p. 162°/19 mm., $d_{4°}^{20·0°}$ 1·0340, $n_D^{20·0°}$ 1·4852, $[R_L]_D$ 57·43 (Found: C, 69·2; H, 8·2. $C_{12}H_{17}O_2N$ requires C, 69·5; H, 8·2%).

Hydrolysis of the Cyano-ester (II; $n = 4$).—(i) *With potassium hydroxide* (see p. 2430). The *iso*quinoline *derivative* (VII; $n = 4$) obtained, m. p. 206° (Found: C, 65·1; H, 6·8. $C_9H_{11}O_2N$ requires C, 65·5; H, 6·5%), gave a faint reddish colour with $FeCl_3$.

(ii) *With hydrochloric acid* (see p. 2430). The hydrolysis was distinctly slower in this case and the whole of the solid hydrolysis product was sol. in Na_2CO_3 aq. and consisted of the acid (V; $n = 4$) although a small amount (perhaps 5% of the ester hydrolysed) was recovered as the *iso*quinoline derivative, m. p. 206°, on evaporation of the acid mother-liquor.

(iii) *With sulphuric acid* (see p. 2430). The solid product consisted entirely of *ethyl 2-carboxy-*Δ^1-cyclo*hexenylmalonamate*, needles, m. p. 167—168°, from AcOEt–C_6H_6 (Found: C, 59·0; H, 7·2. $C_{14}H_{21}O_5N$ requires C, 59·3; H, 7·3%). A small amount of the acid (V; $n = 4$) was recovered by extracting the mother-liquors, remaining after the separation of the amide, with Et_2O; no *iso*quinoline derivative appeared to be formed.

2-Carboxy-Δ^1-cyclo*hexenylacetic Acid* (V; $n = 4$).—The *acid*, obtained as described above, crystallised from H_2O in clusters of needles, m. p. 166°

(decomp.) (Found : C, 58·5; H, 6·6; *M*, dibasic, 184·6. $C_9H_{12}O_4$ requires C, 68·7; H, 6·5%; *M*, 184·1). The *ethyl* ester (VIII; $n = 4$), prepared through the Ag salt, had b.p. 162°/20 mm., $d_{4°}^{20·0°}$ 1·0634, $n_{D}^{20·0°}$ 1·4746, $[R_L]_D$ 63·53 (calc., 62·64) (Found : C, 64·8; H, 8·1. $C_{13}H_{20}O_4$ requires C, 65·0; H, 8·3%).

Ozonisation. The ester gave as sole product an oil, b. p. 145—155°/21 mm., which developed a purple colour with $FeCl_3$ and formed a phenylhydrazine *derivative*, plates, m. p. 172°, analogous to that obtained from the lower homologue (Found : C, 67·5; H, 6·6. $C_{23}H_{26}O_3N_4$ requires C, 67·9; H, 6·4%), and a semicarbazone, m. p. 248°; it was evidently ethyl $\beta\zeta$-diketoazelate. No ethyl *cyclo*hexanonecarboxylate, ethyl glyoxylate, or oxalic acid was detected.

Methylation. This was carried out with "molecular" K as described on p. 2431; the new *ester* (IX; $n = 4$) had b. p. 158°/17 mm., $d_{4°}^{20·0°}$ 1·0527, $n_{D}^{20·0°}$ 1·4752, $[R_L]_D$ 67·99 (calc., 67·26) (Found : C, 66·3; H, 8·4. $C_{14}H_{20}O_4$ requires C, 66·1; H, 8·6%). The ester was hydrolysed to the acid, which was recrystallised from C_6H_6–petroleum. From the less sol. portion, a small amount of the parent acid was isolated; the new *acid* crystallised in fine clusters of flattened needles, m. p. 136—137° (Found : C, 60·5; H, 7·3. $C_{10}H_{14}O_4$ requires, C, 60·6; H, 7·0%).

An attempt was made to prepare this acid by the hydrolysis of the methylated nitrile (IV; $n = 4$) with HCl aq. as described on p. 2430. The product separated as a solid on cooling and was recrystallised from C_6H_6; the greater part formed fine needles, m. p. (indefinite) 172°, and still contained N (Found : C, 51·9; H, 7·2. $C_{10}H_{17}O_5N$ requires C, 51·9; H, 7·4%); none of the acid (V; $n = 4$) appeared to be formed.

Hydroxy-anhydride (X).—The acid (V; $n = 4$) was recovered unchanged after treatment with AcCl even in a sealed tube, but the dehydration was readily carried out as described on p. 2431; on removal of the Ac_2O the residue did not solidify and was therefore distilled under reduced press. The principal fraction, b. p. about 177°/6 mm., was contaminated by a coloured impurity and did not solidify, but its reactions showed that it consisted for the most part of the desired hydroxy-anhydride : it gave a fine violet colour with $FeCl_3$, behaved approximately as a monobasic acid on titration, and reacted with NH_2Ph in C_6H_6, forming the *semianilide* of the acid (V; $n = 4$), flattened needles, m. p. 135—136°, from dil. EtOH (Found: C, 69·1; H, 6·6. $C_{15}H_{17}O_3N$ requires C, 69·5; H, 6·5%). On treatment with 25% KOH aq., followed by acidification, the hydroxy-anhydride yielded the original acid unaccompanied by any other compound. No second anhydride, corresponding to the compound $C_{10}H_{10}O_4$ (p. 2431), was obtained in this expt.

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