CCCLXII.—*The Chemistry of the Three-carbon System. Part VIII. Tautomeric Systems terminated by a Phenyl Group.*

By Reginald Patrick Linstead and Leslie Thomas Douglas Williams.

The tautomeric substances described in the earlier papers of this series have without exception the general structure :

$$\underset{\alpha\beta\text{-Phase.}}{\mathrm{R{-}CH[H]{-}CR^1{=}\underset{|}{C}{-}X}} \rightleftharpoons \underset{\beta\gamma\text{-Phase.}}{\mathrm{R{-}CH{=}CR^1{-}\underset{|}{C}[H]{-}X}}$$

where R, R^1 are positive groups—alkyl groups or portions of an alicyclic ring—and X is a negative activating group containing one or more double or triple bonds. The αβ-phase is stabilised by conjugation with these double or triple bonds, the βγ-phase by the decrease in strain or free energy which appears to be brought about by the introduction of a double bond into certain branched chains. The substances investigated have been those in which the two phases have approximately equal stabilities and in which the activating force has been sufficient to produce mobility.

Tautomeric substances are also known in which mobility in the system is induced by negative substituents at both ends of the three-carbon chain, *e.g.*, the glutaconic acids and esters and their cyano- and carbethoxy-derivatives. Many of these molecules are sufficiently symmetrical for the occurrence of semi-aromatic or normal structure (Thorpe, J., 1905, **87**, 1670). Little systematic work has, however, been carried out on negatively substituted systems in which there is no such symmetry and in which the tautomerism is of the type described in the earlier papers of this series. It is with the object of increasing such knowledge that a number of propene systems terminated by a phenyl group have been studied.

The presence of a substituent phenyl group in a three-carbon system should not in itself cause mobility, as it now appears that this is connected with the ability of the mobile hydrogen to leave the system temporarily and pass into the activating group. This consideration provides an explanation for the static nature of the αγ-diphenylpropenes (Ingold and Piggott, J., 1922, **121**, 2381). On the other hand, the double bond of a substituent side-chain should show a strong tendency to become conjugated with the double bonds of a benzene nucleus—numerous examples of this phenomenon have been recorded—and therefore the phenyl group, if properly placed, should produce a marked effect on the position of equilibrium in the three-carbon system.

Examples of this effect are found in the γ-phenylbutenoic acids, styrylacetic acid * (I) and γ-phenylcrotonic acid (II), which are two distinct, crystalline substances.

(I.) $CHPh{:}CH{\cdot}CH_2{\cdot}CO_2H$ $CH_2Ph{\cdot}CH{:}CH{\cdot}CO_2H$ (II.)

These were first examined in detail by Fittig and his collaborators (*Annalen*, 1882, **216**, 97, 115; 1894, **283**, 297), who showed that in the presence of sodium hydroxide an equilibrium mixture of the two acids together with the corresponding β-hydroxy-acid was formed. The equilibrium was abnormal, however, in that there was present only a very small amount of the αβ-acid (II). Styrylacetic acid has since been made from phenylacetaldehyde by Vorländer (*Annalen*, 1906, **345**, 244) and by Fichter and Latzko (*J. pr. Chem.*, 1906, **74**, 327), using the Döbner method. As a result of many experiments we find that the acid is best made by condensing phenylacetaldehyde in alcoholic solution with malonic acid, a small amount of diethylamine being used as condensing agent. The acid product is exclusively styrylacetic acid; no substituted malonic acids nor any γ-phenylcrotonic acid can be detected, but some ethyl styrylacetate can be isolated from the neutral product of the reaction.

The action of sodium hydroxide on the acid under more vigorous conditions than those of Fittig (*loc. cit.*) has been investigated. The action of 40 times the theoretical amount of the alkali in 20% solution produced a mixture of 0·5% of the αβ-acid, 10% of the β-hydroxy-acid (V), 50% of unchanged βγ-acid, and a trace of lactone. Allowance being made for the recovery of unchanged acid, the yield of the hydroxy-acid is about 26%. Fittig, using 10 times the theoretical amount of 20% alkali, obtained less than 1% of the αβ-acid and a little more than this amount of the β-hydroxy-acid. In our experiments, the time of boiling was 100 hours as against the 20 to 80 hours of Fittig.

With a view to determine the effect of the phenyl group on the

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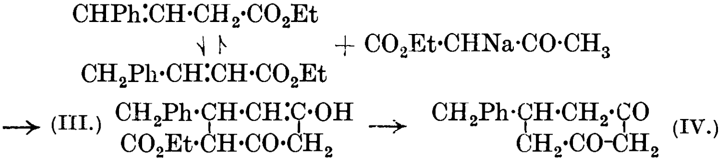
* We have followed Beilstein ("Organische Chemie," 4th edn., vii, 293) in using the name "styrylacetic" in the place of "phenyl*iso*crotonic" for the acid (I), as the older name implies a structural relationship with crotonic acid which does not exist. Other compounds in the series have been named correspondingly.

mobility of the system, the action of sodium ethoxide on ethyl styrylacetate was investigated. An orange colour was produced immediately, but no definite proof of the formation of a sodio-derivative has yet been obtained, nor has the ester been alkylated. The ester can be condensed with ethyl sodioacetoacetate to give the sodio-derivative of the ester (III), which passes on hydrolysis into 3 : 5-diketo-1-benzyl*cyclo*hexane (IV). In the presence of sodium ethoxide, therefore, the ester becomes mobile and the αβ-phase then condenses with ethyl sodioacetoacetate in the usual way.



$$\begin{matrix} CHPh{:}CH{\cdot}CH_2{\cdot}CO_2Et \\ \rightleftharpoons \\ CH_2Ph{\cdot}CH{:}CH{\cdot}CO_2Et \end{matrix} + CO_2Et{\cdot}CHNa{\cdot}CO{\cdot}CH_3$$

$$\longrightarrow \text{(III.)} \begin{matrix} CH_2Ph{\cdot}CH{\cdot}CH{:}C{\cdot}OH \\ CO_2Et{\cdot}CH{\cdot}CO{\cdot}CH_2 \end{matrix} \longrightarrow \begin{matrix} CH_2Ph{\cdot}CH{\cdot}CH_2{\cdot}CO \\ CH_2{\cdot}CO{-}CH_2 \end{matrix} \text{(IV.)}$$

In these additive reactions, the ester is unique among βγ-butenoic esters : even ethyl Δ^1-*cyclo*hexenylacetate fails to give addition products under similar conditions.

For comparison with the ester, the corresponding ketone, *styrylacetone* (V), was prepared. The phenyl ketone (VI) has been synthesised by Wieland and Stenzel (*Ber.*, 1907, **40**, 4825), who showed that it readily enolises and that the methylene group

(V.) $CHPh{:}CH{\cdot}CH_2{\cdot}CO{\cdot}CH_3$ $CHPh{:}CH{\cdot}CH_2{\cdot}COPh$ (VI.)

condenses with benzaldehyde, both reactions indicating the presence of a mobile hydrogen atom.

The condensation of phenylacetaldehyde with acetone by means of sodium methoxide, aqueous sodium hydroxide, aqueous potassium cyanide, or alcoholic potassium hydroxide failed to give the ketone (V), and its condensation with ethyl acetoacetate, with diethylamine or sodium ethoxide as condensing agent, led to the production of high-boiling gums. The ketone was readily prepared, however, by the action of zinc methyl iodide on styrylacetyl chloride, its structure thus being proved, and the βγ-position of the double bond was confirmed by its oxidation to benzaldehyde. It reacted immediately with sodium in alcohol, giving a deep red solution. Attempts to alkylate it either in alcoholic or in ethereal solution (compare Kon, this vol., p. 1792) led to the production of high-boiling gums.* In the course of one such alkylation, however, an interesting side reaction was observed. The reaction was carried out in the usual way in a flask open to the air and a 30% yield of

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* The production of gums and resins in the course of this work was probably due in many instances to fission of the compounds at the double bond followed by auto-condensation of the aldehydes so formed.

styrylacetic acid was obtained in addition to the neutral products. This curious example of aërial oxidation is unique in our experience, although many similar experiments have been performed with ketones of this type. The ethyl iodide used, which had been made by the phosphorus method, contained a sub-analytical trace of a strongly odorous phosphorus compound. As the ethylphosphines are known to absorb oxygen readily from the air, this may possibly have been the active catalytic agent.

The ketone (V) resembles the corresponding ester in that the equilibrium mixture formed by the action on it of sodium ethoxide adds on ethyl sodiomalonate very readily with the formation of the resorcinol ester (III) already prepared from the ester, together with its sodio-derivative. The structures of these two substances were shown by their hydrolysis to diketobenzyl*cyclo*hexane (IV), which was identical with the compound previously obtained.

It was obviously of great interest to prepare the αβ-isomerides of styrylacetic acid and styrylacetone. The αβ-acid, γ-phenylcrotonic acid (II), can be prepared only in minute quantities, either by the action of sodium hydroxide on the βγ-acid or from the β-hydroxy-acid (VII) by dry distillation; it is also formed to the almost complete exclusion of styrylacetic acid by the action of acetic anhydride on the β-hydroxy-acid. The product is identical with Fittig's acid in its properties and gives phenylacetaldehyde on oxidation with permanganate.

(VII.) $CH_2Ph{\cdot}CH(OH){\cdot}CH_2{\cdot}CO_2H$ $CH_2Ph{\cdot}CH_2{\cdot}CHBr{\cdot}CO_2H$ (VIII.)
$CH_2Ph{\cdot}CH_2{\cdot}CBr(CO_2H)_2$ (IX.)

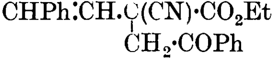
Attempts to prepare the acid by the action of secondary bases on either of the acids (VIII) and (IX) gave γ-phenylbutyric acid as the sole product (compare Hope and Perkin, J., 1909, **95**, 1360).

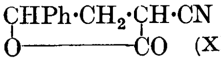
We have therefore been unable to develop a more successful method for the preparation of γ-phenylcrotonic acid than that from the β-hydroxy-acid already mentioned, and with the small quantity of material available our experiments were confined to an observation of the effect of alkali on the acid. When the acid was treated with an excess of 10% sodium hydroxide solution in the cold, styrylacetic acid was formed in good yield and no other acid could be isolated.

The next substance investigated was ethyl α-cyano-α-styrylacetate (X), which provided an interesting contrast with ethyl α-cyano-*cyclo*hexylideneacetate, from which it differs in that it normally has the βγ-structure. Like the *cyclo*hexylidene ester, however, in the presence of alcoholic ammonia it gives good yields of addition products derived from the αβ-form.

The ester (X) was first synthesised by Haworth (J., 1909, **95**, 482), who showed that the α-hydrogen atom could be replaced by sodium and that the sodio-derivative thus formed reacted with ω-bromoacetophenone to give the substance (XI). In addition, the cyano-ester (X), in the presence of alkali, added on water at the double bond to give, finally, the cyano-lactone (XII).

(X.) $CHPh{:}CH{\cdot}CH(CN){\cdot}CO_2Et$

(XI.) 
$CHPh{:}CH.C(CN){\cdot}CO_2Et$ with $CH_2{\cdot}COPh$ on the C


$CHPh{\cdot}CH_2{\cdot}CH{\cdot}CN$, O——CO (XII.)

These reactions led Haworth to give to the substance the βγ-formula (X), and he used this view in support of his contention that aldehydes pass through the enolic form when reacting with the sodium derivatives of tautomeric esters such as ethyl cyanoacetate.

We have prepared the compound both by Haworth's method and by the condensation of phenylacetaldehyde and ethyl cyanoacetate in presence of diethylamine. Its identity with Haworth's compound was shown by the formation of the substitution product (XI). From a knowledge of the behaviour of related substances it was obvious that neither of the reactions used by Haworth could provide definite proof of the βγ-structure of the ester, as it was possible that movement of the double bond in the three-carbon system had taken place under the experimental conditions used. Determination of the optical properties, a method previously used with much success in similar problems, was considered untrustworthy for the following reasons :

(1) The exaltation due to conjugation of a phenyl group with a double bond in a side chain has no very constant value.

(2) No αβ-substances could be prepared for comparative purposes.

(3) In all these compounds there is selective absorption of light of a wave-length approaching that of the (sodium) light used in the determination of refractive index. Hence the Lorentz-Lorenz law no longer provides a trustworthy basis for calculation (compare Hunter, J., 1923, **123**, 1671).

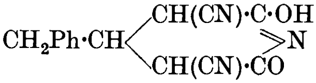
The exaltation of the molecular refractivity of ethyl α-cyano-α-styrylacetate over the calculated value was, however, of the same order as that found in styrylacetic ester, and it was probable, therefore, that the substance had the βγ-formula. We were able to confirm this decision by chemical methods, for although the substance was unusually stable to most oxidising agents, it was quantitatively converted into benzoic acid by the action of a mixture of chromic and acetic acids. Neither phenylacetaldehyde nor phenylacetic acid could be detected in the oxidation product, although a separate experiment showed that phenylacetaldehyde was oxidised only to phenylacetic acid, and not, by oxidation of the side chain, to benzoic acid under the same conditions.

It was impossible to prove or disprove the presence of a small quantity of the αβ-isomeride by oxidation, but that such a trace was present, and, in short, that the substance is an equilibrium mixture containing a large proportion of the βγ-form, was shown very clearly by the following experiment. When ethyl α-cyanostyrylacetate was treated with alcoholic ammonia and ethyl cyanoacetate in the cold, addition to the αβ-phase readily occurred with the production of α-cyano-γ-phenylbutyramide (XV) and 3 : 5-dicyano-6-hydroxy-4-benzyl-2-pyridone (XVI), the latter being isolated in the form of its mono-ammonium salt. These had been formed from cyanostyrylacetamide (XIII) and the dihydropyridone (XIV) by a process of auto-oxidation and reduction similar to that found by Guareschi (*Atti R. Accad. Sci. Torino*, 1898—1899, **34**, 565) and Day and Thorpe (J., 1920, **117**, 1466).

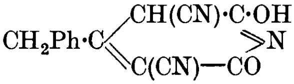
$CHPh{:}CH{\cdot}CH(CN){\cdot}CO{\cdot}NH_2$ (XIII.)

$CH_2Ph{\cdot}CH_2{\cdot}CH(CN){\cdot}CO{\cdot}NH_2$ (XV.)

(XIV.)



$$CH_2Ph{\cdot}CH{<}\begin{matrix}CH(CN){\cdot}C{\cdot}OH\\ \gg N\\ CH(CN){\cdot}CO\end{matrix}$$



$$CH_2Ph{\cdot}C{\lessgtr}\begin{matrix}CH(CN){\cdot}C{\cdot}OH\\ \gg N\\ C(CN){-}CO\end{matrix}$$

(XVI.)

The pyridone (XVI) resembles other substances in the same group in not giving a glutaconic or glutaric acid on hydrolysis with sulphuric acid.

The sodio-derivative of ethyl cyanostyrylacetate reacts in alcoholic solution with methyl iodide to form the corresponding α-methyl ester. This loss of the mobile hydrogen atom is followed by elimination of the carbethoxy-group with the formation of a methylated nitrile, probably having the formula

$$CHPh{:}CH{\cdot}CHMe{\cdot}CN,$$

and ethyl carbonate. This reaction is in accordance with previous observations on the subject (Rogerson and Thorpe, J., 1905, **87**, 1702; Ingold and Thorpe, J., 1919, **115**, 143; Birch, Kon, and Norris, J., 1923, **123**, 1369).

This nitrile and related compounds are readily converted into naphthalene derivatives—a transformation which will be discussed in a future paper. Ethyl α-cyanostyrylacetate itself does not form a naphthalene derivative when treated with cold concentrated sulphuric acid; addition of water to the double bond occurs, followed by hydrolysis and lactone formation. The final product is a cyano-lactone apparently identical with that (XII) isolated by Haworth (*loc. cit.*).

In general, this investigation shows that the chief effect of the

γ-phenyl group is to confer an unusual degree of stability on the double bond in the $\beta\gamma$-position. The fact that ethyl α-cyano-α-styrylacetate exists almost completely in the $\beta\gamma$-phase shows that in its attraction for a double bond the phenyl group is stronger than the very powerful cyano-ester group. If the β-carbon as well as the γ-carbon atom in the propene system carries a phenyl group, this effect is lost; *e.g.*, in $\beta\gamma$-diphenylcrotonic acid (Fichter, *loc. cit.*) and in $\beta\gamma$-diphenylcrotonolactone (Thiele, *Annalen*, 1901, **319**, 196).

EXPERIMENTAL.

Styrylacetic Acid (*γ-Phenyl-Δ^{β}-butenoic Acid*) (I).

A solution of malonic acid (50 g.), phenylacetaldehyde * (60 g.), and 10 drops of diethylamine in 130 c.c. of absolute alcohol was boiled under reflux for 6 hours; the product was poured into an excess of 2*N*-sodium carbonate and extracted with ether. The acid that crystallised from the acidified aqueous solution was recrytallised from water or light petroleum. It melted at 87° and did not depress the m. p.s of samples prepared by the methods of Jayne and Fittig (*loc. cit.*) and Fichter and Latzko (*loc. cit.*) (Found: C, 74·4; H, 6·2. Calc.: C, 74·0; H, 6·2%). The yield was 60%, but was sometimes lower owing to partial esterification. Changes in solvent, concentration, or duration of heating led to decreased yields.

The condensation of ethyl bromoacetate with phenylacetaldehyde was attempted by various methods with a view to preparing the β-hydroxy-acid corresponding to styrylacetic acid. The use of magnesium or zinc in benzene, or of zinc in ether as condensing agents led alike to the formation of high-boiling gums.

Potassium styrylacetate forms white plates, m. p. 245° (decomp.), from a concentrated aqueous solution (Found: K, 19·3. $C_{10}H_9O_2K$ requires K, 19·5%).

Styrylacetyl chloride, formed by the action of thionyl chloride on the acid, readily solidified on removal of the excess of the reagent. It crystallised from light petroleum in clusters of flattened needles, m. p. 42° (Found: Cl, 19·9. $C_{10}H_9OCl$ requires Cl, 19·6%). On treating it with anhydrous formic acid, the parent acid is re-formed.

Ethyl styrylacetate was formed as a by-product in the preparation of the acid and was isolated from the ethereal extract. The amount of esterification depended directly on the time of reaction. After refractionation, the product had optical properties in good agree-

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* In this and other condensations the best yield is obtained when the phenylacetaldehyde has been freshly distilled. The aldehyde polymerises on standing, but may be kept in ethereal solution for a month or more with but little change.

ment with those obtained for the pure ester (see below) and its identity was confirmed by oxidation with ozone in chloroform solution and by hydrolysis. By decomposition of the ozonide with water followed by distillation in steam from an acid medium, benzoic acid was obtained. Hydrolysis of the ester with 50% aqueous potassium hydroxide gave potassium styrylacetate, from which the acid, m. p. 86—87°, was obtained.

The pure ester was prepared in excellent yield by esterifying the acid in the presence of sulphuric acid, or through the acid chloride. It had b. p. 164—165°/25 mm. and 184°/44 mm., $d_{4^\circ}^{20\cdot5^\circ}$ 1·0340, $n_{D}^{20\cdot5^\circ}$ 1·53271, $[R_L]_D$ 56·73 (calc., 55·21, Brühl's value for C_6H_5, 25·21, being used). It gave no colour with alcoholic ferric chloride (compare Vorländer, *loc. cit.*), an immediate red colour with sodium ethoxide, and an orange colour with " molecular " sodium in ether.

Action of Sodium Hydroxide on Styrylacetic Acid.—The method was essentially that of Fittig (*Annalen*, 1894, **283**, 297), but the conditions were more drastic, styrylacetic acid being boiled with 20% sodium hydroxide solution (40 times the quantity necessary for neutralisation) for 100 to 110 hours. In a typical experiment, 50 g. of styrylacetic acid gave 6 g. of the hydroxy-acid and 4 g. of mixed unsaturated acids, 23 g. of styrylacetic acid being recovered unchanged. The β-hydroxy-γ-phenylbutyric acid (VII) formed needles from the carbon disulphide solution and had m. p. 96°. The unsaturated acids in the filtrate from the hydroxy-acid were freed from carbon disulphide and, on standing, yielded a small quantity of styrylacetic acid. The oily residue was converted into barium salts which, on fractional crystallisation from water, gave the powdery salt of styrylacetic acid and 2 g. of a gummy salt. The latter, on acidification, gave a mixture of the βγ-acid (needles, m. p. 84°) and the αβ-acid (plates, m. p. 58°) in about equal quantities. The yield of αβ-acid was 0·8 g. The loss (about 40%) was due mainly to the formation of resinous material.

γ-Phenylcrotonic acid was also produced when β-hydroxy-γ-phenylbutyric acid (10·6 g.) was boiled under reflux with acetic anhydride (20 c.c.) for 3 hours. The bright red, heavy product was boiled in a current of steam until it was free from acetic acid. The residue was extracted with ether, the extract dried, and the ether removed. The residual oil was converted in the usual way into a gummy barium salt, which was dried in a vacuum desiccator (yield, 9 g.). A hot, filtered, aqueous solution of the salt, on acidification and cooling, deposited crystals of phenylcrotonic acid, and more were obtained on concentrating the mother-liquor. After complete evaporation, the semi-solid residue was drained on porous tile, more phenylcrotonic acid being thus obtained (total yield, 2 g. or 21%).

γ-Phenylcrotonic acid forms white, shimmering leaflets, m. p. 58—59°, from water (Fittig gives 65°). The melting point of a mixture with the 87°-acid is much lower. On oxidation with alkaline permanganate the acid gives phenylacetaldehyde. The acid chloride, made by means of thionyl chloride, is a liquid which does not solidify in a freezing mixture.

3 : 5-*Diketo*-1-*benzyl*cyclo*hexane* (IV).—Pure ethyl styrylacetate (b. p. 164—165°/25 mm.) (9·5 g.) was added to ethyl sodioacetoacetate prepared from 6·5 g. of acetoacetic ester and 1·15 g. of sodium in 15 c.c. of ethyl alcohol. The red solution was boiled under reflux for 4 hours, becoming almost completely solid, and thereafter heated on the steam-bath for 12 hours. The solid sodium derivative was filtered off (6·5 g.), and the filtrate freed from alcohol by suction. The semi-solid residue was dissolved in water and extracted with ether, but only a small quantity of the ester (III) was thus obtained. From the neutral fraction 1·5 g. (= 16%) of ethyl styrylacetate were recovered. Allowance being made for this, the yield of the sodium derivative was 55%.

On treatment with hydrochloric acid, the sodium derivative gave an oily ester (III), which developed a purple coloration in presence of alcoholic ferric chloride. The sodium derivative (6·5 g.) was boiled with a solution of 30 g. of sodium carbonate crystals in 18 c.c. of water for 20 hours, carbon dioxide and alcohol being freely evolved. The brown solution was acidified with hydrochloric acid and exhaustively extracted with ether. From the dried extract a gum was obtained which readily solidified on being rubbed with a little cold ether. It was recrystallised from boiling ether with the aid of animal charcoal (yield, 2 g. or 46%). When hydrolysed under these conditions, the ester (III) yielded the same product.

3 : 5-*Diketo*-1-*benzyl*cyclo*hexane* (IV), thus obtained, forms glistening plates, m. p. 118°. It is insoluble in water, light petroleum, or chloroform, soluble in alcohol, acetone, or hot ether, and sparingly soluble in cold ether (Found : C, 77·6; H, 7·0. $C_{13}H_{14}O_2$ requires C, 77·2; H, 7·0%). It gives a much weaker colour with ferric chloride than the corresponding ester (III), it resinifies readily in contact with hydrolytic solvents, and dissolves slowly but completely in sodium bicarbonate solution.

On boiling diketobenzyl*cyclo*hexane with baryta solution, ring fission occurred and a gummy acid was formed which could not be obtained pure. In this respect it resembles diketophenyl*cyclo*hexane (Vorländer, *Annalen*, 1897, **294**, 273).

Styrylacetone (V).

Styrylacetyl chloride was allowed to react with zinc methyl iodide as described in J., 1923, **123**, 1361. The acid product extracted by 10% sodium hydroxide solution consisted of a small amount of styrylacetic acid. The neutral product, after removal of benzene, was fractionated under reduced pressure, the new ketone being obtained, b. p. 145—165°/20 mm. (yield, 30 to 45%). The substitution of methyl acetate for ethyl acetate did not improve the yield.

Styrylacetone is a mobile liquid with a faint smell. It is pale yellow when freshly prepared, but the colour slowly deepens. It has b. p. 262°/75 mm., 150°/15 mm., and distils under normal pressure almost without decomposition. It gives no colour with ferric chloride.

The *semicarbazone* is very readily formed and crystallises from dilute alcohol in lustrous plates, m. p. 160° (Found : C, 66·2; H, 7·2. $C_{12}H_{15}ON_3$ requires C, 66·3; H, 7·0%). No second semicarbazone is formed.

The structure of the ketone was confirmed by oxidation with ozone. The ozonide was decomposed with water and the benzaldehyde produced was identified as the semicarbazone, m. p. 219—220°.

Action of Sodium Ethoxide on Styrylacetone.—(a) *Attempted alkylation.* The ketone (10 g.) was treated with 1·53 g. of sodium in 20 c.c. of absolute alcohol, moisture being carefully excluded. A red colour developed immediately, but it faded on the addition of ethyl iodide (6 c.c.). The mixture was worked up in the usual way. The neutral fraction gave a high-boiling gum (9 g.) and the acid fraction gave 3 g. of styrylacetic acid. The weights of the products indicated that alkylation had occurred, but although the experiment was repeated a number of times under various conditions, an alkylated ketone could not be isolated.

(b) *Formation of* 3 : 5-*diketo*-1-*benzyl*cyclo*hexane* (IV). Equimolecular quantities of styrylacetone and ethyl sodiomalonate were heated together in alcoholic solution for 16 hours; the mixture then partly solidified. The products were worked up as described on p. 2743. The yields were smaller, 25% of the sodium compound and 16% of the ester (III) being obtained. These were hydrolysed separately in the manner already described. The product in each case was 3 : 5-diketo-1-benzyl*cyclo*hexane. This was identified with the substance previously prepared from ethyl styrylacetate by its melting point, characteristic crystalline form, and by a mixed melting-point determination.

Experiments with ω-Bromostyrene.

ω-Bromostyrene, prepared by Nef's method (*Annalen*, 1899, **308**, 267), had b. p. 105°/17 mm. Attempts to condense it with the sodio-derivatives of ethyl malonate, acetoacetate, and cyanoacetate in alcoholic, benzene, or xylene solution failed.

Experiments on the Elimination of Hydrogen Bromide from α-Bromo-γ-phenylbutyric Acid and α-Bromo-α-(β-phenylethyl)malonic Acid.

β-Phenylethyl bromide was prepared in excellent yield by the action of 40% hydrobromic acid on β-phenylethyl alcohol in the presence of sulphuric acid. The heavy product, after being separated, washed, and dried, had b. p. 109°/22 mm. and 92°/11 mm.

The bromide was converted into α-bromo-α-(β-phenylethyl)-malonic acid (IX) by Fischer and Schmitz's method (*Ber.*, 1906, **39**, 2208). The bromo-acid crystallised from toluene in needles, m. p. 156°, and on distillation gave α-bromo-γ-phenylbutyric acid (VIII), b. p. 183°/9 mm., a liquid which did not solidify in a freezing mixture.

The bromophenylbutyric acid (7 g.) in ethereal solution was left in contact with an excess of diethylamine for a week. No bromine-free product could be isolated from the reaction mixture.

The bromomalonic acid (IX) (6·5 g.) was heated with pyridine (2 mols.) at 160—180° for ½ hour. The acid product, after being freed from pyridine and charred material, was recrystallised from hot water, shimmering leaflets, m. p. 50°, of γ-phenylbutyric acid, identified by the melting point of a mixture with a sample of the acid made by Fischer and Schmitz's method (*loc. cit.*), being obtained.

Ethyl α-Cyano-α-styrylacetate (X).

A mixture of phenylacetaldehyde and ethyl cyanoacetate (0·25 g.-mol. of each) was cooled in ice and, after 2·5 c.c. of diethylamine had been slowly added, left at room temperature for 24 hours or more. The viscous neutral product, after separation in the usual way, was fractionated under reduced pressure, the fraction, b. p. 180—202°/15 mm., being collected separately and refractionated.

Ethyl α-cyano-α-styrylacetate prepared in this way is fairly mobile when freshly distilled, but becomes viscous on standing. This is not, however, due to irreversible polymerisation, as the mobility is regained on redistillation. The pure ester has b. p. 192°/16 mm. (Haworth, *loc. cit.*, gives 195—197°/20 mm.), $d_{4°}^{17·5°}$ 1·0912, $n_{D}^{17·5°}$ 1·53635, $[R_L]_D$ 61·22 (calc., 59·64). The yield obtained by this method varies from 25 to 32%, and compares favourably with that obtained by Haworth's method. If the reaction is carried out at 0°, the yield is lowered.

The product was identified with that prepared by Haworth by the formation of the ω-bromoacetophenone compound, which melted at 109—110° and did not depress the melting point of a sample prepared by Haworth's method.

When the condensation was carried out in presence of sodium ethoxide, a solid by-product was found in the neutral fraction of the condensate. This formed small plates, m. p. 220°, from acetic acid (Found : C, 81·3; H, 6·3. $C_{18}H_{17}ON$ requires C, 82·1; H, 6·5%). It was probably the hydroxy-nitrile,

$$CHPh{:}CH{\cdot}CH(CN){\cdot}CH(OH){\cdot}CH_2Ph,$$

formed by the action of a second molecule of phenylacetaldehyde on ethyl α-cyano-α-styrylacetate.

The ester (X) was stable to ozonised oxygen and to alkaline permanganate, but chromic acid broke the side chain at the double bond. The ester (2·1 g.) dissolved in glacial acetic acid (5 c.c.) was treated with three times the theoretical quantity of chromic acid in 20 c.c. of acetic acid. After ½ hour's heating, the solution was poured into 200 c.c. of water, cooled, and extracted with ether. The extract was freed from acetic acid by washing with water, dried, and evaporated, 1 g. of benzoic acid being thus obtained.

In a control experiment, phenylacetaldehyde (1 g.) in 5 c.c. of acetic acid was treated with 4 g. of chromic acid in 15 c.c. of acetic acid. The vigorous reaction was carried out as before and the products were worked up in the same way. The acid product was entirely phenylacetic acid, which was identified in the usual way.

The cyano-ester readily formed a sodio-derivative which reacted with ω-bromoacetophenone and with methyl iodide in alcoholic solution. (A description of the products obtained on methylation in alcohol will be given in a future paper.) Methylation in the presence of "molecular" sodium in ether led to the formation of Haworth's cyanolactone as the sole product. This compound was isolated as a resinous solid which could be crystallised with considerable difficulty from methyl alcohol and then melted at 85—90° (Found : N, 6·9. Calc.: N, 7·5%). The substance was readily soluble in alkali hydroxides and in ammonia solution. On boiling with 20% sodium hydroxide solution, ammonia was evolved. It appeared very probable that the substance was a mixture of two stereoisomeric forms, but no separation could be effected. The same substance was obtained in good yield by the action of cold concentrated sulphuric acid on ethyl α-cyano-α-styrylacetate, a reaction which confirms the structure assigned to it by Haworth.

Action of Ethyl Cyanoacetate and Ammonia on Ethyl α-Cyano-α-styrylacetate.—A mixture of ethyl cyanostyrylacetate (20·4 g.) and ethyl cyanoacetate (10·6 g.), cooled to 0°, was treated with

38 c.c. of absolute alcohol, previously saturated in a freezing mixture with ammonia. The mixture having been kept for 24 hours at 0°, the solid product was separated, washed with a little alcohol, and dried (yield, 14 g. or 55%). It was almost entirely the *mono-ammonium* salt of 3 : 5-*dicyano*-6-*hydroxy*-4-*benzyl*-2-*pyridone*, which crystallised from water in felted masses and from methyl alcohol in fine, white needles, charring without melting at 320° (Found : N, 20·4. $C_{14}H_{12}O_2N_4$ requires N, 20·9%). On treatment with hydrochloric acid 3 : 5-*dicyano*-6-*hydroxy*-4-*benzyl*-2-*pyridone* was obtained, which crystallised from dilute hydrochloric acid in lustrous leaflets, m. p. 279° (Found : C, 62·5, 62·6, 62·2; H, 5·0, 4·2, 4·2; N, 15·6. $C_{14}H_{11}O_3N_3$ requires C, 62·4; H, 4·1; N, 15·1%). It is readily soluble in hot water, alcohol, or benzene, insoluble in ether, and sparingly soluble in dilute acids and in acetic acid. The unsaturated nature of the 3 : 4-bond is confirmed by the fact that on hydrolysis of the pyridone with sulphuric acid under the conditions of Thole and Thorpe (J., 1911, **99**, 422) no β-benzylglutaric acid can be obtained, the product being a nitrogenous acid giving a fluorescent green solution in alkalis.

The viscous filtrate from the ammonium salt of the pyridone, when left in a vacuum desiccator, slowly deposited α-cyano-γ-phenylbutyramide contaminated with cyanoacetamide. In one experiment, 11 g. of the parent ester gave 4·6 g. of the cyanobutyramide and only a trace of cyanoacetamide. Usually, however, cyanoacetamide was present to the extent of more than 50% in this residue, from which it could be recovered by boiling with water.

α-*Cyano*-γ-*phenylbutyramide* (XV) crystallises from dilute methyl alcohol in shining, flattened needles, m. p. 151—152° (Found : C, 70·4; H, 6·5. $C_{11}H_{12}ON_2$ requires C, 70·2; H, 6·4%). It is considerably more soluble in alcohol than the other products of the reaction. It is insoluble in water and in alkalis, and does not decolorise permanganate.

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