

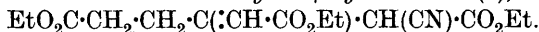
CCXLII.—*The Addition of Ethyl Sodiocyanoacetate and Ethyl Sodiomalonnate to Ethyl Muconate.*

By ERNEST HAROLD FARMER.

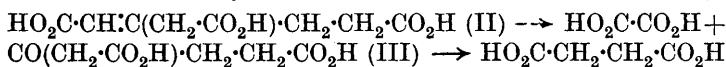
AMONG the very numerous exceptions to Thiele's theory of conjugation, the case of ethyl muconate,  $\text{EtO}_2\text{C}\cdot\text{CH}:\text{CH}\cdot\text{CH}:\text{CH}\cdot\text{CO}_2\text{Et}$ , is of considerable interest. Although the muconic system follows the rule in its 1 : 4-type of hydrogen addition, it has been shown recently by Chandrasena and Ingold (this vol., p. 1306) that ethyl muconate adds on bromine at the 1 : 2-position, a property which is unusual with symmetrical, conjugated chains. In view of this different behaviour of symmetrical addenda in relation to a symmetrical, conjugated system it seemed desirable to investigate the attachment of unsymmetrical addenda to ethyl muconate, and in this paper the addition of ethyl sodiocyanoacetate and ethyl sodiomalonnate is dealt with.

According to Hinrichsen (*Chem. Ztg.*, 1901, **316**, 43), addenda the components of which have an opposite polar character attach themselves at the 1 : 2-position. Ethyl muconate might therefore be expected to obey this rule were it not that even among the additive reactions of unsymmetrical, conjugated systems, on which alone Hinrichsen appears to have based his generalisation, there is at least one striking exception. Vorländer and his collaborators have shown (*Annalen*, 1906, **345**, 206) that although methyl cinnamylideneacetate, cinnamylideneacetone, and cinnamylideneacetophenone add on the components of ethyl malonnate at the 1 : 2-position, methyl sorbate,  $\text{CH}_3\cdot\text{CH}:\text{CH}\cdot\text{CH}:\text{CH}\cdot\text{CO}_2\text{Me}$ , with the same substance yields a 1 : 4-additive product.

Remarkably enough, ethyl muconate follows neither of these courses, the product (90 per cent.) from ethyl sodiocyanoacetate being *ethyl*  $\Delta^4$ -butene- $\alpha\delta$ -dicarboxylate- $\beta$ -cyanoacetate (I),



That the ester is correctly represented by this formula is seen from a study of its derivatives. By hydrolysis, a tricarboxylic acid (II) is obtained the constitution of which follows from its oxidation by alkaline potassium permanganate to a mixture of oxalic and succinic acids, probably by way of  $\beta$ -ketoadipic acid (III); no trace of tricarballic acid could be detected. Accompanying

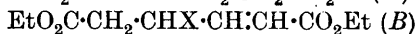


the acid (II) is 2 : 6-dihydroxypyridine-4- $\beta$ -propionic acid (IV),  $\text{HO}_2\text{C}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{C} \begin{smallmatrix} \text{CH}\cdot\text{C}(\text{OH}) \\ \text{CH}:\text{C}(\text{OH}) \end{smallmatrix} \text{N}$ , the production of which recalls

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many similar occurrences during the hydrolysis of cyanoglutaconic esters and indicates that the parent ester is of the latter type.

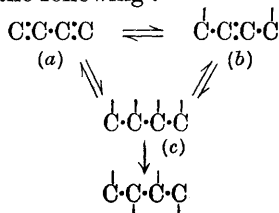
If, therefore, the addition be regarded as of the 1 : 2-type (B),



it is obvious that to yield the structure (A) the double bond must move from the  $\alpha$ - to the  $\alpha'$ -position, a phenomenon for which no parallel is to be found outside cyclic compounds. It is highly improbable that such a double movement occurs during addition, and that it is not brought about by hydrolysis is shown by the oxidation products of the ester (I) itself. The latter with alkaline potassium permanganate yields oxalic acid and ethyl hydrogen  $\alpha$ -cyano- $\beta$ -keto adipate (V),  $\text{HO}_2\text{C}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CH}(\text{CN})\cdot\text{CO}_2\text{Et}$  (Best and Thorpe, T., 1909, **95**, 1523), a derivative of the acid (III) assumed above to be an intermediate product of the oxidation of the tricarboxylic acid (II). It is necessary, therefore, to regard the addition as of the 1 : 3-type, such as has been observed in the case of normal ethyl  $\beta$ -methylglutaconate (Thorpe, T., 1919, **115**, 679), and of ethyl glutaconate (Ingold and Thorpe, T., 1921, **119**, 492).

Confirmation of this view regarding the additive process is gained from the similar action of ethyl sodiomalonate on ethyl muconate. In this case, the initial ester, *ethyl  $\Delta^{\alpha}$ -butene- $\alpha\delta$ -dicarboxylate- $\beta$ -malonate* (90 per cent.),  $\text{EtO}_2\text{C}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{C} \begin{smallmatrix} \text{CH}\cdot\text{CO}_2\text{Et} \\ \text{CH}(\text{CO}_2\text{Et})_2 \end{smallmatrix}$  (VI), yields the foregoing tricarboxylic acid (II) on hydrolysis with mineral acids, whilst alcoholic sodium hydroxide produces a tetra-sodium salt corresponding with the above ester (VI), oxidisable to oxalic and succinic acids.

Thus it is clear that addition of ethyl cyanoacetate and ethyl malonate to ethyl muconate does not yield products with the components of the addendum in the 1 : 4-position after the manner of the addition of hydrogen to muconic acid or of bromine to butadiene, and only by sacrificing the directness of the facts can it be made to appear of a much modified 1 : 2-type. Therefore, to embrace all the phases of activity, views of the potentialities of the muconic four-carbon system must be extended and represented in some such way as the following :



Here the mobility of the system is represented as such that transformation from a state of ordinary unsaturation (*a*), with its 1 : 2-addition, to one of conjugation (*b*) with the associated 1 : 4-addition, can take place; further, under suitable conditions either may pass into a third state (*c*), where by the exercise of free valencies a 1 : 3-type of addition can occur.

A new investigation into the addition of esters to conjugated systems has been commenced with the hope of gaining further knowledge of the types of addition that occur and the circumstances of their manifestation.

### EXPERIMENTAL.

*Ethyl Δ<sup>α</sup>-Butene-αδ-dicarboxylate-β-cyanoacetate* (I).—Sodium (2.3 grams) was "molecularised" under xylene and the latter replaced by absolute ether. To the cold mixture, ethyl cyanoacetate (13 grams) was added and the reaction allowed to proceed to completion. A dilute ethereal solution of well-dried ethyl muconate (20 grams) was then poured in, with shaking, and after the addition of a little absolute alcohol (30 c.c.) the containing flask was closed with a soda-lime tube and the whole kept at room temperature. The sodio-compound gradually dissolved to yield a clear reddish-brown liquid, and after one week this was shaken up with water, the ethereal layer separated, washed, and dried in the usual way, and the solvent evaporated, the residual yellow oil being almost pure *ethyl butenedicarboxylatemalonate* (yield 90 per cent.).

The ester distilled with some decomposition at 210°/20 mm. as a rather viscous, pale yellow oil, but at pressures above 20 mm. it decomposed almost entirely (Found: C = 57.81; H = 6.76. C<sub>15</sub>H<sub>21</sub>O<sub>6</sub>N requires C = 57.88; H = 6.75 per cent.).

The alkaline aqueous layer yielded on acidification a small amount of a viscous, brown oil which gave an intense purple colour with ferric chloride. The amount was insufficient for a complete examination, but the substance appeared to consist essentially of an ethyl hydrogen ester of butenedicarboxylic-cyanoacetic acid admixed with a ketonic product of secondary condensation.

*Ethyl Δ<sup>α</sup>-Butene-αδ-dicarboxylate-β-malonate* (VI).—The preparation of this substance by the addition of ethyl sodiomalonate to ethyl muconate was effected in precisely the same way as the preceding one, except that no alcohol was added. *Ethyl butenedicarboxylatemalonate* was thus obtained as a pale yellow, fairly mobile oil. After removal of traces of ethyl malonate by steam distillation, an almost pure product was obtained (yield 90 per cent.). After distillation, which can be carried out at low pressures with only slight decomposition, it was obtained as a colourless

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oil, b. p.  $215^{\circ}/14$  mm. (Found : C = 56.8; H = 7.2.  $C_{17}H_{26}O_8$  requires C = 57.0; H = 7.2 per cent.).

*Ethyl Hydrogen  $\Delta^{\alpha}$ -Butene- $\alpha\delta$ -dicarboxylate- $\beta$ -malonate*.—The alkaline aqueous liquor yielded on acidification a small amount of red oil which gave an intense purple coloration with ferric chloride. On hydrolysis with concentrated hydrochloric acid, it yielded  $\Delta^{\alpha}$ -butene- $\alpha\delta$ -dicarboxylic- $\beta$ -acetic acid (II), and, after purification by reprecipitation from a solution of its sodium salt, gave figures which indicate that it is the triethyl hydrogen ester of butenedicarboxylicmalonic acid. The coloration with ferric chloride appears to be due to the presence of a trace of some ketonic condensation product (Found : C = 54.53; H = 6.30.  $C_{15}H_{22}O_8$  requires C = 55.54; H = 6.66 per cent.).

*2 : 6-Dihydroxypyridine-4-propionic Acid (IV)*.—Ethyl butenedicarboxylatecyanoacetate (60 grams) was mixed with an equal volume of concentrated sulphuric acid and kept for five days. The hydrolysis was completed by adding water (120 c.c.) and boiling for twelve hours, removing the condenser at intervals to expel alcohol, but keeping the volume constant by addition of water. The sulphuric acid was removed by adding the boiling solution to the calculated quantity of barium hydroxide dissolved in 2 litres of boiling water. After rapid filtration by the aid of the pump, the clear filtrate deposited, on cooling, a considerable quantity of a solid crystallising in pale brownish-yellow flakes, which was recognised as a 2 : 6-dihydroxypyridine.

The liquor from which this substance separated was found still to contain a little sulphuric acid. It was therefore treated with small quantities of barium chloride solution until no more barium sulphate was precipitated. The filtered solution was evaporated to dryness several times with small quantities of hydrochloric acid. The residue having been extracted with acetone, the undissolved portion consisted mainly of the hydrochloride of the base. This was decomposed as accurately as possible with standard alkali, and the liberated base filtered off.

*2 : 6-Dihydroxypyridine-4-propionic acid* possesses marked acidic and basic properties. It acts as a dibasic acid, as might be expected of a substance with its constitution, and dissolves in mineral acids to produce salts. The *sulphate* and the *hydrochloride* are obtained as small, colourless needles on dissolving the compound in 50 per cent. sulphuric and concentrated hydrochloric acids respectively. Both these salts dissolve readily in cold water without appreciable dissociation.

*Dihydroxypyridinepropionic acid* is insoluble or only slightly soluble in the usual organic solvents, but in small amount can be

recrystallised from boiling water. Its solutions turn green or purple on standing, and the substance itself, on heating, darkens above  $250^{\circ}$  and decomposes at  $257^{\circ}$  [Found : C = 52.37; H = 4.96.  $C_8H_9O_4N$  requires C = 52.46; H = 4.91 per cent. 0.0862 neutralised 24.8 c.c. of 0.0385*N*-barium hydroxide. Calc. (dibasic), 24.5 c.c.].

*Ethyl  $\Delta^{\alpha}$ -Butene- $\alpha\delta$ -dicarboxylate- $\beta$ -acetate.*—The acetone extract (p. 1818) yielded on evaporation a brown syrup which would not solidify. It was therefore esterified with alcohol and sulphuric acid. The bulk of the ester distilled at  $195\text{--}205^{\circ}/19$  mm. as a colourless, mobile oil which gave, on hydrolysis with mineral acids, good yields of  $\Delta^{\alpha}$ -butene- $\alpha\delta$ -dicarboxylic- $\beta$ -acetic acid.

*$\Delta^{\alpha}$ -Butene- $\alpha\delta$ -dicarboxylic- $\beta$ -acetic Acid (Modification A) (II).*—This substance was obtained, not only from ethyl butenedicarboxylateacetate by hydrolysis with concentrated hydrochloric or dilute sulphuric acid, but also directly from ethyl  $\Delta^{\alpha}$ -butene- $\alpha\delta$ -dicarboxylate- $\beta$ -malonate. The latter ester was boiled with concentrated hydrochloric acid until dissolution was complete, and, on cooling, a quantity of the acid separated out. A further quantity was obtained by concentrating the solution on a steam-bath. Extraction of the remaining liquor with ethyl acetate yielded a syrup from which another small amount of the solid acid was obtained by dissolving in dry ether and keeping for several days. The acid, which is only sparingly soluble in cold water and almost insoluble in dry ether, benzene, or chloroform, was recrystallised for analysis from ethyl acetate, from which it separated in colourless, crystalline aggregates melting at  $179^{\circ}$  without decomposition. Larger quantities were readily recrystallised by dissolving in hot water and adding an equal volume of concentrated hydrochloric acid. The unsaturated nature of the acid was shown by its instantaneous reduction of cold alkaline permanganate [Found : C = 47.62; H = 5.07.  $C_8H_{10}O_6$  requires C = 47.52; H = 4.95 per cent. 0.0608 neutralised 23.5 c.c. of 0.0385*N*-barium hydroxide. Calc. (tribasic), 23.5 c.c.]. The *silver* salt was obtained in the usual way as a white, curd-like precipitate (Found : Ag = 61.5.  $C_3H_7O_6Ag_3$  requires Ag = 61.9 per cent.).

Boiling acetyl chloride slowly converted the acid into its *anhydride*, the conversion being still incomplete after twenty hours. The anhydride was readily extracted from the mixture by boiling benzene, from which it separated in flattened needles melting at  $116^{\circ}$ . It dissolved in alkali with immediate hydration [Found : C = 52.4; H = 4.4; *M* (tribasic) = 184.  $C_8H_8O_5$  requires C = 52.2; H = 4.34 per cent.; *M* = 184]. Conversion into the original acid was brought about both by water and by concentrated potassium hydroxide.

The proportion of syrupy material increased when the process of hydrolysis was prolonged by using more dilute mineral acid. Analysis of the white, curd-like silver salt derived from the syrup gave figures inconsistent with a pure substance, but denoting a decrease of basicity.

*Sodium  $\Delta^{\alpha}$ -Butene- $\alpha\delta$ -dicarboxylate- $\beta$ -malonate.*—Sodium (2.6 grams) was dissolved in absolute alcohol (45 c.c.) and to the cold solution water (5 c.c.) was added. On mixing with this solution ethyl  $\Delta^{\alpha}$ -butene- $\alpha\delta$ -dicarboxylate- $\beta$ -malonate (10 grams) and heating for a short time on the steam-bath, a pale yellow, crystalline sodium salt was precipitated in almost quantitative yield. This was rapidly filtered and washed by repeated trituration with absolute alcohol. After drying in an evacuated desiccator, the pure salt was obtained as a pale yellow, very hygroscopic powder (Found: Na = 27.2.  $C_9H_8O_8Na_4$  requires Na = 27.5 per cent.).

*$\Delta^{\alpha}$ -Butene- $\alpha\delta$ -dicarboxylic- $\beta$ -acetic Acid (Modification B).*—Acidification of the deep yellow, aqueous solution of the tetra-sodium salt with the theoretical amount of dilute hydrochloric acid gave a colourless solution, from which, by repeated shaking with ether, an almost colourless gummy acid was extracted. This, on keeping in an evacuated desiccator, partly solidified, and the solid matter was separated by rubbing the mass with dry ether. The ethereal solution, on long keeping, deposited a further amount of the same substance, but the separation was by no means complete. A rather better result was obtained by repeating the process of desiccation and ether treatment until no further solid would separate.

The solid acid was extremely soluble in cold water, but almost insoluble in benzene or chloroform. It was recrystallised from ethyl acetate, from which it separated in colourless, crystalline aggregates of indefinite shape melting at  $152^{\circ}$ , but these crystals gave low results on analysis owing to retention of the solvent. The acid was therefore recrystallised by heating under reflux with a large volume of pure ether until it dissolved, crystallisation taking place on concentrating the solution. It was thus obtained as a white, crystalline powder still melting at  $152^{\circ}$ . After drying in the steam-oven, it gave the following figures: C = 47.2; H = 5.2 ( $C_8H_{10}O_6$  requires C = 47.5; H = 5.0 per cent.). 0.0632 neutralised 24.2 c.c. of 0.0385*N*-barium hydroxide. Calc. (tribasic), 24.3 c.c. The silver salt was obtained in the usual way as a white, curd-like precipitate (Found: Ag = 62.1.  $C_8H_7O_6Ag_3$  requires Ag = 61.9 per cent.).

That portion of the product of hydrolysis obtained in a solid condition represented only about 3 to 5 per cent. of the whole. The remainder, from which no further solid could be separated in any

way, was dissolved in boiling water and carefully neutralised with ammonia. Treatment of the cold solution with silver nitrate gave a white, curd-like silver salt, from which the acid was regenerated by decomposition with hydrogen sulphide in dry ethereal suspension. Evaporation of the solvent in a vacuum left the acid as a colourless, viscous gum, which on titration gave figures closely approximating to those required by the formula  $C_8H_{10}O_6$  (tribasic). It could not, however, be decided with certainty whether the substance was essentially an unsaturated acid or an isomeric lactonic acid. Complete analysis of the silver salt yielded figures scarcely more conclusive (Found: C = 18.02; H = 1.42; Ag = 60.0.  $C_8H_7O_6Ag_3$  requires C = 18.37; H = 1.34; Ag = 61.9 per cent.).

*Oxidation of (a)  $\Delta^{\alpha}$ -Butene- $\alpha\delta$ -dicarboxylic- $\beta$ -acetic Acid, (b) Sodium  $\Delta^{\alpha}$ -Butene- $\alpha\delta$ -dicarboxylate- $\beta$ -malonate.*—(a) To the less fusible acid (3 grams) in sodium hydrogen carbonate solution at  $0^\circ$ , 3 per cent. potassium permanganate was added drop by drop, with stirring. The equivalent of six atoms of oxygen was added before reduction ceased. The oxidation mixture, decolorised with sulphurous acid and freed from manganese oxide by steam treatment and filtration, was successively treated with dilute hydrochloric acid, ammonia, and calcium chloride. The precipitate thus obtained was found to consist entirely of calcium oxalate. Concentration of the alkaline mother-liquor to small bulk and subsequent acidification gave a liquid from which repeated extraction with ether removed a white, crystalline solid. This was contaminated with a minute amount of syrupy substance, but after washing with dry ether melted sharply at  $185^\circ$ , and proved to be succinic acid (mixed melting point). Careful examination of the residual liquor revealed no trace of tricarballic acid.

(b) The tetra-sodium salt (7 grams) was dissolved in water (300 c.c.) containing sodium hydrogen carbonate (3.5 grams) and the same procedure as above followed, except that the equivalent of only four atoms of oxygen was supplied. The results were identical with those of (a).

*Oxidation of Ethyl  $\Delta^{\alpha}$ -Butene- $\alpha\delta$ -dicarboxylate- $\beta$ -cyanoacetate (I).*—The ester (14 grams), suspended in a solution of sodium hydroxide (14 grams) in water (500 c.c.) at  $0^\circ$ , was mechanically agitated while 3 per cent. potassium permanganate was run in. Reduction of the latter was rapid until the equivalent of three atoms of oxygen had been added, when it ceased. The cold, filtered reaction mixture was extracted many times with ether, and from the extract was obtained a considerable amount of a pale brown syrup which, after keeping for several weeks, partly solidified. Draining of the



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semi-solid mass on a porous tile yielded a white solid, which, after recrystallisation from boiling water, was obtained as colourless needles melting at  $104^{\circ}$ . This substance gave in alcoholic solution a deep red colour with ferric chloride, titrated accurately as a dibasic acid, and agreed in all respects with ethyl hydrogen  $\alpha$ -cyano- $\beta$ -ketoadipate (X) (Found: C = 50.69; H = 5.37. Calc., C = 50.68; H = 5.20 per cent.).

Oxalic acid could readily be obtained from the residues after boiling with alkali to complete the hydrolysis.

I desire to express my thanks to Professor J. F. Thorpe and Dr. C. K. Ingold for the interest they have taken in this research and to the Government Grant Committee of the Royal Society for a grant which has largely defrayed the cost of the materials employed.

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[Received, July 5th, 1922.]

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