

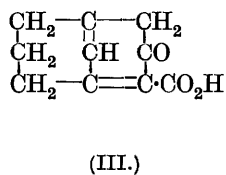
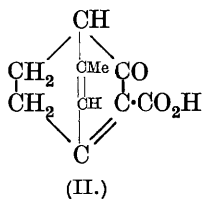
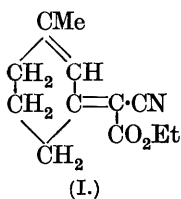
CCIV.—*Properties of Conjugated Compounds. Part I.*  
*Conjugative Associations in Extended “Con-*  
*jugated” Systems.*

By ERNEST HAROLD FARMER and JOHN ROSS.

IN extended conjugated systems of the type  $\text{CH}:\text{CH}\cdot\text{CH}:\text{CH}\cdot\text{C}:\text{O}$ , the characteristic mode of terminal hydrogen addition is usually regarded as due to the conjugative coherence of all the individual unsaturated elements of the chain. Many reactivities of these

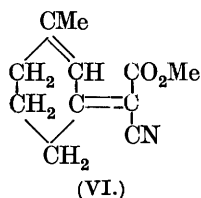
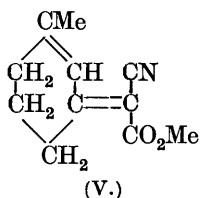
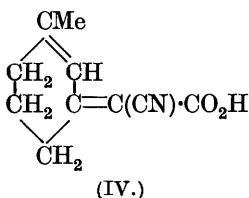
structures, however, appear to be dependent on a state of partial association in which the complex  $\text{CH}_2\text{CH}\cdot\text{C}\cdot\text{O}$  acts as a conjugated unit, the whole behaving as a substituted ethylene or as a  $\beta$ -substituted acrylic acid. As a means of estimating the extent of conjugative association in extended systems, an attempt has been made to examine the degree to which the behaviour of the acrylic "unit" is modified by inclusion in systems of the type in question. Since one of the most important properties of the complex is a normal capacity for change from one conjugated form to another ( $\cdot\text{CH}_2\text{C}\cdot\text{C}\cdot\text{O} \rightleftharpoons \cdot\text{C}\cdot\text{C}\cdot\text{O}\text{H}$ )—a change impossible in extended systems unless the olefinic chain is branched—observations have been made in this respect, certain *cyclohexenyldenecyanoacetic* esters containing the essential structure  $\text{C} \begin{array}{c} \text{C}=\text{C} \\ \diagdown \quad \diagup \\ \text{C} \quad \text{C} \end{array} \text{C}=\text{C}\cdot\text{C}=\text{O}$  being employed for the purpose.

It was shown by Knoevenagel and Mottek (*Ber.*, 1904, **37**, 4464), in their investigation of the reactivity of ketones, that 1-methyl- $\Delta^1$ -*cyclohexen-3-one* reacts with ethyl cyanoacetate in the presence of piperidine, giving ethyl methyl*cyclohexenyldenecyanoacetate* (I). In accordance with the assigned constitution, this substance could be broken down by hydrolysis with caustic alkali into the original ketone and malonic acid; apparently, however, it was unsuitable for our experiments owing to the ease with which it was stated to undergo an astonishing intramolecular change. Thus, according to these authors, hydrolysis with sodium carbonate yielded an acidic compound to be represented by some such formula as (II) or (III), or one of their enolised equivalents.



Further, the silver salt of the substance yielded with methyl iodide a mixture of isomeric esters or ethers for the isomerism of which it was difficult to account. The formulæ assigned were necessitated solely by the analytical results; there was nothing in the behaviour of the substance itself to suggest the presence of the aromatic nucleus which these formulæ imply. Consequently, in reviewing the evidence, the suspicion arose that the acidic compound was a nitrogenous substance, and, if formula (I) were correct, was actually the normal hydrolysis product (IV). Repetition of Knoevenagel

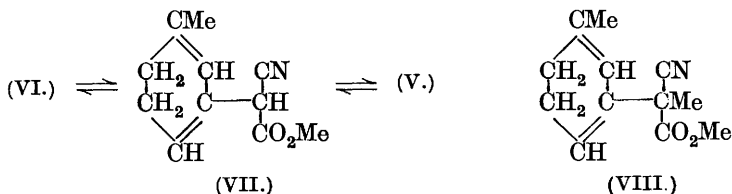
and Mottek's work confirmed this view, thus rendering possible the study of the methylcyclohexenyldenecyanoacetic esters.



The ethyl ester was very readily obtained and was converted by alcoholic alkali into an acid agreeing with formula (IV) analytically, and in melting point and general properties with Knoevenagel and Mottek's supposed dicyclic compound. This rather intractable acid did not appear homogeneous, but could not be separated into components by fractional crystallisation. Esterification, however, yielded the two isomeric methyl esters mentioned above.

Formula (IV) at once suggests the possibility of geometrical isomerism about the extracyclic double bond, and the two isomerides found might be regarded as the maleinoid and fumaroid forms (V and VI). This being so, these two solid methyl esters should be directly obtainable by the condensation of methyl cyanoacetate with the ketone. When this was done, the excellent yield of the two methyl esters obtained left no doubt as to their monocyclic constitution.

As the isomerides or tautomerides concerned in mobility of the  $\alpha\beta$ - $\beta\gamma$  type are usually brought into equilibrium in the presence of alkalis or sodium alkyl oxides, the two methyl methylcyclohexenyldenecyanoacetates were separately treated with alcoholic sodium methoxide. In each case, a similar mixture of three esters was obtained from the product. Two of these were the esters (V) and (VI), and the third must be regarded as the methyl methylcyclohexadienylcyanoacetate (VII). Subsequently this was shown to yield a similar mixture of three isomerides on treatment with sodium methoxide. Since in all three mixtures the proportions of the

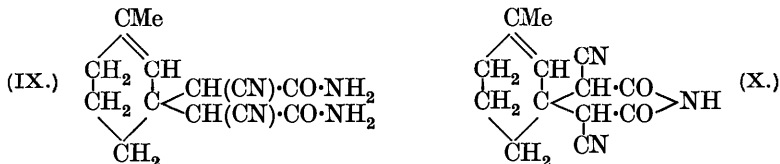


components appeared identical, there is little doubt that an equilibrium holds. Caustic alkali exerted a similar influence during the

hydrolysis of these esters, as was shown by the melting point of the acid mixture obtained and by the nature of the mixture of esters obtained on re-esterification; further, upon repetition of these processes with larger amounts of the ethyl ester first obtained, the third methyl ester was isolated in this case also.

Each of the three esters gave a distinctive dibromide and each could be methylated precisely as the various *cyclopentenyl*- and *cyclohexenyl*-cyanoacetic esters and their tautomerides (Harding and Haworth, J., 1910, **97**, 490; Birch and Kon, J., 1923, **123**, 2440), the product in all cases being one and the same methyl derivative (VIII).

In attempts to prepare the cyanoacetamides of the isomeric esters by means of aqueous ammonia, each gave rise to a dicyanoacetamide (IX) and the ammonium salt of the imide (X), both being identical with the compounds directly obtainable from the ketone and cyanoacetic ester by the Guareschi synthesis. Such syntheses resulting from the reversion of a portion of the cyclic ester into its generators, with the subsequent addition of the liberated cyanoacetic ester (or amide) to the undecomposed portion, have recently been observed in other series (private communication by Miss W. Kilroy).



Among the small portions of ester recovered in these reactions, isomerides other than the original one were obtained. Interconversion of the esters could be secured only by the use of an alkaline equilibrating agent; thus the passage from a fumaroid to a maleinoid form was only possible by way of the third (*cyclohexadienyl*-) form, and in the original condensation of the ketone and methyl cyanoacetate two and only two forms were obtained.

In estimating the effect of conjugative association on the incorporation of the group  $\text{CH}:\text{CH}:\text{C}:\text{O}$  in a larger unit, it is convenient to compare the results obtained above with the evidence furnished by substances containing no double bonds other than those of the acrylic system. Among the latter, considerable, and at present inexplicable, variations occur in the speed of attainment and in the position of equilibrium. In some cases, the  $\alpha\beta$ - and  $\beta\gamma$ -forms are readily isolable and undergo appreciable interconversion only in the presence of a reagent like sodium alkyloxide; in the limiting cases, isomerisation is so rapid (even in absence of a reagent) and the position of equilibrium favours so strongly one form or the other

that the separation of individuals has been impossible.\* In the *cyclohexenyliidene* esters described above, the acrylic group seems to be preserved as a definite unit. Change of the  $\alpha\beta$ - $\beta\gamma$  type, which might conceivably have been suppressed, is here of normal and intermediate character; and in so far as this is the case there is no positive evidence of any considerable tendency for the extended system, of which the acrylic group is a part, to act persistently as a completely conjugated unit.

#### EXPERIMENTAL.

*Condensation of Methyl Cyanoacetate with 1-Methyl- $\Delta^1$ -cyclohexen-3-one.*—A mixture of the ketone (110 g.), the ester (100 g.), and piperidine (10 c.c.) was heated at 120—125° for 6 hours. The cooled product, upon the surface of which a thin aqueous layer had formed, was diluted with ether and thoroughly washed, first with dilute sulphuric acid and then with dilute sodium carbonate solution. The dried ethereal solution was distilled, finally at a very low pressure (the amount of undecomposed material passing over at 1 mm. was double that at 10 mm.); the fraction, b. p. 165—175°/2 mm., solidified on cooling (yield 70%).

A considerable portion of this solid dissolved in boiling petroleum (b. p. 40—60°). The solution deposited one isomeride of *methyl 1-methyl- $\Delta^1$ -cyclohexenyliidene-3-cyanoacetate* in large, needle-shaped prisms, m. p. 74°; these were sometimes colourless, but often had a deep yellow colour which was removed by boiling in petroleum solution with animal charcoal (Found : C, 68.95; H, 6.9; N, 7.5.  $C_{11}H_{13}O_2N$  requires C, 69.05; H, 6.85; N, 7.3%).

The petroleum mother-liquor, after concentration and cooling, deposited flat, colourless prisms, m. p. 60°. This substance, isomeric with that described above (the two are regarded as isomerides of the fumaroid-maleinoid type), represented about 6% of the ester mixture (Found : C, 69.05; H, 6.9; N, 7.45%).

The portion of the ester mixture undissolved by boiling petroleum crystallised from methyl alcohol-petroleum in colourless, hexagonal prisms, m. p. 88°. The nature of this stable, highly nitrogenous substance, which is readily obtainable from the cyanoacetic ester and piperidine alone, has not been determined (Found : C, 63.1; H, 8.0; N, 17.7%).

\* The strictly comparable *cyclohexyliidene*- and *cyclopentyliidene*-cyanoacetic esters are liquids (Birch, Kon, and Norris, J., 1923, 123, 1368) and from the details published it is evident that both the position of equilibrium and the isolability of the separate forms are uncertain. In the present case, equilibrium is attained when the material is divided between the *cyclohexadienyl* and the *cyclohexenyliidene* form in the approximate ratio of 3 : 10.

*Condensation of Ethyl Cyanoacetate with 1-Methyl- $\Delta^1$ -cyclohexen-3-one.*—This condensation, effected by Knoevenagel and Mottek's method (*loc. cit.*), produced an oil from which, by distillation at 1 mm. pressure and refractionation, a mixture of esters, b. p.  $190^\circ/16$  mm., which solidified on cooling, was obtained. The main part of this mixture melted at  $58^\circ$  after recrystallisation from light petroleum. This substance, doubtless one form of ethyl methylcyclohexenyldenecyanoacetate, was used for the repetition of Knoevenagel and Mottek's experiments (Found: C, 70.0; H, 7.5; N, 7.05. Calc. for  $C_{12}H_{15}O_2N$ : C, 70.2; H, 7.4; N, 6.85%).

*Equilibration by Alcoholic Caustic Alkali.*—*Hydrolysis of methylcyclohexenyldenecyanoacetic esters.* The ethyl ester was not appreciably hydrolysed on boiling for 12 hours with 15% hydrochloric acid and was only slowly affected by boiling with sodium carbonate solution in the manner described by Knoevenagel and Mottek. Since prolonged treatment with caustic alkali caused degradation, the ester was boiled for 30 minutes with 10% aqueous-alcoholic caustic potash (alcohol: water = 3:1). The deep brown solution so obtained was cooled, and the hydrolysis product separated by the usual methods into neutral and acidic portions. The acidic portion was a very sticky, brown solid which was recrystallised several times from benzene, decolorised by animal charcoal, and recrystallised from acetone. This acid, which was not homogeneous in crystalline form, melted at  $149^\circ$  (Found: C, 67.6; H, 6.3; N, 7.9; *M*, monobasic, 174. Calc. for  $C_{10}H_{11}O_2N$ : C, 67.8; H, 6.25; N, 7.9%; *M*, 177.1). The ammonium salt was obtained, from the acid and ammonia in ether, as a colourless, crystalline precipitate, which was dried in a vacuum. The silver salt was precipitated as a pale yellow powder from an aqueous solution of the ammonium salt by silver nitrate.

*Separation of the isomeric esters.* The mixture of methyl esters, b. p.  $180$ — $185^\circ/17$  mm., obtained by boiling the silver salt with alcoholic methyl iodide was crystallised from petroleum. The characteristic, needle-like crystals of methyl methylcyclohexenyldenecyanoacetate, m. p.  $74^\circ$ , separated first; then, after concentration, the geometrical isomeride, m. p.  $60^\circ$ , was obtained in large, hexagonal plates. (Both of these were shown by analysis and by direct comparison to be identical with the respective esters described above.) Finally, when the mother-liquor had been evaporated almost to dryness, crystals of methyl 1-methyl- $\Delta^{1,3}$ -cyclohexadienyl-3-cyanoacetate were obtained. These, after recrystallising several times from strongly-cooled methyl alcohol-petroleum, were obtained in colourless needles, m. p.  $42^\circ$  (Found: C, 69.1; H, 7.0; N, 7.5.  $C_{11}H_{13}O_2N$  requires C, 69.05; H, 6.9; N, 7.35%).

The proportions in which the three esters were obtained were (m. p. 74°) : (m. p. 60°) : (m. p. 42°) = 4 : 1 : 1.6.

*Equilibration by Sodium Alkyloxide.*—A mixture of the ester, m. p. 74° (3 g.) and sodium methoxide (1 mol.) in cold methyl alcohol was kept for one hour and then poured into water. The mixture of solid esters (2 g.) obtained by extracting the product with ether yielded, on fractional crystallisation, the three isomeric esters in the approximate proportions 4.2 : 1 : 1.5. Nearly a third of the material suffered hydrolysis during the process.

Similar results were obtained with the other two isomerides.

*Methylation of the Isomeric Esters.*—An equilibrated mixture obtained as described above was heated on a water-bath with an excess of methyl iodide for 30 minutes. The cooled solution was poured into ice-water, and the product extracted with ether. The extract was washed in turn with dilute acid and sodium carbonate solution and dried. Evaporation of the ether yielded an oil two-thirds of which distilled at 160—165°/10 mm. On redistillation it was obtained as a colourless, mobile liquid, b. p. 160°/11 mm. This substance, from its analysis and ready conversion into the corresponding acetonitrile, must be regarded as *methyl 1-methyl- $\Delta^{1:3}$ -cyclohexadienyl-3- $\alpha$ -cyano-propionate* (VIII) (Found : C, 69.95; H, 7.5; N, 7.3.  $C_{12}H_{15}O_2N$  requires C, 70.2; H, 7.4; N, 6.9%).

*Bromination of the Isomeric Methyl Methylcyclohexenylidene-cyanoacetates.*—The esters, m. p. 74° and 60°, yielded, on bromination (1 mol.) in cold chloroform, *dibromides* which crystallised from alcohol-petroleum in large, colourless prisms, m. p. 77° (Found : Br, 45.2%), and fine needles, m. p. 65° (Found : Br, 45.3.  $C_{11}H_{13}O_2NBr$  requires Br, 45.5%) respectively. The ester, m. p. 42°, similarly yielded a yellow, oily dibromide (Found : Br, 44.8%).

These dibromides readily lost hydrogen bromide on treatment with diethylamine, but the products were all liquid and could not be satisfactorily reduced by any of the reagents employed.

*Decarboxylation of the Cyano-esters.*—Decarboxylation of (VIII) by Birch and Kon's method (*loc. cit.*, p. 1374) gave, in good yield, *1-methyl- $\Delta^{1:3}$ -cyclohexadienyl-3-propionitrile* as a colourless, mobile liquid, b. p. 126°/11 mm. (Found : C, 81.9; H, 9.0; N, 9.0.  $C_{10}H_{13}N$  requires C, 81.6; H, 8.9; N, 9.5%).

The purified hydrolysis product of methyl (or ethyl) methylcyclohexenylidene-cyanoacetate (p. 1575) yielded, on heating with water at 180° or on boiling for 30 minutes with 15% hydrochloric acid, a light, neutral oil which, after extraction, drying, and distillation, was obtained as a colourless, mobile, highly refractive liquid, b. p. 118°/10 mm. (Found : C, 80.8; H, 8.3; N, 10.2.  $C_9H_{11}N$  requires C, 81.1; H, 8.3; N, 10.5%).

*Action of Ammonia upon the Three Isomeric Esters.*—The methyl ester, m. p.  $74^{\circ}$  (3 g.), gradually dissolved in concentrated aqueous ammonia, and after 12 hours large crystals, m. p.  $273^{\circ}$ , of 1-methyl- $\Delta^1$ -cyclohexene-3 : 3-dicyanoacetamide (IX) were deposited. A second crop consisted of this substance and the ammonium salt of the cyanimide (X). The latter had m. p.  $188^{\circ}$  (Found : C, 60.1; H, 6.4; N, 21.3.  $C_{13}H_{16}O_2N_4$  requires C, 59.95; H, 6.2; N, 21.5%) and yielded, on acidification of its aqueous solution, the free imide, a white, crystalline powder, m. p.  $195^{\circ}$  (Found : N, 17.1.  $C_{13}H_{13}O_2N_3$  requires N, 17.3%). The dicyanoacetamide, which was insoluble in all the ordinary solvents, was washed in turn with boiling alcohol and boiling water and then had m. p.  $275^{\circ}$  (Found : C, 59.85; H, 6.2; N, 21.4.  $C_{13}H_{16}O_2N_4$  requires C, 59.95; H, 6.2; N, 21.5%). The yields of the condensation products corresponded with the explanation of their formation given in the introduction.

The esters, m. p.  $60^{\circ}$  and m. p.  $42^{\circ}$ , also gave on similar treatment the same two compounds (m. p.  $188^{\circ}$  and m. p.  $275^{\circ}$ ). The quantities of the cyclic imide and dicyanoacetamide produced varied in the different experiments, but the total amount was constant.

*Condensation of Methyl Methylcyclohexenyldenecyanoacetate with Methyl Cyanoacetate.*—To a solution of the ester, m. p.  $74^{\circ}$  (5 g.) and methyl cyanoacetate (2.5 g.) in cold alcohol, ammoniacal alcohol (10 c.c., saturated at  $-10^{\circ}$ ) was added, and the mixture kept at  $0^{\circ}$  for 2 days, much crystalline matter separating. The ammonium salt of the cyclic imide and the dicyanoacetamide described above were thus obtained in 68% yield.

*Condensation of Methylcyclohexenone and Ethyl Cyanoacetate.*—A mixture of methylcyclohexenone (4 g.), ethyl cyanoacetate (8.5 g.), and ammoniacal alcohol (18 c.c., saturated at  $-10^{\circ}$ ) was kept at  $0^{\circ}$  in a closed bottle. The crystals deposited after 1 day consisted almost entirely of cyanoacetamide, but after 3 days 5.5 g. of the almost pure ammonium salt of the imide (X) were obtained.

The authors desire to express their thanks to the Government Grant Committee of the Royal Society (E. H. F.) and to the Chemical Society (J. R.) for grants towards the cost of the investigation, and to Professor J. F. Thorpe for his interest in the work.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,

LONDON, S.W. 7.

[Received, February 17th, 1926.]