ON THE NITRILE-ESTERS OF THE DICARBOXY-GLUTACONIC ACID.

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In the previous paper[1] dealing with the so-called diethyl dicyano-glutaconate the author showed that this substance has the composition $C_{11}H_{12}O_4N_2 \cdot \frac{1}{2}H_2O$ instead of $C_{11}H_{12}O_4N_2$, and its constitution is represented by the formula $(C_{10}H_{12}O_4N)-C(=NH)-NH-CO-(C_{10}H_{12}O_4N)$. The triethyl dicyanoaconitate $C_2H_5OOC(CN)C=C(COOC_2H_5)-CH(CN)COOC_2H_5+\frac{1}{2}H_2O$[2], and the methenylbismalonitrile-imidether $(CN)_2C=CH-CH(CN)C(NH)-OC_2H_5+\frac{1}{2}H_2O$[3], are also combined with half a molecule of water. In order to examine the presence of such a tendency as of combining with water, and at the same time expecting some interesting results which would arise from their being the derivatives of glutaconic acid, the author synthesized and investigated the following nitrile-esters of the dicarboxyglutaconic acid.

(1) This journal **2** (1927), 26.
(2) G. Errera und F. Perciabosco, *Ber.*, **34** (1901), 3704.
(3) W. Zoernig, *J. prakt. Chem.* **74** (1906), 435.

By the condensation of one of diethyl ethoxymethylene-malonate $(C_2H_5OOC)_2C=CHOC_2H_5$, ethyl ethoxymethylene-cyanoacetate $C_2H_5OOC(CN)C=CHOC_2H_5$, and ethoxymethylene-malonitrile $(CN)_2C=CHOC_2H_5$, with one of diethyl sodio-malonate $CHNa(COOC_2H_5)_2$, ethyl sodio-cyanoacetate $CHNa(CN)COOC_2H_5$, and sodio-malonitrile $CHNa(CN)_2$, nine methenyl compounds are to be formed, which are the nitrile-esters of the dicarboxyglutaconic acid. They are:

(I) Tetraethyl propylene-α, α, γ, γ-tetracarboxylate (or tetraethyl dicarboxyglutaconte), $(C_2H_5OOC)_2C=CH-CH(COOC_2H_5)_2$;

(II) Triethyl α-cyanopropylene-α, γ, γ-tricarboxylate (or triethyl α-cyano-γ-carboxyglutaconate), $(C_2H_5OOC)_2C=CH-CH(CN)COOC_2H_5$;

(III) Triethyl γ-cyanopropylene-α, α, γ-tricarboxylate, $C_2H_5OOC(CN)C=CH-CH(COOC_2H_5)_2$;

(IV) Diethyl α, α-dicyanopropylene-γ, γ-dicarboxyate, $(C_2H_5OOC)_2C=CH-CH(CN)_2$;

(V) Diethyl γ, γ-dicyanopropylene-α, α-dicarboxylate, $(CN)_2C=CH-CH(COOC_2H_5)_2$;

(VI) Diethyl α, γ-dicyanopropylene-α, γ-dicarboxylate (or diethyl dicyanoglutaconate), $C_2H_5OOC(CN)C=CH-CH(CN)COOC_2H_5$;

(VII) Ethyl α, α, γ-tricyanopropylene-γ-carboxylate, $C_2H_5OOC(CN)C=CH-CH(CN)_2$;

(VIII) Ethyl α, γ, γ-tricyanopropylene-α-carboxylate, $(CN)_2C=CH-CH(CN)COOC_2H_5$;

(IX) α, α, γ, γ-Tetracyanopropylene, $(CN)_2C=CH-CH(CN)_2$.

Of course the above condensations will give first the α-sodio-derivatives of these compounds. All of them, except (I) which is well known as the tetraethyl dicarboxyglutaconate, have never been closely investigated, and most of them have never been synthesized. Errera[1] carried out the condensation of diethyl ethoxymethylene-malonate with ethyl sodio-cyanoacetate, and the oily substance obtained by him was probably the nitrile-ester (II), but with no analytical determination of its composition, he transformed it into the diethyl dihydroxydinicotinate. The compound which had been considered to be the diethyl α, γ-dicyanopropylene-α, γ-dicarboxylate (VI), the so-called diethyl dicyanoglutaconate, was clearly explored by the author as stated above. The compound obtained by Zoernig[2] in the condensation of malonitrile, chloroform, and sodium ethylate was not the tetranitrile (IX), but its imidether semihydrate.

The first two compounds (I) and (II) are not described in this paper, because the tetraethyl dicarboxyglutaconate had no important relation to the

(1) *Ber.*, **31** (1898), 1243.

(2) Loc. cit.

present investigation, and the triethyl α-cyanopropylene-α, γ, γ.tricarboxylate had been synthesized by Errera if not in a satisfying manner. The present author has synthesized the other seven compounds, or, strictly speaking, performed the seven condensations which would give the seven compounds.

The general procedure of the condensations of the ethoxymethylene compounds with sodium compounds was very simple.[1] These reactions proceeded smoothly at the ordinary temperature in the absolute alcoholic solutions. The resulting solutions of the sodium derivatives of the methenyl compounds were coloured more or less deep red, but, besides the inevitable formation of the colouring by-product which might be very small in quantity, no side reactions seemed to occur. On evaporating the alcohol in vacuo over sulphuric acid (heating was avoided in fear of any secondary reaction) the solutions left the crystalline mass of the sodium compounds. As these sodium compounds are generally easily soluble in water, a considerable loss could not be avoided in the recrystallisation from water.

Some of the sodium compounds were obtained in coloured appearance, and others in colourless state. From the analogy of the constitution all of them should be colourless and the colours of some of them must be due to impurities which can be difficultly removed.

(III) **Triethyl γ-cyanopropylene-α, α, γ-tricarboxylate.** Sodium was dissolved in absolute alcohol, and diethyl malonate was added. Ethyl ethoxymethylene-cyanoacetate in powder was added to this solution under cooling in ice water. The solution became red, and on evaporating the alcohol in vacuo over sulphuric acid, a coloured crystalline mass was obtained. After washing with ether the crystals were again dried over sulphuric acid. This crystalline sodium compound, triethyl α-sodio-γ-cyanopropylene-α, α, γ-tricarboxylate, is hygroscopic, and absorbs heat when dissolved in water. It gave an oily substance when its aqueous solution was acidified with dilute hydrochloric acid, which was extracted with ether. This ethereal solution was shaken with the aqueous solution of sodium carbonate and the aqueous layer was again acidified and extracted with fresh ether. This second ethereal solution was washed with water, dried with calcium chloride, and evaporated in vacuo. In this way an oily substance was obtained, which gradually crystallised on keeping it in the desiccator. After dried to a constant weight in vacuo in the desiccator it was analysed. 0.2378 Gr. of the substance gave 10.5 c.c. of nitrogen at 24.0° and 758 mm. (Found : N=4.91. $C_{13}H_{17}O_6N$ requires N=4.94%.) According to the mode of formation and the expected result in analysis, this substance is the triethyl γ-cyanopropylene-α, α, γ-tricarboxylate, $C_2H_5OOC(CN)C=CH-CH(COOC_2H_5)_2$.

(1) Cf L. Claisen, *Ann.*, **297** (1897), 1.

This substance has an acid character and dissolves in the aqueous solution of sodium carbonate, evolving carbon dioxide.

It can be induced from the studies on the following cases that the condensation of diethyl ethoxymethylene-malonate with ethyl sodio-cyano-acetate will give the same product as that described above, and there is no difference between triethyl *α*-cyanopropylene-*α*, *γ*, *γ*-tricarboxylate and triethyl *γ*-cyanopropylene- *α*, *α*, *γ*-tricarboxylate,

(IV) **Diethyl *α*, *α*-dicyanopropylene-*γ*, *γ*-dicarboxylate.** When diethyl ethoxymethylene-malonate was added to the alcoholic solution of sodio-malonitrile a reddish solution was obtained. The solution was filtered from a little amount of solid. The viscous mass which remained after the evaporation of the alcohol was dissolved in water and the solution was shaken with ether to remove substances soluble in ether. On adding dilute hydrochloric acid to the aqueous solution a brown oil separated, which was extracted with ether, but soon from both the aqueous and ethereal solutions colourless crystals separated out. As the colouring impurities were taken into ether, the crystals from aqueous solution were quite colourless, which were collected, washed with cold water and ether, and dried in vacuo over sulphuric acid. 0.1552 Gr. of the substance gave 14.2 c.c. of nitrogen at 23.5° and 760 mm.; 0.2359 gr. of the substance gave 0.4199 gr. of CO_2 and 0.1253 gr. of H_2O. (Found: N=10.23; C=48.56; H=5.94. $C_{11}H_{12}O_4N_2 \cdot 2H_2O$ requires N=10.29: C=48.51; H=5.93%.) This crystalline compound was not the diethyl *α*, *α*-dicyanopropylene-*γ*, *γ*-dicarboxylate $C_{11}H_{12}O_4N_2$, but the diethyl *α*, *α*-dicarbamyl-propylene-*γ*, *γ*-dicarboxylate, $(C_2H_5OOC)_2C=CH-CH(CONH_2)_2$. The oily substance which existed for a short time was probably the dinitrile.

When the viscous mass obtained by evaporation of alcohol from the condensation mixture was left in the desiccator for a few days, it took gradually crystalline form. This crystalline substance was twice recrystallised from a small amount of water. 0.3504 Gr. of the substance dried in vacuo over sulphuric acid decreased by 0.0116 gr. on dehydrating at 140−150°. (Found: H_2O=3.31. $C_{11}H_{11}O_4N_2Na \cdot \frac{1}{2}H_2O$ requires H_2O=3.37%.) 0.3388 Gr. of the dehydrated substance gave 34.0 c.c. of nitrogen at 26° and 756 mm. (Fonnd: N=11.02. $C_{11}H_{11}O_4N_2Na$ requires N=10.9%.) According to the mode of formation this is diethyl *α*-sodio-*α*, *α*-dicyanopropylene-*γ*, *γ*-dicarboxylate.

(V) **Diethyl *γ*, *γ*-dicyanopropylene-*α*, *α*-dicarboxylate.** In the case of the condensation of ethoxymethylene-malonitrile with diethyl sodio-malonate, the resulting solution was not so intensely coloured as in the case of (IV) and the formed sodium compound crystallised easily on evaporating the solvent.

The sodium compound was dissolved in water and dilute hydrochloric acid was added. A brown oily substance deposited at once, but, on stirring, dissolved again in the mother liquor and soon colourless crystalline substance separated out, which was collected, washed with a small amount of water several times and dried in vacuo over sulphuric acid. 0.2596 Gr. of the substance gave 24.5 c.c. of nitrogen at 27.5° and 758.4 mm. (Found: N=10.31, $C_{11}H_{12}O_4N_2 \cdot 2H_2O$ requires N=10.29%.)

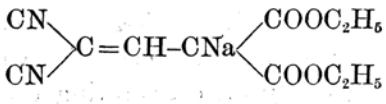
The compound obtained in this case was also a diamide. The constitution should be $(H_2NCO)_2C=CH-CH(COOC_2H_5)_2$, the isomer of $(C_2H_5OOC)_2C=CH-CH(CONH_2)_2$ described in (IV).

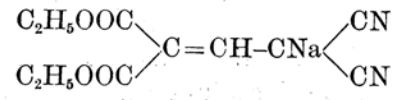
Recrystallised from alcohol, the sodium compound became nearly colourless crystals. 0.5245 Gr. of the substance dried at 150° gave 0.1413 gr. of Na_2SO_4. 0.3220 Gr. of the substance dried at 150° gave 32.5 cc. of nitrogen at 27° and 757 mm. (Found: Na=8.72; N=11.03. $C_{11}H_{11}O_4N_2Na$ requires Na=8.92; N=10.9%.) The sodium compound crystallised from water contains half a molecule of water. 0.3440 Gr. of the substance decreased by 0.0113 gr. on dehydrating at 140–150°. (Found: H_2O=3.29. $C_{11}H_{11}O_4N_2Na \cdot \frac{1}{2}H_2O$ requires H_2O=3.37%.) According to the mode of formation this is diethyl α-sodio-γ, γ-dicyanopropylene-α, α-dicarboxylate.

Considered from the mode of formation the two kinds of diamides described in (IV) and (V) may differ in the position of the double union only. But as it is expectable from the fact that the α- and γ-positions in glutaconic acid are the same,[1] these two diamides have been found identical. The one, the other, and their mixture melted at the same point 139-140°, solidified then and gradually decomposed when heating was continued.

The coincidence in composition (water of crystallisation) of the sodium derivatives of diethyl α, α-dicyanopropylene-γ, γ-dicarboxylate and of diethyl γ, γ-dicyanopropylene-α, α-dicarboxylate suggested the identity of these two sodium compounds. Really they have been found identical. These two specimens of sodium compounds and their mixture melted at the same point 238–239° (not corr.). It is no wonder that the specimens of the identical sodium compounds gave the identical diamides.

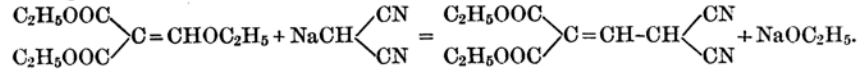
For the identity of the α- and γ-positions in glutaconic acid $HOOCCH=CH-CH_2COOH$, it is necessary that at least one of the methylene hydrogen atoms remains unsubstituted. There exists, however, no mobile hydrogen atom in the sodium compounds as shown by the formulæ,


(A)


(B)

(1) J. F. Thorpe, *J. Chem. Soc.* **87** (1905), 1669.

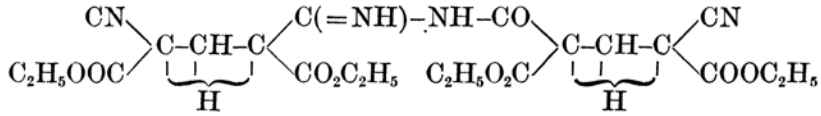
The compound represented by (A) can not be identical with the compound represented by (B). Therefore the constitution of the sodium compounds formed through two ways of condensation must be limited to either of them. Whichever formula it may possess, how two ways of condensation led to the same product can be explained on the assumption that the condensation of an ethoxymethylene compound with a sodium compound proceeds in two stages. In the first stage sodium ethylate is split off from the ethoxymethylene compound and the sodium compound, for instance,



And then the sodium ethylate reacts with the methenyl compound, yielding the sodium derivative of the methenyl compound and alcohol. Now, the methenyl compound formed intermediately has the mobile hydrogen atom, and there is no difference between α- and γ-positions. Thus the condensation of diethyl ethoxymethylene-malonate with sodio-malonitrile and the condensation of ethoxymethylene-malonitrile with diethyl sodio-malonate will give the same intermediate compound, and the second stage of the condensation, where the mobile hydrogen atom is replaced by sodium, will be the same.

The identity of the diamides may not be directly due to their glutaconic structure, but to the identity of the sodium derivatives ; and the fundamental cause of the identity of the sodium compounds lies in their glutaconic structure. Although it is not yet decided whether the constitution of the sodium compound is (A) or (B) it can be safely said that the diamide $C_{11}H_{16}O_6N_2$ is the diethyl α, α (= γ, γ)-dicarbamylpropylene-γ, γ (= α, α)-dicarboxylate.

(VI) **Diethyl α, γ-dicyanopropylene-α, γ-dicarboxylate.** That the condensation of ethyl ethoxymethylene-cyanoacetate with ethyl sodio-cyanoacetate gave the same substance as that synthesized from ethyl cyanoacetate, chloroform, and sodium ethylate, was explained in the previous paper.[1] The constitutional formula previously given to the diethyl dicyanoglutaconate semihydrate can now be written in a more expanded form, for it has become known that the double bond of the propylene nucleus is not fixed. Thus in the following way :



or in any other ways in which the propylene nucleus has a symmetrical structure.[2]

(1) This journal **2** (1927), 240.
(2) Cf. J. F. Thorpe, *J. Chem. Soc.*, **87** (1905) 1669.

(VII) **Ethyl α, α, γ-tricyanopropylene-γ-carboxylate.** The sodium derivative of this compound was obtained in coloured crystalline mass by the evaporation of alcohol from the red solution which resulted on adding ethyl ethoxymethylene-cyanoacetate to the alcoholic sodio-malonitrile. As this sodium compound was very easily soluble in water, alcohol, acetone, ethyl acetate, and pyridine, it was not recrystallised in fear of the loss of the substance. The crystalline mass was washed with ether, dried, and dissolved in cold water. On adding hydrochloric acid to the aqueous solution and rubbing the wall of the vessel with a glass rod, a crystalline precipitate in yellowish brown colour separated out, which was collected, washed with water, and dried in the desiccator. 0.1892 Gr. of the substance dried at 100° gave 36.1 c.c. of nitrogen at 22.5° and 751 mm. 0.2953 Gr. of the substance gave 0.5874 gr. of CO_2 and 0.1071 gr. of H_2O. (Found: N=21.20; C=54.27; H=4.06. $C_9H_7O_2N_3 \cdot \frac{1}{2}H_2O$ requires N=21.21; C=54.54; H=4.04%.) The obtained substance corresponded in composition to ethyl α, α, γ-tricyanopropylene-γ-carboxylate *semihydrate*. This specimen was yellowish brown and melted at about 190°.

In order to investigate whether this substance is identical with that obtained in the case of (VIII), the sodium compound prepared by another experiment was recrystallised three times from water, when it was obtained as greyish violet crystals. 0.5428 Gr. of the substance decreased by 0.0433 gr. on dehydrating at 130–140°% (Found: H_2O=7.98. $C_9H_6O_2N_3Na \cdot H_2O$ requires H_2O=7.86%.) The aqueous solution of this coloured sodium compound gave light green crystals of the semihydrate of the free nitrile-ester on acidifying.

When the sodium compound was dissolved by heating in a saturated aqueous solution of sodium chloride, the solution separated into two layers. The crystals which separated on cooling the solution in two layers were twice recrystallised from hot water. In this way nearly colourless crystals were obtained, which gave the light yellow semihydrate. This yellew specimen was probably the purest, but the colouring impurities in the brown or green specimen had nearly no perceptible effect on the melting point and the analytical results.

(VIII) **Ethyl α, γ, γ-tricyanopropylene-α-carboxylate.** By an analogous procedure the sodium derivative was obtained. This substance was easily soluble in water, acetone, ethyl acetate, and pyridine. On acidifying the aqueous solution of the sodium compound yellow crystalline substance precipitated, which was collected, washed with water, and dried in the desiccator. 0.1490 Gr. of the substance (no decrease in weight when dried at 120–130°) gave 27.7 c.c. of nitrogen at 22.5° and 755 mm. 0.1842 Gr. of the substance gave 34.6 c.c. of nitrogen at 23.5° and 754 mm. 0.2370 Gr. of the

substance gave 0.4710 gr. of CO_2 and 0.0868 gr. of H_2O. 0.3022 Gr. of the substance gave 0.5991 gr. of CO_2 and 0.1100 gr. of H_2O. (Found: N=20.77, 20.83; C=54.22, 54.08; H=4.10, 4.07. $C_9H_7O_2N_3 \cdot \frac{1}{2}H_2O$ requires N=21.21; C=54.54; H=4.04%.) Decided from the analytical results this specimen was not pure and melted gradually by the time when the temperature reached 185°.

To obtain a pure specimen the preparation was repeated, when the sodium compound became quite colourless on recrystallising it twice from hot water. 0.3111 Gr. of the substance decreased by 0.0250 gr. on dehydrating at 130–140°. (Found: H_2O=8.04: $C_9H_6O_2N_3Na \cdot H_2O$ requires H_2O=7.86%.) 0.2861 Gr. of the dehydrated substance gave 52.8 c.c. of nitrogen at 28.5° and 752.3 mm. (Found: N=19.88. $C_9H_6O_2N_3Na$ requires N=19.91%.) This purified sodium compound was transformed into the semihydrate of the free nitrile-ester. 0.1423 Gr. of the substance dried at 120° gave 27.4 c.c. of nitrogen at 27.5° and 759 mm. (Found: N=21.44. $C_9H_7O_2N_3 \cdot \frac{1}{2}H_2O$ requires N=21.21%.)

The semihydrate in (VII) stands in the same relation to the semihydrate in (VIII) as the diamide in (IV) to the diamide in (V). The yellow purest specimen of the semihydrate described in (VII), the yellow semihydrate from the purified sodium compound described in (VIII), and their mixture melted exactly at the same point 190° (corr.). The sodium derivatives obtained through two ways of condensation also coincided in water of crystallisation, and proved to be identical. These two specimens and their mixture melted at the same point 241–242° (not corr.). An analogous discussion may be made on these compounds, and it may be said that the compound obtained from the sodium derivative is the semihydrate of ethyl α, α, γ (= α, γ, γ)-tricyanopropylene-γ (= α)-carboxylate, and its constitution is represented by the formula $(C_8H_7O_2N_2)$–CO–NH–C(=NH)–$(C_8H_7O_2N_2)$.

(IX) $\alpha, \alpha, \gamma, \gamma$-Tetracyanopropylene. Soon after the addition of ethoxymethylene-malonitrile to the alcoholic solution of sodio-malonitrile, fine crystals separated out until the solution was filled with them, which were collected and recrystallised from hot water. In this way colourless fine needles of the sodium derivative of $\alpha, \alpha, \gamma, \gamma$-tetracyanopropylene were obtained, which had one molecule of water of crystallisation. 0.6551 Gr. of the substance decreased by 0.0648 gr. on heating at 135–140°. (Found: H_2O=9.89. $C_7HN_4Na \cdot H_2O$ requires H_2O=9.89%.) 0.1327 Gr. of the dehydrated substance gave 40.5 c.c. of nitrogen at 22.5° and 756 mm. (Found: N=34.14. C_7HN_4Na requires N=34.15%.)

The alcoholic mother liquor of the crystallised condensation product gave a crystalline mass on evaporating it to dryness. The solid which remained undissolved when this crystalline mass was treated with hot water, was recrystallised from alcohol. 0.1581 Gr. of the substance gave 43.2 c.c. of nitrogen at 23.5° and 752 mm. 0.1138 Gr. of the substance gave 30.3 c.c. of nitrogen at 23° and 752.5 mm. (Found : N=30.21, 29.55%.) This substance did not contain sodium, was not changed by treating with dilute hydrochloric acid, and melted at 211–212° without decomposition. 0.1133 Gr. of the substance treated with hydrochloric acid gave 30.5 c.c. of nitrogen at 26° and 757 mm. 0.2292 Gr. of the substance gave 0.4836 gr. of CO_2 and 0.0893 gr. of H_2O. 0.2194 Gr. of the substance gave 0.4617 gr. of CO_2 and 0.0860 gr. of H_2O. (Found : N=29.60 ; C=57.56, 57.41 ; H=4.36, 4.39. $C_7H_2N_4 \cdot C_2H_5OH$ requires N=29.78 ; C=57.43 ; H=4.29%.) No investigation was made on the constitution and the mechanism of formation of this compound.

The sodio-tetracyanopropylene seemed to behave in a different manner towards hydrochloric acid. It deposited neither solid nor liquid, when acidified with the acid. The warm aqueous solution of the sodium compound, acidified with hydrochloric acid, gave the crystals of the original sodium compound on cooling. The acidified solution of this compound, after standing for three weeks, also gave the original substance on evaporating to dryness in the desiccator, the desiccator being filled with the fume of hydrochloric acid. But when the acidified solution of the sodium compound was extracted with ether several times and the aqueous layer was evaporated on the water bath, the residue consisted of sodium chloride alone. The ethereal solution was dehydrated with calcium chloride and evaporated in vacuo over sulphuric acid, when colourless crystals remained, which soon decomposed into a brown amorphous substance. Further the following experiment clearly shows the behaviour of the compound in question.

3.640 Gr. ($\frac{1}{50}$ mol.) of sodio-tetracyanopropylene $C_7HN_4Na \cdot H_2O$ were dissolved in water, acidified with hydrochloric acid, and shaken with ether five times. The aqueous layer was separated quantitatively and evaporated on the water bath, when 1.177 gr. of sodium chloride was obtained. The ethereal extracts were evaporated on the aqueous solution of 1.169 gr. ($\frac{1}{50}$ mol) of sodium chloride, so that the solute in the ethereal solution could enter into the aqueous layer as the ether was evaporated. After the disappearance of the ethereal layer, the aqueous solution was evaporated in vacuo in the desiccator in which concentrated sulphuric acid and soda-lime were placed. This solution, on evaporating to dryness, gave 3.643 gr. of sodio-tetracyanopropylene $C_7HN_4Na \cdot H_2O$. This experiment indicates the perfect reversibility of the reaction $C_7HN_4Na + HCl \gtrless C_7H_2N_4 + NaCl$, and the distinct

existence of the compound $C_7H_2N_4$ which matches hydrochloric acid in strength.

The equilibrium state in the aqueous solution containing C_7HN_4Na, HCl, $C_7H_2N_4$, and NaCl, probably owes its existence to the fact that the compound $C_7H_2N_4$ is soluble in water and has no tendency of combining with water and forming an insoluble substance as in the cases of other nitrile-esters of the dicarboxyglutaconic acid.

Triethyl cyanocarboxyglutaconate is so strong in acidity that it decomposes carbonates, forming its own salt, and tetracyanopropylene matches hydrochloric acid. The continued investigation on the acid character of the latter will bring some interesting results.

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