

Citation:

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Chemistry. — "*Glutaconic acid*". (I). By Dr. P. E. VERKADE. (Communicated by Prof. J. BÖESEKEN).

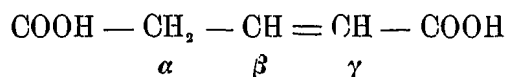
(Communicated in the meeting of November 27, 1915).

In a series of very interesting communications¹⁾ entitled: "The chemistry of the glutaconic acids" J. F. THORPE has given a fairly complete survey of the peculiar structure and isomerism phenomena noticed more in particular in the case of the alkyl and aryl derivatives of glutaconic acid and their anhydrides, dicarboxy-esters etc.

A short time before the appearance of the first publication of this series (in 1911) I had noticed, in an effort *to determine the hydration constant of the glutaconic anhydride*, deviations in the normal progress of the hydration process which could not then be explained, but the explanation of which is now very simple owing to the above mentioned investigations of THORPE (according to which this anhydride must be regarded as 6. hydroxy- α . pyrone). In other words the results obtained by THORPE *by means of a purely chemical process* were confirmed by a physico-chemical method.

It speaks for itself that I subsequently tried to also confirm other peculiarities of these acids by a physico-chemical investigation; in the subjoined, a start is made with the publication of the results attained.

By various ways, which need not be discussed here, THORPE²⁾ has demonstrated that in the glutaconic acid molecule:



the α and the γ position are identical. It appeared, for instance, that from the α Et. γ Me. α -carbethoxyglutaconate:



as well as from α Me. γ Et. α -carbethoxyglutaconate:



the same acid was formed by a very careful hydrolysis (*where a reversal was excluded*). A true methylene group (CH_2 —) is not present in these acids; one of the H-atoms of this group is *mobile*

¹⁾ THORPE, Soc. **87**, 1669 (1905) etc.

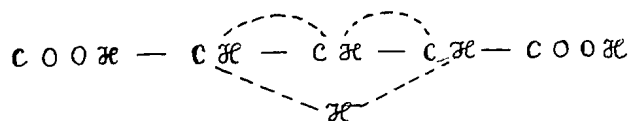
THORPE and THOLE, *ibid.* **99**, 2187, 2208 (1911).

THORPE and BLAND, *ibid.* **101**, 856, 871, 1557, 1739 (1912).

THORPE and WOOD, *ibid.* **103**, 276, 1579, 1752 (1913); **105**, 282 (1914).

Soc. **87**, 1669 etc.; **99**, 2187,

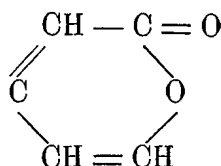
and is simultaneously under the influence of both the α - and the γ -carbon atom, which is best symbolised as follows:



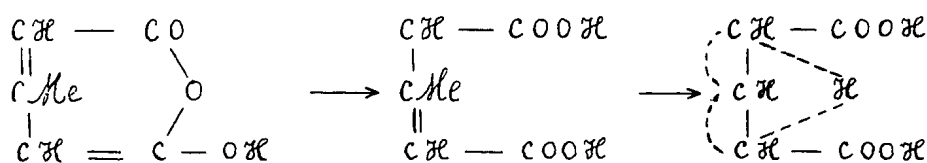
In this case the double bond is “floating”. In one of the following communications I hope to elucidate this formula by a model.

[In the $\alpha\alpha$ -dialkyl-substituted acids these mobile hydrogen atoms are wanting. These acids, in fact, form a separate class where the double bond is fixed and thus a pure cis-trans isomerism occurs.]

If an acid belonging to the “mobile class” is dehydrated under definite conditions a *hydroxyanhydride* is formed, namely a derivative of the α -pyrone:



If now this hydroxyanhydride is rehydrated in turn the original *normal* acid is generally regenerated, for instance:



Hence, the formation of the normal acid is preceded by that of another one, the *labile* acid. In some cases — where the hydrogen atoms were less mobile, — this labile acid has been successfully isolated, namely by hydration of the hydroxyanhydride with an excess of strong alkali, or with dilute alkali in presence of *casein* as anticatalyst.

This labile acid possesses two bonds and, therefore, should be obtainable in two forms (cis and trans); this indeed has succeeded with β -phenyl- α -glutaconic acid¹⁾ so that we now know three isomerides of the acid, which is certainly the most powerful support for THORPE's conceptions. The other labile acids are, as yet, known in one form only; probably (with the exception of the α -benzyl- β -methylglutaconic acid) this is always the cis-form.

¹⁾ Soc. 103, 1579.

Now what about the relation of the glutaconic acid in regard to this theory?

I. Glutaconic acid may be obtained by a number of very different processes, which will be discussed here, briefly.

A. Method of CONRAD and GUTHZEIT¹⁾. By condensation of 2 mols. of malonic ester and 1 mol. of chloroform with sodium ethoxide, Na-dicarboxylglutaconic ester is formed which is then separated and saponified.

With this method of preparation are closely connected:

1. that from *isoaconitic* ester²⁾ which is formed for instance, by incomplete saponification of the dicarboxylglutaconic ester.

2. that from 6. *ethoxy. α pyrone 3.5 dicarboxylic ester*³⁾ (formed by distillation of the dicarboxyl ester etc.).

The melting points of the acids thus obtained mostly vary between 130°—134°.

B. PECHMANN-BLOISE⁴⁾ based on the saponification of the glutaconic ester formed by cleavage of acetic acid from the *acetyl- β -oxyglutaric acid*.

C. Method of MORGENSTERN and ZERNER⁵⁾. By saponification with strong alkali of the *β -oxyglutaric dinitrile* obtained by the action of potassium cyanide or dichlorohydrin a little glutaconic acid was also formed. The melting point is given here as 129—129°.5.

D. Method of VON PEGMANN⁶⁾, which is based on the decomposition of *cumalic acid* (*α -pyrone 3 carboxylic acid*) by boiling with baryta. The acid so obtained is stated to melt at 132—134°.

E. Method of BUCHNER⁷⁾. The acid is formed by the saponification of the dimethyl ester formed in company with that of *Trans* 1. 2. trimethylene dicarboxylic acid by cleavage of nitrogen from the *acryldiazoacetic ester* (pyrazoline 3.5. dicarboxylic ester.)

The acid so obtained melted at 127—128°.

In addition there occur in the literature a few other methods of preparation or formation, of less importance.

In RICHTER's Lexicon a distinction is made between:

cis-propen. *$\alpha\gamma$. dicarbonsaure* (cis-Glutakonsaure)
and isom-propen. *$\alpha\gamma$. dicarbonsaure* (Glutakonsaure).

The statements in the literature relating to the above syntheses

¹⁾ Ann. **222**. 253 (1883); Ber. **15**. 2841 (1882) etc.

²⁾ CONRAD and GUTHZEIT: loc. cit.

³⁾ GUTHZEIT and DRESSEL: Ber. **22**. 1425 (1889).

⁴⁾ Ann. **261**. 157 (1891); Ber. **24**. 3250 (1891), Bull. (3) **29**. 1013 (1903).

⁵⁾ Sitz. ber. Akad. Wien **119**. 589 (1910).

⁶⁾ Ann. **264**. 301 (1891).

⁷⁾ Ber. **23**. 703 (1890), Ann. **273**. 238 (1893).

are however distributed arbitrarily over these two "isomerides" so that this distinction is quite worthless.

A serious investigation as to the eventual identity of all these kinds of glutaconic acid has never been taken in hand; the investigators have always been content to *pronounce this identity* on account of the melting point of the different acids¹⁾ which was always fairly well the same. Still a similar investigation would be of importance; suppose the identity of all the acids was established, it would then be evident that there exists **one** form of glutaconic acid which exceeds over all other possible isomerides by a very great stability, for this variety was formed *in all kinds of conditions*. A similar great difference in stability does not occur as far as I know with a series of cis-transisomerides. Hence, I have endeavoured in the first place to furnish the proof for this identity.

It should be mentioned here that PERKIN and TATTERSALL²⁾ have tried in various ways to obtain a second isomerides of glutaconic acid, but always without success. They always obtained either the acid already known or the *trans-trimethylenedicarboxylic acid*.

II. The question whether to the known glutaconic acid appertains the cis- or the trans-formula has been decided by BUCHNER³⁾ in favour of the cis-formula and this on account of the ready formation of anhydride on boiling with acetyl chloride. This way of arguing is not satisfactory; it is generally known that fumaric acid on treatment with acetyl chloride⁴⁾, phosphorus pentoxide⁵⁾ or pentachloride⁶⁾ is converted into maleinic anhydride. Moreover, the formation of anhydride proceeds anything but rapid.

If to the glutaconic acid appertains the symmetric structure suggested by THORPE it may be expected that this acid will possess neither all the characteristic properties of the cis- nor all those of a trans-acid, but will behave either as a cis or trans in reactions or definite properties, which can give exclusive evidence as to cis- or trans-positions of the carboxyl groups.

I have been able to demonstrate the correctness of this view in the case of a few reactions and properties.

¹⁾ Compare BUCHNER: Ber. 27. 881 (1894).

²⁾ Soc. 87. 361 (1905).

³⁾ loc. cit.

⁴⁾ ANSCHUTZ: Ber. 14. 2792 (1881). PERKIN: Ber. 15. 1073 (1882).

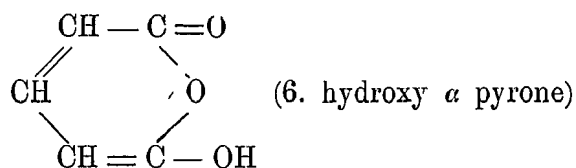
⁵⁾ TANATAR: Journ. Russ. phys. chem. Ges. 22. 312.

⁶⁾ VOLHARD: Ann 268. 255 (1892), 273. 31 (1893).

III. It was possible *à priori* that in this acid wherein we assume the presence of a floating double bond the reduction velocity should be different from that of an acid with an ordinary double bond. I have, therefore reduced glutaconic acid and also aconitic acid ¹⁾ (where we meet with a similar mobile hydrogen atom) according to the methods of PAAL, SKITA, and WILLSTÄTTER, measured the velocities of these reductions, and compared them with those of some other unsaturated acids. And indeed some peculiar differences now came to light.

Whether the velocity measured is a true *reaction velocity* or some kind of *diffusion velocity* does not matter here. For in the latter case some differences in diffusion power would have been noticed between these two kinds of double bonds. The reduction experiments executed, however, elucidated this question somewhat; hence, I will again refer to the mechanism of these reduction processes more fully.

IV. According to THORPE's investigations ²⁾ glutaconic acid yields an hydroxyanhydride:



which on hydration under different conditions — hence, also with strong alkali or in the presence of casein — reproduces the same acid (mp. 137°). The labile acid whose formation precedes that of the normal acid is, therefore, very unstable.

The question now arose, however, whether the existence of this labile acid (of the labile acids, respectively) might not be demonstrated by a physico-chemical process. For this it was necessary to observe as accurately as possible the course of the hydration of the hydroxyanhydride under various conditions and at different temperatures. These experiments will also be communicated fully in what follows.

Preparation of glutaconic acid by different methods.

A. The object was attained most rapidly by the process of CONRAD

¹⁾ BLAND and THORPE: Soc. 101 1490 (1912).

²⁾ Soc. 101. 863 (1912).

and GUTHZEIT; this however, is expensive as it starts with malonic acid and yields at most only 20 %.

The reaction between Na-malonic ester and chloroform took place entirely according to the directions of CONRAD and GUTHZEIT, but with sufficient precautions much larger quantities (say 100 grams) can be operated with. The yield of Na-dicarboxylglutaconic ester recrystallised from alcohol is bad (40—42 % of the theoretical) but as demonstrated by COUTELLE¹⁾ in a very elaborate research it cannot be improved.

From this Na-compound the ester was liberated with dilute acetic acid. The saponification of this dicarboxylglutaconic ester to glutaconic acid has been studied elaborately by GUTHZEIT and BOLAM²⁾. They found that a saponification of the esters with alkalis gave very bad results as a considerable portion decomposed into malonic acid and formic acid; on the other hand the saponification with hydrochloric acid proceeded fairly rapidly. This, I have carried out as follows:

Portions of 30 grams of the ester were boiled with thrice the volume of hydrochloric acid (10 % HCl) and half the volume of alcohol in a MONTAGNE³⁾ reflux apparatus until the evolution of carbon dioxide has ceased, which took about seven hours.

According to GUTHZEIT and BOLAM the reaction mixture must now be evaporated until a separation of crystals takes place at the surface; sometimes this succeeds, but frequently the crystallisation does not set in and a viscid syrup is obtained chiefly consisting of β -oxyglutaric acid formed by the action of water on the glutaconic acid. The best plan, however, is as follows:

The liquid is neutralised with sodium hydroxide saturated with ether, again acidified with sulphuric acid and then extracted continuously with ether. After drying over calcium chloride the ethereal solution is mixed with benzene and then left to itself, on evaporation of the ether a yield is obtained of 50 % of the theoretical quantity of glutaconic acid which is nearly white and melts above 130°.

The crude acid was titrated with baryte:

0.1749 gram required	26.55 cc.	Ba(OH) ₂	0.1009 n.	M. 130.6
0.1468 ,, ,,	22.77 ,, ,,		0.1009 ,,	M. 130.7
				Theory M. 130.05.

The purification of the acid took place by recrystallisation from

¹⁾ J. pr. (2) 73. 49 (1906).

²⁾ J. pr. 54. 372 (1896); 58. 407 (1898).

³⁾ Chem. Weekbl. 7. 375 (1910).

ether-benzene or by precipitation of the ethereal solution with petroleum ether. Amyl acetate¹⁾ as recommended by TUTIN¹⁾ is less suitable because glutaconic acid is still too soluble therein.

The acid melted finally without decomposition at 136°—138°.

B. Very splendid results are obtained by the process of VON PECHMANN—BLAISE. Starting with citric acid, acetodicarboxylic acid was prepared according to the directions of JERDAN²⁾ and this was reduced to β -oxyglutaric acid by VON PECHMANN's process, after which the glutaconic diethylester was obtained according to BLAISE via β -oxyglutaric ester and acetyl- β -oxyglutaric acid. The yields are those stated by BLAISE: 500 grams of crude acetonedicarboxylic acid gave \pm 140 grams of glutaconic ester b.p. 128°—132° at 15 m.m.

I saponified this ester by boiling with 10% aqueous potassium hydroxide, using a little more than the theoretical quantity, until all had dissolved. The solution was then acidified with sulphuric acid and continuously extracted with ether. This saponification was fairly well quantitative.

The acid when recrystallised as stated above melted at 136°—138°.

C. According to the method of MORGENSTERN and ZERNER a prolonged boiling *with strong aqueous potassium hydroxide* of β -oxyglutaricdinitrile we should expect, *a priori*, no glutaconic acid but β -oxyglutaric acid instead. However, FICHTER and DREYFUS³⁾ showed that β -oxyglutaric acid (analogous to the monobasic oxy-acids investigated by FITTIG⁴⁾) is converted on boiling with alkali into glutaconic acid. In the synthesis of MORGENSTERN and ZERNER, glutaconic acid is, therefore, a *secondary* product and I only needed to investigate the acid obtained by FICHTER and DREYFUS method.

Pure β -oxyglutaric acid was obtained from the crude syrup of this acid⁵⁾ by warming for a few days with copper acetate. The Cu-salt was filtered off, washed with water and alcohol and decomposed with H₂S, when the aqueous solution of the acid was evaporated to dryness in vacuum.

10 grams of that acid yielded, after 24 hours boiling with 50 grams of 10% potassium hydroxide, on extraction with ether 5 grams of glutaconic which after purification melted at 135°—137°.

¹⁾ Soc. 91. 1144 (1907).

²⁾ Soc 75. 809 (note) (1899).

³⁾ Ber. 33, 1452 (1900).

⁴⁾ Ann 283, 58 (1894).

⁵⁾ The non-crystallisation of this crude syrup is attributed by VON PECHMANN JENISCH (loc. cit.) to the presence of a *hypothetical lactide-like substance*. In reality, this syrup contains considerable quantities of β -oxyglutaric ester (formed on evaporation of the alcoholic extracts) as was convincingly shown on distillation.

For preparing large quantities of glutaconic acid this method is certainly the one to be most recommended; it is cheap and gives relatively high yields.

D. 10 grams of cumalinic acid were boiled with 60 grams of barium hydroxide in a reflux apparatus until the bright red liquid was nearly colourless, which took ± 15 hours. After removing the barium carbonate precipitate, the filtrate was shaken with ether, the barium was precipitated with sulphuric acid and after filtration the liquid was extracted continuously with ether.

I so obtained 1.7 gram of glutaconic acid, melting after the usual recrystallisation at 135° — 137° . The yield amounted to 18% of the theory thus corresponding with VON PECHMANN's statement.

E. The linking of diazoacetic ethyl ester to acrylic methyl ester was carried out as follows.

An equimolecular mixture of both esters was heated in a reflux apparatus for 2 days at $\pm 50^{\circ}$. The reaction then takes place without any sensible generation of heat or elimination of nitrogen.

The (generally thick-fluid) reaction product was heated in the same flask at $\pm 180^{\circ}$ and kept at this temperature until no more nitrogen was evolved. The residual oil was then distilled and the fraction 107 — 117° at 10 m.m. was collected. The yield of the mixture of glutaconic acid and trimethylenedicarboxylic ester as 66% of the theoretical amount.

The ester mixture was now boiled with 10% aqueous potassium hydroxide, slightly in excess of the theoretical quantity, until all has just dissolved; the whole was acidified with sulphuric acid and continuously extracted with ether.

Owing to the extraordinary resemblance in properties between glutaconic and *trans*-trimethylenedicarboxylic acid (in all solvents these acids are both more or less soluble to the same extent whilst the salts also do not exhibit serious differences) the separation is very troublesome; it further appeared that in addition to these acids another *cis*-trimethylenedicarboxylic acid was present (although in smaller quantities) which might have been expected theoretically. By fractional crystallisation from water, from ether (with or without addition of benzene) and from ethyl acetate, I finally succeeded in obtaining the three acids in a pure condition.

a. *Trans*-trimethylene 1.2 dicarboxylic acid is, of the three acids, the one most soluble in ether and least soluble in ethyl acetate. It possessed all the properties communicated for this acid by BUCHNER (loc. cit.). M.p. 175° .

b. *Glutaconic acid* melts after repeated recrystallisations from ether-

benzene at 136°—138°. In contrast with the acids mentioned under *a* and *c* it instantly reduced alkaline permanganate.

c. Cis-trimethylene 1.2 dicarboxylic acid has not been found by BUCHNER in this synthesis. This ether is the first to pass into ether as it is very insoluble in water. The m.p. was 139° in agreement with the statements in the literature; on mixing with acid *b* or otherwise prepared glutaconic acid a considerable melting point depression occurred. The acid did not reduce alkaline permanganate and was not attacked by sodium amalgam at boiling heat.

0.1131 gram required: 8.35 cc. N/9.48 baryta M = 130.2

Theory M = 130.05

I hope to refer to a few properties of these trimethylenedi carboxylic acids later.

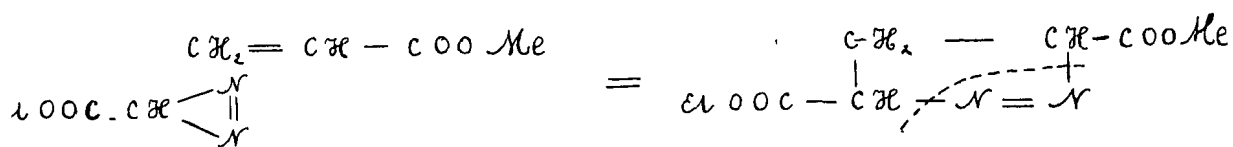
Identity of the glutaconic acids obtained.

The glutanic acid obtained according to the methods A—E had always fairly well the same melting point (136°—138°); moreover, on mixing the various specimens the melting point remained quite unchanged. The appearance of the crystal-mass and the relative solubilities are the same for all specimens investigated. It is, therefore, certain that *all the methods investigated yield the same acid.*

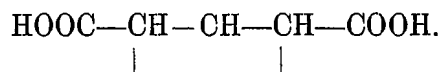
The identity of these acids is confirmed by the results to be discussed in the communication to follow; all kinds of the acid behaved in the reactions to be stated, *in exactly the same manner.* In each method of preparation it was tried carefully whether eventually an isomeric glutaconic acid was present, but always without any result, however.

The BÜCHNER diazoacetic ester synthesis has also a double theoretical importance.

1st. Let us imagine the linking as follows:



If now nitrogen is split off we obtain the glutaconic acid in the *symmetric* form as first proposed by PERKIN and TATTERSALL¹⁾



2nd. The formation of cyclopropane derivatives beside an isomeric

¹⁾ Soc. 87, 361 (1905).

unsaturated acid¹⁾ is interesting because it again shows the *slight difference in energy* between 3-ring and double bond, a fact also already noticed by others.²⁾ The difference in tension in the 3-rings and 2-rings is *not so considerable by a long way* as demanded by the ring-tension theory of VON BAERER. That this theory does not hold good has been demonstrated by me previously by means of quantitative measurements.³⁾

Properties of glutaconic acid.

The properties of this acid have already been frequently described; attention may be called to a few facts only.

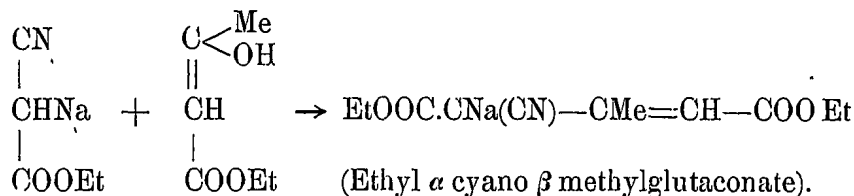
a. The melting point, after keeping the acid for months over phosphorus pentoxide in vacuum is still quite unchanged. Hence, there is no question of anhydride formation in these circumstances.

b. On evaporating an aqueous solution of the acid we obtain beside a little β -oxyglutaric acid a brown sticky mass, from which is extracted by ether a very impure brown-coloured glutaconic acid. The acid, therefore, appears to partly resinify.

c. With ferric chloride no discoloration takes place in alcoholic solution, but in aqueous solution a *brownish-red* coloration occurs. Contrary to CONRAD and GUTHZET's statement⁴⁾ this solution remains unchanged on boiling and no ferric hydroxide is deposited.

Attempt to find a new synthesis of glutaconic acid.

By THORPE and ROGERSON⁵⁾ β -alkyl derivatives of glutaconic acid have been prepared by condensation of Na-cyanacetic ester with acetylacetic ester or alkyl derivatives thereof, for instance



On saponification with strong hydrochloric acid these esters yielded the desired acid in varying quantity *often beside pyridine derivatives*.

¹⁾ The unsaturated condition of glutaconic acid is also shown by the conversion into dibromo-acid dioxylglutamic acid, with bromine and potassium permanganate, respectively.

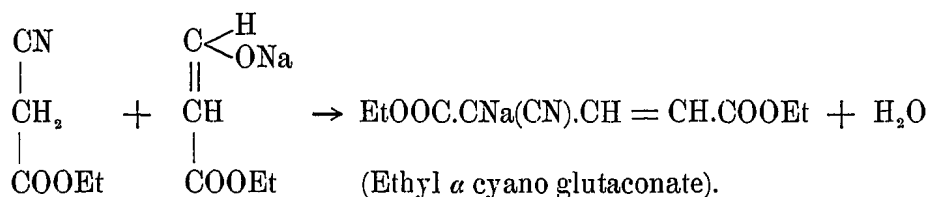
²⁾ BÖESEKEN: Overzicht der koolwaterstoffen I, p. 209 and 266.

³⁾ Handelingen XVe Ned. Natuur- en Geneesk. Kongres, p. 234.

⁴⁾ Ann. 222, 254 (1883).

⁵⁾ Soc. 87, 1685 (1905).

The suspicion now arose that the (readily obtainable) Na-formylacetic ester would react with cyanoacetic acid as follows:



This indeed appeared to be so.

60 grams of Na-formylacetic ester (which according to a statement in the literature only consists of the desired compound to the extent of about 70 %) were dissolved in 150 cc. of absolute alcohol. Immediately afterwards 45 grams of cyanoacetic ester were added and the whole heated on a boiling waterbath for \pm half an hour (until the decomposition sets in). The yellow gelatinous contents of the flask were then taken up with dilute hydrochloric acid and the liquid shaken with ether. After washing with dilute soda solution and water the ether was evaporated. The result was 30—35 grams (\pm 45 % of the theory) of a pale yellow, very thick viscid oil.

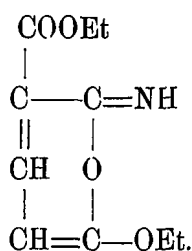
In its properties this ester completely resembled the α -cyanoglutaconic ester obtained by GUTHZEIT and EYSEN¹⁾ from *iso*-imidodicarboylglutaconic ester with α -cyanoglutaconic ester prepared with aqueous sodium hydroxide. It had a very bitter taste, gave a carmine-red colour with ferrichloride in alcoholic solution and could not be distilled under any circumstances.²⁾

By saponifying the ester with acids or alkalis GUTHZEIT and EYSEN could isolate *neither glutaconic acid nor any other product of hydrolysis*. I have myself tested this saponification with dilute potassium hydroxide, potassium methoxide, hydrochloric acid (10 % HCl), concentrated sulphuric acid and 30 % hydrogen peroxide + potassium hydroxide and tested the reaction fluids carefully with regard to the presence of glutaconic acid, malonic acid ethyl-2.6-dioxypyridine.5. carboxylate, 2.6.dioxypyridine.5. carboxylic acid and 2.6.dioxypyridine, all products which might be expected here in consequence of the research of THORPE and ROGERSON. The result, however, was always negative.

The acid thus prepared is, therefore, certain to have another structure. Probably it possesses an *iso-imido* structure: for instance

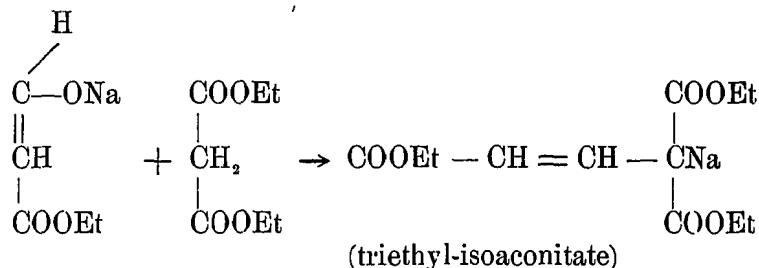
¹⁾ J. pr. Chem. (2) **80**. 34 (1909).

²⁾ The cyanoaconitic esters prepared by ERRERA PASCIABOSCO (Ber. **34**. 3704) cannot be distilled even in vacuum without decomposition.



In harmony with this is the fact that in all the saponification methods investigated ammonia is *readily* split off. There ought then to be formed 6. *ethoxy a pyrone derivatives*; the carmine coloration which occurs with all saponification products when exposed to the air certainly points in this direction.¹⁾

An effort to effect condensation of the Na-formylacetic ester with malonic ester to *isoaconitic ester*:



ended in failure. The two esters certainly react on each other, but form Na-malonic ester and *free* formylacetic ester, the latter of which is subsequently converted into formylglutaconic ester and trimesinic ester.²⁾ It is, therefore, a simple double decomposition. Nor has THORPE succeeded in getting the malonic ester to react with acetyl-acetic ester.

Chemistry. — “*On Black Phosphorus*” I³⁾. By Prof. A. SMITS, G. MEYER, and R. PH. BECK. (Communicated by Prof. J. D. VAN DER WAALS).

(Communicated in the meeting of November 27, 1915).

1. Introduction.

Besides a second modification of white P, BRIDGMAN⁴⁾ obtained last year a black form by subjecting white P at 200° to a pressure of from 12000 to 13000 kg. per c.m².

¹⁾ So, for instance, several of the anhydrides of the glutaconic series (which are hydroxypyrene derivatives) obtained by THORPE and others give a dark wine red coloration when their neutral solution is exposed to the air.

²⁾ Compare also WISLICENUS and BINDEMANN. *Ann.* **316**. 18 (1901).

³⁾ In the translation of the Dutch communication some passages have been changed.

⁴⁾ *Journ. Amer. Chem. Soc.* **36**, 1344 (1914).