

The assistance of Professor S. M. McElvain is gratefully acknowledged.

Summary

The reaction between phenol and benzoyldiphenylmethyl bromide gives *p*-bromophenol and diphenylacetophenone.

The compounds described as phenylbenzoin monophenyl ether and benzopinacone monophenyl ether by Schuster² are in reality diphenylacetophenone and $\alpha,\alpha,\beta,\beta$ -tetraphenylethanol.

Diphenylacetophenone and $\alpha,\alpha,\beta,\beta$ -tetraphenylethanol are smoothly cleaved by alcoholic potassium hydroxide, giving in the one case benzoic acid and diphenylmethane, and in the other benzophenone and diphenylmethane.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY, HARVARD UNIVERSITY]

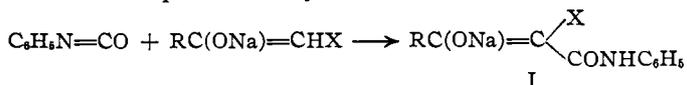
THE COURSE OF ADDITION OF SODIUM ENOL ALKYL MALONIC AND SODIUM ENOL ALKYL CYANACETIC ESTERS TO UNSATURATED ESTERS

BY ARTHUR MICHAEL AND JOHN ROSS

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According to the law of chemical neutralization,¹ the course of an addition reaction involving the use of an enolic sodium derivative will be such as to produce a compound in which the sodium is in a better neutralized state. The attainment of the maximal heat of formation in the addition reaction depends upon the neutralization of the positive energy of the metal and this energy factor determines the utmost possible degradation of chemical energy. This generalization is well illustrated in the reactions of sodium enol derivatives with phenyl isocyanate.² With the sodium enol derivatives of acetoacetic, malonic, formyl, acetic, benzoylacetic esters and diacylmethane, the reaction takes place smoothly to give in most cases almost quantitative yields of anilides, thus



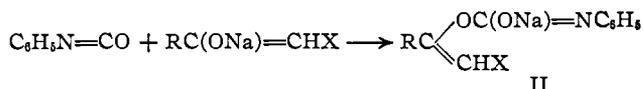
In these derivatives the α -hydrogen atoms of the enolic sodium mother substances are replaced by the negative $-\text{CONHC}_6\text{H}_5$ group, and, hence, the sodium atoms are better neutralized in the C-addition products (I). When there is no α -hydrogen atom in the sodium compound, this simple reaction cannot take place. For example, with the sodium enol derivatives of ethylmalonic and ethylacetoacetic esters maximal possible energy degradation is attained by the phenyl isocyanate polymerizing mainly

¹ Michael, *J. prakt. Chem.*, 60, 293 (1899); *THIS JOURNAL*, 32, 990 (1910).

² Michael, *Ber.*, 38, 22 (1905).

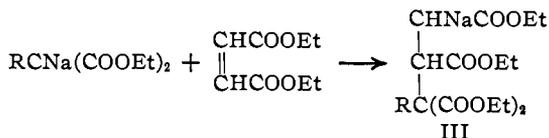
to the much less energetic isocyanurate and a small amount of the same neutral sodium product of destructive decomposition is formed from each sodium enolic ester.

A second course of these reactions would be the formation of sodium enol O-addition products, that is, of sodium enolic urethan derivatives

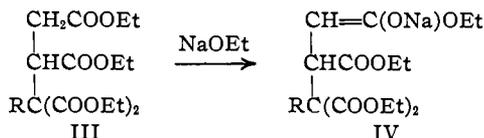


According to the law of chemical neutralization, such a procedure is not possible, since the metal in the compound (II) would be much less neutralized than in the original sodium enolates. Indeed, the tendency to form sodium enol urethans is so slight that sodium ethoxide does not unite with phenyl isocyanate, but entirely converts it into isocyanurate.

Auwers, Köbner and Meyenberg³ showed that sodium enol alkylmalonic esters readily added to fumaric ester, and, from the addition product upon hydrolysis, obtained α -alkyl tricarballic acids. The addition reaction was written⁴



Since Michael⁵ showed that the addition products of sodium enol methylmalonic ester and sodium enol ethylmalonic ester with fumaric ester readily gave sodium derivatives, which could be methylated upon treatment with methyl iodide, it was apparent that the original addition compound could not be a γ -alkyl γ -carbethoxy tricarballic ester (III), unless such an ester formed a stable sodium derivative (IV) at the α -carbethoxy group



Michael concluded from his experiments that these esters gave stable enolic sodium derivatives (IV), but the recent examination of such addition reactions with α,β -unsaturated, monobasic olefinic esters⁶ made it probable that the alkyl group migrated in the addition of sodium enol alkylmalonic esters to the unsaturated dibasic ester, thus forming compounds containing a malonic ester residue that would give stable sodium

³ Auwers, Köbner and Meyenberg, *Ber.*, **24**, 2890 (1891).

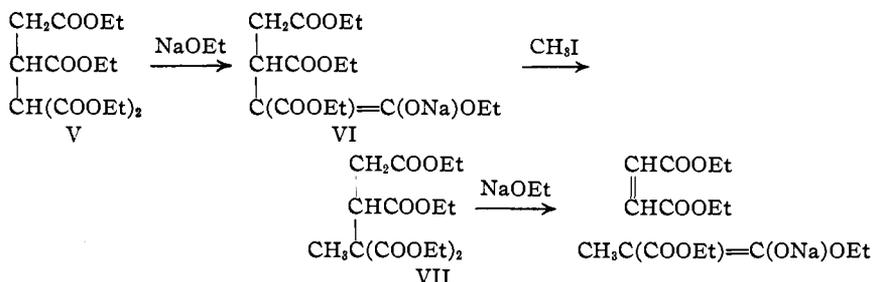
⁴ Ethyl is more conveniently represented by Et throughout this paper.

⁵ Michael, *Ber.*, **33**, 3731 (1900).

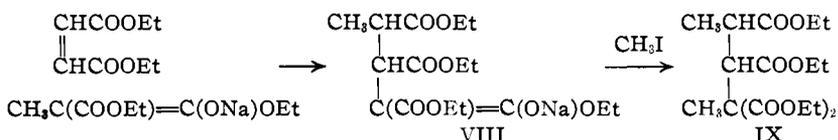
⁶ Michael and Ross, *THIS JOURNAL*, **52**, 4598 (1930).

enol derivatives and could therefore be alkylated. In order to ascertain whether this had occurred, these reactions were re-examined.

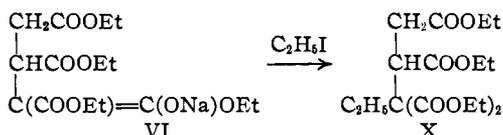
Butane $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic ester (VII) was prepared by methylation of the sodium derivative of propane $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic ester (VI). Upon treatment with anhydrous sodium ethoxide, in ether at 0° , followed by methyl iodide, the butane derivative (VII) mainly underwent retrogression to form fumaric ester and sodium enol methylmalonic ester



The sodium enol methylmalonic ester thus formed was converted by the methyl iodide into dimethylmalonic ester. This course of the reaction is in marked contrast to that of the addition product of sodium enol methylmalonic and fumaric esters, which under parallel conditions methylate to give a quantitative yield of α,γ -dimethyl γ -carbethoxytricarballic ester (IX).⁷ The first addition reaction therefore takes place with migration of methyl, *i. e.*



It was further shown that pentane $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic ester (X) prepared by action of ethyl iodide upon the sodium derivative of propane $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic ester (VI) remained unchanged upon treatment in the cold with sodium ethoxide and methyl iodide

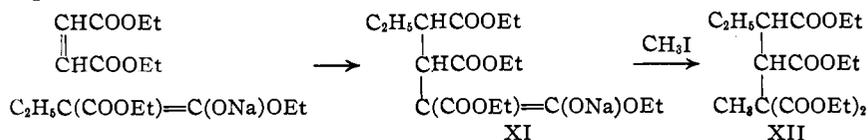


Upon treatment of the addition product of sodium enol ethylmalonic ester to fumaric ester in the cold with sodium ethoxide and methyl iodide, the tetracarboxylic ester is methylated with facility.⁸ It therefore follows

⁷ Michael, Ref. 5, p. 3763.

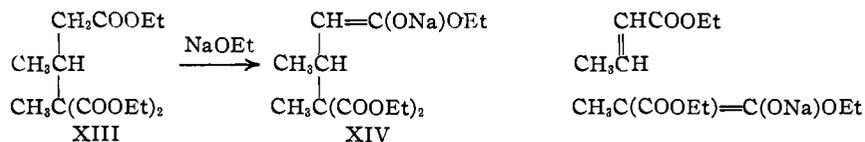
⁸ Michael, *ibid.*, p. 3746.

that in the latter addition reaction the ethyl group has migrated to the α -position, thus



The retrogression reaction that occurred when the free esters from the addition products of sodium enol alkylmalonic esters to crotonic ester were treated with sodium⁹ was later shown by Ingold¹⁰ and Kohler and Butler¹¹ to take place by the action of sodium ethoxide upon similar addition products. Ingold considered that such reversal of the additive process indicated that the additive process itself was a balanced reaction which proceeded until a definite equilibrium was attained under the conditions in which the reaction was carried out. The following view offers an insight into the mechanism of the retrogression reaction.

Michael¹² explained the formation of acetoacetic ester from ethyl acetate and sodium through the primary formation of $\text{CH}_2=\text{C(ONa)OEt}$ and Scheibler and Marhenkel¹³ on isolating this compound, proved the correctness of this view. It therefore seemed probable that the capacity of the ester (XIII) to form a sodium derivative at the α -carbethoxyl group as in (XIV) was due to the near spatial negative influence of the four oxygen atoms upon the C and H₂ of the CH₂ group. However, the strong positive influence of the sodium introduced into ester (XIII) must decrease the affinity for each other of the two C atoms of (XIV) attached to the methyl groups, and the very considerable positive free chemical energy of the sodium in (XIV) is able to attain a much better neutralization by the retrogression of (XIV) into sodium enol malonic and crotonic esters.



The intermediate formation of such a sodium derivative as (XIV) is, therefore, not improbable.

That pentane $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic ester (X) did not undergo retrogression upon treatment with sodium ethoxide and methyl iodide may have been due to incapacity to form such a sodium derivative as in

⁹ Michael, Ref. 5, p. 3749.

¹⁰ Ingold, *J. Chem. Soc.*, 119, 1976 (1921).

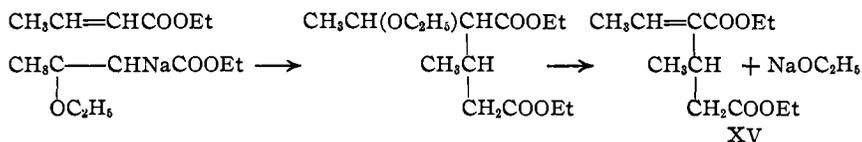
¹¹ Kohler and Butler, *THIS JOURNAL*, 48, 1040 (1926).

¹² Michael, *Ber.*, 38, 1933 (1905).

¹³ Scheibler and Marhenkel, *Ann.*, 458, 1 (1927).

(XIV), owing to the influence of the more positive character of the ethyl compared with the methyl group.

It was thought that separation of the ethyl group from the directly attached carbon atom of sodium enol ethylmalonic ester would not take place as readily as the separation of the methyl group of sodium enol methylmalonic ester, and that the difference might be reflected in the yields of addition product obtained. The reaction between sodium enol ethylmalonic and crotonic ester was therefore examined. Contrary to the behavior of sodium enol methylmalonic ester,⁶ only slight addition was found to occur; the crotonic ester mainly polymerized to the sodium derivative of a dimeric ester, α -ethylidene β -methylglutaric ester (XV) which v. Pechmann¹⁴ had obtained by the action of sodium ethoxide, and Michael¹⁵ by the action of sodium on crotonic ester. This reaction was expressed by v. Pechmann as follows¹⁶



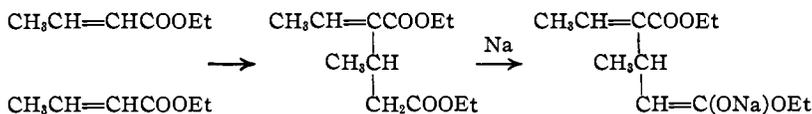
The fact that the sodium derivative of enol ethylmalonic ester causes the polymerization of crotonic ester while that of methylmalonic ester does not, is to be attributed to the more energetic state of the metal in the first ester. Addition of sodium enol ethylmalonic ester to crotonic ester would require the migration of the ethyl group, and apparently polymerization of the crotonic ester takes place more readily.

Since no addition product was obtained in the above reaction, attention was directed to the ease of migration of alkyl groups during the addition of sodium enol alkyl cyanacetic esters to unsaturated esters. J. F.

¹⁴ V. Pechmann, *Ber.*, 33, 3340 (1900).

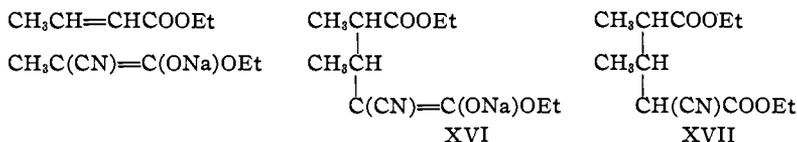
¹⁵ Michael, *ibid.*, 33, 3760 (1900).

¹⁶ There is no evidence that crotonic ester unites with sodium ethylate and the existence of the assumed sodium β -ethoxybutyric ester is improbable, apart from the assumption of the direct union of sodium with carbon. The assumed intermediate stage is therefore untenable as is also the last step, since Michael showed that the sodium derivative of the dimeric crotonic ester appears as the final reaction product. The reaction represents a polymerization by addition, resulting in the better neutralization of the sodium

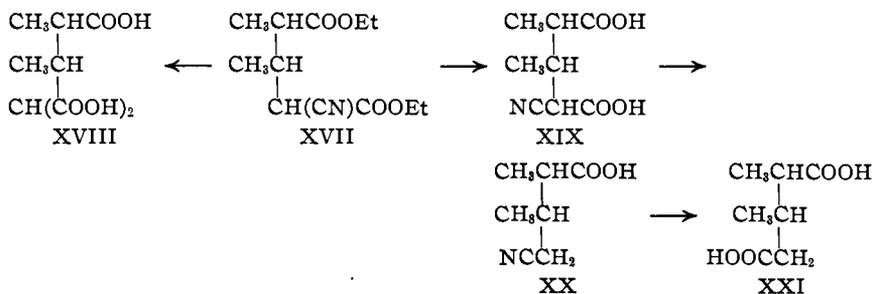


Although the sodium addition product contains the group $-\text{CH}=\text{C}(\text{ONa})\text{OEt}$, it does not suffer retrogression because crotonic ester does not give a sodium derivative. This is an interesting point in support of the theoretical views upon the retrogression reaction discussed above.

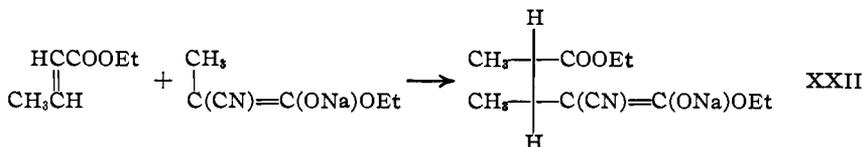
Thorpe¹⁷ concluded that in the addition of sodium enol α -cyano propionic ester to β,β -dimethylacrylic ester, the parts of the addendum appeared to be CH_3 and $-\text{C}(\text{CN})=\text{C}(\text{ONa})\text{OEt}$. Upon examination of the addition of sodium enol α -cyanopropionic ester to crotonic ester, it was found that addition also occurred with migration of the methyl radical to the α -C atom of the latter ester, that is, the addendum functioned as CH_3 and $-\text{C}(\text{CN})=\text{C}(\text{ONa})\text{OEt}$



The product, α,β -dimethyl γ -cyanoglutaric ester (XVII), is apparently a stereomeric form of the cyano ester obtained by the addition of sodium enol cyanacetic ester to tiglic ester.⁶ Upon saponification (XVII) gave a sirupy cyano acid (XIX) which upon treatment with hydrochloric acid gave very little α,β -dimethylglutarimide, but mainly a liquid cyano acid (XX). This was converted into *trans* α,β -dimethylglutaric acid, which was identified by its di-anilide. Hydrolysis of the cyano ester gave a tricarboxylic acid (XVIII), which was not identical with the corresponding acid prepared through the addition of sodium enol cyanacetic ester to tiglic ester, and was therefore apparently a stereomer of that acid

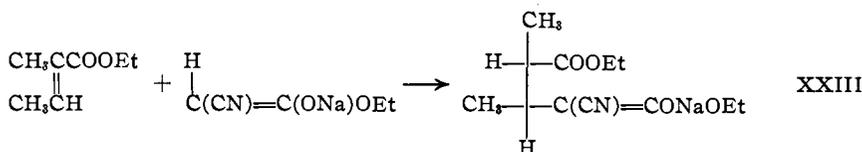


Considering the addition reaction in each case to take place as a *trans* process,¹⁸ the following stereomeric compounds would be expected to be formed



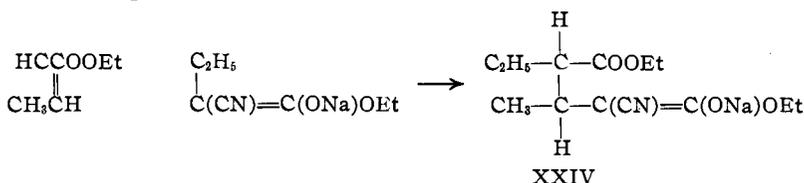
¹⁷ J. F. Thorpe, *J. Chem. Soc.*, **77**, 923 (1900).

¹⁸ See Michael, *J. prakt. Chem.*, **52**, 289 (1895); *THIS JOURNAL*, **40**, 1674 (1918).

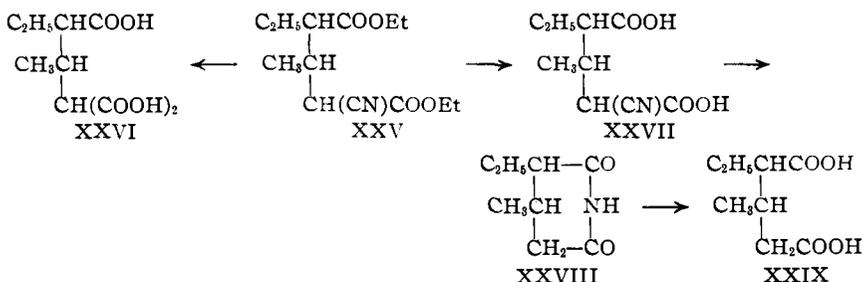


It agrees with this interpretation, that the addition of sodium enol cyanacetic ester to tiglic ester gave a cyano ester stereomeric with the product of addition of sodium enol α -cyanopropionic ester to crotonic ester.

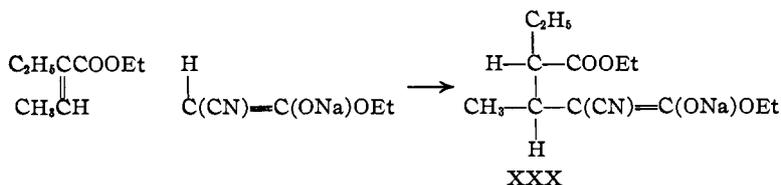
Results parallel to those with sodium enol α -cyanopropionic ester were obtained in the addition of sodium enol α -cyanobutyric ester to crotonic ester. A 33% yield of α -ethyl- β -methyl- γ -cyanoglutaric ester (XXV) was obtained from the addition product (XXIV), showing that the parts of the addendum were C_2H_5 and $\text{C}(\text{CN})=\text{C}(\text{ONa})\text{OEt}$. With *trans* addition the reaction proceeds as follows



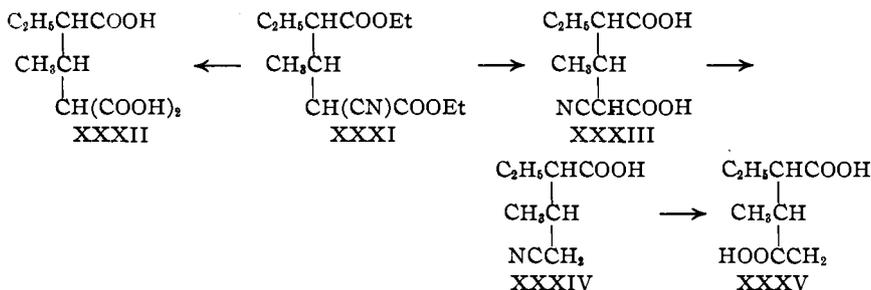
Upon saponification of the ester (XXV), a cyano acid (XXVII) melting at 147° was obtained, which upon treatment with hydrochloric acid was almost completely converted into α -ethyl- β -methylglutarimide, m. p. 92° , together with a small amount of a stereomeric imide, m. p. 102° . Since both imides gave the same *cis* α -ethyl- β -methylglutaric acid, m. p. 88° (XXIX), upon hydrolysis, it is considered that they are related to one another as *cis* and *trans* with respect to the methyl and ethyl groups and the plane of the imide ring. Through saponification with caustic potash, the ester (XXV) gave α -ethyl- β -methyl- γ -carboxyglutaric acid (XXVI), melting at 143° . These reactions are represented by



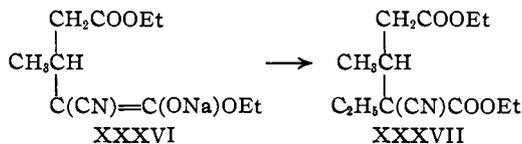
Addition of sodium enol cyanacetic ester to α -ethylcrotonic ester gave a stereomeric form (XXX) of the sodium derivative of the ester (XXIV)



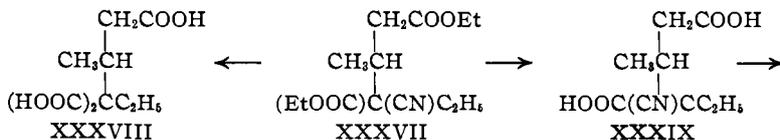
Through saponification with alcoholic potash, the ester from (XXX) yielded a cyano acid, m. p. 132° (XXXIII), and complete hydrolysis led to a tricarboxylic acid (XXXII), melting at 141° . When boiled for thirty minutes with hydrochloric acid, the cyano acid (XXXIII) gave a very small amount of the imide (XXVIII) melting at 92° with a sirupy cyano acid (XXXIV) as the main product. The latter, when completely hydrolyzed, gave *trans* α -ethyl- β -methylglutaric acid, m. p. 101°

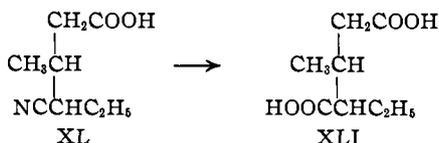


For comparison with the above compounds, β -methyl- γ -ethyl- γ -cyano-glutaric ester (XXXVII) was prepared by the action of ethyl iodide upon the sodium derivative of β -methyl- γ -cyanoglutaric ester (XXXVI)



From the product of saponification with caustic potash, a cyano acid (XXXIX) was obtained, melting at 139° , which upon treatment with hydrochloric acid gave a sirupy cyano acid (XL) with a very small amount of the two isomeric β -methyl- α -ethylglutarimides, m. p. 92° and m. p. 102° . Upon complete hydrolysis with hydrochloric acid, the cyano acid gave *trans* α -ethyl- β -methylglutaric acid, m. p. 101° (XLI).





γ -Ethyl- β -methyl- γ -cyanoglutaric acid (XXXIX) after long boiling with 25% caustic potash, yielded the corresponding tricarboxylic acid (XXXVIII) which could not be obtained crystalline. The difficulty of hydrolysis of this substituted ethyl cyanoacetic acid is undoubtedly due to the influence of the ethyl and $-\text{CH}(\text{CH}_3)\text{CH}_2\text{COOEt}$ groups upon the cyanacetic residue. The greater stabilizing influence of the ethyl compared with the methyl group as a substituent is similarly exhibited in the difficulty of saponifying diethylmalonic ester, in comparison with the relative ease of saponification of dimethylmalonic ester.¹⁹

It would appear from the above reactions that addition of sodium enol cyano esters to α,β -unsaturated esters can take place with the *selective synthesis* of one of the stereomeric forms. It was shown above that if the primary addition reaction is considered a *trans* process then the addition of sodium enol cyanoacetic ester to α -ethylcrotonic ester would give a cyano ester stereomeric with the product of addition of sodium enol α -cyanobutyric ester to crotonic ester. When both stereomeric forms appeared, as occurred in the additions to cinnamic and α -methylcinnamic esters,²⁰ it is apparent that racemization had taken place during the addition reaction. This must also be the case when the same single stereomer was formed, as in the addition of sodium enol malonic to tiglic ester and of sodium enol methylmalonic to crotonic ester. McKenzie and Wren²¹ and others have connected the presence of the phenyl group as favoring racemization. The action of free alkali or of sodium ethoxide in promoting racemization is well known, so that racemization would be expected to occur in the presence of a strongly alkaline material, such as sodium enol malonic ester. The absence of racemization when the sodium enol cyano esters are added to olefinic unsaturated esters is an indication of the neutrality and stability of the sodium enol cyano ester addition product in these particular cases.

In the addition of sodium enol alkyl cyanacetic esters to crotonic ester, it was noticed that always with the main product varying small quantities of higher boiling esters were formed, which gave a deep red color with alcoholic ferric chloride. Analyses indicated that they consisted of an addition product of one molecule of the alkyl cyanacetic ester to one molecule of crotonic ester. Hydrolysis with hydrochloric acid of the prod-

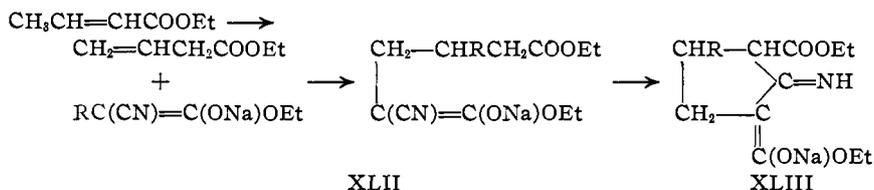
¹⁹ Michael, *J. prakt. Chem.*, 72, 546 (1905).

²⁰ Ref. 6, p. 4608.

²¹ McKenzie and Wren, *J. Chem. Soc.*, 117, 680 (1920).

uct from α -cyanopropionic and crotonic esters gave a ketone, which readily gave a semicarbazone. However, the yield of the ketone was very small, and, possibly due to the difficulty experienced in purifying this small quantity of material, the melting point and analysis of the semicarbazone did not correspond well to the expected derivative of a dimethylcyclopentanone. Notwithstanding, it was thought that this ketone might have been derived from an imino compound produced by ring-formation involving the cyano group and the H attached to the α -carbon atom.

Although crotonic ester shows no tendency to change into vinylacetic ester, yet as a hypothesis it may be supposed that in the presence of the energetic sodium enol alkyl cyanacetic ester, crotonic ester may exhibit a tendency to function in its β,γ -form



By the action of sodium ethoxide, such δ -cyano esters as (XLII) readily form sodium derivatives of cyclic imino compounds (XLIII) in which the sodium is better neutralized than in the open-chain derivatives.²²

In a somewhat analogous case, the addition of sodium enol malonic ester to citraconic ester,²³ it has been shown²⁴ that, as well as the normal addition compound, α -methylpropane- $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic ester, there is also formed butane- $\alpha,\beta,\delta,\delta$ -tetracarboxylic ester, which would appear to have been produced by addition to itaconic ester. The latter tetracarboxylic ester is readily converted by sodium ethoxide into a cyclopentanone-carboxylic ester and, hence, the product of addition of sodium enol malonic ester to citraconic ester is largely the sodium derivative of this cyclic keto ester, because in this compound the sodium secures better neutralization and in the formation the maximum energy degradation is attained. To achieve this, hydrogen from the methyl group migrates during the reaction with change in the position of unsaturation so that the citraconic ester functions during the process of addition as does itaconic ester.

The possibility indicated by the formation of high-boiling esters of an apparently cyclic structure, apparently derived from vinylacetic ester and suggesting that addition could take place at the β,γ -carbon atoms of an olefinic ester, was of sufficient interest as to warrant further examina-

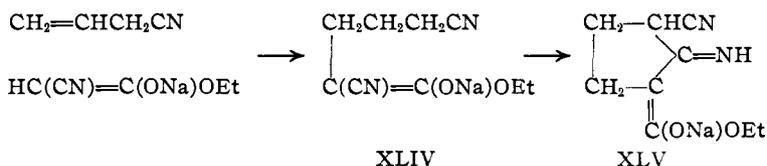
²² Best and Thorpe, *J. Chem. Soc.*, 95, 685 (1909).

²³ Michael, *Ber.*, 33, 3757 (1900).

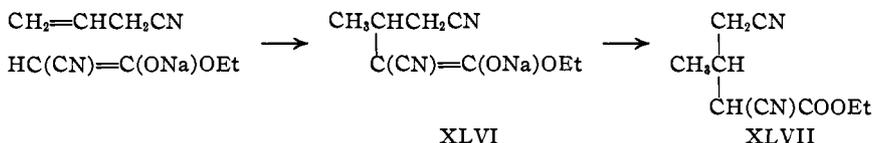
²⁴ Hope, *J. Chem. Soc.*, 101, 892 (1912); Ingold, Shoppee and Thorpe, *ibid.*, 1477 (1926).

tion of reactions where this type of addition might be expected to be favored.

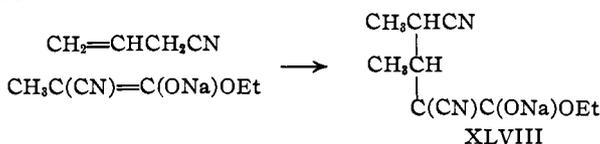
Allyl cyanide was chosen as a readily accessible β,γ -unsaturated compound of the same type as vinylacetic ester. If this added sodium enol cyanacetic ester in the above manner, then the ethyl compound of 2-imino-3-cyanocyclopentane-1-carboxylate (XLV) would be formed, a compound that has been described by Thorpe and Best.²²



When this reaction was carried out in alcohol, or alcohol-free benzene, none of the cyclic imino compound could be detected. A very good yield of sodium derivative of β -methyl α -carbethoxyglutaronitrile (XLVI) was obtained

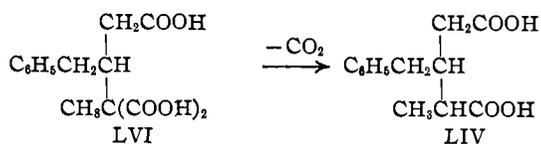


Similarly sodium enol α -cyanopropionic ester and allyl cyanide gave sodium enol α,β -dimethyl- γ -carbethoxyglutaronitrile (XLVIII) by migration of CH_3 , although in this case a quantity of resinous material was also formed



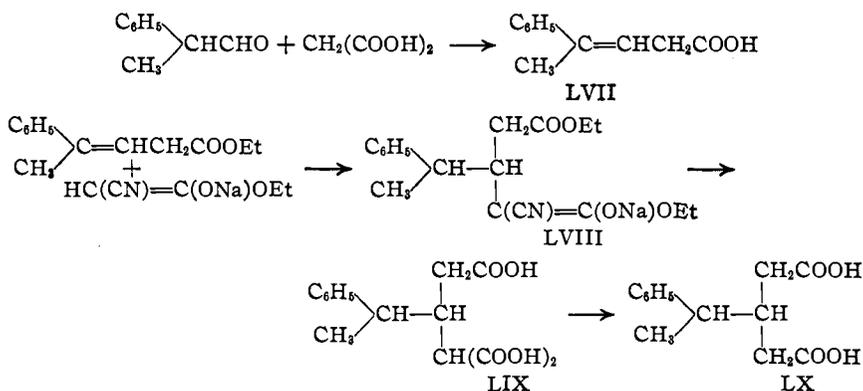
The absence of β,γ -addition with allyl cyanide may be due to the great tendency of this nitrile to rearrange to the more stable α,β -unsaturated isomer. Since styrylacetic acid (β,γ -derivative) is known to be far more stable toward alkali than γ -phenylcrotonic acid (α,β -isomer)²⁵ addition to styrylacetic ester was therefore examined. Vorländer and Strunck showed that sodium enol malonic ester adds to styrylacetic ester apparently through the α,β -derivative to give β -benzyl- γ -carbethoxyglutaric ester (XLIX). However, there is obviously no means of deciding from the structure of the addition product, at which carbon the hydrogen of the addendum had united

²⁵ Vorländer and Strunck, *Ann.*, **239**, 345 (1906).



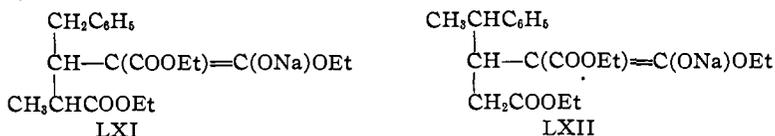
Evidently to establish the constitution of the tricarboxylic acid, m. p. 118°, and of the dicarboxylic acid, m. p. 97°, derived from it, it was necessary to compare it with γ -methyl- γ -phenyl- β -aceticbutyric acid (LX).

For this purpose hydratropic aldehyde was condensed with malonic acid in the presence of diethylamine, and the ester of the γ -methyl- γ -phenylbutenoic acid (LVII) so obtained was treated with sodium enol cyanacetic ester



The cyano ester was hydrolyzed to the tricarboxylic acid (LIX) melting at 162°, which upon heating lost carbon dioxide and gave γ -methyl- γ -phenyl- β -aceticbutyric acid, m. p. 88° (LX).

In the addition of sodium enol methylmalonic ester to styrylacetic ester, the methyl group evidently assumed the α -position and isomerization of the styrylacetic ester to γ -phenylcrotonic ester occurred. This rearrangement may have anteceded the addition but it is more probable that it took place during the process and that it was associated with the maximal neutralization of the positive energy of the sodium. A comparison of the structures of the two possible addition products (LXI) and (LXII)



shows that the negative radicals of (LXI) are more symmetrically arranged about the positive nucleus $\text{CH}-\text{C}(\text{COOEt})=\text{C}(\text{ONa})\text{OEt}$ and that (LXI) should therefore be the intramolecularly better neutralized compound.

Experimental

A. Addition of Alkylmalonic Esters to Fumaric Ester

Propane- $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic ester was prepared by the addition of malonic ester to fumaric ester in the presence of a small amount of sodium ethoxide;²⁶ yield, 90% of theory, b. p. 187° (5 mm.).

Propane- $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic acid was prepared from the above ester by saponification with 20% barium hydroxide solution and decomposing the sparingly soluble barium salt obtained with acid. The tetracarboxylic acid was extracted with ether and crystallized from the ether solution as a fine powder, m. p. 153°.

Anal. Calcd. for $C_7H_8O_8$: C, 38.19; H, 3.64. Found: C, 38.36; H, 3.80.

Butane- $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic ester was obtained by adding 22 g. of propane- $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic ester to an ethereal suspension of anhydrous sodium ethoxide prepared from 1.8 g. of sodium, and methylating by addition of 10 g. of methyl iodide to the solution of sodium derivative, the mixture being cooled in ice. After standing for eight hours at room temperature, the product was worked up in the usual way; yield 21 g. of ester boiling at 180° (3 mm.).

Anal. Calcd. for $C_{16}H_{27}O_8$: C, 55.34; H, 7.78. Found: C, 55.50; H, 7.95.

Upon treatment of this ester with an ethereal suspension of sodium ethoxide, followed by methyl iodide, the main products were those of fission into fumaric and methylmalonic esters; 16 g. of ester was added to sodium ethoxide from 1.2 g. of sodium and after five minutes 8 g. of methyl iodide was added, the whole mixture standing at 0° for twelve hours. Upon working up there were obtained: 10 g. of ester, b. p. 95–120° (10 mm.), fumaric, dimethylmalonic esters; 4 g. of ester, b. p. 120–180° (3 mm.), unchanged ester.

Butane- $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic acid was obtained by saponifying the ester with 20% caustic potash or barium hydroxide solution. The acid was liberated with hydrochloric acid and extracted with ether. It crystallized in transparent nodules from ether or acetone and ligroin and melted at 170°.

Anal. Calcd. for $C_8H_{10}O_8$: C, 41.03; H, 4.27. Found: C, 40.82; H, 4.46.

Butane- $\beta,\gamma,\delta,\delta$ -tetracarboxylic ester is formed when fumaric ester is added to methylmalonic ester in the presence of an equivalent of sodium ethoxide in ethereal solution. This ester was previously obtained by Auwers, Köbner and Meyenberg,²⁷ and Michael²⁸ but described as butane- $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic ester. Michael showed that this ester formed a sodium derivative, which readily reacted with methyl iodide and gave a quantitative yield of pentane- $\beta,\gamma,\delta,\delta$ -tetracarboxylic ester and which, upon hydrolysis, gave α,γ -dimethyltricarballic acid.

Butane- $\beta,\gamma,\delta,\delta$ -tetracarboxylic acid was prepared by saponifying the ester with caustic potash. It was extracted with ether and crystallized from an ether-ligroin mixture in large nodules. There was no change in melting point upon fractional crystallization, so it was concluded that this acid, melting at 176°, was probably a pure stereomeric form. Hope²⁹ obtained an acid, melting at 155°, which he considered to be a mixture of two stereomeric forms, from the ester obtained in the addition of sodium enol malonic ester to citraconic ester.

Anal. Calcd. for $C_8H_{10}O_8$: C, 41.03; H, 4.27. Found: C, 41.21; H, 4.42.

²⁶ Ruhemann and Cunnington, *J. Chem. Soc.*, 73, 1007 (1898).

²⁷ Auwers, Köbner and Meyenberg, *Ber.*, 24, 2890 (1891).

²⁸ Michael, *ibid.*, 33, 3761 (1900).

²⁹ Hope, *J. Chem. Soc.*, 101, 901 (1912).

Pentane- $\beta,\gamma,\delta,\delta$ -tetracarboxylic acid was prepared by saponification of the ester obtained upon treating the above butane- $\beta,\gamma,\delta,\delta$ -tetracarboxylic ester with sodium ethoxide and methyl iodide at 0°. Recrystallized from acetone-ligroin mixture, m. p. 166°.

Anal. Calcd. for $C_9H_{12}O_8$: C, 43.54; H, 4.84. Found: C, 43.28; H, 4.90.

Pentane- $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic Ester.—Prepared by treating sodium enol propane- $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic ester with ethyl iodide, in ethereal solution, in the cold. The ester boiled at 180° (3 mm.).

Anal. Calcd. for $C_{17}H_{20}O_8$: C, 56.51; H, 8.03. Found: C, 56.65; H, 8.00.

Nine grams of ester was added to sodium ethoxide from 0.7 g. of sodium and after five minutes 8 g. of methyl iodide was added, the whole mixture standing on ice for twelve hours. Upon working up, there was obtained 8 g. of ester, b. p. 180° (3 mm.), which proved to be unchanged ester, since upon saponification it gave pentane- $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic acid, m. p. 177°.

Pentane- $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic acid was obtained by saponifying the ester with caustic potash. It crystallized from ether in nodules, m. p. 177°.

Anal. Calcd. for $C_9H_{12}O_8$: C, 43.54; H, 4.84. Found: C, 43.35; H, 4.77.

Pentane- $\alpha,\alpha,\beta,\gamma$ -tetracarboxylic ester was obtained when fumaric ester was added to sodium enol ethylmalonic ester, formed by adding ethylmalonic ester to an equivalent of anhydrous sodium ethoxide suspended in ether. This ester, previously described as pentane- $\alpha,\beta,\gamma,\gamma$ -tetracarboxylic ester, was obtained by Michael,²⁸ who also showed that it formed a sodium derivative which, upon methylation, gave a quantitative yield of hexane- $\beta,\beta,\gamma,\delta$ -tetracarboxylic ester.

Pentane- $\alpha,\alpha,\beta,\gamma$ -tetracarboxylic acid was prepared by saponifying the ester with caustic potash. It crystallized from ether or acetone-ligroin in transparent nodules, melting at 179° with decomposition, and, since no separation was obtained upon fractional crystallization, it was concluded that this acid represented a single stereomeric form.

Anal. Calcd. for $C_9H_{12}O_8$: C, 43.54; H, 4.84. Found: C, 43.75; H, 5.05.

Hexane- $\beta,\beta,\gamma,\delta$ -tetracarboxylic acid was prepared by saponifying the ester obtained by treating pentane- $\alpha,\alpha,\beta,\gamma$ -tetracarboxylic ester with sodium ethoxide and methyl iodide in ether solution at 0°. Recrystallized from acetone-ligroin mixture, m. p. 170°.

Anal. Calcd. for $C_{10}H_{14}O_8$: C, 45.80; H, 5.34. Found: C, 45.72; H, 5.51.

B. Addition of Alkylcyanacetic Esters to Crotonic Ester

Addition of α -Cyanopropionic Ester to Crotonic Ester.— α -Cyanopropionic ester was prepared by methylation of sodium enol cyanacetic ester and freed from unchanged cyanacetic ester by shaking with successive small quantities of 5% caustic potash.

To a solution of 4.7 g. of sodium dissolved in 70 cc. of absolute alcohol, 25.5 g. of α -cyanopropionic ester was added, followed by 23 g. of crotonic ester. The mixture was heated on the water-bath for twenty-four hours. The cooled product was then poured into 500 cc. of ice water containing 13 g. of acetic acid and extracted with ether. The ethereal extract was washed with 10% sodium carbonate, followed by distilled water, the neutral esters dried and fractionated. Some low-boiling material came over first and then two main fractions were collected: 24 g., representing a 50% yield of γ -cyano- α,β -dimethylglutaric ester, distilled at 145–148° (3 mm.). This was a colorless liquid, which gave no coloration with alcoholic ferric chloride.

Anal. Calcd. for $C_{12}H_{16}O_4N$: C, 59.75; H, 7.88. Found: C, 59.65; H, 7.95.

Eleven grams of ester, collected between 160 and 185° (3 mm.), gave a deep red coloration with alcoholic ferric chloride. After redistillation, a fraction boiling at 182° (3 mm.) was obtained which was analyzed.

Anal. Calcd. for $C_{12}H_{19}O_4N$: C, 59.75; H, 7.88; N, 5.82. Found: C, 59.47; H, 7.6; N, 5.7.

Upon hydrolyzing 3 g. of this high-boiling ester with hydrochloric acid (1:1), a small quantity of a ketonic compound, b. p. 50–120° (10 mm.), was obtained together with a sirupy acid. The ketonic compound with semicarbazide acetate gave a crystalline semicarbazone within one hour. This was recrystallized from dilute aqueous alcohol and melted at 224°.

Anal. Calcd. for $C_7H_{13}ON_3$: C, 54.2; H, 8.38; N, 27.1. Found: C, 54.79; H, 7.34; N, 19.0.

These figures do not correspond with any simple derivative of cyclopentanone.

α,β -Dimethyl- γ -cyanoglutaric acid was obtained by saponification of α,β -dimethyl- γ -cyanoglutaric ester, b. p. 145–148° (3 mm.), with 20% caustic potash containing a small amount of alcohol. Immediately upon warming, the ester dissolved. After acidifying the well-cooled solution, the cyano acid was extracted with ether. It was a sirup which resisted all attempts to make it crystallize.

Anal. Calcd. for $C_8H_{11}O_4N$: C, 51.89; H, 5.95. Found: C, 51.56; H, 6.03.

When boiled for one hour with concentrated hydrochloric acid, the above α,β -dimethyl- γ -cyanoglutaric acid gave a small amount of α,β -dimethylglutarimide, m. p. 112°, together with a sirupy cyano acid from which, on treatment with alkali, a liquid α,β -dimethylglutaric acid was prepared. This was characterized as a *trans* derivative by conversion into α,β -dimethylglutaric dianilide. The α,β -dimethylglutaric acid was mixed with an excess of aniline and heated at 180° for one hour. The neutral dianilide thus formed crystallized in fine needles from mixture of ether and ligroin and melted at 216°.

Anal. Calcd. for $C_{19}H_{27}O_2N_2$: C, 73.53; H, 7.1. Found: C, 73.27; H, 7.31.

The above α,β -dimethylglutaric dianilide was identical with the dianilide prepared from an authentic sample of the *trans* α,β -dimethylglutaric acid.

α,β -Dimethyl- γ -carboxylglutaric acid was prepared by complete hydrolysis of the ester boiling at 147° (3 mm.), or of the above cyano acid by boiling it with 20% caustic potash for eight hours when ammonia ceased to be evolved. The acid solidified on standing and was recrystallized from an ether–ligroin mixture as fine prisms, m. p. 142°.

Anal. Calcd. for $C_8H_{12}O_6$: C, 47.07; H, 5.88. Found: C, 46.95; H, 6.00.

This acid was shown by mixed melting point to be not identical with the α,β -dimethyl- γ -carboxylglutaric acid, m. p. 145°, obtained by condensation of the enolic sodium derivative of malonic or cyanacetic esters with tiglic ester. From the ease of hydrolysis of the parent ester, and the general properties of the acid, it is probable that it is a stereomer of α,β -dimethyl- γ -carboxylglutaric acid.

α,β -Dimethyl- γ -cyanoglutaric acid was obtained as an uncrystallizable sirup by saponifying the addition product of sodium enol cyanacetic ester to tiglic ester.³⁰

Anal. Calcd. for $C_8H_{11}O_4N$: C, 51.89; H, 5.95. Found: C, 51.63; H, 6.10.

Upon boiling with concentrated hydrochloric acid, it gave some α,β -dimethylglutarimide, m. p. 113°, together with a cyano acid. Alkali hydrolysis of this acid, however, gave *trans* α,β -dimethylglutaric acid, characterized by the dianilide, m. p. 216°.

³⁰ Michael and Ross, Ref. 6, p. 4607.

β,γ -Dimethyl- γ -cyanoglutaric acid was prepared, for comparison with the above cyanoglutaric acids, by the action of methyl iodide upon the sodium derivative of β -methyl- γ -cyanoglutaric ester. It readily crystallized in large prisms, m. p. 152°, and upon boiling with hydrochloric acid gave about equal quantities of α,β -dimethylglutarimide and the *trans* cyano acid. Thorpe and Young³¹ synthesized this acid by the same method, but gave the melting point as 132–133°.

Anal. Calcd. for $C_8H_{11}O_4N$: C, 51.89; H, 5.95. Found: C, 51.78; H, 5.96.

Attempted Addition of Sodium Enol Ethylmalonic Ester to Crotonic Ester.— α -Carboxybutyric ester was obtained by treating sodium enol malonic ester with ethyl iodide, and the product was purified from malonic ester by shaking four times with a third of its volume of 25% caustic potash.

Four and eight-tenths grams of sodium was pulverized and dissolved in 9.5 g. of absolute alcohol in ether solution. To the anhydrous sodium ethoxide, 38 g. of α -carboxybutyric ester was added, followed by 23 g. of crotonic ester and the mixture heated on the water-bath for six hours. The ice-cooled mixture was then washed with water containing a little more than an equivalent quantity of acetic acid. The ether solution was extracted with 10% sodium carbonate, followed by distilled water, dried and the neutral esters distilled; 35 g. of ester boiled up to 150° (25 mm.), consisting mainly of unchanged α -carboxybutyric ester and with some crotonic ester; 7 g. distilled from 140–152° (4 mm.), which consisted of α -ethylidene β -methylglutaric ester (or so-called dicrotonic ester). This was proved by analysis of the acid, m. p. 129°, obtained upon saponification of this ester.³²

Anal. Calcd. for $C_8H_{12}O_4$: C, 55.82; H, 7.56. Found: C, 56.04; H, 7.3.

There was also obtained 4 g. of ester boiling at 152–159° (4 mm.), which upon saponification gave a sirupy, uncrystallizable acid. The small yield of this material did not permit further examination, although it probably represented the addition product of ethylmalonic to crotonic ester.

Addition of Sodium Enol α -Cyanobutyric Ester to Crotonic Ester.— α -Cyanobutyric ester was prepared from sodium enol cyanacetic ester and ethyl iodide. The product was shaken with successively small amounts of 5% caustic potash in order to remove unchanged cyanacetic ester.

A solution of 4.7 g. of sodium in 70 cc. of absolute alcohol was mixed with 28 g. of α -cyanobutyric ester and then with 23 g. of crotonic ester, and the mixture heated on the water-bath for twenty-four hours. The cooled product was poured into 500 cc. of water containing 13 g. of acetic acid and the solution extracted with ether. The ethereal extract was washed with 10% sodium carbonate, then with distilled water, dried and the neutral esters distilled. About 25 g. distilled up to 140° (15 mm.), which consisted of unchanged esters. The 17 g. that passed over at 153° (3 mm.) proved to be γ -cyano- α -ethyl- β -methylglutaric ester, representing a 33% yield. It was a colorless liquid which gave no color with alcoholic ferric chloride.

Anal. Calcd. for $C_{13}H_{21}O_4N$: C, 61.18; H, 8.23. Found: C, 60.95; H, 8.30.

There was also obtained a fraction of ester, boiling at 160–165° (3 mm.), which gave a deep red coloration with alcoholic ferric chloride. This higher-boiling ester was probably homologous with the similar ester formed in the addition of sodium enol α -cyanopropionic ester to crotonic ester.

Anal. Calcd. for $C_{13}H_{21}O_4N$: C, 61.18; H, 8.23. Found: C, 60.56; H, 8.01.

γ -Cyano- α -ethyl- β -methylglutaric acid was obtained by saponification of the ester,

³¹ Thorpe and Young, *J. Chem. Soc.*, **83**, 357 (1903).

³² V. Pechmann, *Ber.*, **33**, 3340 (1900); and Michael, *ibid.*, **33**, 3760 (1900).

b. p. 153° (3 mm.), with alcoholic potash, the mixture being gently boiled until the ester had dissolved. Upon acidifying, the acid was extracted with ether and crystallized in prisms from a mixture of ether and ligroin, m. p. 147°. This cyano acid accounted for 60% of the product of saponification; only a residual sirup remained.

Anal. Calcd. for $C_8H_{13}O_4N$: C, 54.26; H, 6.53. Found: C, 54.15; H, 6.7.

α -Ethyl- β -methylglutarimides.—Boiling the above cyano acid with hydrochloric acid (1:1) gave a mixture of two isomeric imides. The main product melted at 92° and crystallized in fine needles from an ether-ligroin mixture.

Anal. Calcd. for $C_8H_{13}O_2N$: C, 61.94; H, 8.38. Found: C, 62.16; H, 8.6.

From the mother liquor the second imide melting at 102°, which crystallized in large prisms, was obtained. By boiling the above-mentioned sirupy cyano acid, more of this imide, m. p. 102°, was obtained. This was apparently formed from a stereomeric *cis* form of the α -ethyl- β -methyl- γ -cyanoglutaric acid, which may occur in four racemic forms.

Anal. Found: C, 62.05; H, 8.5.

Cis α -Ethyl- β -methylglutaric acid was obtained by hydrolysis of the above imide, m. p. 92°, by boiling with hydrochloric acid for six hours. It crystallized in prisms from a mixture of chloroform and ligroin and melted at 88°.

Anal. Calcd. for $C_8H_{14}O_4$: C, 55.18; H, 8.04. Found: C, 55.13; H, 8.16.

α -Ethyl- β -methyl- γ -carboxylglutaric acid was obtained by complete hydrolysis of the ester, b. p. 153° (3 mm.), or of the cyano acid, m. p. 147°, with caustic potash. It crystallized in fine prisms, melting at 143°.

Anal. Calcd. for $C_8H_{14}O_6$: C, 49.53; H, 6.42. Found: C, 49.56; H, 6.53.

Addition of Sodium Enol Cyanacetic Ester to α -Ethyl Crotonic Ester.—To a solution of 2.3 g. in 35 cc. of absolute alcohol, 11.3 g. of cyanacetic ester was added, followed by 14.2 g. of α -ethylcrotonic ester (b. p. 160°). The mixture was heated on the water-bath for twenty-four hours and the material worked up as usual; yield, 60% of addition product.

α -Ethyl- β -methyl- γ -cyanoglutaric ester distilled at 154° (4 mm.).

Anal. Calcd. for $C_{13}H_{21}O_4N$: C, 61.18; H, 8.23. Found: C, 61.06; H, 8.40.

α -Ethyl- β -methyl- γ -cyanoglutaric acid was prepared by saponifying the above ester with alcoholic potash. It crystallized in large prisms, melting at 132°.

Anal. Calcd. for $C_8H_{13}O_4N$: C, 54.26, H, 6.23. Found: C, 54.22; H, 6.08.

Upon boiling the cyano acid with hydrochloric acid, a small amount (5%) of a mixture of the α -ethyl- β -methylglutarimides was obtained, but the main product was a sirupy cyano acid that could not be crystallized. This was apparently α -ethyl- β -methyl- γ -cyanobutyric acid, since, upon complete hydrolysis, it gave *trans* α -ethyl- β -methylglutaric acid, m. p. 101°. This acid crystallized in large prisms from a mixture of chloroform and ligroin. It had previously been prepared by v. Pechmann,³² from α -ethylidene- β -methylglutaric acid, who only described one form, which from the above synthesis is apparently the *trans* stereomer.

Anal. Calcd. for $C_8H_{14}O_4$: C, 55.18; H, 8.06. Found: C, 55.25; H, 8.18.

α -Ethyl- β -methyl- γ -carboxylglutaric acid was obtained by complete hydrolysis of the ester, b. p. 154° (4 mm.), or of the cyano acid, m. p. 132°, with caustic potash. It crystallized in needles, m. p. 141°.

Anal. Calcd. for $C_8H_{14}O_6$: C, 49.53; H, 6.42. Found: C, 49.82; H, 6.69.

Ethylation of γ -Cyano- β -methylglutaric Ester.— γ -Cyano- β -methylglutaric ester was prepared by the addition of crotonic ester to sodium enol cyanacetic ester in alcoholic

solution. The ester distilled as a colorless liquid, b. p. 147° (3 mm.).³³ To a suspension of sodium ethoxide prepared by the action of 4.8 g. of absolute alcohol upon 2.5 g. of pulverized sodium, 23 g. of γ -cyano- β -methylglutaric ester was added. After standing until the formation of the soluble sodium derivative was completed, 17 g. of ethyl iodide was added and the mixture stood for two hours at room temperature. After warming on the steam-bath for half an hour, the product was worked up in the usual way. γ -Ethyl- β -methyl- γ -cyanoglutaric ester boiled at 152° (4 mm.).

Anal. Calcd. for $C_{13}H_{21}O_4N$: C, 61.18; H, 8.23. Found: C, 61.29; H, 8.42.

γ -Ethyl- β -methyl- γ -cyanoglutaric acid was obtained through saponification with alcoholic potash. It crystallized from ether-ligroin mixture in long prisms, m. p. 139°. The amount of this cyano acid accounted for 80% of the product of saponification.

Anal. Calcd. for $C_9H_{13}O_4N$: C, 54.26; H, 6.53. Found: C, 54.11; H, 6.63.

Upon boiling γ -ethyl- β -methyl- γ -cyanoglutaric acid with dilute hydrochloric acid for one hour, there was formed a small amount of the two α -ethyl- β -methylglutarimides (less than 5%), but the main product was a sirupy cyano acid which could not be crystallized. It was apparently α -ethyl- β -methyl- γ -cyanobutyric acid, since, upon complete hydrolysis, it gave *trans* α -ethyl- β -methylglutaric acid, m. p. 101°.

γ -Ethyl- β -methyl- γ -carboxyglutaric acid.—Upon boiling γ -ethyl- β -methyl- γ -cyanoglutaric ester, or the corresponding cyano acid, with 30% caustic potash for twenty-four hours, a sirupy tricarboxylic acid was obtained which could not be crystallized.

Anal. Calcd. for $C_9H_{14}O_6$: C, 49.53; H, 6.42. Found: C, 49.28; H, 6.62.

When boiled with hydrochloric acid, the tricarboxylic acid lost carbon dioxide to form a mixture of *cis* and *trans* α -ethyl- β -methylglutaric acids.

C. Addition to β,γ -Unsaturated Compounds

Addition of Sodium Enol Cyanacetic Ester to Allyl Cyanide.—Allyl cyanide was prepared from cuprous cyanide by the method described in "Organic Syntheses" (Vol. VIII, p. 4); 5.7 g. of sodium was dissolved in 85 cc. of absolute alcohol and 28 g. of cyanacetic ester added. After cooling, 17 g. of allyl cyanide was added and, as there was a noticeable evolution of heat as the solid derivative dissolved, the flask was placed in ice water. The mixture was gently refluxed upon the water-bath for sixteen hours. The product was cooled, mixed with dilute acetic acid and extracted with ether; 40 g. of β -methyl- γ -carbomethoxyglutaronitrile, b. p. 160° (3 mm.), was obtained, being a yield of 90%.

Anal. Calcd. for $C_9H_{12}O_2N_2$: C, 59.99; H, 6.66. Found: C, 59.75; H, 6.80.

When the addition was carried out in xylene using alcohol-free sodium enol cyanacetic ester, prepared by precipitation from ether solution, the product was the same.

In each case the constitution of the cyano ester was proved by hydrolysis with 20% caustic potash, when β -methyl- γ -carboxyglutaric acid was obtained, m. p. 139° (Ref. 6, p. 4604).

Addition of Sodium Enol α -Cyanopropionic Ester to Allyl Cyanide.—Thirty-two grams of α -cyanopropionic ester was added to a solution of 5.7 g. of sodium in absolute alcohol and then 17 g. of allyl cyanide, carrying out the operation as above. The neutral products, 12 g., distilling up to 110° (15 mm.), consisted apparently of unchanged material; 17 g. distilled at 152° (3 mm.) which was α,β -dimethyl- γ -carbomethoxyglutaronitrile, and a resinous residue weighing 12 g. remained in the flask.

Anal. Calcd. for $C_{10}H_{14}O_2N_2$: C, 61.85; H, 7.22. Found: C, 61.72; H, 7.36.

Upon hydrolysis with 20% caustic potash, the cyano ester gave α,β -dimethyl- γ -

³³ Darbishire and Thorpe, *J. Chem. Soc.*, **87**, 1716 (1905).

carboxylglutaric acid, m. p. 142°. This was identified by analysis, direct comparison and a mixed melting point with a sample of the acid, prepared by addition of sodium enol α -cyanopropionic ester to crotonic ester.

Addition of Sodium Enol Cyanacetic Ester to Styrylacetic Ester.—To a solution of 1.2 g. of sodium in 20 cc. of absolute alcohol, was added 5.8 g. of cyanacetic ester, followed by 9.5 g. of styrylacetic ester, and the mixture heated for sixteen hours on the water-bath. After working up in the usual way, a yield of 10 g. of addition product, boiling at 193° (3 mm.), was obtained. The formation of enolic compounds could not be detected.

Anal. Calcd. for $C_{17}H_{21}O_4N$: C, 67.33; H, 6.93. Found: C, 67.15; H, 7.10.

β -Benzyl- γ -carboxylglutaric acid was obtained through treatment of the above ester with caustic potash. It crystallized in large transparent prisms, melting at 158° with decomposition. This acid should be identical with the acid obtained by Vorländer and Strunck³⁴ through the addition of sodium enol malonic ester to styrylacetic ester, although their acid melted at 146°.

Anal. Calcd. for $C_{13}H_{14}O_6$: C, 58.64; H, 5.26. Found: C, 58.41; H, 5.35.

The above acid gave β -benzylglutaric acid on heating to 165° for thirty minutes. It crystallized in large prisms from an ether-ligroin solution and, like Vorländer and Strunck's acid, melted at 102°.

γ -Methyl- β -benzyl- γ -cyanoglutaric ester was obtained by treatment of the sodium derivative of the above ester in ether solution with methyl iodide. It boiled at 194° (3 mm.).

Anal. Calcd. for $C_{13}H_{23}O_4N$: C, 68.14; H, 7.25. Found: C, 68.22; H, 7.41.

γ -Methyl- β -benzyl- γ -carboxylglutaric acid was prepared through hydrolysis of the above cyano ester with caustic potash. It crystallized in large prisms from acetone-ligroin mixture and melted at 177° with decomposition.

Anal. Calcd. for $C_{14}H_{16}O_6$: C, 59.99; H, 5.71. Found: C, 60.18; H, 5.93.

α -Methyl- β -benzylglutaric acid.—This acid was heated at 180° for thirty minutes and the decomposition product crystallized from a mixture of ether and ligroin. Only one acid was isolated and this melted at 139° after recrystallization.

Anal. Calcd. for $C_{13}H_{16}O_4$: C, 66.1; H, 6.78. Found: C, 66.23; H, 6.90.

Addition of Sodium Enol Methylmalonic Ester to Styrylacetic Ester.—To a suspension of anhydrous sodium ethoxide prepared from 2.3 g. of sodium, 17.5 g. of methylmalonic ester was added, followed by 19 g. of styrylacetic ester and the mixture was heated upon the water-bath for six hours. After working up as usual, 15 g. of unchanged esters, b. p. up to 120° (10 mm.) was obtained and 15 g. of the addition product ester, boiling at 197° (3 mm.). There was also a small amount of high-boiling ester which distilled at 222° (3 mm.).

Anal. Calcd. for $C_{19}H_{28}O_6$: C, 65.13; H, 7.43. Found: C, 65.28; H, 7.61.

α -Methyl- β -benzyl- γ -carboxylglutaric acid.—The ester, boiling at 197° (3 mm.), was saponified with caustic potash. After acidifying, the tricarboxylic acids were extracted with ether. Upon addition of ligroin, an acid crystallized out which melted at 197° upon purification.

Anal. Calcd. for $C_{14}H_{16}O_6$: C, 59.99; H, 5.71. Found: C, 59.71; H, 6.00.

A second isomeric α -methyl- β -benzyl- γ -carboxylglutaric acid was obtained from the mother liquor left after crystallizing out the form of m. p. 197°. It was recrystallized from chloroform and melted at 118°.

Anal. Found: C, 59.81; H, 5.9.

³⁴ Vorländer and Strunck, *Ann.*, 345, 239 (1906).

α -Methyl- β -benzylglutaric Acid.—When the α -methyl- β -benzyl- γ -carboxyglutaric acid, melting at 195°, was decomposed by heating at 200° for twenty minutes, a mixture of the two forms of α -methyl- β -benzylglutaric acid was obtained. These were separated by crystallization from chloroform-ligroin mixture. The main product was the stereomer, m. p. 139°, identical with the acid obtained above from γ -methyl- β -benzyl- γ -carboxyglutaric acid. The other isomer present in small amount melted at 97°.

When α -methyl- β -benzyl- γ -carboxyglutaric acid, m. p. 118°, was heated at 150° for thirty minutes, the product consisted entirely of α -methyl- β -benzylglutaric acid, m. p. 97°.

Anal. Calcd. for $C_{13}H_{16}O_4$: C, 66.10; H, 6.78. Found: C, 66.18; H, 6.95.

Synthesis of γ -Methyl- γ -phenyl- β -aceticbutyric Acid.—Hydratropic aldehyde, prepared by Claisen's method³⁵ was condensed with malonic acid, by boiling a mixture of the aldehyde and malonic acid in alcoholic solution for six hours in the presence of a few drops of diethylamine. The product was poured into water, and extracted with ether. The acid was extracted from the ether solution by washing with sodium carbonate solution. Upon acidifying with hydrochloric acid an oil was obtained which was taken up in ether. The acid thus obtained was esterified by boiling with absolute alcohol containing a little sulfuric acid. The ester obtained was fractionally distilled and gave two main fractions; γ -methyl- γ -phenylbutenoic ester boiled at 156° (10 mm.).

Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.47; H, 7.84. Found: C, 76.24; H, 8.06.

A smaller amount of the higher-boiling fraction of ester, 175–182° (10 mm.), was apparently γ -methyl- γ -phenyl- α -carbethoxybutenoic ester.

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.56; H, 7.25. Found: C, 69.32; H, 7.40.

γ -Methyl- γ -phenylbutenoic acid was obtained by saponification of the above ester, b. p. 156° (10 mm.); it remained a sirup. Mayer and Stamm³⁶ previously obtained this acid, m. p. 75–78°, through the action of methylmagnesium iodide upon benzoylpropionic ester.

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 75.00; H, 6.82. Found: C, 74.73; H, 7.06.

γ -Methyl- γ -phenyl- α -carboxybutenoic Acid.—Upon saponification of the ester, b. p. 175–182° (10 mm.), an acid was obtained melting at 151° with evolution of gas.

Anal. Calcd. for $C_{12}H_{12}O_4$: C, 65.46; H, 5.45. Found: C, 65.23; H, 5.60.

Addition of Sodium Enol Cyanacetic Ester to γ -Methyl- γ -phenylbutenoic Ester.—To a solution of 1.2 g. of sodium in 20 cc. of alcohol was added 5.7 g. of cyanacetic ester, followed by 10 g. of γ -methyl- γ -phenylbutenoic ester, and the mixture heated for twelve hours upon the water-bath. The product was worked up in the usual manner and 9 g. of ester, b. p. 198° (3 mm.), was obtained. This was the addition product, γ -methyl- γ -phenyl- α -cyano- β -aceticbutyric ester.

Anal. Calcd. for $C_{13}H_{15}O_4N$: C, 68.14; H, 7.25. Found: C, 68.26; H, 7.38.

γ -Methyl- γ -phenyl- α -carboxy- β -aceticbutyric acid was obtained through saponifying the above ester with caustic potash. The acid crystallized in large prisms from an acetone-ligroin mixture which melted at 162° with decomposition.

Anal. Calcd. for $C_{14}H_{16}O_5$: C, 59.99; H, 5.71. Found: C, 60.18; H, 5.64.

γ -Methyl- γ -phenyl- β -aceticbutyric acid was prepared by heating the above tri-carboxylic acid to 165° for thirty minutes. The acid crystallized from a mixture of ligroin and ether in fine needles melting at 88°.

Anal. Calcd. for $C_{12}H_{16}O_4$: C, 66.10; H, 6.78. Found: C, 66.11; H, 6.63.

³⁵ Claisen, *Ber.*, 38, 702 (1905).

³⁶ Mayer and Stamm, *ibid.*, 56, 1424 (1923).

Summary

1. The course of addition of a derivative of the sodium enol malonic ester type to an α,β -unsaturated ester proceeds according to the law of chemical neutralization. That addition product is therefore formed in which the positive energy of the sodium atom is best neutralized, since the maximal energy degradation is thus realized.

2. It has been shown that in the addition of sodium enol alkyl malonic esters to fumaric ester, the alkyl group migrates so that the addendum parts are alkyl and $-\text{C}(\text{COOEt})=\text{C}(\text{ONa})\text{OEt}$.

3. In the addition of sodium enol alkyl cyanacetic esters to crotonic ester, the addendum parts are similarly alkyl and $-\text{C}(\text{CN})=\text{C}(\text{ONa})\text{OEt}$.

4. In the addition to crotonic ester, the yield of addition product was greater in the case of sodium enol methylcyanacetic ester (50%) than with sodium enol ethylcyanacetic ester (33%). However, the yield of addition product is determined by several complex factors so that it is not possible from these experiments to make any statement regarding the relative ease of migration of the methyl and ethyl groups in these addition reactions.

5. In these reactions, the maximal chemical neutralization of the sodium is realized by the sodium remaining attached to the carbonyl oxygen atom in the malonic or cyanacetic groups. The sodium atom, however, becomes better neutralized than it was in the addendum by the spatial negative influence of the acquired carboxyl group.

6. Esters of the type $\text{CHX}(\text{COOEt})-\text{CHY}-\text{CZ}(\text{COOEt})_2$ [where $\text{X} = \text{R}$ or H , $\text{Y} = \text{R}$, H or COOEt and $\text{Z} = \text{R}$ or H , also R is an alkyl or aryl radical], apparently form enolic sodium derivatives containing the group $-\text{CH}=\text{C}(\text{ONa})\text{OEt}$, but these immediately decompose to form ethylenic α,β -esters and sodium alkylmalonic esters. The retrogression of the free ester (A) by sodium is probably due to the formation of such an enolic sodium derivative. It would follow from this relationship that the sodium atom involved in the addition reactions specified under 2 and 3 above cannot migrate during the addition process. However, if the single carboxyl group of (A) can form an enolate, an amount of sodium corresponding to the relative acidity of the two enolic forms of ester (A) ($\text{Z} = \text{H}$), would migrate to the single carboxyl group according to the partition principle,³⁷ and spontaneous retrogression would lead to the re-formation of a further quantity of this sodium enol derivative. Thus, by this process, in agreement with the partition principle, an apparent balanced state would be achieved between the two possible stable sodium derivatives.

7. It has not been found possible to obtain addition to the γ -carbon atom of a β,γ -unsaturated ethylenic ester or nitrile. Addition occurs

³⁷ Michael, *J. prakt. Chem.*, 60, 6 (1899).

in the case of allyl cyanide and styrylacetic ester at the α - and β -carbon atoms, with migration of an α -hydrogen atom.

CAMBRIDGE, MASSACHUSETTS

NOTES

Some New *p*-Bromophenacyl Esters.—In using the method of Reid and Judefind [THIS JOURNAL, 42, 1043 (1920)] for the identification of organic acids, we have prepared the following *p*-bromophenacyl esters which are not listed by these authors: trimethylacetate, m. p. 76.5°; isocaproate, m. p. 77.3°; enanthate, m. p. 69.2°; isoheptylate, m. p. 75.5°; pelargonate, m. p. 63.5°.

CONTRIBUTION FROM THE
CHEMICAL LABORATORY OF THE
UNIVERSITY OF WASHINGTON
SEATTLE, WASHINGTON

S. G. POWELL

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Preparation of *N*-*o*-Chlorobenzoyl-*o*-chlorobenzenesulfonamide.—Several years ago an investigation was undertaken in this Laboratory having for its object the preparation of diphenic sulfinide ("Diphen-saccharin"). It was hoped that this compound might be sweet, or at least that its preparation would throw some light on the general problem of sweet taste *vs.* molecular structure. The method attempted was the internal condensation of chlorobenzoylchlorobenzenesulfonamide by loss of two atoms of chlorine from the molecule.

Preparation of *N*-*o*-Chlorobenzoyl-*o*-chlorobenzenesulfonamide, $\text{Cl-C}_6\text{H}_4\text{CONHSO}_2\text{C}_6\text{H}_4\text{Cl}$.—Ten grams of *o*-chlorobenzenesulfonamide was treated with 9.5 g. of *o*-chlorobenzoyl chloride and the mixture heated (180–190°) in an oil-bath for one hour. The dark brown mass was dissolved in acetone, the solution filtered, and the solid again precipitated by the use of petroleum ether. The solid was heated on a clay plate (70–80°) until it was perfectly dry and odorless. Repeated crystallizations from dilute ethanol or dilute acetic acid finally gave a product with a constant melting point of 154–155°; white platelets, having a faint bitter taste, yield about 11 g.

Anal. Calcd. for $\text{C}_{13}\text{H}_9\text{O}_2\text{Cl}_2\text{NS}$: C, 47.27; H, 2.72; N, 4.24; Cl, 21.52; S, 9.70. Found: C, 47.24; H, 2.60; N, 4.19; Cl, 21.40; S, 9.76.

In attempting to prepare diphenic sulfinide from the compound named above, it was heated alone and in different solvents, and treated with metals and other reagents under a variety of conditions. Seventy-two experiments were carried out, only two of which gave any indication of success. In these cases the material was heated in amyl alcohol solution with copper