

10. Researches on Acetylenic Compounds. Part XXIX. The Reaction between Nickel Carbonyl and Disubstituted Acetylenes.

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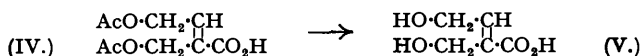
Treatment of disubstituted acetylenes with nickel carbonyl in aqueous-alcoholic acetic acid gives $\alpha\beta$ -disubstituted acrylic acids. The stereochemical configuration of the products and, in the case of unsymmetrical acetylenes, the direction of the addition reaction are discussed.

IN various summaries of work in the acetylene field carried out in Germany during the war (see *inter al.* Reppe, *Experientia*, 1949, 5, 93; "Acetylene Chemistry," translation, Meyer and Co., 1949, p. 156) it is stated that the reaction between nickel carbonyl and acetylene, which gives acrylic acid or its derivatives, can be extended to both mono- and di-substituted acetylenes. The application of this reaction, suitably termed the "Reppe carboxylation reaction," to mono-substituted acetylenes has already been examined in detail (Jones, Shen, and Whiting, *J.*, 1950, 230), and this paper deals with its use with certain types of disubstituted acetylenes.

Treatment of the symmetrical hydrocarbons, dec-5-yne and tolan (I; $R^1 = R^2 = \text{Bu}$ and Ph, respectively) with nickel carbonyl under the conditions previously found to be most favourable for mono-substituted acetylenes, *i.e.*, in aqueous-ethanolic acetic acid at 65–75°, gave the expected acids (II; $R^1 = R^2 = \text{Bu}$ and Ph, respectively) in *ca.* 40% yields. In the latter case the product was the "trans"- α -phenylcinnamic acid (III), m. p. 173°, which gives *cis*-stilbene



on decarboxylation; it therefore seems that *cis*-addition of the hydrogen and carboxyl groups takes place during the reaction. Confirmation of this view was obtained when but-2-yne-1 : 4-diol diacetate (I; $R^1 = R^2 = \text{AcO}\cdot\text{CH}_2$) was treated with nickel carbonyl. The product, the crystalline acid (IV), obtained in 53% yield, gave on alkaline hydrolysis the crystalline dihydroxy-acid (V). Now the *cis*- γ -hydroxy- $\alpha\beta$ -ethylenic acids obtained by semihydrogenation

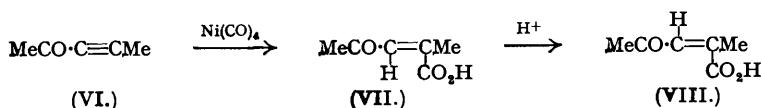


of the corresponding acetylenes (Haynes and Jones, *J.*, 1946, 954) lactonised very readily. The failure of (V) to cyclise even on being heated to 100° thus proves the *trans*-configuration of the carboxyl and hydroxymethyl substituents, and hence the *cis*-addition of hydrogen and carboxyl to the acetylenic diacetate during the reaction.

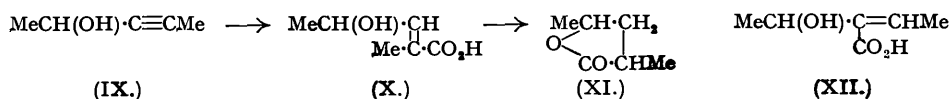
Treatment of either hex-1-yne-1-carboxylic acid (I; $R^1 = \text{Bu}$, $R^2 = \text{CO}_2\text{H}$) or its ethyl ester under the standard conditions resulted in exothermic reactions and the formation, in *ca.* 30% yields, of *n*-butylfumaric acid and of its crystalline monoethyl ester (II; $R^1 = \text{CO}_2\text{Et}$, $R^2 = \text{Bu}$), respectively. These reactions constitute further clear cases of *cis*-addition. As a synthesis of pure monoesters of monosubstituted fumaric acids, this reaction may be of some synthetic importance, since such esters, with unambiguous structures, are not otherwise easily accessible.

When the ketones, oct-3-yn-2-one and pent-3-yn-2-one (I; $R^1 = \text{Bu}$ and Me, respectively; $R^2 = \text{Ac}$) were treated with nickel carbonyl, exothermic reactions occurred and the corresponding acids were obtained in 30–40% yields; the position of the carboxyl group was indicated by their stability, and the direction of the addition is thus analogous to that observed with the acetylenic acid and ester. The product, m. p. 31°, from oct-3-yn-2-one was homogeneous, and analogy with the reactions discussed above suggests that it must be the *trans*-isomer of (II; $R^1 = \text{Ac}$, $R^2 = \text{Bu}$) *i.e.*, that obtained by *cis*-addition to the triple bond. The product from pent-3-yn-2-one (VI), however, was very water-soluble and could be isolated only by continuous ether-extraction of its strongly acidified solution; it proved to be a heterogeneous solid, m. p. 70–75°, from which two isomers, m. p.s 96–97° and 100–101° (VII and VIII), were separated in low yield by fractional crystallisation. The former resembled the acid obtained from oct-3-yn-2-one in its properties and can thus be assigned the *trans*-configuration (VII); the latter, presumably formed by acid-catalysed isomerisation, is the corresponding *cis*-form (VIII) (which actually exists in solution as the tautomeric cyclic pseudo-acid). The properties, chemical and spectrographic, of these keto-acids have been extensively investigated and leave no room for

doubt regarding the assigned configurations; they will be reported, in relation to analogous cases, in a later publication.



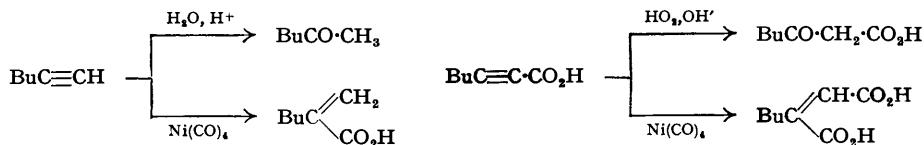
The failure of secondary and tertiary ethynylcarbinols to react readily with nickel carbonyl has already been mentioned (Jones, Shen, and Whiting, *loc. cit.*). In view of the apparent reluctance of the carboxyl group to enter at a position adjacent to a secondary carbinol grouping, it might be expected that pent-3-yn-2-ol (IX) would give (X), rather than (XII), on treatment with nickel carbonyl. In contrast to the ethynylcarbinols, (IX) reacted readily with nickel carbonyl under the usual conditions, and gave as the acidic reaction product a syrup, b. p. 90° (bath temp.)/10⁻⁶ mm., which gave analytical data in good agreement with (X) or (XII); the yield, 60%, was unusually high, but the product appeared to be somewhat heterogeneous (striations on distillation, etc.). On hydrogenation with a platinum catalyst (uptake exactly as calculated for one double bond) and distillation, only a 65% yield of α - γ -dimethylbutyrolactone (XI)



was obtained. A less volatile residue remained, which gave a heterogeneous, high-boiling liquid on distillation, either directly or over potassium hydrogen sulphate. It follows that only about 70% of the crude product could have consisted of (X); if (XII) had been present to a significant extent, however, α -ethylcrotonic acid, m. p. 45°, should have been isolated. The nature of the acidic compounds accompanying (X) therefore remains uncertain; etherification of the hydroxyl group in (X) is one possibility.

Certain other experiments on disubstituted acetylenes require brief discussion. But-2-yne-1 : 4-diol reacted exothermically with nickel carbonyl, but no reaction product could be isolated. This is hardly surprising, since (V), prepared from its diacetate, was somewhat unstable (*e.g.*, it could not be reacetylated with acetic anhydride and pyridine). The apparent "success" of the reaction with but-2-yne-1 : 4-diol recalls the similar vigorous reaction observed with propargyl alcohol. The Mannich bases (I; R¹ = CH₂·NEt₂, R² = Bu, and Ph) failed to react exothermically and were to some extent recovered unchanged. The vinylacetylene, 1-cyclohex-1'-enylhex-1-yne, failed to react exothermically and was recovered in 65% yield; the diacetylenes, diphenyldiacetylene, dodeca-5 : 7-diyne, and hexa-2 : 4-diyne, were to some extent decomposed by nickel carbonyl, somewhat exothermally, with the formation of black polymeric material but no appreciable quantity of acidic product; the first two hydrocarbons were recovered in yields of 75 and 60%.

Two conclusions can be drawn concerning the direction of addition in the Reppe carboxylation reaction. The first is that the carbonyl group attacks that carbon atom which in acid-, alkali-, or mercury-salt-catalysed hydration accepts the oxygen atom :



The second is that the reaction only occurs readily when the carbonyl group can attack a triply-bonded carbon atom which is linked to one of a limited number of groups. These are (R = alkyl or aryl) :

Groups facilitating carboxylation (A).

R, CH₂·OH, CH₂·OAc or CHR·OAc, CH₂·CH₂·OH or CH₂·CHMe·OH, CH₂·CH₂·OAc

CH₂·CH₂·O—CH—O—CH₂·CH₂·CH₂·CH₂, CH₂·CH₂·CH₂·OH.

Groups hindering carboxylation (B).

H, CHR·OH or CR₂·OH, CR₂·OAc, CH₂·CMe₂·OH,

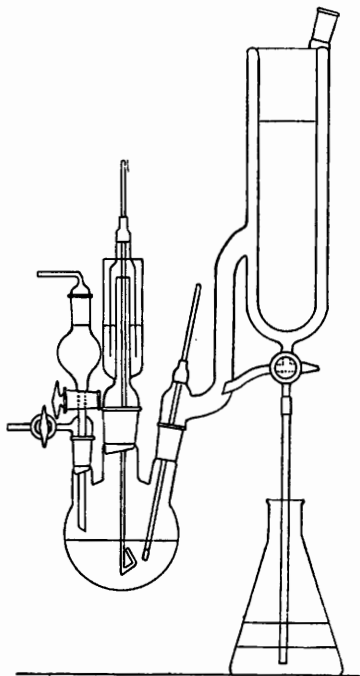
Ac, CO₂H, CO₂Et.

In a compound $\text{XC}\equiv\text{CY}$, if both X and Y are groups of type A, rapid reaction occurs; if they are both of type B, no rapid reaction occurs; if X is of type A and Y is of type B, a rapid reaction will take place and the product will be $\text{XC}(\text{CO}_2\text{H})=\text{CHY}$. The one outstanding exception is the case of acetylene itself; otherwise this rule covers all the vigorously exothermic reactions so far observed. It would nevertheless be unwise to regard it as more than a very tentative generalisation from somewhat limited experience; however, it makes possible certain predictions, e.g., that acetylenedicarboxylic ester would fail to react vigorously. This has been verified; mellitic ester (15% yield) was the only product isolated.

Somewhat similar limitations to the applicability of the Mannich reaction with acetylenic compounds have been observed (Jones, Marszak, and Bader, *J.*, 1947, 1578)

EXPERIMENTAL.

General Method.—The technique used was essentially similar to that previously described (Jones, Shen, and Whiting, *loc. cit.*), except that the apparatus was as now shown. The condenser contains a mixture of carbon tetrachloride and solid carbon dioxide; by turning the three-way tap it could be employed for either reflux or distillation. An atmosphere of nitrogen was maintained throughout the experiment; at the end of the exothermic reaction ether was added, and the excess of nickel carbonyl was removed by co-distillation, an electric heating-mantle being used. This apparatus could also be employed when quantitative determination of unreacted nickel carbonyl was necessary.



Dec-5-ene-5-carboxylic Acid.—Dec-5-yne (13.8 g.) (Hennion, *J. Amer. Chem. Soc.*, 1937, **59**, 1310), ethanol (30 c.c.), water (1.5 c.c.), and glacial acetic acid (4 c.c.) were warmed to 75° and treated with a solution of nickel carbonyl (5 c.c.) in ethanol (5 c.c.). An exothermic reaction occurred; when complete, the excess of carbonyl was removed, and isolation of the acid fraction (by means of sodium hydroxide solution) gave the acid (8.0 g., 44%), b. p. 122°/0.5 mm., n_D^{20} 1.4644 (Found: C, 72.05; H, 10.9. $\text{C}_{11}\text{H}_{20}\text{O}_2$ requires C, 71.7; H, 10.95%). On fractionation of the neutral portion of the reaction mixture the corresponding ethyl ester (1.6 g., 8%) was obtained; it had b. p. 93°/0.8 mm., n_D^{20} 1.4509 (Found: C, 73.8; H, 11.4. $\text{C}_{13}\text{H}_{24}\text{O}_2$ requires C, 73.5; H, 11.4%). A by-product (1.4 g.), b. p. 148°/0.5 mm., n_D^{17} 1.4744, was also isolated (Found: C, 82.1; H, 12.45. $\text{C}_{20}\text{H}_{38}\text{O}$ requires C, 82.1; H, 12.4%). Light absorption: Maximum, 2420 Å.; $E_{1\text{cm}}^{1\%} = 460$. It formed a dinitrophenylhydrazone which failed to crystallise even after chromatographic purification; its constitution was not investigated further.

Dec-5-ene-5-carboxylic acid gave an *S*-benzylthiuronium salt, which formed needles, m. p. 129°, from aqueous methanol (Found: C, 65.6; H, 8.45. $\text{C}_{19}\text{H}_{30}\text{O}_2\text{N}_2\text{S}$ requires C, 65.1; H, 8.65%), and a *p*-phenylphenacyl ester which formed plates, m. p. 42°, from aqueous methanol (Found: C, 79.2; H, 7.8. $\text{C}_{25}\text{H}_{30}\text{O}_3$ requires C, 79.3; H, 8.0%). Its *p*-nitrobenzyl ester formed needles, m. p. 29°, from methanol. Esterification of the acid with ethanol and sulphuric acid gave an ester, b. p. 70°/0.05 mm., n_D^{17} 1.4508 agreeing well with the constants of the material isolated from the neutral fraction.

trans-α-Phenylcinnamic Acid (cf. Reppe, *op. cit.*, p. 156).—Tolan (13.5 g.), ethanol (40 c.c.), water (1.5 c.c.), and acetic acid (3.5 c.c.) were allowed to react with nickel carbonyl (4 c.c.) in ethanol (10 c.c.) at 70°. Isolation of the acidic fraction, after removal of excess carbonyl, and recrystallisation gave the acid (6.3 g., 38%) as needles, m. p. 172–173°, from benzene–light petroleum. Distillation of the neutral fraction gave the corresponding ethyl ester (2.0 g., 10%), b. p. 142°/0.8 mm., n_D^{17} 1.5986, which solidified on storage and then had m. p. 31° (Müller, *Ber.*, 1893, **26**, 659, gives m. p. 172° for the acid; Auwers and Eisenlohr, *J. pr. Chem.*, 1911, **84**, 87, give b. p. 214–215°/28 mm., $n_D^{18.6}$ 1.5972, m. p. 28°, for the ethyl ester). Hydrolysis of the ethyl ester (0.5 g.) with aqueous-methanolic sodium hydroxide solution at 20° for 18 hours, followed by isolation of the acid fraction and recrystallisation gave the acid (0.2 g.), m. p. 173° undepressed on admixture with the specimen obtained directly from the reaction.

1:4-Diacetoxybut-2-ene-2-carboxylic Acid (IV).—A solution of but-2-yne-1:4-diol diacetate (19 g.) (Valette, *Ann. Chim.*, 1948, **3**, 644), ethanol (40 c.c.), water (2.5 c.c.), and acetic acid (4.5 c.c.) was treated with a solution of nickel carbonyl (6 c.c.) in ethanol (10 c.c.) at 65°. Isolation of the acid fraction gave a solid which was crystallised from benzene to give the diacetoxy-acid (12.5 g., 53%), as needles, m. p. 65° (Found: C, 49.9; H, 5.6. $\text{C}_9\text{H}_{12}\text{O}_6$ requires C, 50.0; H, 5.6%). Fractionation of the neutral portion gave (a) a liquid (1.2 g., 5%), b. p. 60°/0.1 mm., n_D^{17} 1.4450, which appeared to be the somewhat impure ethyl ester corresponding to the diacetoxy-acid (Found: C, 56.4; H, 6.95; OEt, 18.3. $\text{C}_8\text{H}_{11}\text{O}_4\cdot\text{CO}_2\text{Et}$ requires C, 54.1; H, 6.45; OEt, 18.4%); and (b) a substance, b. p. 150° (bath temp.)/10⁻³ mm., n_D^{18} 1.4710, which solidified when kept and was recrystallised from methanol to give prisms, m. p. 98° (0.4 g.) [Found: C, 56.1; H, 6.35%; *M*(ebullioscopic), 276. $\text{C}_{12}\text{H}_{14}\text{O}_6$ requires C, 56.3; H, 6.25%; *M*, 256].

Its saponification value corresponded to the presence of 3·2 ester groupings per molecule; it showed a light-absorption maximum at 2300 Å., $\epsilon = 10,000$. No structure can be suggested for this substance.

1 : 4-Dihydroxybut-2-ene-2-carboxylic Acid (V).—The corresponding diacetoxy-acid (9·9 g.) was treated with a solution of potassium hydroxide (10 g.) in water (20 c.c.) and ethanol (60 c.c.). After 16 hours at 20° the solution was diluted, strongly acidified, and extracted continuously with ether for two days. Evaporation of the ether gave a dark syrup which slowly crystallised on being kept at 0°; recrystallisation from benzene-dioxan yielded the *dihydroxy-acid* (0·9 g.) as prisms, m. p. 89–90° (Found : C, 45·4; H, 6·25. $C_4H_6O_4$ requires C, 45·5; H, 6·1%). No moderately-volatile material (b. p. >20°/0·2 mm.) was obtained on distillation of the hygroscopic syrup obtained by evaporating the mother-liquors.

4-Hydroxypent-2-ene-2-carboxylic Acid (X).—A solution of pent-3-yn-2-ol (IX) (16·8 g.) (Iositch *et al.*, *J. Russ. Phys. Chem. Soc.*, 1909, **41**, 529; *Bull. Soc. chim.*, 1910, **8**, 889) in ethanol (50 c.c.), water (4 c.c.), and acetic acid (8 c.c.) was treated with a solution of nickel carbonyl (8 c.c.) in ethanol (15 c.c.) at 75° in the usual way, an exothermic reaction taking place. After removal of excess of carbonyl, the acidic fraction was isolated by continuous ether extraction, washing with potassium hydrogen carbonate solution and continuous re-extraction after acidification. The dried extract was concentrated by evaporation and distilled at 85–90° (bath temp.)/10⁻⁵ mm., to give a viscous oil (15·1 g., 60%), n_D^{20} 1·4908 (Found : C, 55·5; H, 7·9. Calc. for $C_6H_{10}O_2$: C, 55·35; H, 7·8%). As the oil could not be induced to crystallise it was impossible to estimate the proportion of the 4-hydroxypent-2-ene-2-carboxylic acid present; from the analytical data it cannot have contained much non-isomeric material, and the hydrogenation data given below show that the proportion of the expected acid cannot have been less than 65%. It readily gave a crystalline *p-nitrobenzyl* ester (prisms, m. p. 98°, from benzene-light petroleum), which is assumed to be that of the principal component (Found : C, 58·6; H, 5·65. $C_{11}H_{15}O_2N$ requires C, 58·85; H, 5·7%). *Hydrogenation*: the oily acid (6·0 g.) was dissolved in methyl acetate and shaken in hydrogen in the presence of platinum oxide (25 mg.); absorption ceased after the uptake of 99% of the volume calculated for the reduction of one double bond. The removal of catalyst, evaporation of the solvent, and distillation of the residue gave α -dimethylbutyrolactone (XI) (3·4 g., 65%), b. p. 50°/0·1 mm., 110°/18 mm., n_D^{20} 1·4296 (Found : C, 62·7; H, 8·6. Calc. for $C_6H_{10}O_2$: C, 63·1; H, 8·85%). Treatment with hydrazine hydrate gave the hydrazide of γ -hydroxy- α -methylvaleric acid as needles, m. p. 117–118°, from ethyl acetate. (Boorman and Linstead, *J.*, 1935, 267, give b. p. 81°/10 mm., n 1·4289, for the lactone and m. p. 118° for the hydrazide.) The residue from the distillation of the lactone (1·6 g.) was distilled at 140–190° (bath temp.)/10·5 mm. over potassium hydrogen sulphate to give a heterogeneous liquid (1·0 g.); no crystalline material could be isolated.

n-Butylfumaric Acid.—Hex-1-yne-1-carboxylic acid (9·5 g.) (Haynes and Jones, *J.*, 1946, 503), ethanol (30 c.c.), acetic acid (4 c.c.), and water (2 c.c.) were treated with nickel carbonyl (5 c.c.) in ethanol at 75° by the general method. Isolation of the acidic fraction gave, after recrystallisation from benzene-ethanol, *n*-butylfumaric acid (3·6 g., 28%), m. p. 169–170° (Fittig and Fichter, *Annalen*, 1899, **304**, 250, give m. p. 170°). A small amount of a liquid, b. p. 130°/0·2 mm., n_D^{20} 1·4660, was obtained on distilling the non-crystalline portion of the acid fraction; it probably consisted of a mixture of impure monoethyl esters.

o-*n*-Butyl- β -carbethoxyacrylic Acid.—Ethyl hex-1-yne-1-carboxylate (6·0 g.) (Haynes and Jones, *loc. cit.*) in ethanol (25 c.c.), acetic acid (4 c.c.), and water (1·5 c.c.) was treated with a solution of nickel carbonyl (3 c.c.) at 65°. An exothermic reaction occurred, and isolation of the acidic product gave the *half-ester* (2·0 g., 25%), as a liquid, b. p. 120°/0·1 mm., which solidified on storage and was recrystallised from light petroleum (b. p. 40–60°) to give needles, m. p. 45° (Found : C, 60·1; H, 7·6. $C_{10}H_{16}O_4$ requires C, 60·0; H, 8·05%). *Hydrolysis*. Treatment of the half-ester with excess of potassium hydroxide solution at 20° gave on isolation the dicarboxylic acid, m. p. 167° undepressed on admixture with a specimen obtained as above.

2-Keto-oct-3-ene-4-carboxylic Acid.—A solution of oct-3-yn-2-one (9·3 g.) (Nieuwland, *J. Amer. Chem. Soc.*, 1936, **58**, 1862) in ethanol (25 c.c.), water (2 c.c.), and acetic acid (6 c.c.) was treated with nickel carbonyl (5 c.c.) at 65°, and a smooth exothermic reaction took place. Distillation of the acidic portion of the reaction product furnished the *keto-acid* (5·1 g., 40%) as a liquid, b. p. 115°/0·1 mm., n_D^{20} 1·4713, which crystallised on storage. On recrystallisation from light petroleum (b. p. 60–80°) at –40° it formed plates, m. p. 30–31° (Found : C, 63·55; H, 8·1. $C_8H_{14}O_3$ requires C, 63·55; H, 8·2%).

4-Ketopent-2-ene-2-carboxylic Acid.—To a solution of pent-3-yn-2-one (7·0 g.) (Braude, Jones, Sondheimer, and Toogood, *J.*, 1949, 609) in methanol (35 c.c.), water (2 c.c.), and acetic acid (4 c.c.), nickel carbonyl (5 c.c.) was added at 65°; an exothermic reaction took place, a brown coloration becoming evident whenever the rate of addition was increased. After removal of excess of carbonyl, isolation of the acidic fraction by ether extraction gave a heterogeneous solid (3·15 g., 30%), m. p. 70–75°. Recrystallisation from water gave, in small yield, the *trans-acid* as plates, m. p. 96–97° unchanged on further recrystallisation (Found : C, 56·25; H, 6·55. Calc. for $C_6H_8O_3$: C, 56·25; H, 6·25%). Two recrystallisations of the acid, m. p. 70–75°, from benzene gave the *cis-acid* as needles, m. p. 100–101° unchanged on further recrystallisation (Found : C, 56·5; H, 6·4%). A mixture of the two forms melted at 68–78°. The evidence upon which the assigned configurations have been based will be given in a forthcoming publication [Ajello and Cusmano, *Gazzetta*, 1940, **70**, 512, give m. p. 98° for an acid of this constitution but unknown configuration; Baxter, Norris, and Morris, *J.*, 1949, 95, give m. p. 102–102·5° (“needles from benzene”) for what was in all probability the *cis*-form].

From the neutral fraction a *methyl ester* (350 mg.), b. p. 44–46°/0·2 mm., was isolated by distillation. It solidified completely on being kept, and was recrystallised from light petroleum (b. p. 40–60°) at –40° to give prisms, m. p. 41° (Found : C, 58·85; H, 7·15. $C_7H_{10}O_3$ requires C, 59·1; H, 7·1%).

Ethyl Melliolate.—Ethyl acetylenedicarboxylate (3·6 g.) in ethanol (25 c.c.) water (0·5 c.c.), and acetic acid (11·5 c.c.) was treated slowly with nickel carbonyl (1·5 c.c.) in ethanol (5 c.c.) at 65–70°

for 10 minutes. No exothermic reaction occurred; removal of excess of carbonyl and isolation of the neutral fraction gave a blue semi-solid mass, which was filtered off. On recrystallisation, the solid portion gave ethyl mellitate (0.65 g., 18%), m. p. 74° (Found: C, 56.25; H, 6.2. Calc. for $C_{24}H_{30}O_{12}$: C, 56.45; H, 5.9%) (Kraut and Busse, *Annalen*, 1875, **177**, 273, give m. p. 72.5—73°). Distillation of the mother-liquors gave unchanged ethyl acetylenedicarboxylate (0.63 g., 17%), b. p. 48—50°/0.2 mm., n_D^{20} 1.4410, m. p. 1°; no other substance could be isolated from the neutral fraction, nor was any appreciable quantity of acidic product formed.

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