931. *Researches on Acetylenic Compounds. Part LVIII.* The Structure of an Anomalous Reppe Carboxylation Product.*

By P. J. Ashworth, G. H. Whitham, and M. C. Whiting.

Interaction of nickel carbonyl and 1-bromo- or 1-iodo-hept-2-yne yields the *cyclo*pentenone derivative (I). Its structure, deduced from degradative and spectroscopic evidence, was proved by the rational synthesis of the dihydro-derivative (V) of its lower homologue.

After the investigations described in the preceding paper, the action of nickel carbonyl on 1-bromohept-2-yne was examined, the reaction conditions being those employed for the corresponding chloride. Again the main product was 2-butylbuta-2 : 3-dienoic acid, but a second acid, m. p. 106—107°, was also formed, and was separated by fractional crystallisation. A much smaller quantity of the new acid was formed, along with the allenic acid, when the corresponding toluene-*p*-sulphonate was used, while the iodide gave it as the main product.

The new acid possessed the empirical formula $C_{16}H_{24}O_3$ and (from the volatility of its ester) was clearly monomeric. It showed an absorption maximum at 2940 Å (ε 15,000). Infrared bands at 1709, 1665, and 1635 cm.$^{-1}$ could not be usefully interpreted and attempts were therefore made to prepare a methyl ester. This ester was not formed at an appreciable rate in methanolic sulphuric acid, but was obtained with diazomethane. It showed an ultraviolet absorption spectrum similar to that of the acid, and infrared bands at 1730 and 1706 cm.$^{-1}$. The former was clearly the carbonyl stretching frequency of an ester group, and the latter that of a ketonic function. The ester in fact formed a 2 : 4-dinitrophenylhydrazone, which had $\lambda_{\text{max.}}$ 3970 Å in ethanol, and was therefore doubly conjugated;[1] if, however, the ketone group is conjugated, then its infrared stretching frequency indicates that it must be present in a five-membered ring.

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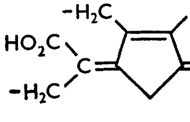
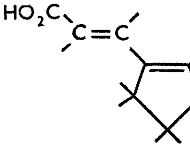
* Part LVII, preceding paper.

[1] Braude and E. R. H. Jones, *J.*, 1945, 498.

Further progress was made by catalytic hydrogenation. With platinic oxide in ethyl acetate, the new acid absorbed one mol., giving a crystalline acid $C_{16}H_{26}O_3$ with $\lambda_{max.}$ 2380 Å. Its methyl ester showed strong infrared bands at 1740 and 1706 cm.$^{-1}$, indicating that the ketonic function was still conjugated but the ester group no longer so. The 2 : 4-dinitrophenylhydrazone had $\lambda_{max.}$ 3870 Å, indicating one conjugated ethylenic linkage.[1] Further, if the dihydro-acid was a *cyclo*pentenone, it must be αβ-disubstituted, since 2- and 3-monosubstituted (monomethyl)*cyclo*pentenones [2,3] absorb maximally at only 2290 and 2250 Å, respectively; 2 : 3-dimethyl*cyclo*pentenone [2] has $\lambda_{max.}$ 2370 Å.


(A)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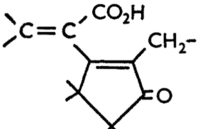
(C)

There are thus only three possible partial formulæ (A–C), if these spectroscopic results are to be fully explained, and of these structures, (C), a vinylogous β-keto-acid, would require that the acid $C_{16}H_{24}O_3$ or at least its dihydro-derivative should be readily decarboxylated. In fact, both these acids were stable to high temperatures and to hydrolytic conditions. Formula B cannot be expanded to any structure even remotely related to that of the starting material. On the other hand, (A) can be expanded to (I), which might be formed from a symmetrical precursor (II) obtained from two molecules of iodoheptyne and two carbon monoxide residues. The diketone (II) might well be sufficiently unstable, through strain and through the unfavourable orientation of the two polar carbonyl groups, to undergo a reversed Claisen condensation in the presence of water alone, or helped by the nickel salts present (weak Lewis acids), giving the acid (I). This is not a necessary assumption, as the four groupings might instead be held in a nickel complex until the attack of a water molecule resulted in direct transformation to the acid (I).

Ozonolysis of the new acid gave no volatile carbonyl compounds, and no keto-fraction could be isolated. Valeric acid (0·6 mol.) was obtained, along with non-crystallisable material. Vigorous hydrogenation resulted in an uptake of exactly 3 mols., giving a non-ketonic product transparent in the ultraviolet region down to 2000 Å (hence, directly, the acid must be monocyclic), which was partly dehydrated to a lactone on distillation. Assuming *cis*-addition, one would expect to obtain four stereoisomeric hexahydro-derivatives from the acid (I), two of which could lactonise; the carbonyl stretching frequency, 1770 cm.$^{-1}$, observed for the lactone produced is intermediate between those [4] of normal γ-(*ca.* 1780 cm.$^{-1}$) and δ-lactones (*ca.* 1740 cm.$^{-1}$), and therefore not implausible for a strained δ-lactone such as (III). For somewhat similar lactones, Wilder and Winston [5] found a band at 1760 cm.$^{-1}$. The Zimmerman test for $-CH_2\cdot CO-$ in the acid (I) was positive. Although no crystalline product could be obtained, the crude product of reduction of the methyl ester by lithium aluminium hydride showed $\lambda_{max.}$ 2410 Å, in good agreement with 2450 Å calculated [6] for the glycol (IV). All these results are consistent with the structure (I), as is the failure to effect acid-catalysed esterification, since a model reveals steric hindrance in the corresponding transition state—this is the only evidence for the configuration about the exocyclic linkage assumed here.

Several attempts were made to complete the degradation of the acid (I) by a further reversed Claisen condensation, which should give αα′-dibutyl-ββ′-dimethylmuconic acid or one of its derivatives. All were unsuccessful, the ester surviving, *e.g.*, after three hours in boiling 10% sodium methoxide solution. A rational synthesis of a compound related

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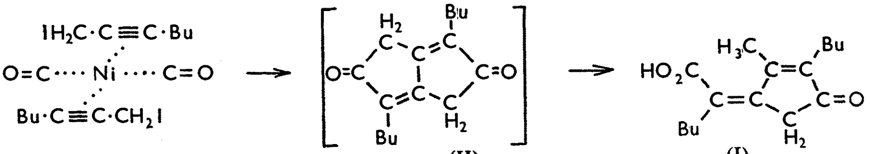
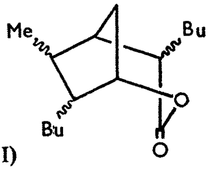
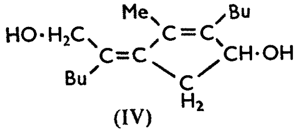
[2] Hennion and Davis, *J. Org. Chem.*, 1951, **16**, 1289.
[3] Acheson and Robinson, *J.*, 1952, 1131.
[4] R. N. Jones, Humphries, and Dobriner, *J. Amer. Chem. Soc.*, 1950, **72**, 956.
[5] Wilder and Winston, *ibid.*, 1955, **77**, 5598.
[6] Woodward, *ibid.*, 1942, **64**, 72.

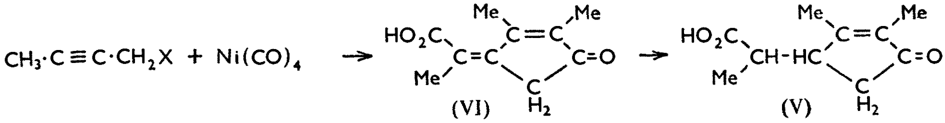
to (I) was therefore considered necessary, and the choice fell upon the dihydro-derivative (V) of the analogous acid (VI) in which methyl groups replace the *n*-butyl groups.


(II) (I)


(III)


(IV)

It proved necessary first to find a more convenient route to but-2-yn-1-ol than published procedures. 2 : 3-Dichlorobutan-1-ol was prepared, but gave a poor yield on dehydrochlorination; 3-chlorobut-2-en-1-ol, however, was dehydrochlorinated by sodamide in liquid ammonia in much better yield than by potassium hydroxide.[7] Conversion into the acetylenic chloride and metathesis with sodium iodide proceeded normally, but 1-iodobut-2-yne gave only a minute yield of the expected keto-acid (VI) on treatment with nickel carbonyl, the main product being dimethylmaleic anhydride. This implies a new variant of the Reppe carboxylation, in which the acetylene and carbon monoxide are involved in the ratio 1 : 2, not hitherto observed. It has not been investigated further, except that the order of addition of the reactants was shown not to affect the result.


(VI) (V)

When 1-bromobut-2-yne was employed, the yield of acid (VI) was comparable with that obtained from 1-bromohept-2-yne, although the other product was again dimethylmaleic anhydride, rather than the allenic acid. When the chloride was employed, a small yield of the acid (VI) was obtained—whereas 1-chlorohept-2-yne gave no trace of acid (I), according to spectroscopic measurements—and the expected 2-methylbuta-2 : 3-dienoic acid was obtained in quantity. Dimethylmaleic anhydride was not formed in this reaction, and hence cannot be a normal product from the allenic acid and nickel carbonyl. The reasons for the different behaviour of the two homologous sets of halides are not obvious, but *n*-butylmethylmaleic anhydride might well have been formed in small yield from the iodoheptyne, and yet escaped detection.

Hydrogenation of acid (VI) readily gave acid (V) under conditions similar to those used for the higher homologue. The analogy between the two series was proved by abundant spectroscopic data, and further evidence for the structures (I) and (VI) was made available by pK_a measurements on the more soluble lower homologues; values of 3·1 and 4·4 for acids (VI) and (V), respectively, testify to the C=O grouping cross-conjugated to the carboxyl residue in acid (VI), and the interruption of the conjugation, and hence of the transfer of polarisation, in acid (V).

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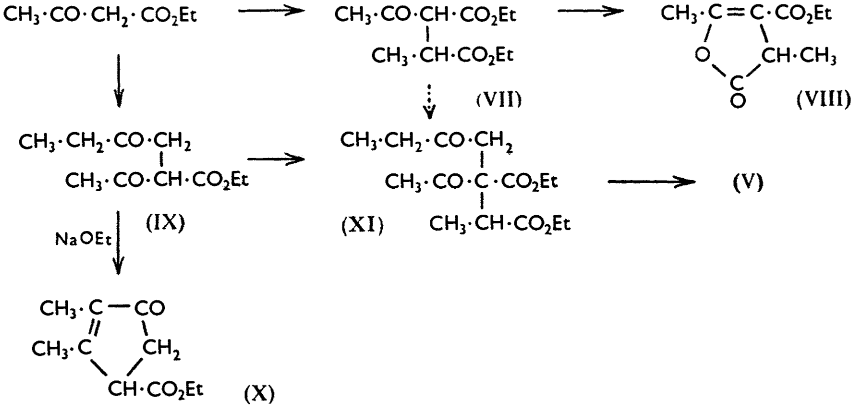
[7] Hatch and Nesbit, *J. Amer. Chem. Soc.*, 1950, **72**, 727.

The synthesis envisaged for the dihydro-derivative (V) was based upon the work of Willstätter and Clark,[8] and involved condensation of ethyl acetoacetate successively with ethyl α-bromopropionate and 1-chlorobutan-2-one, as shown.

The first reaction gave the expected ester [9] (VII), but attempts to effect further alkylation failed. This was traced to the rapid cyclisation of the sodium derivative of (VII) to the enol-lactone (VIII), recognised by its absorption band at 1810 cm.$^{-1}$; an analogous reaction has been observed previously.[10]



The order of alkylation was therefore inverted, although it was realised that the interaction of a monosubstituted acetoacetic ester and a secondary halide would be unlikely to give a good yield in the final stage. The diketo-ester (IX) was obtained without difficulty. Condensation with ethyl α-bromopropionate gave a product which was fractionally distilled. The lowest-boiling fraction absorbed intensely at 2380 Å and so consisted essentially of the *cyclo*pentenone (X), which was isolated as its 2 : 4-dinitrophenylhydrazone. This cyclisation of ester (IX) took place under the action of ethoxide alone. The second fraction consisted mainly of the unchanged diketo-ester (IX); the highest-boiling fraction also absorbed intensely at ~2380 Å, and was probably a mixture of the desired ester (XI) and its cyclisation product. Alkaline hydrolysis gave a syrupy acidic fraction which was subjected to paper chromatography; a spot, developed either by 2 : 4-dinitrophenylhydrazine or by a pH indicator, was found with an R_F value corresponding to that of acid (V). After fractional precipitation, a crystalline specimen of the latter, identical with the product obtained by the hydrogenation of acid (VI), was obtained in small yield. It is not known in which order the condensation, cyclisation, decarbethoxylation, and (possibly) epimerisation steps had occurred, but the formation of acid (V) from ethyl α-bromopropionate and ester (IX) provides the necessary confirmation of the structures assigned to the anomalous Reppe carboxylation products.

EXPERIMENTAL

Reaction between 1-*Bromohept*-2-*yne and Nickel Carbonyl.*—1-Bromohept-2-yne [11] (6·7 g.) was added to a stirred mixture of ethanol (30 c.c.), acetic acid (4·6 c.c.), sodium acetate (6·4 g.), water (1·5 c.c.), and nickel carbonyl (6 c.c.) at 45° during 20 min. No exothermal reaction ensued. The mixture was worked up and the acid fraction was isolated as a crystalline solid. Repeated recrystallisation from light petroleum (b. p. 60—80°) gave 2-*butyl*-4-1′-*carboxypentylidene*-3-*methyl*cyclo*pent*-2-*enone* (I) as plates (0·5 g., 10%), m. p. 103—105°, raised to 106—107° on recrystallisation from aqueous ethanol (Found: C, 72·55; H, 9·5%; equiv., 259. $C_{16}H_{24}O_3$

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[8] Willstätter and Clark, *Ber.*, 1914, **47**, 291.

[9] Conrad, *Annalen*, 1877, **188**, 226.

[10] Sprankling, *J.*, 1897, **71**, 1163.

[11] Newman and Wotiz, *J. Amer. Chem. Soc.*, 1949, **71**, 1295.

requires C, 72·7; H, 9·15%; equiv., 264). Evaporation of the mother-liquors from the initial crystallisation followed by recrystallisation of the residue from light petroleum (b. p. 40—60°) gave 2-butylbuta-2 : 3-dienoic acid (0·6 g., 11·5%), m. p. 68°.

*Reaction between Hept-2-yn-1-yl Toluene-*p*-sulphonate and Nickel Carbonyl.*—Hept-2-yn-1-yl toluene-*p*-sulphonate (5 g.; prepared from hept-2-yn-1-ol by the method of Eglinton and Whiting[12]) in ethanol (5 c.c.) was added during 30 min. to a stirred mixture of ethanol (30 c.c.), acetic acid (4·6 c.c.), sodium acetate (6·4 g.), water (1·5 c.c.), and nickel carbonyl (6 c.c.) at 40°. The solution became green and crystalline sodium toluene-*p*-sulphonate appeared. Working up gave a solid acid fraction; trituration of this with warm light petroleum (b. p. 40—60°) followed by filtration and crystallisation of the undissolved solid from aqueous ethanol gave the acid (I) (0·05 g., 2%), m. p. 103—105°. Evaporation of the filtrate and crystallisation of the residue from light petroleum (b. p. 40—60°) yielded 2-butylbuta-2 : 3-dienoic acid as prisms (0·81 g., 31%), m. p. 68—70°.

Reaction between 1-Iodohept-2-yne and Nickel Carbonyl.—1-Iodohept-2-yne (33·1 g.)[13] was added during 30 min. to a stirred mixture of ethanol (90 c.c.), acetic acid (18 g.), sodium acetate (24 g.), water (5 c.c.), and nickel carbonyl (20 c.c.) at 40°. No exothermal reaction ensued. Isolation of the acid fraction, after removal of excess of nickel carbonyl, gave an oil which partly crystallised on addition of light petroleum (b. p. 40—60°). Filtration and recrystallisation from light petroleum (b. p. 60—80°) gave the acid (I) (2·8 g., 14·5%), m. p. 102—105°. Evaporation of the mother-liquors followed by recrystallisation from light petroleum (b. p. 40—60°) afforded 2-butylbuta-2 : 3-dienoic acid, m. p. 66—68° (0·97 g., 5%). Distillation of the neutral fraction gave ethyl 2-butylbuta-2 : 3-dienoate (4·6 g., 17%), b. p. 89°/14 mm., n_D^{17} 1·4589.

Methyl Ester of the Acid (I).—The acid (1 g.) in ether (10 c.c.) was treated with ethereal diazomethane until evolution of nitrogen ceased and a yellow colour persisted. After being washed with sodium carbonate solution to remove unchanged acid (120 mg. recovered) the solution was dried and distilled, yielding the *methyl ester* (0·72 g., 78%), b. p. 180° (bath)/0·01 mm., n_D^{18} 1·5152 (Found: C, 72·55; H, 9·05. $C_{17}H_{26}O_3$ requires C, 73·35; H, 9·4%). The 2 : 4-*dinitrophenylhydrazone* crystallised in bright red needles from ethyl acetate–ethanol and had m. p. 136—137° (Found: C, 60·3; H, 6·35; N, 12·4. $C_{23}H_{30}O_6N_4$ requires C, 60·25; H, 6·6; N, 12·2%).

Hydrogenation of Acid (I).—The acid (364 mg.) was hydrogenated in " AnalaR " ethyl acetate (25 c.c.) with platinic oxide (100 mg.) (uptake 0·95 mol.). After filtration, evaporation, and crystallisation from light petroleum (b. p. 40—60°) 2-*butyl*-4-1′-*carboxypentyl*-3-*methyl*-cyclo*pent*-2-*enone* was obtained as prisms (270 mg., 74%), m. p. 83—85° (Found: C, 72·5; H, 9·7. $C_{16}H_{26}O_3$ requires C, 72·2; H, 9·85%). This dihydro-acid (390 mg.) with diazomethane gave a *methyl ester* (290 mg., 71%, b. p. 180° (bath)/0·1 mm., n_D^{18} 1·4787 (Found: C, 73·0; H, 10·0. $C_{17}H_{28}O_3$ requires C, 72·8; H, 10·05%), whose 2 : 4-*dinitrophenylhydrazone* crystallised as red needles (from ethyl acetate–ethanol), m. p. 115—116° (Found: C, 60·0; H, 7·3, N, 12·3. $C_{23}H_{32}O_6N_4$ requires C, 60·0; H, 7·00; N, 12·15%),

Zinc Dust–Acetic Acid Reduction of the Acid (I).—A solution of the acid (500 mg.) in acetic acid (20 c.c.) was heated under reflux and zinc dust (5 g.) was added in portions during 1 hr. After cooling, water was added and the solution was extracted with ether. Evaporation of the dried extract gave an oil which slowly solidified and crystallised from light petroleum (b. p. 40—60°) to give the dihydro-acid (290 mg., 58%), m. p. and mixed m. p. 85—86°.

Complete Hydrogenation of Acid (I).—The acid (337 mg.) was hydrogenated in acetic acid (20 c.c.) over platinic oxide (200 mg.) (uptake 2·94 mols.). Filtration, evaporation, and distillation gave a liquid, b. p. 180° (bath)/0·01 mm., n_D^{18} 1·4665 (Found: C, 74·55; H, 11·2. Calc. for $C_{16}H_{30}O_3$: C, 71·05; H, 11·2%. Calc. for $C_{16}H_{28}O_2$: C, 76·15; H, 11·2%), evidently a mixture of hydroxy-acid and lactone.

Ozonolysis of the Acid (I).—A slow stream of ozonised oxygen was passed through a solution of the acid (516 mg.) in ethyl acetate (20 c.c.) for 2 hr. at 18°. After evaporation of the solvent and decomposition of the ozonide by zinc dust (2 g.) and warm water, the neutral and the acid fraction were isolated with ether. Evaporation of the former left a negligible residue which did not react with 2 : 4-dinitrophenylhydrazine reagent, while the latter yielded *n*-valeric acid (120 mg.), identified as the amide, m. p. (after three recrystallisations from benzene) and mixed m. p. 104—105°

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[12] Eglinton and Whiting, *J.*, 1950, 3650.

[13] Toussaint and Wenzke, *J. Amer. Chem. Soc.*, 1935, **57**, 669.

2 : 3-*Dichlorobutan*-1-*ol*.—Chlorine (114 g.) in carbon tetrachloride (100 c.c.) was added to a stirred and cooled solution of but-2-en-1-ol (114 g.), at −40° to −50°. The mixture was allowed to warm to room temperature and the solvent was evaporated. Distillation of the residual oil gave 2 : 3-*dichlorobutan*-1-*ol* (94 g., 41%), b. p. 62°/5 mm. n_D^{19} 1·4783 (Found: C, 33·55; H, 5·70. $C_4H_8OCl_2$ requires C, 33·60; H, 5·65%). A considerable quantity of heterogeneous high-boiling material remained.

But-2-*yn*-1-*ol*.—(a) *From* 2 : 3-*dichlorobutan*-1-*ol*. 2 : 3-Dichlorobutan-1-ol (94 g.) was added dropwise to a solution of sodamide (from sodium, 55 g.) in liquid ammonia (800 c.c.) during 2 hr. After 12 hours' stirring the complex was decomposed with ammonium chloride (128 g.), ether (600 c.c.) was added, and the mixture was set aside until the ammonia had evaporated. Evaporation of the dried ethereal solution followed by distillation gave but-2-yn-1-ol (23 g., 49%), b. p. 45°/16 mm., n_D^{20} 1·4542.

(b) *From* 3-*chlorobut*-2-*en*-1-*ol*. 3-Chlorobut-2-en-1-ol (134 g.) was added during 30 min. to a suspension of sodamide (from sodium, 65 g.) in liquid ammonia (3 l.). The mixture was stirred overnight, then ammonium chloride (148 g.) was added in portions at a rate that permitted control of the reaction. The ammonia was allowed to evaporate and the residue was extracted thoroughly with ether (5 × 250 c.c.). The ether was removed through a 20 cm. Fenske column; distillation of the residue yielded 66—75 g. (75—85%) of but-2-yn-1-ol, b. p. 55°/18 mm., n_D^{20} 1·4550.

1-*Iodobut*-2-*yne*.—1-Chlorobut-2-yne [14] (5·3 g.) was stirred and heated under reflux with sodium iodide (10 g.) in acetone (100 c.c.) for 15 hr. After filtration of the sodium chloride and washing with ether the filtrate was distilled to a small bulk to remove most of the acetone. The sodium chloride was dissolved in water; ether-extracts of the solution together with the residue from the above distillation were washed with sodium thiosulphate solution, dried, and evaporated through a short Fenske column. Distillation of the residue gave the iodide (6·7 g., 63%), b. p. 51—52°/16 mm., n_D^{18} 1·5859, with the expected very simple infrared spectrum.

1-*Bromobut*-2-*yne*.—But-2-yn-1-ol (100 g.) in dry ether (80 c.c.) and pyridine (1 c.c.) were treated with phosphorus tribromide (140 g.) in ether (53 c.c.) at such a rate as to maintain gentle boiling. After being heated under reflux for a further 2 hr. the solution was cooled and the colourless ether layer was removed and washed with potassium hydrogen carbonate solution (50 c.c.), then water (50 c.c.). Evaporation of the ether and distillation gave the *bromide* (105 g., 55%), b. p. 82°/136 mm., n_D^{21} 1·5113 (Found: C, 36·4; H, 4·0. C_4H_5Br requires C, 36·1; H, 3·8%).

Reaction between 1-*Iodobut*-2-*yne and Nickel Carbonyl*.—1-Iodobut-2-yne (10 g.) was added to a stirred mixture of ethanol (23·5 c.c.), acetic acid (4·8 g.), sodium acetate (6·4 g.), water (1 c.c.), and nickel carbonyl (6·4 c.c.) at 45° during 20 min. No exothermal reaction ensued so the reaction mixture was kept at 40° for a further 30 min. After cooling and removal of excess nickel carbonyl by co-distillation with ether (100 c.c.), the residue was treated with 5% sulphuric acid (100 c.c.), extracted with ether, and separated into acid and neutral fractions. The acid fraction was isolated as brown crystals. 4-1′-*Carboxyethylidene*-2 : 3-*dimethyl*cyclo*pent*-2-*enone* (VI) which remained after extraction with light petroleum (b. p. 40—60°) recrystallised from ether (100 mg., 1%) and had m. p. 199° (Found: C, 66·35; H, 6·65. $C_{10}H_{12}O_3$ requires C, 66·65; H, 6·7%). Light absorption: max. at 2040 and 2940 Å (ε 8000 and 15,000 respectively). Evaporation of the light petroleum extracts followed by recrystallisation from light petroleum (b. p. 40—60°) gave dimethylmaleic anhydride as plates (1 g., 14%), m. p. 94·5° (Found: C, 57·15; H, 4·8. Calc. for $C_6H_6O_3$: C, 57·15; H, 4·75%).

Reaction between 1-*Bromobut*-2-*yne and Nickel Carbonyl*.—Nickel carbonyl (38·5 c.c.) was added to a stirred mixture of 1-bromobut-2-yne (50 g.), ethanol (85 c.c.), acetic acid (33 g.), sodium acetate (40·7 g.), and water (3 c.c.) at 45°. No exothermal reaction ensued, but on working up a solid acid fraction was obtained. Trituration with warm light petroleum (b. p. 40—60°) followed by filtration and crystallisation of the undissolved solid from ether gave the acid (VI) (1·2 g., 5%), m. p. 199°. Evaporation of the filtrate and recrystallisation of the residue from light petroleum (b. p. 40—60°) yielded dimethylmaleic anhydride (1·3 g., 3%), m. p. 94·5°.

Reaction between 1-*Chlorobut*-2-*yne and Nickel Carbonyl*.—Nickel carbonyl (19 c.c.) was added to a stirred mixture of 1-chlorobut-2-yne (30 g.), ethanol (70 c.c.), acetic acid (21 g.), sodium acetate (28 g.), and water (3 c.c.) at 45°. No exothermal reaction ensued. Isolation

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[14] Hatch and Chiola, *J. Amer. Chem. Soc.*, 1951, **73**, 360.

of the acid fraction, after removal of the excess of nickel carbonyl in the usual way, gave a light brown solid. Extraction with light petroleum (b. p. 40—60°) and crystallisation of the undissolved solid from ether gave the acid (VI) (300 mg., 2%), m. p. 199°. Evaporation of the mother-liquors followed by recrystallisation of the residue from light petroleum (b. p. 40—60°) afforded 2-*methylbuta*-2 : 3-*dienoic* acid as needles (5 g., 15%), m. p. 70° (Found: C, 61·15; H, 6·05. $C_5H_6O_2$ requires C, 61·2; H, 6·1%).

Hydrogenation of Acid (VI).—The acid (500 mg.) was hydrogenated in ethyl acetate with platinic oxide (uptake 1 mol.). After filtration, evaporation, and crystallisation from benzene containing 10% of light petroleum (b. p. 60—80°), 4-1′-*carboxyethyl*-2 : 3-*dimethyl*cyclo*pent*-2-*enone* (V) was obtained (350 mg., 70%), having m. p. 123—124° (Found: C, 66·15; H, 7·75. $C_{10}H_{14}O_3$ requires C, 65·95; H, 7·75%). Light absorption: max. at 2360 Å (ε 14,000).

Methyl Ester of Acid (V).—Treatment with standardised ethereal diazomethane (1 mol.) and crystallisation from methanol gave the *methyl ester* (65%), m. p. 78° (Found: C, 67·95; H, 7·15. $C_{11}H_{16}O_3$ requires C, 67·3; H, 8·2%).

Determination of the Dissociation Constants.—The acids were dissolved in distilled water and their p*K* values were determined by potentiometric titration with carbonate-free 0·01N-sodium hydroxide, a glass electrode and a Cambridge pH meter at 25° being used.

Ethyl 4-*Oxopentane*-2 : 3-*dicarboxylate* (VII).—Sodium (9 g.) was added to ethyl acetoacetate (42 g.) in dry ethanol (100 c.c.). When reaction had ceased, ethyl α-bromopropionate (63 g.) was added and the mixture was heated under reflux for 12 hr., cooled, poured into water, and extracted with ether. Evaporation, and distillation of the residue, yielding the ester (38 g.), b. p. 83·5°/0·05 mm., n_D^{20} 1·4340 (Found: C, 57·20; H, 7·65. Calc. for $C_{11}H_{18}O_5$: C, 57·40; H, 7·80%).

1-*Chlorobutan*-2-*one.*—Potassium hydroxide (72 g.) was dissolved in hot propan-1-ol (275 c.c.) in a 3-l. three-necked flask. Two dropping funnels and a Fenske column were fitted and the column was connected through a condenser and adaptor to a 3-l. filter-flask fitted with a calcium chloride drying tube and cooled in ice. The contents of the flask were cooled and dry ether (600 c.c.) was added. Methyl *N*-nitrosourethane (120 c.c.) and dry ether were slowly added from the two funnels, and when the flask was warmed ether and diazomethane co-distilled, the quantity of ether in the flask being kept constant. When the condensed liquid became colourless, the distillate was transferred to a 3-l. three-necked flask equipped with mechanical stirrer, dropping funnel, and condenser. Propionyl chloride (27·6 g.) in dry ether (50 c.c.) was showly added, nitrogen being evolved. After 2 hr., the diazo-ketone solution was cooled in ice-water and treated with dry hydrogen chloride until effervescence ceased. Water (400 c.c.) was added and the ethereal layer was separated, washed with potassium hydrogen carbonate solution, and dried ($MgSO_4$). The ether was removed through a short Fenske column, and the residue on distillation gave 1-chlorobutan-2-one (25 g., 81%), b. p. 65°/50 mm., n_D^{20} 1·4352.

Ethyl 2 : 5-*Dioxoheptane*-3-*carboxylate* (IX).—Dry ether (100 c.c.) was added to sodium (6·8 g., powdered under boiling xylene). Ethyl acetoacetate (39 g.), diluted with dry ether (50 c.c.), was slowly added while the ether refluxed. The sodio-derivative, after being kept overnight at room temperature, was cooled in a salt–ice bath and 1-chlorobutan-2-one (28·6 g.) in dry ether (50 c.c.) was slowly added. The mixture was stirred for 20 hr. at room temperature and 2 hr. on the steam-bath. The precipitated sodium chloride was dissolved in water (100 c.c.). Isolation of the keto-ester followed by distillation yielded *ethyl* 2 : 5-*dioxoheptane*-3-*carboxylate* (27 g., 54%), b. p. 85°/0·01 mm., n_D^{25} 1·4430 (Found: C, 59·7; H, 7·9. $C_{10}H_{16}O_4$ requires C, 60·0; H, 8·0%).

Reaction between Ethyl 2 : 5-*Dioxoheptane*-3-*carboxylate and Ethyl* α-*Bromopropionate.*—Sodium (2·4 g.) was added to the diketo-ester (17 g.) in dry ethanol (50 c.c.). When the reaction had ceased, ethyl α-bromopropionate (18·5 g.) was added, and the mixture was heated under reflux for 4 hr. Isolation of the neutral fraction with ether and distillation gave three groups of fractions:

(*a*) B. p. *ca.* 65°/0·01 mm., n_D^{17} 1·4659 (3·2 g.). This had $\lambda_{max.}$ 2350 Å (ε 9000) and gave the 2 : 4-*dinitrophenylhydrazone*, m. p. 142°, $\lambda_{max.}$ 3870 Å (ε 31,000), of ethyl 2 : 3-dimethyl-4-oxo*cyclo*pent-2-enecarboxylate (Found: C, 52·75; H, 5·1; N, 15·05. $C_{16}H_{18}O_6N_4$ requires C, 53·0; H, 5·0; N, 15·45%).

(*b*) B. p. *ca.* 95°/0·1 mm., n_D^{17} 1·4575 (3·0 g.), which appeared to be a mixture of the foregoing *cyclo*pentenone with a larger proportion of starting material and had $\lambda_{max.}$ 2380 Å (ε 4100).

(*c*) B. p. 120° (bath temp.)/10^{-4} mm., n_D^{17} 1·4720 (2·8 g.), which had $\lambda_{max.}$ 2390 Å (ε 9000) and appeared to be essentially the desired condensation and cyclisation product, probably with partial loss of the tertiary ethoxycarbonyl grouping.

Fraction (*c*) (1·3 g.) was treated with 10% methanolic sodium hydroxide, giving a syrupy acid (730 mg.) which was dissolved in benzene (25 c.c.). Addition of light petroleum (5 c.c.) precipitated brown polymeric matter which was removed. Further addition of light petroleum precipitated a solid which was recrystallised from benzene–light petroleum, giving the acid (V) (113 mg.), m. p. 124°, undepressed on admixture with a specimen prepared as above.

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