Researches on Acetylenic Compounds. Part XLVIII. The Prototropic Rearrangements of Some Diacetylenic Dicarboxylic Acids.*

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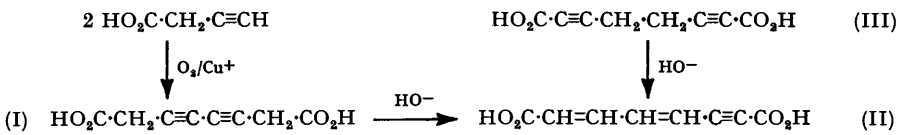
Studies on prototropic isomerisation have been extended to diacetylenic dicarboxylic acids, from which conjugated dienyne- and tetraene-dicarboxylic acids are obtained.

The preceding paper describes the rearrangements observed when acetylenic dicarboxylic acids are heated in alkaline solutions, a frequent result being the formation of conjugated diene systems. The scope and limitations of this reaction with analogous diacetylenic acids have now been investigated.

Oxidation of octa-3 : 5-diyne-1 : 8-diol with chromic acid gave an acidic product from which it proved impracticable to separate the pure acid (I). Oxidative coupling of but-3-ynoic acid at 35° gave a heterogeneous product, but at 10° an excellent yield of the acid (I) was obtained. Alternatively ethyl but-3-ynoate was coupled to give the ester of (I) in good yield.

The acid (I) rearranged to an isomeric acid (II) in 10% potassium hydroxide solution at 55°. Spectroscopic measurements suggested that the yield was about 60%, but the product was both heterogeneous and unstable, and only 15% of a pure acid, presumably



the *trans-trans*-isomer, could be isolated on crystallisation. It decomposed without melting, but gave a methyl ester, m. p. 114—115°. Alternatively the crude isomerisation product was esterified, giving a complex mixture from which two esters, m. p.s 114—115° and 56—57°, were isolated in low yield by chromatography and fractional crystallisation. From infra-red data these were clearly stereoisomers, and there were indications that the other possible stereoisomers of (II) were present in the crude rearrangement product.

* Part XLVII, preceding paper.

Complete hydrogenation of the rearranged acid gave suberic acid. Of the possible structures (II—VI), (III), (IV), and (V) fail to explain the strong light-absorption band at 2920 Å shown by the rearranged acid ($\varepsilon = 30{,}500$ and 17,500 for the pure material and the crude mixture of stereoisomers, respectively), while the absence of absorption in the infra-red at *ca.* 1970 cm.$^{-1}$ eliminates the allenic structures (IV) and (V). The intense bands near 2195 and 2220 cm.$^{-1}$ shown by the acid and both esters strongly support structure (II) rather than (VI), since the symmetrical environment of the triple bond in

(IV) $HO_2C{\cdot}CH{=}C{=}CH{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CO_2H$ $\qquad$ $HO_2C{\cdot}CH{=}C{=}CH{\cdot}CH{=}C{=}CH{\cdot}CO_2H$ (V)

$HO_2C{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CO_2H$ (VI)

(VI) should lead to an infra-red inactive stretching frequency as in acetylenedicarboxylic acid. An attempt was made to prove structure (II) by indirect hydration; the dimethyl ester was treated with diethylamine, and the adduct (cf. Ruhemann *et al.*, *J.*, 1898, **73**, 723) was hydrolysed with dilute mineral acid (Moureu and Lazennac, *Bull. Soc. chim.*, 1906, **35**, 1190), giving the crystalline hydration product in 50% overall yield. It appeared from its ultra-violet absorption spectrum to exist entirely in the enolic form (VII), and on treatment with concentrated alkali it hydrolysed only to the corresponding acid, instead of undergoing the desired ketonic or acidic fission. As an alternative, the acid (II) was treated with mercuric sulphate and sulphuric acid; hydration was then accompanied by decarboxylation. The resultant keto-acid, (VIII), was smoothly degraded by hypoiodite to iodoform and *trans-trans*-muconic acid, which could only have been derived, ultimately, from (II).

$$MeO_2C{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}CO_2Me \xrightarrow[HCl]{NHEt_2;} MeO_2C{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}C(OH){=}CH{\cdot}CO_2Me \quad \text{(VII)}$$

$$HO_2C{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}CO_2H \xrightarrow{Hg^{++}/H_2SO_4} HO_2C{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}CO{\cdot}CH_3 \quad \text{(VIII)}$$

The acid (III) (Lespieau, *Ann. Chim.*, 1912, **27**, 137), when treated with 12% potassium hydroxide solution at 65°, similarly gave a solution showing intense absorption at 2920 Å. Isolation of the acidic product gave again apparently a mixture of stereoisomers of (II), although in this case only the methyl ester, m. p. 114—114·5°, could be isolated; the spectroscopic yield of acid was again about 60%, and 25% of the *trans-trans*-isomer could be obtained by recrystallisation. Preparatively this is the best route to (II).

Under comparable conditions both diacetylenic acids (I and III) underwent rearrangement according to a first-order law, the rate constant for (I) being about seven times larger than that for (III). In the second case the sequence of events is fairly obvious; the reaction rate observed is comparable with that of the transformation of pent-2-ynoic into penta-2 : 3-dienoic acid (*J.*, 1954, 3201), and probably corresponds to the slow formation of octa-2 : 3-dien-5-ynedioic acid, which would then more rapidly isomerise to (II), *i.e.* :

$$^-O_2C{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CO_2^- \rightleftharpoons {}^-O_2C{\cdot}CH{=}C{=}CH{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CO_2^-$$

$$\downarrow$$

$$^-O_2C{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}CO_2^-$$

The isomerisation of octa-3 : 5-diyndioic acid (I) must be more complex, however, and attempts were made to detect intermediate products. When it was treated with 10% sodium carbonate solution no alteration in the ultra-violet absorption spectrum was observed at room temperature, but at 62° changes occurred which are illustrated in the Figure. Clearly the slow formation of (II) is preceded by the fairly rapid formation, to equilibrium, of a substance with $\lambda_{max.}$ 2190 Å. The acidic product when isolated at this stage contained much starting material, but the non-crystalline material from the mother-liquors showed

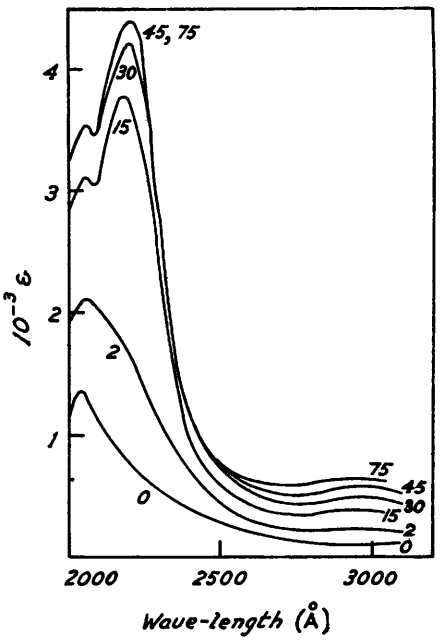
intense absorption at 1970 cm.$^{-1}$ in the infra-red, characteristic of an allenic grouping. This substance must be either (IV) or (V):

$$^{-}O_2C\cdot CH_2\cdot C{\equiv}C\cdot C{\equiv}C\cdot CH_2\cdot CO_2^{-} \overset{(i)}{\rightleftharpoons} {}^{-}O_2C\cdot CH{=}C{=}CH\cdot C{\equiv}C\cdot \dot{C}H_2\cdot CO_2^{-}$$

$$\Big\updownarrow (ii)$$

$$^{-}O_2C\cdot CH{=}CH\cdot CH{=}CH\cdot C{\equiv}C\cdot CO_2^{-} \overset{(iii)}{\longleftarrow} {}^{-}O_2C\cdot CH{=}C{=}CH\cdot CH{=}C{=}CH\cdot CO_2^{-}$$

By analogy with simpler systems (preceding papers and unpublished work) it would be expected that reaction (ii) would be somewhat, but not greatly, slower than (i), with (iii) slower still; also that the anion of (V) would predominate over that of (IV) at equilibrium. The equilibrium between these anions and that of (I), however, might well favour the latter, in which the presumably strong interaction of two conjugated acetylenic linkages is possible—a factor not involved in the related equilibria involving but-3-ynoic and buta-2 : 3-dienoic anions. If the light absorption at 2190 Å is attributed essentially to (V), for which the predicted spectrum would be a composite of butadiene and (acrylic acid × 2), but rather more intense (Celmer and Solomons, *J. Amer. Chem. Soc.*, 1953, **75**, 1372, and unpublished work from these laboratories), we may assume $\varepsilon = 50{,}000$, approximately, and deduce that at equilibrium about 10% of the anion of (V) is present, together with a smaller amount of the anion of (IV), the remainder being the diacetylenic isomer.



Figures indicate timei n minutes.

Preliminary experiments with the dimethyl ester of (I) and 1% aqueous potassium carbonate or 1% triethylamine in aqueous dioxan revealed a similar but less favourable situation. The formation of an initial absorption band at *ca.* 2200 Å was followed by a rapid increase in optical density at 2500—3100 Å and obvious darkening. When the reaction was interrupted, products showing intense infra-red absorption bands at 1960 cm.$^{-1}$ indicated the presence of allenes.

The diacetylenic acid (IX) was prepared by oxidative coupling of pent-4-ynoic acid (Eglinton and Whiting, *J.*, 1953, 3052). In boiling 10% potassium hydroxide it gave a 20% yield (spectroscopic) of deca-2 : 4 : 6 : 8-tetraenedioic acid (X); this is an attractive preparative method, of added interest since this acid is a component of the antibiotic fumagillin (Shenck, Hargie, Tarbell, and Hoffman, *J. Amer. Chem. Soc.*, 1953, **75**, 2274). As an alternative route, the acid (XI) was prepared by carboxylation of octa-1 : 7-diyne. Isomerisation under varied conditions failed to reveal the unmistakable spectrum of (X) but a sparingly soluble acid, clearly (XII), was obtained in small yield. No other compounds could be isolated from the experiments with either (IX) or (XI), indicating the relative importance of addition of HO^{-}, followed by fission, in these cases; both $-C{\equiv}C-C{\equiv}C-$ and $-C{\equiv}C-CO_2^{-}$ systems are known to undergo addition reactions with, for

$$\text{(IX)}\quad HO_2C\cdot CH_2\cdot CH_2\cdot C{\equiv}C\cdot C{\equiv}C\cdot CH_2\cdot CH_2\cdot CO_2H \longrightarrow HO_2C\cdot[CH{=}CH]_4\cdot CO_2H\quad \text{(X)}$$

$$\underset{\text{(XI)}}{HO_2C\cdot C{\equiv}C\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot C{\equiv}C\cdot CO_2H} \longrightarrow \underset{\text{(XII)}}{HO_2C\cdot CH_2\cdot C{\equiv}C\cdot CH_2\cdot CH_2\cdot C{\equiv}C\cdot CH_2\cdot CO_2H}$$

example, EtO^{-} with relative ease. Thus the presence of αβ- (or βγ-) acetylenic linkages in particular is undesirable if a prototropic rearrangement leading to a polyene-acid is required.

Ultra-violet light-absorption data are summarised below (λ are recorded in Å) :

Substance	$\lambda_{max.}$	$10^{-3}\varepsilon$	$\lambda_{max.}$	$10^{-3}\varepsilon$	$\lambda_{max.}$	$10^{-3}\varepsilon$	λ_{max}	$10^{-3}\varepsilon$
I	2080	1·3	2300 *	0·62	2400	0·54	2540	0·32
I; Me ester	2150	1·7	—	—	2400	0·72	2540	0·32
I; Et ester	2150	2·0	—	—	2400	0·72	2540	0·40
IX	—	—	2250	0·47	2380	0·42	2530	0·25
IX; Me ester	—	—	2250	0·45	2390	0·36	2530	0·21
III	2060	11·7						
III; Me ester	2070	12·4						
XI	2070	13·0						
XI; Me ester	2080	12·7						
II	—	—	—	—	2920	30·5		
II; Me ester [a]	2100	6·1	—	—	2920	37·5	3040 *	29
II; Me ester [b]	2100	7·0	—	—	2930	30	3060 *	23
VII	2320	3·4	3380	39·5				
VII; in NaOH	2630	6·0	4160	35				
VIII	2720	23						
VIII [c]	2620	16·3	3020	12·3	3915	38		

* Inflexion. [a] M. p. 115°. [b] M. p. 57°. [c] Methyl ester 2 : 4-dinitrophenylhydrazone.

The diacetylenic acid (I) and its esters show appreciable interaction between the methoxycarbonyl groupings and the unsaturated system, resulting in the appearance of a new maximum near 2100 Å, but not in the hyperchromic and bathochromic displacements characteristic of hyperconjugative auxochromes like hydroxyl or chloro (cf. Armitage and Whiting, *J.*, 1952, 2005). Data for the methyl ester of (X) are included in the next paper; infra-red spectra are summarised below, except for those of the stereoisomeric esters of (II), for which extensive comparisons with model compounds are required to establish the configurations of the ethylenic linkages.

Experimental

Melting-points were determined on the Kofler block. Ultra-violet spectra were obtained with a Unicam SP500 Spectrophotometer known to give results little affected by scattered light even at 2000—2150 Å when appropriate precautions were taken, low optical densities and 1-mm. cells being used as a matter of routine in this region. Infra-red spectra were recorded with a Perkin-Elmer Model 21 Spectrophotometer. " Light petroleum " refers to the fraction, b. p. 40—60°, unless otherwise stated.

Octa-3 : 5-diynedioic Acid (I).—But-3-ynoic acid (2·1 g.), ammonium chloride (10 g.), cuprous chloride (6 g.), and water (30 c.c.) were shaken in oxygen until absorption was complete; external cooling to *ca.* 10° was necessary to prevent darkening and a reduction in yield. 3N-Hydrochloric acid was added to dissolve copper salts, and the suspension was extracted continuously with ether. Evaporation gave the essentially pure *acid* in quantitative yield; crystallisation from water gave plates, m. p. 210° (decomp.) (Found : C, 57·6; H, 3·7. $C_8H_6O_4$ requires C, 57·85; H, 3·65%). Hydrogenation over platinum (uptake 3·8 mols.) gave suberic acid in 80% yield. The *methyl* ester was obtained by treating the diacetylenic acid with 5% sulphuric acid in methanol for 14 days at 18°; it had b. p. 130°(bath temp.)/1 mm., m. p. 53° (Found : C, 62·0; H, 5·3. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·2%).

Diethyl Octa-3 : 5-diynedioate.—This *ester* was obtained in 63% yield by oxidative coupling of ethyl but-3-ynoate, or in 80% yield from the diacid, as long needles, m. p. 60°, from aqueous ethanol (Found : C, 64·8; H, 6·25. $C_{12}H_{14}O_4$ requires C, 64·85; H, 6·35%).

Isomerisation of Octa-3 : 5-diynedioic Acid (I).—A solution of the acid (2·00 g.) in potassium hydroxide solution (10%; 60 c.c.) was heated to 55° for 1 hr., the intensity of absorption at 2920 Å having then become constant. Cooling and acidification gave a precipitate (1·51 g.) (Found : equiv., 93·0. $C_8H_6O_4$ requires equiv., 83·0), $\varepsilon_{max.}$ at 2910 Å = 17,500. Continuous extraction of the filtrate with ether gave a syrup (0·35 g.) without significant absorption in the ultra-violet.

The crude *acid* (1·26 g.) was treated with the theoretical quantity of diazomethane in ether. When the colour had disappeared, an acidic fraction (260 mg.; $\lambda_{max.}$ 2900 Å, ε = 10,700) and a neutral fraction (967 mg.) were separated. Chromatography on deactivated alumina from benzene gave (*a*) 216 mg. of esters, m. p. 23—45°, $\lambda_{max.}$ 2930, ε = 25,600, (*b*) 341 mg. of higher-melting and more intensely-absorbing fractions, and (*c*) gummy material eluted with chloroform. Fractions (*a*) and (*b*) still behaved as mixtures of closely-similar substances, but by further

chromatography followed by two crystallisations from light petroleum fraction (*a*) yielded *dimethyl octa*-trans-2 : cis-4-*dien*-6-*ynedioate* (42 mg.) as plates, m. p. 56—57° (Found : C, 61·85; H, 5·15. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·2%). Fraction (*b*) gave the ester, m. p. 114—115°, described below, in small yield on similar treatment.

In a similar experiment the crude acid (4·0 g.) was crystallised from water, the only satisfactory solvent, giving *octa*-trans-2 : trans-4-*dien*-6-*ynedioic acid* (II) (0·81 g.) as microscopic plates which decomposed above 150° without melting (Found : C, 57·6; H, 3·7. $C_8H_6O_4$ requires C, 57·85; H, 3·65%). This recovery varied little in several experiments; no homogeneous product could be isolated from the mother-liquors. Hydrogenation (uptake 3·85 mols.) gave suberic acid in almost quantitative yield. The *dimethyl* ester was obtained in 45% yield from the recrystallised acid, separating in prisms, m. p. 114—115°, from 10% sulphuric acid in methanol during 14 days at room temperature (Found : C, 62·1; H, 5·4. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·2%).

Isomerisation of Octa-2 : 6-*diynedioic Acid*.—This acid (2·0 g.), potassium hydroxide (6·0 g.), and water (50 c.c.) were heated to 65° for 1·5 hr. Acidification and isolation with ether gave a crude product (1·8 g.) which was crystallised from water, giving octa-2 : 4-dien-6-ynedioic acid (0·50 g.); this had ultra-violet light-absorption properties identical with those of the acid obtained as above. Esterification gave the same methyl ester, m. p. 114—115°.

Dimethyl 3-*Hydroxyocta*-2 : 4 : 6-*trienedioate* (VII).—Dimethyl octa-2 : 4-dien-6-ynedioate, m. p. 114—115° (170 mg.), chloroform (4 c.c.), and diethylamine (0·2 c.c.) were set aside for 16 hr. Evaporation of the solvent below 20° gave an oil which was shaken with 5% hydrochloric acid (10 c.c.) for 40 min. Isolation with ether and crystallisation from aqueous ethanol gave the *hydroxy*-ester (92 mg.), m. p. 126·5—128° (Found : C, 56·7; H, 5·75. $C_{10}H_{12}O_5$ requires C, 56·6; H, 5·7%); its infra-red spectrum in carbon tetrachloride included bands at 3465 (O–H), 1720, 1705 (C=O), and 1612 cm.$^{-1}$ (C=C).

6-*Oxohepta*-2 : 4-*dienoic Acid*.—Octa-2 : 4-dien-6-ynedioic acid (320 mg.), mercuric sulphate (*ca.* 10 mg.), and sulphuric acid (2·5N; 25 c.c.) were heated to 95° for 10 min. Isolation of the acidic fraction with ether gave a solid which was extracted with hot benzene; evaporation of this solution and crystallisation gave the *keto-acid* (177 mg.) as needles, m. p. 140—142° (Found : C, 59·85; H, 5·8. $C_7H_8O_3$ requires C, 60·0; H, 5·75%). The 2 : 4-*dinitrophenylhydrazone* of the methyl ester formed scarlet needles, m. p. 214—218° (Found : C, 50·7; H, 4·35; N, 16·5. $C_{14}H_{14}O_6N_4$ requires C, 50·3; H, 4·2; N, 16·75%).

Muconic Acid.—The keto-acid (95 mg.), sodium hydroxide solution (5%; 4 c.c.), and potassium iodide (700 mg.) were treated with 12% sodium hypochlorite solution at 20° until precipitation of iodoform (170 mg., 66%) ceased. Acidification gave *trans-trans*-muconic acid (39 mg., 40%), m. p. *ca.* 300°, $\lambda_{max.}$ 2610 Å, ε = 25,000. Esterification gave the dimethyl ester, m. p. and mixed m. p. 157—158°.

Deca-4 : 6-*diynedioic Acid* (IX).—Pent-4-ynoic acid (2·5 g.), cuprous chloride (6·0 g.), ammonium chloride (10 g.), and water (33 c.c.) were shaken in oxygen until uptake was complete. Addition of 5N-hydrochloric acid dissolved the copper salts, and filtration gave the insoluble diacetylenic *acid*, which separated from hot water as microscopic needles which decomposed without melting above 220° (yield 1·65 g.) (Found : C, 61·65; H, 5·3. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·2%). Hydrogenation (uptake 4·15 equiv.) gave sebacic acid, m. p. and mixed m. p. 132·5—133°, in quantitative yield. The dimethyl ester was obtained at 20° with 9% methanolic sulphuric acid for 14 days (yield 63%); it formed leaflets, m. p. 36° (Found : C, 64·85; H, 6·55. Calc. for $C_{12}H_{14}O_4$: C, 64·85; H, 6·35%). Christiansen and Sorensen (*Acta Chem. Scand.*, 1952, **6**, 893) give m. p. 37·5°, but their specimen, from published ultra-violet data, must have contained a more highly unsaturated impurity.

Dimethyl Deca-2 : 4 : 6 : 8-*tetraenedioate* (*Diester of* X).—The above acid (600 mg.) was heated in potassium hydroxide solution (10%; 20 c.c.) under reflux for 3 hr. Acidification gave the rearranged acid which was separated by centrifugation (320 mg.); it could not easily be purified, and was therefore heated with thionyl chloride (5·5 c.c.) for 1 hr. Removal of excess of reagent gave the crystalline dichloride which was treated with methanol. After sublimation at 150°/0·02 mm. and crystallisation from *cyclo*hexanol the ester (110 mg.) had m. p. 209—212° (Kuhn and Grundmann, *Ber.*, 1936, **69**, 1757, give m. p. 212°) (Found : C, 64·7; H, 6·4. Calc. for $C_{12}H_{14}O_4$: C, 64·85; H, 6·35%).

Deca-2 : 8-*diynedioic Acid* (XI).—A solution of ethylmagnesium bromide, prepared in ether from magnesium (2·64 g.), was treated with octa-1 : 7-diyne (5·3 g.), and the mixture was heated under reflux for 1·5 hr. The suspension of the Grignard complex was transferred to a 250-c.c. autoclave containing solid carbon dioxide (*ca.* 100 g.). After 18 hr. excess of carbon dioxide

was released, sulphuric acid was added, and the solution was extracted continuously with ether. Evaporation of the dried extract and crystallisation of the residue from nitromethane gave the *acid* (6·2 g., 67%) as plates, m. p. 159—161° (Found: C, 61·95; H, 5·3. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·2%). Its infra-red spectrum included an intense band at 2236 cm.$^{-1}$ (–C≡C–, conjugated). Hydrogenation (uptake 4·2 equiv.) gave sebacic acid, m. p. and mixed m. p. 133°. The *methyl* ester, prepared with methanolic sulphuric acid at room temperature, formed needles, m. p. 35·5—36·5°, from light petroleum (b. p. 30—40°) (Found: C, 65·0; H, 6·45. $C_{12}H_{14}O_4$ requires C, 64·85; H, 6·35%).

Deca-3 : 7-*diynedioic Acid* (XII).—The above acid (500 mg.) and potassium hydroxide solution (15%; 20 c.c.) were heated under reflux for 20 min.; isolation of the acidic fraction gave a syrup which was treated with ether, the isomeric *acid* (49 mg.) separating. Crystallisation from nitromethane gave the pure product, m. p. 170—183° (decomp.) (Found: C, 62·0; H, 5·35. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·2%). The *dimethyl* ester was prepared with diazomethane. After sublimation and crystallisation from light petroleum, then twice from aqueous methanol the yield was 54% of needles, m. p. 40·5—41° (Found: C, 65·0; H, 6·35. $C_{12}H_{14}O_4$ requires C, 64·85; H, 6·35%). Both acid and ester showed only weak absorption at *ca.* 2200 cm.$^{-1}$. Neither absorbed intensely in the ultra-violet (cf. deca-2 : 7-diynedioic acid, above), ε being about 850 at 2020 Å in each case and falling steeply at longer wave-lengths.

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