

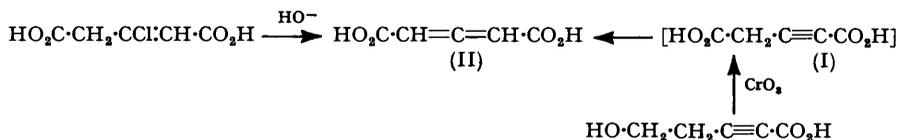
*Researches on Acetylenic Compounds. Part XLVII.\* The Prototropic Rearrangements of Some Acetylenic Dicarboxylic Acids.*

By E. R. H. JONES, G. H. MANSFIELD, and M. C. WHITING.

[Reprint Order No. 5305.]

Prototropic rearrangements of some acetylenic dicarboxylic acids, yielding allenic or conjugated dienic isomers, are described. "Glutinic acid" is shown to have an allenic (II) rather than an acetylenic (I) structure.

THE simplest acetylenic dicarboxylic acid capable of prototropy is "glutinic acid" (I), first described by Burton and Pechmann (*Ber.*, 1887, 20, 148) as the product of the action of potassium hydroxide on  $\beta$ -chloroglutaconic acid. This method was much improved by van der Zanden (*Rec. Trav. chim.*, 1935, 54, 289). The original structure has not, so far as is known, been questioned; nevertheless repetition of van der Zanden's work gave an acid which possessed structure (II) rather than (I), although its properties agreed well with the



literature description. Its ultra-violet absorption spectrum showed intense rising absorption at low wave-lengths, reaching  $\epsilon = 27,200$  at  $2000 \text{ \AA}$ . This is consistent with (II), for which one would predict a spectrum similar to that of acrylic acid ( $\lambda_{\text{max}}$  below  $2000 \text{ \AA}$ , where  $\epsilon = 7500$ ) but with molar extinction coefficients rather more than twice as great (Celmer and Solomons, *J. Amer. Chem. Soc.*, 1953, 75, 1375, and unpublished work from these laboratories). It is quite inconsistent with (I), for which strong resemblance to tetrolic acid ( $\lambda_{\text{max}}$   $2055 \text{ \AA}$ ,  $\epsilon = 6300$ ) would be expected. Infra-red data confirmed this conclusion; the crystalline acid in Nujol suspension showed no absorption in the  $2250\text{-cm.}^{-1}$  region, where all  $\alpha\beta$ -acetylenic acids absorb strongly, but did absorb at  $1970 \text{ cm.}^{-1}$ , just as does buta-2 : 3-dienoic acid. The methyl ester, prepared with diazomethane, showed maxima at  $1970 \text{ cm.}^{-1}$  (allene) and  $1720 \text{ cm.}^{-1}$ , the latter band indicating the presence of only one type of carbonyl group, and consistent in its position with an  $\alpha\beta$ -ethylenic ester system; it was almost transparent near  $2200 \text{ cm.}^{-1}$ .

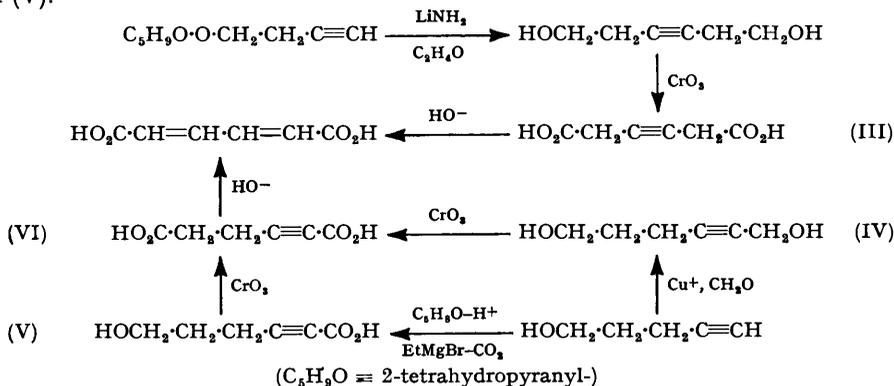
Consideration of the method of synthesis from chloroglutaconic acid suggested that the formation of (II) rather than (I) was to be expected. Kinetically, attack of hydroxyl ion on the doubly-activated protons of the methylene group should certainly predominate; thermodynamically, the equilibrium between (II) and (I) would probably favour the allenic isomer, though here the analogies available are less decisive (see preceding papers). An independent synthesis of (I) was therefore attempted; 5-hydroxypent-2-ynoic acid (Haynes and Jones, *J.*, 1946, 954) was oxidised with chromic acid in acetone, the use of even bicarbonate solution being avoided in the isolation of the product in the hope of preventing isomerisation. The product, obtained in 23% yield, again proved to be (II); thus equilibration of (I) and (II) must take place even in neutral or acidic solutions. Such exceptional mobility is, of course, understandable by analogy with the behaviour of glutaconic acid and its derivatives.

The two acids homologous to (I) were next examined.

One isomer (III) was readily obtained by oxidising the corresponding diprimary glycol (Raphael and Roxburgh, *J.*, 1952, 3875). The other (VI) was formed in the same way from the isomeric glycol (IV) (Paul and Tchelitcheff, *Bull. Soc. chim.*, 1953, 418) in much lower yield, and the alternative route *via* the hydroxy-acid (V) was therefore investigated, with equally mediocre results. In both cases the crude acid (VI) was contaminated with succinic acid, which was on one occasion isolated pure. Eglinton, Jones, and Whiting (*J.*, 1952, 2873) have discussed the abnormally rapid hydration of pent-4-yn-1-ol in acidic solution in

\* Part XLVI, preceding paper.

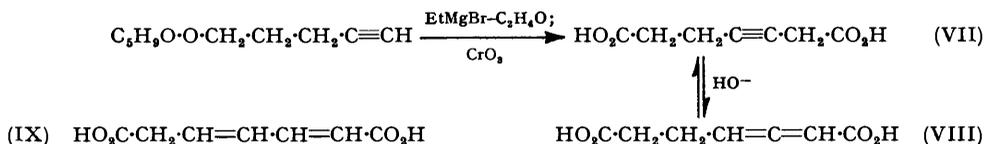
terms of intramolecular nucleophilic attack by the hydroxyl group concerted with addition of a proton at C<sub>(5)</sub>; presumably the hydroxy-acid (V), probably the first product from (IV), could undergo a similarly accelerated hydration reaction, giving a product convertible by further oxidation or hydrolysis into succinic acid. Mr. B. L. Shaw has observed (personal communication) that pent-4-ynoic acid similarly undergoes rapid hydration to lævulic acid, so that (VI) itself probably undergoes hydration during its preparation from (IV) and (V).



The acid (III) rearranged to *trans-trans*-muconic acid in 9% potassium hydroxide solution at 40°; the yield was 44% (spectroscopic) and almost this quantity was isolated. Its isomer (VI) rearranged with greater difficulty (at 103° with the same reagent) and gave only a 23% yield (spectroscopic; 8% isolated). Presumably the hexa-2 : 3-dienedioic acid anion was the intermediate in both cases; the lower yield of muconic acid from (VI) might be due to either (a) a larger temperature coefficient for the rate of the competing hydration reaction than for the prototropic shift, or (b) some direct hydration of the anion of (VI) preceding its rearrangement to the allenic anion.

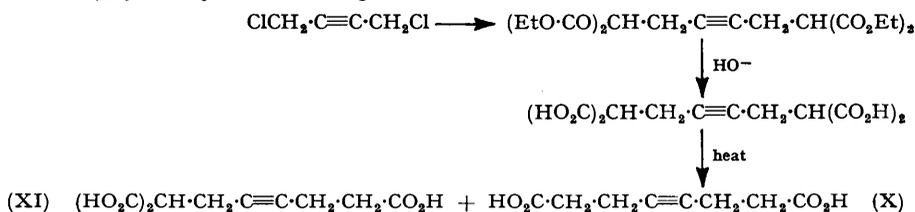
An ester, believed to be that of but-1-yne-1 : 3 : 4-tricarboxylic acid, and so related to (VI), gave muconic acid on vigorous alkaline hydrolysis (E. H. Ingold, *J.*, 1925, 127, 1199). 1 : 4-Dichlorobut-2-yne and cuprous cyanide gave a dinitrile which underwent alkaline hydrolysis with rearrangement to muconic acid (Dr. J. Elvidge, personal communication).

The next acid examined, hept-3-ynedioic acid (VII), was prepared by the obvious route :



It was subjected to alkaline conditions of increasing severity, but no light absorption of appreciable intensity above 2200 Å could be discerned. Isolation of the product of the action of 9% potassium hydroxide solution at 90° and examination of its infra-red absorption spectrum indicated the presence of the allenic acid (VIII); evidently the equilibrium between (VII) and (VIII) is fairly readily established, but (VIII) is further converted into fission products rather than into (IX) or sorbic acid.

Finally the acid (X) was prepared. Johnson (*J.*, 1946, 1011) described the formation of this acid in 7% yield by the following route :



He did not isolate either of the intermediates, the entire non-volatile fraction from the malonic ester condensation being hydrolysed to a syrupy acid which was pyrolysed at 160—180° to give a non-crystalline product. This was esterified, a small quantity of the methyl ester of (X) and a much larger quantity of a higher-boiling product, formulated as the ester of (XI), being obtained. It was stated that (X) was formed only if the scale of the decarboxylation reaction was small.

This scale-variability seemed surprising and the reaction sequence was therefore reinvestigated. The tetracarboxylate was separated by distillation from much non-volatile material, presumably of the type  $[C(CO_2Et)_2 \cdot CH_2 \cdot C \equiv C \cdot CH_2]_n$ . A crystalline tetracarboxylic acid was readily obtained which when carefully purified gave at 160° an almost quantitative yield of pure (X), whatever the scale of the experiment. When the crude tetra-acid, containing a trace of mineral acid as a result of the continuous-extraction process necessary for its isolation, was heated at 160° in nitrogen, the decarboxylation product was non-crystalline and gave, on esterification, a main fraction of much higher boiling point than the ester of (X). This had physical properties approximating to those quoted by Johnson for the ester of (XI), but analytical data were in poor agreement with such a constitution, and it was clearly heterogeneous. Presumably acid-catalysed attack by a carbonyl group on the triple bond, giving initially an enol-lactone (cf. the behaviour of pent-4-ynoic acid mentioned above), is involved; Johnson's evidence, *i.e.*, production of some suberic acid by decarboxylation following hydrogenation under vigorous conditions, is compatible with such a hypothesis.

The acid (X), like its analogue hex-4-ynoic acid, underwent isomerisation only under drastic conditions, indeed it was appreciably less reactive, perhaps because of the additional negative charge on the anion. After 16 hours in a 17% solution of potassium hydroxide in ethylene glycol at 167° it gave a 55% yield of deca-3 : 5-dienedioic acid. This high-melting acid, like (X), was readily characterised as a crystalline dimethyl ester.

#### EXPERIMENTAL

Melting-points were measured on the Kofler block, and ultra-violet and infra-red spectra were normally determined in 95%-alcoholic and carbon tetrachloride solutions, respectively.

*Penta-2 : 3-dienedioic Acid* (II).—A solution of chromic acid (6N in 12N-sulphuric acid; 11 c.c.) was added to a stirred, cooled solution of 5-hydroxypent-2-ynoic acid (1.9 g.; Haynes and Jones, *J.*, 1946, 954) in acetone (50 c.c.) at 20°. After 2 hr. water was added and the mixture was extracted continuously with ether. Evaporation of the dried extract and crystallisation of the residue from ether-light petroleum (b. p. 40—60°) gave the allenic acid (0.5 g.), m. p. 149—150° undepressed on admixture with a specimen prepared by van der Zanden's method (*loc. cit.*). The methyl ester was prepared with diazomethane; it had b. p. 90° (bath temp.)/0.2 mm.,  $n_D^{19}$  1.4853 (Makulec, Malachawski, and Manitus, *Chem. Zentr.*, 1929, 1328, give b. p. 101°/6 mm.,  $n_D^{19}$  1.4878).

*Hex-3-ynedioic Acid* (III).—Chromic acid (as above; 35 c.c.) was added to a stirred, cooled solution of hex-3-yne-1 : 6-diol (3.0 g.) in acetone (100 c.c.) at 20°. After 2 hr. water was added and the product was isolated by continuous extraction with ether. Evaporation and crystallisation of the residue from water gave the acid (1.8 g.), m. p. 174—175° (Found : C, 50.85; H, 4.4.  $C_6H_8O_4$  requires C, 50.7; H, 4.3%). Light absorption : no maximum above 2000 Å, where  $\epsilon = 315$ . The methyl ester, prepared with 2.5% sulphuric acid in methanol at 65°, formed needles, m. p. 64—65° (Found : C, 56.45; H, 5.65.  $C_8H_{10}O_4$  requires C, 56.5; H, 5.9%).

*6-Hydroxyhex-2-ynoic Acid* (V).—5-2'-Tetrahydropyranyloxy-pent-1-yne (21 g.) in benzene (30 c.c.) was added to a solution of ethylmagnesium bromide in benzene, prepared from magnesium (3.3 g.). The mixture was stirred for 1 hr. at 20° and 1 hr. at 50°, cooled, and poured on to a large excess of solid carbon dioxide in a steel autoclave, which was sealed. After 24 hr., release of excess of carbon dioxide, and cautious decomposition with dilute sulphuric acid gave a benzene layer containing the tetrahydropyranyl ether of the desired acid. Evaporation of the solvent and treatment with sulphuric acid (2N; 400 c.c.) for 24 hr., followed by continuous extraction with ether, and evaporation of the extract, gave a solid residue. Crystallisation from ether-light petroleum yielded *6-hydroxyhex-2-ynoic acid* (3.0 g.), m. p. 65—66° (Found : C, 56.4; H, 6.35.  $C_6H_8O_3$  requires C, 56.2; H, 6.3%). Light absorption : maximum, 2070 Å;  $\epsilon = 6100$ . A Nujol mull showed intense infra-red absorption at 2240  $cm^{-1}$  and other expected frequencies.

*Hex-2-ynedioic Acid* (VI).—(a) Chromic acid (as above; 35 c.c.) was added to a stirred, cooled solution of hex-2-yne-1 : 6-diol (3.0 g.; Paul and Tchelitcheff, *Bull. Soc. chim.*, 1953, 418) in acetone (25 c.c.) below 38° during 20 min. The upper layer was evaporated under reduced pressure, and the residue extracted with tetrahydrofuran (3 × 25 c.c.) at 50°, leaving a residue containing chromium. Evaporation of the tetrahydrofuran gave a solid which was purified by crystallisation from ether–light petroleum, yielding the *acid* (0.7 g.), m. p. 139–140° (Found : C, 51.0; H, 4.55. C<sub>6</sub>H<sub>6</sub>O<sub>4</sub> requires C, 50.7; H, 4.3%). Light absorption : maximum, 2060 Å;  $\epsilon = 5300$ . A Nujol mull showed intense absorption at 2250 cm.<sup>-1</sup>.

(b) Similar oxidation of 6-hydroxyhex-2-ynoic acid (2.3 g.) with chromic acid (12 c.c.), and crystallisation of the crude product from nitromethane gave the dicarboxylic acid (0.6 g.), m. p. 139–140°, undepressed on admixture with material prepared as above.

*Rearrangement of the Hexynedioic Acids.*—In trial experiments, a solution of the hexynedioic acid in 9% potassium hydroxide (100 c.c. per g.) was heated to 40° or 103° (under reflux), samples being withdrawn at intervals and added to an excess of sulphuric acid. In this solvent *trans-trans*-muconic acid has  $\lambda_{\max}$ , 2655 Å,  $\epsilon = 30,100$ ; the samples withdrawn were examined in the region 2300 to 2800 Å, where all absorbed maximally at 2655 Å; the muconic acid content could readily be determined.

In preparative experiments the isomerised acid was isolated by continuous extraction with ether. The muconic acid was identified by conversion into the *trans-trans*-dimethyl ester, m. p. and mixed m. p. 157–158°. No attempt was made to isolate any of the *cis-trans*- or the *cis-cis*-isomer, which might also be present, and since these acids absorb less intensely than the *trans-trans*-isomer (Elvidge, Linstead, Sims, and Orkin, *J.*, 1950, 2238) the yields calculated from spectroscopic data are minimal.

*Hept-3-yne-1 : 7-diol.*—5-2'-Tetrahydropyranloxy-pent-1-yne (22.0 g.) in benzene (50 c.c.) was added to a solution of ethylmagnesium bromide in benzene, prepared from magnesium (3.5 g.). The mixture was heated to 40° for 1 hr., then cooled and treated with ethylene oxide (20 c.c.); a very viscous complex then separated, stirring becoming impossible. After 3 hr. at 65° the mixture was cooled and treated with dilute sulphuric acid. The ethereal extract of the aqueous phase was added to the benzene layer, and the solvents were removed, leaving the tetrahydropyranyl ether of the desired glycol as an oil. Treatment with methanolic sulphuric acid (4%; 200 c.c.) for 7 hr. at 20°, followed by neutralisation with sodium methoxide and evaporation of the filtrate, gave a residue containing mineral salts. Extraction with ethyl acetate, evaporation, and distillation gave the *glycol* (8.5 g.), b. p. 102–104°/0.05 mm.,  $n_D^{20}$  1.4870 (Found : C, 65.85; H, 9.0. C<sub>7</sub>H<sub>12</sub>O<sub>2</sub> requires C, 65.6; H, 9.4%). The *bis*-3 : 5-*dinitrobenzoate*, crystallised from benzene, had m. p. 131–132° (Found : N, 10.6. C<sub>21</sub>H<sub>16</sub>O<sub>12</sub>N<sub>4</sub> requires N, 10.8%).

*Hept-3-ynedioic Acid* (VII).—Chromic acid solution (as above; 31 c.c.) was added to a solution of the above glycol (3.05 g.) in acetone (50 c.c.) at 20° during 30 min. After 2 hr., water was added and the solution was extracted continuously with ether. Evaporation of the ether and recrystallisation of the residue from nitromethane gave *hept-3-ynedioic acid* (0.71 g.), m. p. 155–157° (Found : C, 53.85; H, 5.05%; equiv., 77. C<sub>7</sub>H<sub>8</sub>O<sub>4</sub> requires C, 53.8; H, 5.2%; equiv., 78). Light absorption : no maximum above 2000 Å, where  $\epsilon = 290$ .

*Tetraethyl Hex-3-yne-1 : 1 : 6 : 6-tetracarboxylate.*—1 : 4-Dichlorobut-2-yne (50 g.) was condensed with sodiomalonic ester, prepared from diethyl malonate (215 g.) and sodium (25 g.), by Johnson's method (*loc. cit.*), except that the crude product was distilled directly, giving the *tetracarboxylic ester* (70.1 g.), b. p. 146°/0.05 mm.,  $n_D^{20}$  1.4551 (Found : C, 58.65; H, 7.3. C<sub>18</sub>H<sub>26</sub>O<sub>8</sub> requires C, 58.4; H, 7.1%).

*Hex-3-yne-1 : 1 : 6 : 6-tetracarboxylic and -1 : 6-dicarboxylic (Oct-4-ynedioic) Acids.*—The above ester (13 g.) was heated under reflux with potassium hydroxide solution (10%; 100 c.c.) for 16 hr. Acidification, continuous extraction with ether, and evaporation gave a residue (8.8 g.), m. p. 152–158°, which was crystallised from nitromethane to give the pure *tetracarboxylic acid* (7.9 g.), m. p. 163–164° (Found : C, 46.55; H, 4.1; equiv., 64.8. C<sub>10</sub>H<sub>10</sub>O<sub>8</sub> requires C, 46.55; H, 3.9%; equiv., 64.5). Light absorption : no maximum above 2000 Å, where  $\epsilon = 615$ .

The pure tetracarboxylic acid (9.2 g.) was heated to 175° in an atmosphere of nitrogen for 40 min. After the acid had melted and effervesced, the dicarboxylic acid (5.5 g.) solidified and had m. p. 200–206° (Johnson, *loc. cit.*, gives m. p. 208–209°). Light absorption : no maximum above 2000 Å, where  $\epsilon = 320$ . Treatment with methanolic sulphuric acid (80 c.c.; 6%) for 5 days at 20° gave the dimethyl ester (5.9 g.), m. p. 28–30° (Johnson, *loc. cit.*, gives m. p. 30–32°).

The tetracarboxylic ester, in carbon tetrachloride, and the tetracarboxylic and dicarboxylic

acids in Nujol mulls, showed no absorption of appreciable intensity in the region 1600—1650  $\text{cm}^{-1}$ , characteristic of  $\alpha\beta$ -ethylenic acids and esters.

*Octa-2 : 4-dienedioic Acid.*—Oct-4-ynedioic acid (1.5 g.) was heated under reflux with a solution of potassium hydroxide (5 g.) in ethylene glycol (25 c.c.) for 16 hr. Acidification, dilution with water, and continuous extraction with ether, and recrystallisation of the extract from water gave the rearranged *acid* (0.9 g.), m. p. 221—222° (Found : C, 56.7; H, 6.15.  $\text{C}_8\text{H}_{10}\text{O}_4$  requires C, 56.5; H, 5.9%). Light absorption : maximum, 2540 Å;  $\epsilon = 23,700$ . The *dimethyl* ester was prepared with cold methanolic sulphuric acid; after sublimation and recrystallisation from light petroleum at  $-70^\circ$  it had m. p. 37—38° (Found : C, 60.6; H, 7.05.  $\text{C}_{10}\text{H}_{14}\text{O}_4$  requires C, 60.6; H, 7.1%). Light absorption : maximum, 2580 Å;  $\epsilon = 29,400$ . The acid, examined in a Nujol mull, showed intense bands at 1630 and 1610  $\text{cm}^{-1}$ .

The authors thank the Department of Scientific and Industrial Research for a Maintenance grant (to G. H. M.). Microanalyses and infra-red spectroscopic measurements were by Mr. E. S. Morton and Mr. H. Swift, and by Miss W. Peardon and Miss J. Shallcross, respectively.

THE UNIVERSITY, MANCHESTER.

[Received, April 13th, 1954.]

---