SYNTHESIS OF ACIDS IN THE POLYACETYLENIC SERIES

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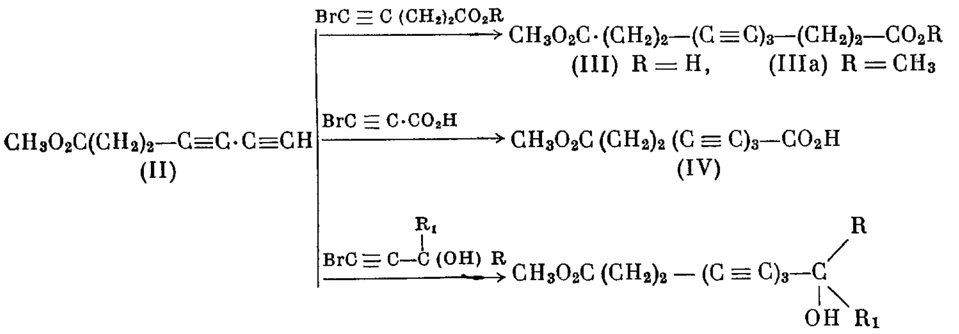
We found a convenient method for the synthesis of the methyl ester of 4,6-heptadienoic acid (II),* based on the alkaline cleavage of the readily available methyl ester of 8-methyldeca-4,6-diyn-8-oloic acid:

$$CH_3O_2C\,(CH_2)_2C \equiv CH + BrC \equiv C \cdot C\,(OH)\,(CH_3)\,C_2H_5 \xrightarrow{Cu_2Cl_2}$$

$$\rightarrow CH_3O_2\,(CH_2)_2\,(C \equiv C)_2\text{—}C\,(OH)\,(CH_3)\,C_2H_5 \qquad (I)$$

$$(I)\ \xrightarrow[140\text{—}150^\circ]{KOH} \underset{(II)}{HC \equiv C \cdot C \equiv C \cdot CH_2CH_2COOCH_3} + C_2H_5COCH_3$$

As is known, the 4,6-heptadiynoic acid fragment is a component part of the molecule in the series of polyacetylenic compounds produced by certain microorganisms [1]. In connection with this it seemed of interest to use compound (II) for the synthesis of a number of tri- and tetraacetylenic compounds, related to the natural products. It was shown that the methyl ester of 4,6-heptadiynoic acid (II), under the conventional oxidative condensation conditions [2], easily reacts with different bromoacetylenes to yield the difficulty available acids of the triacetylenic series:



(V) $R = H$, $R_1 = C_2H_5$, (VI) $R = CH_3$, $R_1 = C_2H_5$; (VII) $RR_1 = \text{—}(CH_2)_5\text{—}$

Thus, the reaction of (II) with 5-bromo-4-pentynoic acid gave, in good yield, the monomethyl ester of dodeca-4,6,8-triyn-1,12-dioic acid (III) as an unstable crystalline product, which changed to an insoluble purple polymer after standing for a short while. This product was also characterized as the diester (IIIa), which was obtained in the reaction with the methyl ester of 5-bromo-4-pentynoic acid. In a similar manner we synthesized from bromopropiolic acid the monomethyl ester of deca-4,6,8-triyn-1,10-dioic acid (IV), the ultraviolet spectrum of which exhibits absorption characteristic for the triacetylenic alcohol isolated from the culture fluid of Merulius lacrymans [1]. Using the bromo derivatives of various acetylenic alcohols as the second components in this reaction, we obtained the esters of several hydroxytriacetylenic acids (V)-(VII). These products proved to be very unstable when chromatographed on aluminum oxide, and only the methyl ester of dodeca-4,6,8-triyn-10-oloic acid (V) was isolated in the crystalline state. We found that the tertiary hydroxy esters (VI) and (VII) could not be isolated in the pure state, and they were characterized only by the ultraviolet spectra.

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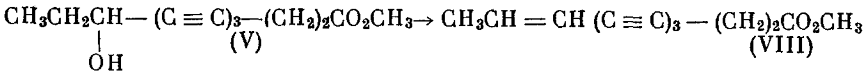
* The method of preparation will be described later.

$R(C \equiv C)_3-CH_2CH_2CO_2CH_3$	M.p., °C (solvent)	Yield, %	Found, %		Calculated, %		λ, mμ (in alcohol)
			C	H	C	H	
R = HO_2C- (IV)	108-109 (with decomp.) (ethyl acetate–petroleum ether)	74	64.67	4.01	64.70	3.95	221, 256, 271, 287, 305, 326 (ε 12,500, 850, 1320, 2310, 2960, 2080)
R = $HO_2C \cdot CH_2CH_2-$ (III)	110-112 (with decomp.) (petroleum ether–benzene)	86	66.92	5.40	67.27	5.21	246, 256, 273, 310, 328
R = $CH_3O_2C \cdot CH_2CH_2$ (IIIa)	41 (hexane)	82	68.38	5.71	68.28	5.73	226, 238, 256, 305, 322, 344 (ε 56,900, 62,100, 10,900, 421, 436, 267)
R = C_2H_5CHOH (V)	61 (hexane)	56	71.66	6.54	71.54	6.47	239, 274, 291, 310, 328 (ε 620, 295, 451, 565, 417)
R = $C_2H_5C(CH_3)(OH)$ (VI)	–	–	–	–	–	–	239, 247, 276, 292, 311, 328
R = $(CH_2)_5C(OH)$ (VII)	–	–	–	–	–	–	241, 258, 277, 293, 311, 329 (ε 855, 384, 490, 716, 934, 758)
R = $CH_3O_2C \cdot CH_2CH_2C \equiv C-$ (IX)	86 (hexane)	92	71.15	5.63	71.10	5.22	227, 238, 267, 279, 302, 316, 334.5, 359 (ε 171,000, 271,000, 1700, 2600, 710, 1130, 1660, 1420).

In studying some of the chemical properties of hydroxy esters (V-VII) it was established that the methyl ester (V) when heated in benzene with p-toluenesulfonic acid is readily dehydrated with the formation of an unstable liquid product, which, on the basis of the data of the ultraviolet spectrum, was assigned the structure of dodeca-4,6,8-triyn-10-enoic acid (VIII):



$$\underset{\mathrm{OH}}{\mathrm{CH_3CH_2CH}}-(\mathrm{C}\equiv\mathrm{C})_3-\underset{\text{(V)}}{}(\mathrm{CH_2})_2\mathrm{CO_2CH_3}\rightarrow \mathrm{CH_3CH}=\mathrm{CH}\,(\mathrm{C}\equiv\mathrm{C})_3-\underset{\text{(VIII)}}{(\mathrm{CH_2})_2\mathrm{CO_2CH_3}}$$

$$\underset{\text{(II)}}{\mathrm{CH_3O_2C\cdot(CH_2)_2{-}C\equiv C\cdot C\equiv CH}} \rightarrow \underset{\text{(IX)}}{\mathrm{CH_3O_2C\,(CH_2)_2{-}(C\equiv C)_4{-}(CH_2)_2{-}CO_2CH_3}}\cdot$$

Besides the above described transformations, we obtained the dimethyl ester of tetradeca-4,6,8,10-tetrayn-1,14-dioic acid (IX) in good yield by the oxidative dimerization of the methyl ester of hepta-4,6-diynoic acid (II). (IX) represented a comparatively stable crystalline product, having an absorption spectrum characteristic for tetra-acetylenic systems. A specific feature of the absorption spectrum of this compound (as was also mentioned previously in [3]) is the presence of a second group of bands in the visible portion of the ultraviolet spectrum, differing sharply in extinction and distinctly shifted toward the long-wave region, which do not appear in the di- and tri-acetylenic compounds.

The constants, analyses, and the data of the ultraviolet spectra for the compounds obtained by us are given in the table.

EXPERIMENTAL

Monomethyl ester of dodeca-4,6,8-triyn-1,12-dioic acid (III). To a solution of 0.01 mole of methyl ester (II) in 6 ml of methanol, containing 0.001 mole of cuprous chloride, 0.001 mole of hydroxylamine hydrochloride and 0.018 mole of ethylamine as 40% aqueous solution, was added in drops, with vigorous stirring, 0.01 mole of 5-bromo-4-pentynoic acid in 10 ml of methanol, previously neutralized with aqueous ethylamine solution. The reaction mixture was treated with 10% hydrochloric acid solution and the product was extracted with ether. After purification through the Na salt using bicarbonate and recrystallization we obtained monoester (III). Infrared spectrum: 1726 (—COOH) and 1744 cm^{-1} (—$\mathrm{COOCH_3}$).

Monomethyl ester of deca-4,6,8-triyn-1,10-dioic acid (IV). Obtained in the same manner as described above from (II) and bromopropiolic acid [4]. Infrared spectrum: 1710, 1741, 2113 and 2192 cm^{-1}.

Methyl ester of dodeca-4,6,8-triyn-10-oloic acid (V). Obtained from (II) and 1-bromo-1-pentyn-3-ol. The reaction product was purified by chromatographing on neutral aluminum oxide using a mixture of benzene and ether. Infrared spectrum: 1733, 2112 and 2215 cm^{-1}. The same procedure was also used to obtain hydroxy esters (VI) and (VII), which represent viscous yellow oils that could not be made to crystallize, and which decomposed on standing or when chromatographed on aluminum oxide.

Methyl ester of dodeca-4,6,8-triyn-10-enoic acid (VIII). A solution of 0.6 g of (V) in 100 ml of benzene was refluxed for 1.5 h in the presence of 0.03 g of p-toluenesulfonic acid. When the residue was chromatographed we isolated 0.22 g (40%) of a liquid product with a pleasant ethereal odor, and having $\lambda_{\max}$ (in alcohol) 233, 240, 253, 286, 305, 326 mμ (ϵ 35600, 38200, 34600, 12000, 12900, 8950), which corresponds to the presence of vinyltriacetylene [1] in the molecule of the system.

Dimethyl ester of tetradeca-4,6,8,10-tetrayn-1,14-dioic acid (IX). To a solution of 1 g of methyl ester (II) in 100 ml of methanol was added 10 g of $\mathrm{Cu_2Cl_2}$, 30 g of $\mathrm{NH_4Cl}$ and 1 ml of hydrochloric acid in 100 ml of water, and the mixture was shaken at 18-20° for 6 h in an oxygen stream. After the usual workup we obtained (92% yield) dimethyl ester (IX) as yellow crystals with m.p. 86°. Infrared spectrum: 2221 (—C≡C—) and 1725 (—$\mathrm{CO_2CH_3}$) cm^{-1}.

SUMMARY

Based on the methyl ester of hepta-4,6-diynoic acid, we synthesized several dicarboxylic and hydroxy carboxylic acids of the triacetylenic series, and also the dimethyl ester of tetradeca-4,6,8,10-tetrayn-1,14-dioic acid.

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