CHEMISTRY OF POLYENIC AND POLYACETYLENIC COMPOUNDS

COMMUNICATION 8. METHODS OF SYNTHESIZING POLYENIC DICARBOXYLIC ACIDS HAVING EVEN NUMBERS OF DOUBLE BONDS AND ALSO POLYENYNIC DICARBOXYLIC ACIDS

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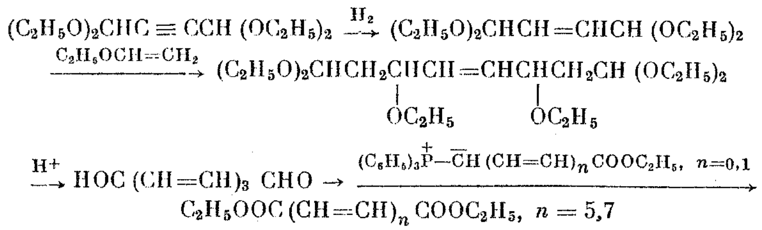
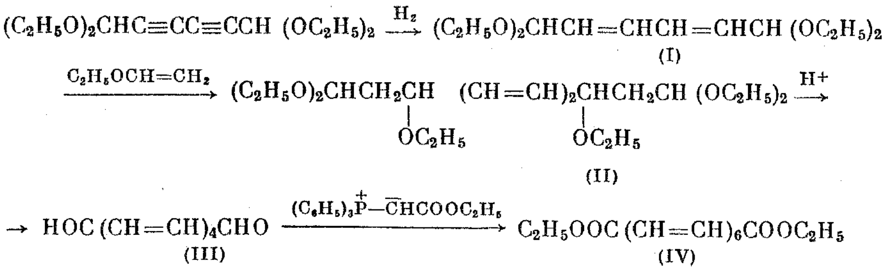
In 1961 [1] we developed the following general method for the synthesis of polyenic dicarboxylic acids having odd numbers of double bonds:



$$(C_2H_5O)_2CHC\equiv CCH(OC_2H_5)_2 \xrightarrow{H_2} (C_2H_5O)_2CHCH{=}CHCH(OC_2H_5)_2$$
$$\xrightarrow{C_2H_5OCH=CH_2} (C_2H_5O)_2CHCH_2\underset{\substack{|\\ OC_2H_5}}{C}HCH{=}CH\underset{\substack{|\\ OC_2H_5}}{C}HCH_2CH(OC_2H_5)_2$$
$$\xrightarrow{H^+} HOC(CH{=}CH)_3CHO \rightarrow \xrightarrow{(C_6H_5)_3\overset{+}{P}-\overset{-}{C}H(CH=CH)_nCOOC_2H_5,\ n=0,1} C_2H_5OOC(CH{=}CH)_nCOOC_2H_5,\ n=5,7$$

As a result, we synthesized descrocetin diethyl ester (diethyl 2,4,6,8,10,12,14-hexadecaheptaenedioate). In the course of this work we determined the detailed geometric configurations of all the compounds obtained.

The present work was concerned with the development of accessible methods of synthesizing polyenic dicarboxylic acids having even numbers of double bonds; many of these are metabolites of fungi and microorganisms: for example, corticrocin (2,4,6,8,10,12-tetradecahexaenedioic acid), a bright-yellow pigment isolated from the mycorrhiza fungus Corticium croceum [2, 3]. The structure of corticrocin was confirmed by synthesis [4, 5], but the method used for its preparation could not be general for the dicarboxylic acids of this series. In the main, for the synthesis of polyenic acids having even numbers of double bonds we followed the scheme that we used for the synthesis of polyenic acids having odd numbers of double bonds, i.e., chain lengthening of diacetals by means of vinyl ethers, combined with the Wittig reaction. We started from 2,4-hexadiynedial bis(diethyl acetal) (I), and the chain lengthening of (I) by means of ethyl vinyl ether in presence of boron trifluoride etherate led to 1,1,3,8,10,10-hexaethoxy-2,6-decadiene (II), whose hydrolysis with a solution of sodium acetate in acetic acid gave 2,4,6,8-decatetraenedial (III). By the Wittig reaction between the dialdehyde (III) and ethyl (triphenylphosphoranylidene)acetate we synthesized diethyl 2,4,6,8,10,12-tetradecahexaenedioate (the diethyl ester of corticrocin) (IV), which was found to be identical with the product prepared from natural corticrocin.



$$(C_2H_5O)_2CHC\equiv CC\equiv CCH(OC_2H_5)_2 \xrightarrow{H_2} \underset{(I)}{(C_2H_5O)_2CHCH{=}CHCH{=}CHCH(OC_2H_5)_2}$$
$$\xrightarrow{C_2H_5OCH=CH_2} \underset{(II)}{(C_2H_5O)_2CHCH_2\underset{\substack{|\\ OC_2H_5}}{C}H(CH{=}CH)_2\underset{\substack{|\\ OC_2H_5}}{C}HCH_2CH(OC_2H_5)_2} \xrightarrow{H^+}$$
$$\rightarrow \underset{(III)}{HOC(CH{=}CH)_4CHO} \xrightarrow{(C_6H_5)_3\overset{+}{P}-\overset{-}{C}HCOOC_2H_5} \underset{(IV)}{C_2H_5OOC(CH{=}CH)_6COOC_2H_5}$$

To determine the geometric configuration of the compounds obtained we studied their infrared spectra in the region of the nonplanar vibrations of C−H bonds (700-1100 cm^{-1}). It was found that the spectrum of 2,4-hexadienedial diacetal (I) contains both vibration bands characteristic for cis bonds and also some characteristic for trans bands, which is probably associated with partial isomerization of cis-cis bonds in the course of catalytic hydrogenation. We have previously observed that trans bonds may be formed to some extent in hydrogenation over Lindlar's catalyst [1]. The chain lengthening of the mixture of geometric isomers of the diacetal (I) by means of the vinyl ether in presence of boron trifluoride etherate does not lead to complete isomerization into the trans form, and as a result a mixture of isomeric ether-acetals (II) is formed (bands due to cis and trans bonds are observed in the infrared spectrum). Such behavior in the hexadienedial diacetal (I) differs from the behavior of cis-2-butenedial bis(diethyl acetal), which, as we observed earlier [1], is completely isomerized into the trans form when undergoing chain lengthening with a vinyl ether under these conditions. However, hydrolysis of the ether-acetal (II) and Wittig chain lengthening of the dialdehyde (III) gave the diethyl ester of completely trans corticrocin (IV). In this way we carried out a new method of synthesizing corticrocin diethyl ester.

We studied also a second possible way of obtaining polyenic acids having even numbers of double bonds, based on the synthesis of enynic monocarboxylic acids with their subsequent oxidative dimerization into polyenynic dicarboxylic acids and hydrogenation of the triple bonds:

$$\mathrm{HC{\equiv}C(CH{=}CH)_{\mathit{n}}CHO} \xrightarrow{(\mathrm{C_6H_5})_3\overset{+}{\mathrm{P}}-\overline{\mathrm{C}}\mathrm{HCOOC_2H_5}} \mathrm{HC{\equiv}C(CH{=}CH)_{\mathit{n}}CH{=}CHCOOC_2H_5} \xrightarrow{\mathrm{O_2}}$$

$$\mathrm{C_2H_5OOOC(CH{=}CH)_{\mathit{n}+1}(C\equiv C)_2(CH=CH)_{\mathit{n}+1}COOC_2H_5} \xrightarrow{\mathrm{H_2}}$$

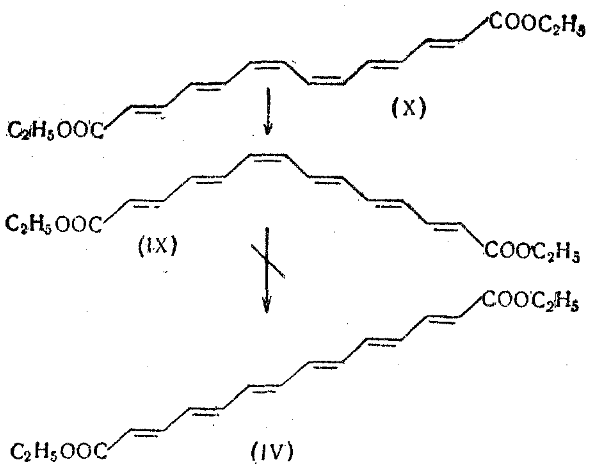
$$\rightarrow \mathrm{C_2H_5OOC}\underset{\text{trans}}{\mathrm{(CH=CH)_{\mathit{n}+1}}}\underset{\text{cis}}{\mathrm{(CH=CH)_2}}\underset{\text{trans}}{\mathrm{(CH=CH)_{\mathit{n}+1}}}\mathrm{COOC_2H_5} \xrightarrow{\mathrm{I_2}\ \text{(ultraviolet)}}$$

$$\rightarrow \mathrm{C_2H_5OOC(CH{=}CH)_{2\mathit{n}+4}COOC_2H_5}, \qquad n = 0{,}1$$

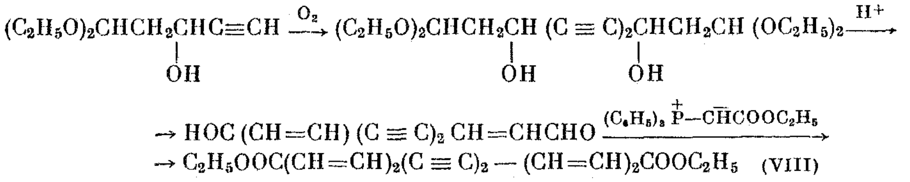
This method made it possible to prepare polyenic dicarboxylic acids having centrally disposed cis-cis bonds. In this scheme of synthesis we used propiolaldehyde and 2-penten-4-ynal, prepared by a new method, namely by the careful hydrolysis of 3-hydroxy-4-pentenal diethyl acetal [6] in presence of p-toluenesulfonic acid. By the reaction of propiolaldehyde and of 2-penten-4-ynal with ethyl (triphenylphosphoranylidene)acetate we obtained ethyl 2-penten-4-ynoate (V) and ethyl 2,4-heptadien-6-ynoate (VI) respectively, and on oxidative dimerization these were converted in high yield into diethyl 2,8-decadiene-4,6-diynedioate (VII) and diethyl 2,4,10,12-tetradecatetraene-6,8-diynedioate (VIII) respectively. Hydrogenation of the resulting diacetylenic acids (VII) and (VIII) in presence of Lindlar's catalyst led to polyenic acids having even numbers of double bonds, of which the central double bonds were of cis configuration, which was confirmed by the appearance of the characteristic frequencies of cis bonds in the infrared spectra of these acids. The following peculiarity of the hydrogenation reaction, which we observed in the case of diethyl 2,4,10,12-tetradecatetraene-6,8-diynedioate (VIII), is noteworthy. When Lindlar's catalyst is used in amounts less (in weight) than that of the sample to be hydrogenated (weight ratio of substance to catalyst of 1.25 and above), hydrogenation is extremely slow and 6-cis-corticrocin diethyl ester (IX) is formed as a result; on the other hand, when an excess of Lindlar's catalyst is used (weight ratio of substance to catalyst 0.5), hydrogenation is considerably quicker and 6,8-dicis-corticrocin diethyl ester (X) is formed. The later readily isomerizes into 6-cis-corticrocin diethyl ester (IX) when boiled in benzene solution in presence of traces of iodine or on ultraviolet irradiation. This experiment directly confirms the possibility of the isomerization of cis bonds into trans bonds in the course of hydrogenation in presence of Lindlar's catalyst. Recently, Dobson and co-workers [7], taking the case of cis-4-undecene, have proved experimentally the possibility of the isomerization of cis bonds into trans bonds over palladium catalysts in an atmosphere of hydrogen, which is in full accord with our observed facts.

Attempts at the further isomerization of 6-cis-corticrocin diethyl ester (IX) into the diethyl ester of completely trans corticrocin (IV) by long boiling with iodine in benzene or toluene with simultaneous ultraviolet irradiation were unsuccessful. The substance either remained unchanged or was resinified.

The cause of the difficulty with which 6-cis-corticrocin diethyl ester (IX) undergoes isomerization is as yet obscure. There is a reference in the literature [8] to the fact that the 9-cis acid of vitamin A cannot be isomerized by the usual methods, but under severe conditions is converted into the retro acid of vitamin A. It was then noted that other 9-cis compounds of the vitamin A series are also incapable of being isomerized by the usual means; however,



the cause of this was not determined. An examination of a molecular model of 6-cis-corticrocin (IX) shows that for this compound a conformation is possible in which the carbonyl of one of the ethoxycarbonyl groups and the double bond adjacent to the second ethoxycarbonyl group are so close that there may be a nonbonded interaction between them of the type of the trans-annular effect. The possibility cannot be excluded that it is in this that the cause of the poor isomerizability of the 6-cis bond lies, for with the occurrence of such electronic interaction between the carbonyl and the double bond this peculiar "folded" conformation of the molecule may be more stable. This question, however, undoubtedly requires further investigation. Apart from the ways examined above, we have developed a further variant of the synthesis of polyenic dicarboxylic acids [taking the example of 6,8-dicis-corticrocin (X)] based on the following scheme of transformations:

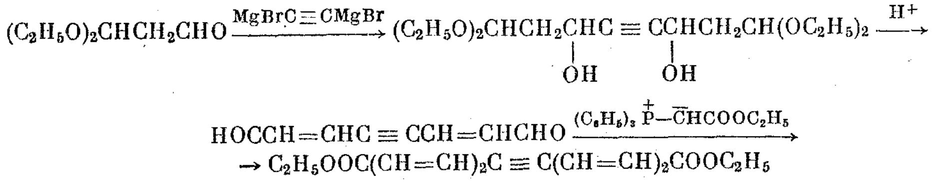


$$(C_2H_5O)_2CHCH_2\underset{OH}{CH}C\equiv CH \xrightarrow{O_2} (C_2H_5O)_2CHCH_2\underset{OH}{CH}(C\equiv C)_2\underset{OH}{CH}CH_2CH(OC_2H_5)_2 \xrightarrow{H^+}$$

$$\rightarrow HOC(CH=CH)(C\equiv C)_2CH=CHCHO \xrightarrow{(C_6H_5)_3\overset{+}{P}-\overset{-}{C}HCOOC_2H_5}$$

$$\rightarrow C_2H_5OOC(CH=CH)_2(C\equiv C)_2-(CH=CH)_2COOC_2H_5 \quad (VIII)$$

In this variant, the first process is the dimerization of the acetylenic hydroxy acetal [6], which is followed by hydrolysis with elimination of the hydroxy groups and formation of the polyenynic dialdehyde, which is converted by the Wittig reaction in the polyenynic dicarboxylic diester (VIII). An analogous scheme may be used also for the preparation of polyenynic acids having odd numbers of multiple bonds.



$$(C_2H_5O)_2CHCH_2CHO \xrightarrow{MgBrC\equiv CMgBr} (C_2H_5O)_2CHCH_2\underset{OH}{CH}C\equiv C\underset{OH}{CH}CH_2CH(OC_2H_5)_2 \xrightarrow{H^+}$$

$$HOCCH=CHC\equiv CCH=CHCHO \xrightarrow{(C_6H_5)_3\overset{+}{P}-\overset{-}{C}HCOOC_2H_5}$$

$$\rightarrow C_2H_5OOC(CH=CH)_2C\equiv C(CH=CH)_2COOC_2H_5$$

Hydrogenation of the resulting polyenynic acids in presence of Lindlar's catalyst gives polyenic dicarboxylic acids having odd numbers of double bonds with a centrally disposed cis bond.

EXPERIMENTAL

2,4-Hexadienedial Bis(diethyl acetal) (I). 29.97 g of 2,4-hexadiynedial bis(diethyl acetal) was hydrogenated in 27 ml of ethyl acetate at 21° (750 mm) in presence of 3.5 g of Lindlar's catalyst. After the absorption of 6012 ml of hydrogen (theory requires 5836 ml) hydrogenation came almost to a stop. Catalyst was filtered off and washed carefully with ethyl acetate. Solvent was distilled off at the water pump, and the residue was distilled. We obtained 21.92 g (73%) of 2,4-hexadienedial bis(diethyl acetal); b.p. 87-90° (0.2 mm), n_D^{21} 1.4528: λ_{max} (in alcohol) 231 mμ (ε 13100); infrared spectrum 993, 751 cm^{-1}. Found: C 65.13; 65.32; H 9.93; 9.98%. $C_{14}H_{22}O_4$. Calculated: C 65.08; H 10.14%.

1,1,3,8,10,10-Hexaethoxy-4,6-decadiene (II). A mixture of 21.92 g of 2,4-hexadienedial bis(diethyl acetal) and one drop of boron trifluoride etherate was heated to 30°, and 12.24 g of ethyl vinyl ether was added gradually at such a rate that the temperature did not exceed 30-35°. The mixture was stirred for 30 minutes at 40-50°, cooled, diluted with ether, washed twice with 5% sodium hydroxide solution and then with water and dried with anhydrous potassium carbonate. After the removal of solvent the residue was distilled, and we obtained 18.15 g (53.2%) of the ether acetal (II); b.p. 145-151° (0.27 mm), n_D^{18} 1.4545; λ_{max} (in alcohol) 232.5 mμ (ε 27900): infrared spectrum: 758, 993 cm^{-1}. Found: C 65.28; 65.56; H 10.38; 10.34%. $C_{22}H_{42}O_5$. Calculated: C 65.63; H 10.52%.

2,4,6,8-Decatetraenedial (III). A mixture of 8.44 g of the ether-acetal (II), 0.35 g of anhydrous sodium acetate, 1 ml of water, 16 ml of 85% acetic acid, and traces of hydroquinone was heated in a stream of nitrogen for one hour at 85-90° (in the bath), cooled, and poured into 600 ml of cold water. The mixture was filtered, and the aqueous layer was extracted with three portions of chloroform. The extract was dried with magnesium sulfate and evaporated. The residue formed crystals of m.p. 163-163.5° (from a mixture of hexane, ether, and ethyl acetate); λ_{max} (in chloroform): 320.5, 334, 352 mμ (ε 22600, 31200, 25400). Found: C 73.48; 73.23; H 6.26, 6.28%. $C_{10}H_{10}O_2$. Calculated: C 74.05; H 6.22%.

Diethyl 2,4,6,8,10,12-Tetradecahexaenedioate (IV) (Corticrocin Diethyl Ester). Unpurified dialdehyde (III), prepared from 8.4 g of the ether-acetal (II), was boiled with 12.6 g of ethyl (triphenylphosphoranylidene)acetate in 50 ml of benzene in a stream of nitrogen for six hours. The solution was evaporated down to one-thrid bulk and cooled. The crystals precipitated were separated and washed with cold alcohol. We obtained 0.5 g of corticrocin diethyl ester, m.p. 204-205.5° (from acetic acid); orange crystals; λ_{max} (in chloroform) 288, 296, 373, 393.5, 417 mμ (ε 3940, 4100, 67000, 103000, 103500); λ_{max} (in benzene) 374, 394, 417 mμ (ε 70000, 114000, 115000), which is in accord with data in the literature [4, 5]. Found: C 71.82; 71.94; H 7.51; 7.43%. $C_{18}H_{22}O_4$. Calculated: C 71.50; H 7.33%.

Ethyl 2-Penten-4-ynoate (V). A mixture of 5.4 g of propiolaldehyde, 42 g of ethyl (triphenylphosphoranylidene)acetate, and 250 ml of dry benzene was left overnight at room temperature and was then boiled for 3.5 hours in a stream of nitrogen. Benzene was carefully vacuum-distilled off, and the residue was extracted several times with hexane. After the removal of solvent fractionation of the residue gave 6 g of a substance having; b.p. 25-27° (0.32 mm), 88-90° (4 mm); n_D^{17} 1.4755; n_D^{19} 1.4751, Without further purification this was used in the further work.

Diethyl 2,8-Decadiene-4,6-diynedioate (VII). A mixture of 5.5 g of ethyl 2-penten-4-ynoate (V), prepared as above, 11.1 g of cuprous chloride, 29.6 g of ammonium chloride, 74 ml of and 40.7 ml of alcohol was shaken in an oxygen atmosphere until absorption ceased. The mixture was extracted several times with ether, and the extract was washed with 1 : 4 hydrochloric acid solution and with water; it was dried with magnesium sulfate, and after evaporation an oil remained, and this crystallized on cooling. We obtained 3.3 g (60%) of the recrystallized dicarboxylic ester; m.p. 37.5-38.5°; λ_{max} (in alcohol) 220, 268.5, 297.7, 317.5, 340 mμ (ε 19200, 29200, 20200, 30000, 28800). Found: C 68.11; 68.27; H 5.66; 5.90%. $C_{14}H_{14}O_4$. Calculated: C 68.28; H 5.73%. Dimethyl 2,8-decadiene-4,6-diynedioate and the corresponding free acid were isolated from extracts of *Polyporus anthracophilus*[9].

Diethyl 4,6-dicis-2,4,6,8-Decatetetraenedioate. 0.3 g of the above-described diacetylenic ester was hydrogenated in 18 ml of ethyl acetate at 20° (756 mm) in presence of 0.5 g of Lindlar's catalyst. After the absorption of 59 ml of hydrogen (theory requires 59.37 ml) the hydrogenation was stopped. Catalyst was filtered off and carefully washed with ethyl acetate. Solvent was vacuum-evaporated, alcohol was added, and the mixture was cooled. We obtained 0.15 g (50%) of white needles, m.p. 83-84°. Infrared spectrum 757, 994 cm^{-1}. Found: C 67.29; 67.21; H 7.20; 7.17%. $C_{14}H_{18}O_4$. Calculated: C 67.18; H 7.25%.

2-Penten-4-ynal. 8 g of 3-hydroxy-4-pentenal diethyl acetal was vigorously stirred with 10 ml of 3% p-toluenesulfonic acid while the mixture was being carefully heated in a water bath. When it reached 70° the mixture became clear and yellowish brown in color. The mixture was cooled rapidly and extracted several times with ether; the ether extract was dried with magnesium sulfate. Ether was removed in a vacuum at room temperature, and the slightly yellowish liquid residue of 2-penten-4-ynal could be used directly in the further work. On distillation we isolated 1.2 g (33.2%) of 2-penten-4-ynal, b.p. (in the bath) 45° (17 mm) [10]. In air the product rapidly polymerizes.

Ethyl 2,4-Heptadien-6-ynoate (VI). By a procedure analogous to that described above for ethyl 2-penten-4-ynoate, from 2 g of 2-penten-4-ynal and 12.3 g of ethyl (triphenylphosphoranylidene)acetate we obtained 1.47 g (39%) of ethyl 2,4-heptadien-6-ynoate; b.p. 64-66° (3 mm); n_D^{16} 1.5503, λ_{max} (in alcohol) 283 mμ (ε 25400) infrared spectrum: 1632, 1652 (weak band), 1715, and 2122 cm^{-1}. Because of its instability, an analytically pure sample of the ester could not be obtained.

Diethyl 2,4,10,12-Tetradecatetraene-6,8-diynoate (VIII). 1.47 g of the above-described heptadienynoic ester was dimerized as described for the 2-buten-4-ynoic ester. The mixture was extracted with chloroform, and the extract was washed with dilute hydrochloric acid and with water; it was dried with magnesium sulfate and evaporated. After recrystallization from alcohol we obtained 1.33 g (90%) of the ester; m.p. 152-153°; λ_{max} (in alcohol) 246, 315.5, 333.5, 357, 383.5 mμ (ε 14300, 28600, 34800, 43000, 41400); infrared spectrum: 1629, 1713, 2215 cm^{-1}. Found: C 72.23; 72.22; H 6.07; 6.07%. $C_{18}H_{18}O_4$. Calculated: C 72.46; H 6.08%.

12.5 g of 3-hydroxy-4-pentynal diethyl acetal was subjected to oxidative dimerization, as described above. The resulting mixture was carefully extracted with ether, and the ethereal solution was washed with sodium carbonate solution; it was dried with magnesium sulfate, and all volatile substances were removed in the vacuum of a water pump. The thick light-colored residue was heated with a mixture of anhydrous sodium acetate, 2 ml of water, and 32 ml of 85% acetic acid for 40 minutes at 85-90° in a stream of nitrogen, and the mixture was then poured onto ice. The orange precipitate formed was separated, washed with water, and vacuum-dried. We obtained 2.7 g of the dialdehyde, which was used in the further work without further purification.

2 g of the unpurified dialdehyde was boiled with 10.4 g of ethyl (triphenylphosphoranylidene)acetate in 10 ml of benzene in a stream of nitrogen for six hours. After the usual treatment we isolated 1.7 g of diethyl 2,4,10,12-tetradecatetraene-6,8-diynoate, m.p. 151-153° (from alcohol), undepressed by admixture of the sample described above.

Diethyl 6,8-dicis-2,4,6,8,10,12-Tetradecahexaenedioate (X) (6,8-dicis-Corticrocin Diethyl Ester). 0.2 g of the above-described diacetylenic ester was hydrogenated in 13 ml of ethyl acetate in presence of 0.4 g of Lindlar's catalyst in the dark. In the usual way we isolated 0.13 g of 6,8-dicis-corticrocine diethyl ester; m.p. 138.5-140° (from a mixture of ethyl acetate and hexane); λ_{max} (in benzene) 368,388,410 mμ (ε 55000, 75500, 66600); infrared spectrum: 757, 992 cm^{-1}. Found: C 71.37; 71.50; H 7.29; 7.46%. $C_{18}H_{22}O_4$. Calculated: C 71.50; H 7.33%.

Diethyl 6-cis-2,4,6,8,10,12-Tetradecahexaenedioate (IX) (6-cis-Corticrocin Diethyl Ester). 0.51 g of diethyl 2,4,10,12-tetradecatetraene-6,8-diynedioate was hydrogenated in 23 ml of ethyl acetate in presence of 0.4 g of Lindlar's catalyst. Hydrogenation was very slow, and while it proceeded crystals were precipitated from the mixture. 83 ml of hydrogen was absorbed (theory requires 84 ml). The mixture was heated to the boil, filtered, and cooled. The precipitated crystals were separated from the mother solution, and a further portion of the substance was isolated by evaporation. In all we obtained 0.26 g of 6-cis-corticrocin diethyl ester; m.p. 189-190.5° (from a mixture of benzene and hexane): λ_{max} (in benzene) 373.5, 394, 417.5 mμ (ε 52600, 86700, 86700); infrared spectrum: 758, 993 cm^{-1}. Found: C 71.50; H 7.33%. When 6,8-dicis-corticrocin diethyl ester was boiled in benzene with traces of iodine for 30 minutes an almost quantitative yield was obtained of 6-cis-corticrocin diethyl ester, m.p. 189-190° (from a mixture of benzene and hexane), undepressed by admixture of the product obtained as above.

Diethyl 2,4,8,10-Dodecatetraen-6-ynoate. A solution of 17.2 g of 3,3-diethoxypropionaldehyde in an equal volume of dry ether was added to Iotsich's reagent (from 1.2 g of magnesium and 5.45 g of ethyl bromide) in 50 ml of dry ether. The resulting mixture was boiled for five hours and then left overnight. After treatment with saturated ammonium chloride solution, the ether layer was separated, and the aqueous layer was carefully extracted with ether. The residue remaining after the removal of ether (12.6 g) was stirred with 15 ml of 3% p-toluenesulfonic acid solution with heating in a water bath until a homogeneous solution was formed. The solution was cooled rapidly and repeatedly extracted with ether. The ether extracts were washed with water and dried with magnesium sulfate. After the removal of ether the residue (3.9 g) was boiled for six hours with 21 g of ethyl (triphenylphosphoranylidene) acetate in a nitrogen atmosphere. Solvent was removed in a vacuum, and the residue was extracted repeatedly with a 1 : 1 mixture of diethyl ether and petroleum ether. Evaporation gave an oil, from which crystals separated on standing; they were filtered off and pressed off on the filter. Crystallization from alcohol gave 0.51 g of a substance of m.p. 119-119.5°. Found: C 70.28; 70.15; H 6.79; 6.58%. $C_{16}H_{18}O_4$. Calculated: C 70.05; H 6.61%.

SUMMARY

1. Three ways of synthesizing polyenic dicarboxylic acids having even numbers of double bonds are proposed.

2. A new method of synthesizing corticrocin diethyl ester is described.

3. The difficulty with which the cis bond in 6-cis-corticrocin diethyl ester is isomerized is pointed out.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.