Synthesis of Long-chain Aliphatic Compounds from Cyclododecatriene

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Dialkyl 1, 16-hexadecandioate, a starting material of 16-membered ring compounds, has been synthesized by the following methods: (1) treating α, ω-dibromoalkane with dialkyl sodiomalonate(1) or potassium cyanide(2); (2) treating the monochloride of α, ω-dicarboxylic acids with organo cadmium compounds;(3) (3) alkylating 1, 3-cyclohexandione with 1, 4-dibromobutene(4) followed by ring opening, and (4) the electrolytic coupling of α, ω-dicarboxylic acids.(5) The present paper reports a synthesis of diethyl 1, 16-hexadecandioate from 1, 5, 9-cyclodecatriene, as well as syntheses of certain long-chain aliphatic compounds as intermediates of the hexadecandioate.

cis, trans, trans-1, 5, 9-Cyclododecatriene was treated with hydrogen peroxide in formic acid to give 2-formoxy-*cis, trans*-5, 9-cyclododecadienol in a 76% yield; its hydrolysis yielded *cis, trans*-5, 9-cyclodecadiene-*cis*-1, 2-diol(6) (I) melting at 160～161°C with small amounts of an isomer melting at 164～165°C.

The 1, 2-diol I gave *cis*-1, 2-cyclododecanediol(7) upon hydrogenation over palladium-charcoal. The configurations of the two olefinic bonds are considered to be cis and trans on the basis of the infrared absorptions of 2-formoxy-*cis, trans*-5, 9-cyclododecadienol and *cis, trans*-5, 9-cyclododecadiene-1, 2-diol isopropylidene ketal (II) near 970 and 700 cm^{-1}.(8) The structure of the isomer melting at 164～165°C is currently under investigation.(9)

The treatment of *cis, trans*-5, 9-cyclododecadiene-*cis*-1, 2-diol with lead tetraacetate yielded *cis, trans*-5, 9-dodecadiene-1, 12-dial (III) in a 63% yield. The compound gave succinic acid in a 91% yield upon ozonolysis followed by oxidative decomposition, thus excluding the possibility of double-bond migration. The configurations of the two olefinic bonds are considered to be cis and trans on the basis of the infrared absorbance of the dialdehyde at 970 cm^{-1} relative to that of *cis, trans, trans*-1, 5, 9-cyclododecatriene.

The dialdehyde was treated with lithium aluminum hydride to give *cis, trans*-5, 9-dodecadiene-1, 12-diol (IV) in a 79% yield.

cis, trans-5, 9-Dodecadiene-1, 12-dial was heated with ethyl hydrogen malonate and catalytic amounts of piperidine in pyridine to give 2, 6, 10, 14-hexadecatetraene-1, 16-dioate (V) in a 71% yield. This compound gave a mixture of oxalic and succinic acid upon ozonolysis followed by hydrolysis. Upon catalytic hydrogenation over palladium-charcoal, the compound absorbed four moles of hydrogen to give diethyl 1, 16-hexadecanedioate (VI). Attempts to prepare diethyl 6, 10-hexadecadiene-1, 16-dioate by partial hydrogenation over palladium-charcoal or Raney-nickel were unsuccessful.

Experimental(10)

2-Formoxy-*cis, trans*-5, 9-cyclododecadienol. — To 1150 g. of formic acid (80%), 1050 g. of acetic anhydride and 3 ml. of concentrated sulfuric acid were added. The solution was then mixed with 440 g. of *cis, trans, trans*-1, 5, 9-cyclododecatriene(11) and hydrogen peroxide (30%) was added dropwise under stirring. The reaction temperature rose to near 100°C after 350 g. of hydrogen peroxide had been added, and the mixture became homogeneous. The solution was stirred until the peroxide disappeared, and then the solvent was removed in a vacuum. From the distillate, 58 g. of cyclododecatriene were recovered unchanged. The residue was distilled to give 398 g. of a fraction boiling at 150～160°C/10 mmHg (76% based on the reacted cyclododecatriene). By redistillation, a fraction boiling at 155°C/10 mmHg was collected.

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1) N. L. Prake, H. W. Carhart and R. Mozingo, *J. Am. Chem. Soc.*, **63**, 617 (1949).

2) P. Chuit and T. Hausser, *Helv. Chim. Acta*, **12**, 850 (1929).

3) A. Kreuchunas, *J. Am. Chem. Soc.*, **75**, 3339 (1953).

4) H. Stetter and W. Dierichs, *Ber.*, **85**, 1061 (1952).

5) L. Ruzicka, M. Stoll and H. Schinz, *Helv. Chim. Acta*, **11**, 1174 (1928).

6) The same diol has been obtained by treating 1, 5, 9-cyclododecatriene with perbenzoic acid; see L. I. Zakharkin and V. V. Korneva, *Doklady Akad. Nauk. S. S. S. R.*, **132**, 1078 (1960).

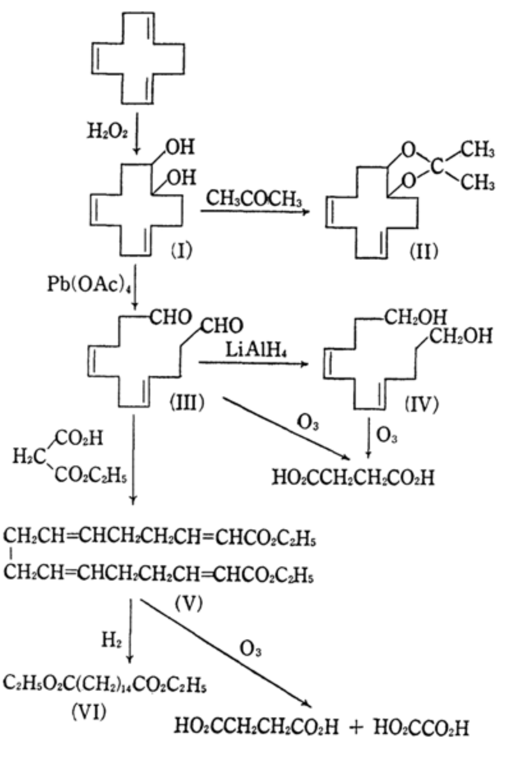
7) V. Prelog and M. Speck (*Helv. Chim. Acta*, **38**, 1786 (1955)) have reported on the infrared spectra of *cis*- and *trans*-1, 2-cyclododecanediol. Both diols can be easily differentiated by the spectra.

8) Both of these compounds are liquid and gave infrared absorptions at the C-H bending region much more clearly than the original diol.

9) The isomer gave analytical data in accord with cyclododecadienediol. On catalytic hydrogenation over palladium-charcoal, two moles of hydrogen were absorbed, and the hydrogenated product gave oxalic acid upon oxidation with pottasium permanganate.

10) All temperatures are uncorrected.

11) G. Wilke, *Angew. Chem.*, **75**, 10 (1963); H. Takahasi and M. Yamaguchi, *J. Org. Chem.*, **28**, 1409 (1963).



Found: C, 69.40; H, 8.85. Calcd. for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99%.

The infrared spectrum of the compound showed the absorptions of the trans and cis double bonds near 970 and 700 cm^{-1}.

***cis, trans*-5, 9-Cyclododecadiene-*cis*-1, 2-diol.**—To a mixture of 500 g. of *cis, trans, trans*-1, 5, 9-cyclododecatriene, 1300 g. of formic acid (80%), 1200 g. of acetic anhydride and 3 ml. concentrated sulfuric acid, 390 g. of hydrogen peroxide (31%) were added. The mixture was stirred until the peroxide disappeared, and then the solvent was removed in a vacuum. From the distillate, 62 g. of the starting cyclododecatriene were obtained. The residue was vigorously refluxed with 1.2 l. of a 20% sodium hydroxide solution for 2 hr. After the mixture had cooled the crystals were filtered, washed with water, and recrystallized from 400 ml. of alcohol to give 320 g. of crude *cis, trans*-5, 9-cyclododecadiene-*cis*-1, 2-diol melting at 150~153°C. The filtrate was concentrated to give 30 g. of the crude 1, 2-diol. The total yield was 66%. A pure specimen was obtained by recrystallization from alcohol; m. p. 160~161°C. The compound showed the infrared absorptions of the trans and cis double bonds at 970 and 700 cm^{-1}.

The mother liquor was distilled in a vacuum to give a fraction boiling at 170~190°C/5 mmHg. This fraction partially crystallized after standing overnight at room temperature, and the solids were filtered to give 2 g. of crystals melting at 156~160°C. By recrystallization from acetone, a pure specimen was obtained; m. p. 164~165°C. Mixed melting point with *cis, trans*-5, 9-cyclododecadiene-*cis*-1, 2-diol showed a depression; m. p. 145~157°C.

Found: C, 73.51; H, 10.26. Calcd. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27%.

***cis, trans*-5, 9-Cyclododecadiene-*cis*-1, 2-diol Isopropylidene Ketal.**—A mixture of 5 g. of *cis, trans*-5, 9-cyclododecadiene-*cis*-1, 2-diol, 50 ml. of acetone and 10 g. of anhydrous copper sulfate was stirred at room temperature for 3 days. After the copper sulfate had been filtered, the acetone was removed and the residue was distilled in a vacuum to give 4.5 g. (69%) of *cis, trans*-5, 9-cyclododecadiene-*cis*-1, 2-diol isopropylidene ketal; b. p. 128~131°C/3 mmHg, m. p. 41~42°C.

Found: C. 76.24; H, 10.27. Calcd. for $C_{15}H_{24}O_2$: C, 76.23; H, 10.24%.

The compound gave the infrared absorptions of the double bonds at 970 and 730 cm^{-1} (liquid).

***cis, trans*-5, 9-Dodecadiene-1, 12-dial.**—Lead tetraacetate was prepared from 450 g. of trilead tetraoxide and 1.4 l. of acetic acid. Into a mixture of 100 g. of *cis, trans*-5, 9-cyclododecadiene-*cis*-1, 2-diol and 150 g. of potassium carbonate in 1 kg. of xylene, lead tetraacetate was stirred in small portions under a nitrogen atmosphere over a 3 hr. period, the mixture was then allowed to stand overnigh after having been stirred for an additional hour. The mixture was filtered, and the solid was washed with xylene. The xylene solutions were washed with water and dried over anhydrous sodium sulfate. After the solvent had been removed, 63 g. of *cis, trans*-5, 9-dodecadiene-1, 12-dial boiling at 140~160°C/4 mmHg were obtained in a 63% yield. A pure specimen was obtained by redistillation; b. p. 147~148°C/4mmHg, n_D^{20} 1.4799, d_4^{20} 0.9625.

Found: C, 73.94; H, 9.42. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34%.

The compound (in a carbon disulfide solution) gave infrared absorptions of the trans and cis double bonds at 970 and 710 cm^{-1} respectively, and the infrared absorbance of this compound in a 6.0 mmol. % carbon disulfide solution at 970 cm^{-1} was of the same degree as that of *cis, trans, trans*-1, 5, 9-cyclododecatriene in a 3.0 mmol. % carbon disulfide solution.

2, 4-Dinitrophenylhydrazone: m. p. 110~111°C.

Found: C, 52.08; H, 4.81; N, 20.09. Calcd. for $C_{24}H_{26}N_8O_8$: C, 51.98; H, 4.72; N, 20.21%.

The Ozonolysis of *cis, trans*-5, 9-Dodecadiene-1, 12-dial.—Ozone was introduced into a solution of 3 g. of the sample and 30 ml. of acetic acid, and the ozonized solution was treated with hydrogen peroxide. When the solution was concentrated, 5 g. of succinic acid melting at 180~182°C was obtained in a 91% yield. Its paper chromatography gave a single spot of succinic acid.

***cis, trans*-5, 9-Dodecadiene-1, 12-diol.**—To a solution of 39 g. of *cis, trans*-5, 9-dodecadiene-1, 12-dial in 100 ml. of ether, 4 g. of lithium aluminum hydride were added over a 2 hr. period; the mixture was then refluxed for 3 hr. while being stirred. After it had stood overnight, the mixture was poured into 100 g. of ice-water and extracted with ether after having been treated with hydrochloric acid. The extracts were washed with water and dried over anhydrous sodium sulfate. After the ether had been removed, the residue was distilled to give 31 g. (79.4%) of a fraction boiling at 165~

170°C/4 mmHg. Redistillation gave *cis*, *trans*-5, 9-dodecadiene-1, 12-diol; b. p. 167~168°C/4 mmHg, n_D^{20} 1.4889, d_4^{20} 0.9558.

Found: C, 72.81; H, 11.13. Calcd. for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18%.

Bis(phenylurethane): m. p. 72.0~72.5°C.

Found: C, 71.35; H, 7.36; N, 6.35. Calcd. for $C_{26}H_{32}N_2O_4$: C, 71.53; H, 7.39; N, 6.42%.

Diethyl 2, 6, 10, 14-Hexadecatetraene-1, 16-dioate.—A solution of 19 g. of *cis*, *trans*-5, 9-dodecadiene-1, 12-dial, 50 g. of ethyl hydrogen malonate, and 1 ml. of piperidine in 70 ml. of pyridine was refluxed under a nitrogen atmosphere for 4 hr. The solution was then concentrated, and the residue was distilled in a vacuum to give 23 g. (71%) of a fraction boiling at 220~230°C/6 mmHg. and 4 g. of residue. A pure specimen was obtained by redistillation; b. p. 196~197°C/2 mmHg, n_D^{20} 1.4899, d_4^{20} 0.9919.

Found: C, 71.36; H, 8.98. Calcd. for $C_{20}H_{30}O_4$: C, 71.23; H, 9.04%.

The ozonolysis followed by the hydrolysis of the compound gave a mixture of oxalic and succinic acid.

Attempts to Synthesize Diethyl 6, 10-Hexadecadiene-1, 16-dioate.—An alcohol solution of 6.7 g. (0.02 mol.) of diethyl 2, 6, 10, 14-hexadecatetraene-1, 16-dioate was hydrogenated over palladium-charcoal (or Raney-nickel). After 1 l. (0.045 mol.) of hydrogen had been absorbed, the catalyst was filtered off and the filtrate was distilled to give 5.5 g. of a fraction boiling at 220~240°C/6 mmHg. The fraction gave a mixture of oxalic, succinic and adipic acid by ozonolysis followed by hydrolysis.

Diethyl 1, 16-Hexadecandioate.—An alcohol solution of 6.7 g. (0.02 mol.) of diethyl 2, 6, 10, 14-hexadecatetraene-1, 16-dioate was hydrogenated over palladium-charcoal (or Raney-nickel) for 7 hr. After 1.7 l. (0.08 mol.) of hydrogen had been absorbed, the catalyst was filtered and the filtrate was distilled to give 5.5 g. of diethyl 1, 16-hexadecandioate boiling at 220~240°C/6 mmHg.

By hydrolysis, this compound gave 1, 16-hexadecandioate; m. p. 119~120°C.

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