Note

Synthesis of Methylene-interrupted (Z, Z)-Octadecadienoic Acids, (Z, E)-, (E, Z)-9, 12-Octadecadienoic Acids and the Corresponding Alcohols

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In order to clarify the substrate specificity for the enzyme system producing C_6 -aldehydes,¹⁾ methylene-interrupted (Z, Z)-octadecadienoic acids (**1a-k**), (Z, E)- and (E, Z)-9, 12-octadecadienoic acids (**3a, b**) were synthesized through unequivocal routes with some modification. (Z, Z)-Octadecadienols (**2a-k**) were also synthesized *via* the corresponding octadecadiynols (**4**), which were synthons of **1**.

i) (Z, Z)-Octadecadienoic acids (**1**) and the corresponding alcohols (**2**). Christie and Holman²⁾ have been reported the synthesis of the complete series of **1**. Our synthetic route offers highly pure **1** and **2**; the diacetylenic alcohols (**4**) were rectified through an effective column *in vacuo* and the derived diacetylenic acids (**5**) were further purified by recrystallization from *n*-pentane. The key step, selective hydrogenation of **5** and **4** under P-2 Ni³⁾ poisoned with a small amount of ethylene diamine in methanol at 5°C, gave the corresponding (Z, Z)-isomers **1** and **2**, respectively, (97~98% purity by GLC analyses). Chromatographic analyses (silver saturated Amberlyst XN 1010)⁴⁾ of the corresponding esters showed the dienoic acids (**1**) to contain ~1% of nonconjugated (E, E)-isomers and (Z)-monoene compounds. The structures of **1** and **2** thus obtained were fully substantiated by IR and ¹H-NMR spectra.

ii) (Z, E)- and (E, Z)-9, 12-Octadecadienoic acids (**3a, b**) and the corresponding alcohols (**8a, b**). The Grignard coupling of 6-bromohexyl tetrahydropyranyl ether with (E)-dodecen-ynyl bromides (**6**)^{5a-c)} was carried out at -10°C *via* organocupper (I) intermediate using catalytic quantities of Li₂CuCl₄^{5d)} to give (E)-octadecenynyl tetrahydropyranyl ethers in good yield without isomerization to conjugated system and the removal of protecting group by *p*-TsOH gave (E)-octadecen-ynyl alcohols (**7**) in high yield as shown in Fig. 1. The hydrogenation of **7** under P-2 Ni³⁾ at 5-10°C, af-

FIG. 1. Synthesis of (Z, E)-, (E, Z)-9, 12-Octadecadienoic Acids (**3a, b**) and the Corresponding Alcohols (**8a, b**).

firmed the desired (Z, E)-octadecadienols (**8**) containing ~8% of contaminant by GLC analyses. The attempted oxidation of dienols (**8**) with CrO₃-H₂SO₄⁶⁾ to the corresponding carboxylic acids (**3**) gave a mixture of geometric and conjugated isomers. Thus, the (Z, E)-octadecadienoic acids (**3**) were prepared *via* the appropriate dienals which were derived by oxidation with CrO₃-pyridine complex⁷⁾, with argentic oxide (AgO)⁸⁾ in THF-water. The dienoic acids (**3**) were purified by TLC on Kieselguhr G impregnated with 10% undecane.⁹⁾ The geometrical purity of **3** was checked by silver saturated resin (Amberlyst XN 1010).⁴⁾ The structures of **3** and **8** thus obtained were confirmed by IR and ¹H-NMR spectra.

EXPERIMENTAL

Infrared spectra were obtained with a Hitachi EPI-G2 spectrometer. NMR spectra were taken in CDCl₃ containing TMS as an internal reference.

(E)-Octadecen-ynyl alcohols (**7**). In usual manner using catalytic quantities (Ca. 0.3%) of Li₂CuCl₄,^{5d)} enynols (**7**) were prepared. IR $\nu_{\text{max}}^{\text{film}}$ cm⁻¹: 3350, 3040, 2950, 2200, 1650, 965, 730. (E)-12-octadecen-9-ynyl alcohol (**7a**): yield; 32.4% from **6a**, bp; 145°C (0.8 mmHg), (E)-9-octadecen-12-ynyl alcohol (**7b**): yield; 32.0% from **6b**, bp; 140°C (0.25 mmHg).

TABLE I. METHYLENE-INTERRUPTED OCTADECADIENOIC ACIDS AND THE CORRESPONDING ALCOHOLS

C ₁₈ -Dienoic; Acids, Alcohols	Yield [%] ^a		Purity [%] (Acids)	¹ H-NMR (Alcohols) [PPM]		
	Acids	Alcohols		olef. H	=C-CH ₂ -C=	-CH ₂ -CH ₂ -O-
(Z, Z)-3, 6; (1a), (2a)	10.4	27.9	99.0	5.32	2.73	2.24
-4, 7; (1b), (2b)	13.5	34.2	98.0	5.29	2.72	2.04
-5, 8; (1c), (2c)	10.4	23.4	99.0	5.28	2.70	2.05
-6, 9; (1d), (2d)	11.7	20.7	98.5	5.28	2.70	2.04
-7, 10; (1e), (2e)	10.0	18.0	98.0	5.27	2.60	2.00
-8, 11; (1f), (2f)	24.0 ^d	24.3	98.0	5.27	2.65	2.01
-9, 12; (1g) ^b , (2g) ^c	—	—	—	5.25	2.67	2.00
-10, 13; (1h), (2h)	15.3	31.5	98.0	5.25	2.68	2.01
-11, 14; (1i), (2i)	10.6	20.7	97.5	5.25	2.69	1.98
-12, 15; (1j), (2j)	10.1	26.1	97.5	5.26	2.70	2.01
-13, 16; (1k), (2k)	6.2	18.0	98.0	5.28	2.60	2.00
(Z, E)-9, 12; (3a), (8a)	18.4	22.7	97.5	5.42	2.76	2.00
(E, Z)-9, 12; (3b), (8b)	17.2	25.2	97.0	5.39	2.72	2.00

^a From ω -acetylenic tetrahydropyranyl ether^b Linoleic acid^c Linoleyl alcohol^d From ω -acetylenic acid

General procedure for hydrogenation with P-2 Ni from acetylenes. With P-2 Ni³⁾ prepared from nickel acetate and sodium borohydride, the acetylenic compound was hydrogenated in methanol containing a small amount (Ca. 0.5%) of ethylene diamine at 5°C, to afford the desired (Z)-olefinic compound in nearly quantitative yield.

General procedure for oxidation via dienals to (Z, E)- and (E, Z)-9, 12-octadecadienoic Acids (3). The (Z, E)- and (E, Z)-9, 12-octadecadienals were prepared with CrO₃-pyridine complex⁷⁾ in CH₂Cl₂. These dienals without further purification were oxidized to (Z, E)- and (E, Z)-9, 12-octadecadienoic acids (3a, b) with AgO in THF-water stirring for 70 hr at room temperature according to the Corey's method⁹⁾. The acids (3) were purified by reverse phase TLC (Kieselguhr Gimpregnated with 10% undecane in *n*-pentane; development solvent, AcOH: CH₃CN=50: 50).⁹⁾ IR $\nu_{\max}^{\text{film}}$ cm⁻¹: 2950, 1700, 1630, 970, 730.

Geometrical purity by silver resin chromatography. The geometrical purity of nonconjugated acids (1 and 3) was checked by silver saturated resin (Amberlyst XN 1010) chromatography of the corresponding methyl esters using methanol according to the method of Emken and Scholfield.⁴⁾ The (Z, Z)-, (Z, E)- and (E, E)-9, 12-octadecadienoates were clearly separated: the order of the relative strength of binding to the resin was the (Z, Z)->(Z, E)->(E, E)-isomer. The resin (Amberlyst XN 1010) was obtained from the courtesy of Rohm and Haas Inc. but is not commercially available.

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