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PRIMATE CHEMICAL COMMUNICATION, PART III[1] Synthesis of the Major Volatile Constituents of the Marmoset (*Saguinus fuscicollis*) Scent Mark

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Abstract—This paper presents the stereospecific synthesis of the long-chain butyrate esters (15 in number) which in addition to squalene comprise the major volatile constituents of the scent mark of the marmoset monkey, *Saguinus fuscicollis*.

Key Words—primate, chemical communication, marmoset monkeys, butyrates, synthesis, *Sanguinus fuscicollis*.

INTRODUCTION

In connection with our continuing studies concerning primate chemical communication, we recently reported on the isolation and identification of the major volatile constituents (1-16) present in the odoriferous scent mark of the marmoset monkey, a South American primate (Smith et al., 1976; Yarger et al., 1977). Although the importance of these substances to marmoset chemical communication is currently unknown, Epple (1974a,b) has demonstrated that the intact scent mark of the marmoset communicates to conspecifics a variety of information including the sex, social status, and identity of the donor monkey.

In order to assign rigorously the structures of the major constituents of

[1]For part II of this series, see Yarger, R.G., Smith, A.B., III, Preti, G., and Epple, G., 1977. *J. Chem. Ecol.* 3:45-56.
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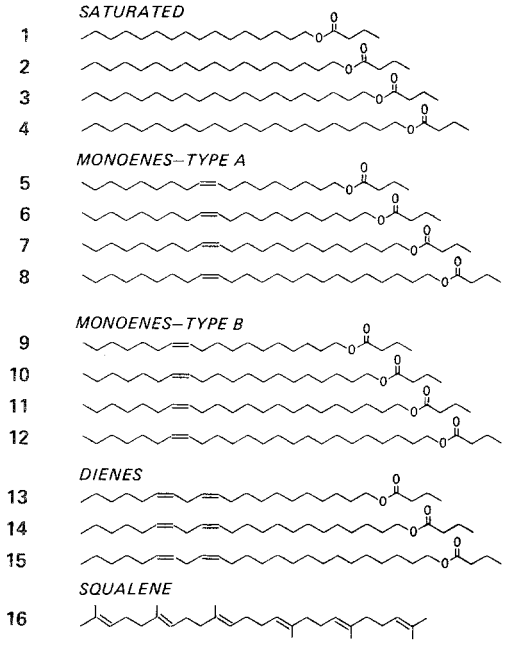
the scent mark, as well as to provide suitable quantities (e.g., 200–500 mg/each) of pure authentic samples of each ester for biological testing, an alternative source of 1–15 was sought. It is with these considerations in mind that we report here our stereospecific approach to these esters.

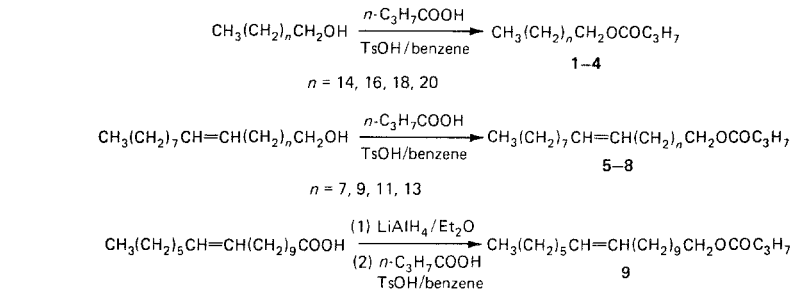
Initial examination of the major components of the scent mark revealed the existence of four major classes of esters, namely saturated butyrates (1–4), monosaturated butyrates (5–12) of two structural types (designated A and B) dependent on the location of the olefinic linkage, and diunsaturated butyrates (13–15). In addition, the configuration of each site of unsaturation was found to be cis. Finally, as often occurs with other mammalian fatty acids, each member of a class differed from the next by a two-carbon unit.



SYNTHETIC STUDIES

We initiated synthetic studies with the structurally simple saturated and monounsaturated butyrate esters (1–8). These esters were easily prepared in high-yield via acid-catalyzed esterification of the corresponding commercially available, albeit expensive, straight-chain alcohols with *n*-butyric acid. Similarly, ester 9 was prepared by esterification of (*Z*)-11-octadecen-1-ol which in turn was available in near-quantitative yield from the $LiAlH_4$ reduction of the corresponding commercially available unsaturated acid, (*Z*)-11-octadecenoic acid. In each case the spectroscopic properties, including the low resolution mass and 220-MHz NMR spectra as well as the high-resolution gas

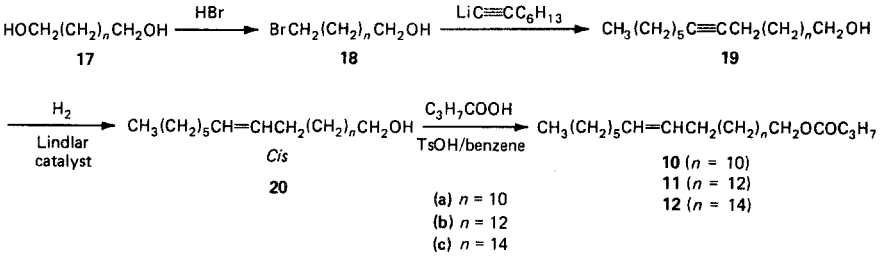
chromatographic retention properties (100-m, SF-96 glass capillary column), were identical to the esters isolated from the marmoset scent mark.



SCHEME 1

We next turned our attention to the preparation of monounsaturated esters 10–12. These esters differ only in the number of methylene units between the ester functionality and the olefinic bond. Our approach employed the synthetic strategy developed several years ago by Hendry and coworkers (1975). Specifically, an eight-carbon synthon containing a precursor of the required cis olefinic bond was added to a difunctionalized carbon chain of appropriate but variable length. A suitable eight-carbon synthon appeared to be the lithium salt of 1-octyne.

To this end, the commercially available diol (17a) was treated with concentrated hydrobromic acid at 85° C for 18 hr with simultaneous heptane extraction. This afforded a crystalline bromo alcohol (18a) melting at 30–31° C in 86% yield after chromatography and recrystallization. Similar treatment of diols 17b and 17c gave bromo alcohols 18b and 18c in 50 and 79% yield, respectively. The bromo alcohols (18a-c) were next transformed to ynols 19a-c via treatment in hexamethyl phosphorus triamide with the lithium

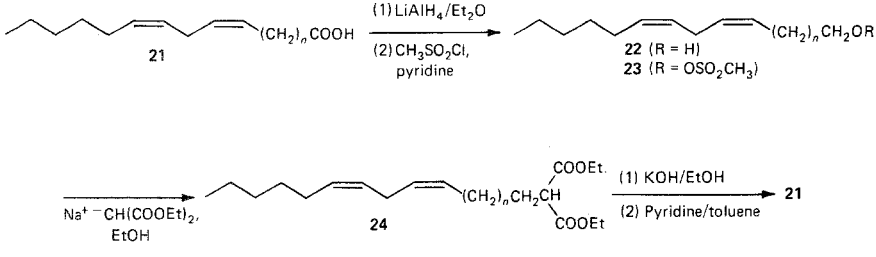


SCHEME 2

salt of 1-octyne, the latter readily prepared from 1-octyne and 1.1 equiv of *n*-butyl lithium. The crystalline ynols (19a-c) were obtained in 60–80% yield. At this point there remained only the stereospecific reduction of the acetylenic linkage to the required cis olefin, and esterification with *n*-butyric acid to

complete the preparation of butyrates 10–12. The former transformation was accomplished via hydrogenation at atmospheric pressure over 5% palladium on barium sulfate poisoned with a small amount of synthetic quinoline, while esterification was effected as described for butyrates 1–18 (*n*-butyric acid, TsOH, and benzene).

The fact that the above transformation led predominantly to the cis unsaturated butyrates was established by high-resolution capillary VPC (100-m, SF-96 glass capillary column). Analysis of various mixtures of oleyl butyrate (5) (C-22 Δ^9 cis) and elaidyl butyrate (C-22 Δ^9 trans) by VPC demonstrated that under our chromatographic conditions as little as 0.5% of elaidyl butyrate was easily detected when added to oleyl butyrate. Similar analysis of our synthetic samples demonstrated in each case that they were >95% configurationally pure.



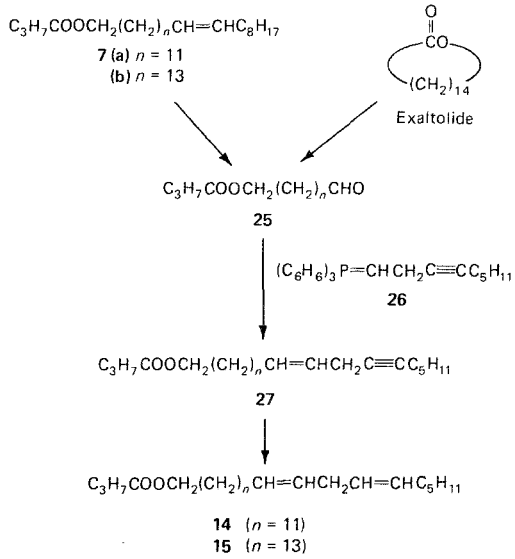
(a) $n = 7$
(b) $n = 9$
(c) $n = 11$
(d) $n = 13$

SCHEME 3

At this point there remained the preparation of the diunsaturated butyrates 13–15 of group four. The availability of (*Z,Z*)-11,14-eicosadienoic acid (21b), albeit expensive, would provide easy access to 13 via the straightforward reduction-esterification sequence employed in the preparation of 9. Butyrates 14 and 15, on the other hand, provided considerably more synthetic challenge. Two possible synthetic strategies appeared feasible. The first, but clearly the least elegant, would involve three consecutive two-carbon malonic ester-chain elongation-reduction sequences on the alcohol derived from readily available (i.e., inexpensive) cis-linoleic acid, followed at each stage by esterification with *n*-butyric acid. This approach by necessity provides alcohol 22b, thereby eliminating the need to acquire the expensive acid 21b.

Alternatively, careful examination of butyrates 14 and 15 suggested that if the appropriate long-chain aldehyde-ester fragments 25a and 25b were readily available, and if condensation with the previously unreported Wittig reagent (26) derived from 1-bromo-3-nonyne followed by subsequent hydro-

genation were in each case effected in a stereospecific cis manner, then an efficient synthetic route to 14 and 15 would be in hand. Interestingly, the aldehyde-ester fragment required for butyrate 14 is present in the previously prepared butyrate 7. Ozonolysis of 7 would provide ready access to aldehyde-ester 25a. Moreover, the C_{15} aldehyde-ester synthon 21b required for the preparation of butyrate 15 appeared to be reasonably accessible from exaltolide. In particular, hydrolysis of the macrocyclic lactone would provide



SCHEME 4

15-hydroxypentadecanoic acid which could in turn be esterified with *n*-butyric acid and subsequently transformed to the requisite aldehyde-ester (21b) by selective reduction of the carboxylic acid functionality with borane-THF (Brown and Korytnyk, 1960) followed by Collins oxidation (Ratcliffe and Rodehorst, 1970). Since the latter synthetic strategies provided the opportunity to explore more interesting chemistry, the decision was made to proceed initially with the preparation of aldehyde-ester (25).

To this end, ozonolysis of 7 followed by reductive work-up with triphenyl phosphine gave 13-oxotridecan-1-yl butyrate (25a) in 52% yield after column chromatography on silica gel. Treatment of this aldehyde with Wittig reagent 26 in THF followed by work-up and column chromatography on silica gel afforded the enyne 27a in 72% yield. Analysis of the product by high-resolution VPC (SF 96 capillary, 100 m × 0.66 mm ID, 200° C) indicated the presence of two compounds in a ratio of 87:13. This ratio corresponds very closely to the cis-trans ratio (86:14) for an analogous Wittig reaction, run

under identical conditions, reported in a comprehensive study by Anderson and Henrick (1975).

Next, the enyne butyrate mixture (27a) was hydrogenated using Lindlar catalyst. The NMR spectrum (220 Hz) of the product mixture indicated the complete disappearance of starting material (i.e., absence of the broad, two-proton singlet at 2.91 ppm corresponding to methylene protons: $=CHCH_2C\equiv$) and of any components possessing a triple bond (i.e., absence of any resonance at 2.16 ppm for methylene protons: $-CH_2CH_2C\equiv$). Signals for allylic methylene (2.03 ppm) and doubly allylic methylene (2.77 ppm) protons were present but integration showed their relative ratio to be 6.8:1.0. The desired diene (14) requires a ratio of only 2:1, thus indicating that overhydrogenation had taken place. Indeed, the high-resolution gas chromatogram displayed four peaks. The retention time of peak A (63.2 min, 47%), corresponded to that of a sample of the desired, naturally occurring diene butyrate 14, while that of peak B (64.6 min, 17%) corresponded to (*Z*)-13-docosenyl butyrate (7). Docosanyl butyrate (4) was not present. Proton NMR and VPC data suggest that peaks C and D (66.3 min, 16%, and 67.5 min, 19%, respectively) were other monoene isomers arising from the starting enyne mixture.

Due to the lack of stereospecificity in the Wittig condensation and the difficulties encountered in the subsequent hydrogenation, we returned to the malonic acid-chain elongation strategy. To this end, commercially available (*Z,Z*)-9,12-octadecadenoic acid (21a) was reduced in 96% yield to the corresponding alcohol (22a) with $LiAlH_4$. Conversion into mesylate 23a proceeded in 90% yield upon treatment of 22a at 0° C with methansulfonyl chloride in pyridine. The resultant mesylate was then homologated with the sodium salt of diethyl malonate. Hydrolysis of the derived diester afforded the corresponding diacid which, without purification, was decarboxylated employing the extremely mild conditions of Cordes et al. (1968); the diacid was heated at reflux for 2 hr in a solution of toluene and pyridine (5:1, v/v). The resultant homologated acid was purified at this point via silica gel chromatography. Reduction of the pure acid (21b) led to alcohol 22b in 90% yield, which was then ready both for conversion to butyrate 13, and further homolgation to alcohols 22c and 22d, respectively. Indeed, a similar series of transformations provided alcohols 22c and 22d in 37 and 39% overall yield from the respective acids (21b and 21c). Final conversion of alcohols 22b-d to butyrates 13-15 was effected in near-quantitative yield as described previously (see above).

Purification of the fifteen butyrates prior to spectroscopic comparison with the authentic butyrates (1-15) was accomplished where necessary by preparative high-pressure liquid chromatography on a silver-loaded macroporous cation exchange column (Warthen, 1976) with final purity being established using high-resolution gas chromatographic analysis on the

aforementioned 100-m SF-96 glass capillary column. In each case the butyrates were >95% configurationally pure and displayed 220 MHz NMR, IR, and VPC retention properties identical to the authentic butyrates.

METHODS AND MATERIALS

Vapor-phase chromatography was performed on a Perkin-Elmer model 990 gas chromatograph using the following column: 3% SF-96 open tubular glass capillary column dynamically coated, 100 m × 0.66 mm ID. The helium carrier gas flow rate was 10 ml/min, and the oven temperature ranged from 180 to 210°C. Compounds isolated were obtained either as colorless oils or white solids. Melting points were obtained on a Thomas Hoover capillary melting point apparatus and are uncorrected. Solutions were dried over $MgSO_4$ unless specified otherwise. IR spectra were obtained for CCl_4 solutions using a Perkin-Elmer model 237 spectrophotometer. NMR spectra were obtained in $CDCl_3$ solutions using a Varian HR-220 (220 MHz) spectrometer. Column chromatographies were performed using Hi-Flosil silica gel 60/200 mesh (Applied Science Laboratories, State College, Pennsylvania). High-pressure liquid chromatography (HPLC) was performed on a Perkin-Elmer model 601 HPLC using a 7-mm ID × 183-cm stainless-steel column packed with silver-loaded macroporous cation exchange resin (37–74 μm, AG MP-5, Bio Rad Laboratories, Richmond, California) eluting with methanol.

Butyrates 1–15: General Esterification Procedure. A solution of approx. 367 mg of cetyl alcohol, 2 ml of *n*-butyric acid, and 40 mg of *p*-toluenesulfonic acid in 40 ml of benzene was heated at reflux gently overnight with the azeotropic removal of H_2O using a micro Dean-Stark trap. The reaction was cooled, diluted with hexane, and washed twice with 5% aqueous NaOH, H_2O, and brine. The solution was dried, and the solvent was removed in vacuo to afford 467 mg (99%) of hexadecyl butyrate (1). Infrared and NMR data for butyrates 1–15 may be found in Yarger et al. (1977).

(Z)-11-Octadecen-1-ol. A solution of 200 mg of (*Z*)-11-octadecenoic acid in 2 ml anhydrous ether was added to a stirred suspension of 260 mg of $LiAlH_4$ in 40 ml of dry ether protected by a drying tube. The reaction mixture was heated at reflux for 3 hr, cooled to room temperature, and sodium sulfate decahydrate was added to consume the excess $LiAlH_4$. The solution was filtered, the residue rinsed with ether, the combined filtrates were evaporated in vacuo to afford 184 mg (97%) of the alcohol as an oil: IR 3340(m), 3005(w), 2935(s), 2855(s), 1460(m) cm^{-1}; NMR (220 MHz) δ 0.87 (t, J = 6Hz, 3H), 1.26 (s, br, 22H), 1.53 (m, 2H), 1.99 (m, 4H), 3.61 (t, J = 6 Hz, 2H), 5.30 (m, 2H).

12-Bromodecan-1-ol (18a). A mixture of 5.0 g of 1,12-dodecanediol and 25 ml of 48% aqueous hydrobromic acid was placed in an apparatus equipped to permit its continuous extraction with heptane. The reaction flask was

stirred and heated at 85° C; the extraction was allowed to proceed overnight. The heptane solution was cooled and diluted with ether. This solution was washed successively with H_2O, aqueous $NaHCO_3$, H_2O, 5% aqueous sodium thiosulfate, and H_2O and dried. The solvent was removed in vacuo and the resulting oil chromatographed on silica gel. Gradient elution with hexane–ether provided 5.65 g (86%) of the pure bromo-alcohol (18a). A sample was recrystallized from hexane: mp 30–31° C (lit. 29° C, Chuit et al., 1927); IR 3360(m), 2940(s), 2860(s), 1460(m), 1050(m) cm^{-1}; NMR (220 MHz) δ 1.27 (s, br, 16H), 1.55 (m, 2H), 1.84 (p, J = 6 Hz, 2H), 3.40 (t, J = 6 Hz, 2H), 3.62 (t, J = 6 Hz, 2H).

14-Bromotetradecan-1-ol (*18b*). Starting with 7.13 g of 1,14-tetradecanediol, the procedure used for the preparation of 18a provided 4.49 g (50%) of bromo-alcohol 18b: mp 40–41° C (lit. 46° C, Chuit et al., 1927); IR 3360(m), 2940(s), 2860(s), 1460(m), 1050(m) cm^{-1}; NMR (220 MHz) 1.25 (s, br, 20H), 1.55 (m, 2H), 1.84 (p, J = 12 Hz, 2H), 3.39 (t, J = 12 Hz, 2H), 3.62 (t, J = 12 Hz, 2H).

16-Bromohexadecan-1-ol (*18c*). Starting with 4.00 g of 1,16-hexadecanediol, the procedure used for the preparation of 18a provided 3.94 g (79%) of bromo-alcohol 18c: mp 52–53° C (lit. 53–54° C, Chuit and Hausser, 1929); IR 3360(m), 2940(s), 2860(s), 1460(m), 1050(m) cm^{-1}; NMR (220 MHz) δ1.25 (s, br, 24H), 1.55 (m, 2H), 1.83 (p, J = 6 Hz, 2H), 3.39 (t, J = 6 Hz, 2H), 3.62 (t, J = 6 Hz, 2H).

13-Eicosyn-1-ol (*19a*). To a stirred solution of 550 mg of 1-octyne in dry THF (distilled from $LiAlH_4$) maintained at −78° C under nitrogen was added 2 ml of *n*-butyllithium (2.5 M in hexane, 1 equiv). After 2 hr, a solution of 530 mg (0.4 equiv) of 12-bromodecan-1-ol (18a) in 1.5 ml of dry HMPA was added and the mixture maintained at −78° C an additional hour. The reaction was allowed to warm at room temperature and was stirred under nitrogen overnight. Water was added, and the mixture was partitioned between water and ether. The ether solution was washed five times with H_2O, once with brine, dried, and the solvent removed in vacuo. The residue was chromatographed on silica gel eluting with a hexane–ether gradient to afford 718 mg (95%) of the pure alkynol 19a. Recrystallization from hexane afforded an analytical sample: mp 37–38° C; IR 3680(w), 2940(s), 2850(s), 1460(m) cm^{-1}; NMR (220 MHz) δ 0.87 (t, J = 7 Hz, 3H), 1.25 (s, br, 26H), 1.48 (m, 2H), 2.12 (t, J = 7 Hz, 4H), 3.61 (t, J = 6 Hz, 2H).

Analysis: calculated for $C_{20}H_{38}O$: C, 81.56; H, 13.01; found: C, 81.79; H, 12.98.

15-Docosyn-1-ol (*19b*). Using the same procedure outlined for the preparation of 19a, 2.00 g of 14-bromotetradecan-1-ol (18b) afforded 1.57 g (71%) of ynol 19b: mp 46.9–47.4° C (hexane); IR 3680(m), 2940(s), 2850(s), 1460(m) cm^{-1}; NMR (220 MHz) δ 0.87 (t, J = 7 Hz, 3H), 1.25 (s, br, 30H), 1.45 (m, 2H), 2.11 (t, J = 7 Hz, 4H), 360 (t, J = 6 Hz, 2H).

Analysis: calculated for $C_{22}H_{42}O$: C, 81.91; H, 13.13; found: C, 81.96; H, 13.12.

17-Tetracosyn-1-ol (19c). Using the same procedure outlined for the preparation of 19a, 1.11 g of 16-bromohexadecan-1-ol (18c) afforded 854 mg (71%) of alkynol 19c: mp 53.0–53.5° C (hexane); IR 3680(w), 2940(s), 2850(s), 1460(m) cm^{-1}; NMR (220 MHz) δ 0.86 (t, J = 7 Hz, 3H), 1.25 (s, br, 34 H), 1.48 (m, 2H), 2.11 (t, br, J = 6 Hz, 4H), 3.60 (t, J = 6 Hz, 2H).

Analysis: calculated for $C_{24}H_{46}O$: C, 82.21; H, 13.23; found: C, 82.37; H, 13.19.

(Z)-13-Eicosen-1-ol (20a). A stirred mixture of 885 mg of 13-eicosyn-1-ol (19a), 24 mg of 5% palladium on barium sulfate (Research Inorganic Chemical Corp., Belleville, New Jersey), and 0.03 ml of synthetic quinoline in 9 ml of anhydrous methanol were hydrogenated at atmospheric pressure and room temperature until the uptake of hydrogen appeared to cease (approximately 1 equivalent of hydrogen absorbed). The mixture was filtered to remove the catalyst. The catalyst was rinsed repeatedly with ether, and the combined filtrates were concentrated in vacuo. The residue was taken up in ether and washed once with water, twice with 5% aqueous hydrochloric acid, twice with water, dried, and the solvent removed in vacuo to afford 885 mg (99%) of the enol 20a as an oil. An analytical sample was prepared by chromatography on silica gel eluting with hexane–ether: IR 3340(m), 3010(w), 2940(s), 2860(s), 1460(m) cm^{-1}; NMR (220 MHz) δ 0.87 (t, J = 7 Hz, 3H), 1.26 (s, br, 26 H), 1.53 (m, 2H), 2.00 (m, 4H), 3.62 (t, J = 6 Hz, 2H), 5.30 (m, 2H).

Analysis: calculated for $C_{20}H_{40}C$, 81.01; H, 13.60; found: C, 80.93; H, 13.66.

(Z)-Docosen-1-ol (20b). Using the same procedure described for the preparation of 20a, 1.56 g of 15-docosyn-1-ol (19b) provided 1.55 (99%) of enol 20b: IR 3340(m), 3010(w), 2940(s), 2860(s), 1460(m) cm^{-1}; NMR (220 MHz) δ 0.87 (t, J = 7 Hz, 3H), 1.25 (s, br, 30H), 1.53 (m, 2H), 1.98 (m, 4H), 3.62 (t, J = 6 Hz, 2H), 5.30 (m, 2H).

Analysis: calculated for $C_{22}H_{44}O$: C, 81.41; H, 13.66; found: C, 81.28; H, 13.62.

(Z)-17-Tetracosen-1-ol (20c). Using the same procedure described for the preparation of 20a, 793 mg of 17-tetracosyn-1-ol (19c) provided 759 mg (95%) of enol 20c: IR 3340(m), 3010(w), 2940(s), 2860(s), 1460(m) cm^{-1}; NMR (220 MHz), δ 0.87 (t, J = 6 Hz, 3H), 1.26 (s, br, 34H), 1.53 (m, 2H), 2.00 (m, 4H), 3.62 (t, J = 6 Hz, 2H), 5.31 (m, 2H).

Analysis: calculated for $C_{24}H_{48}O$: C, 81.74; H, 13.72; found: C, 81.92; H, 13.80.

13-Oxotridecan-1-yl Butyrate (25a). A solution of 742 mg of erucyl butyrate (7) in 20 ml of CH_2Cl_2 was ozonized at −78° C for 4 hr in a Supelco microozonolysis apparatus. The reaction mixture was then thoroughly flushed with N_2, 590 mg of triphenyl phosphine was added, and the reaction

was allowed to warm to room temperature. The solvent was removed in vacuo and the residue was chromatographed on 75 g of silica gel, eluting with a hexane–ether gradient to afford 278 mg (52%) of the aldehyde-ester: IR 2930(s), 2850(m), 2700(w), 1740 (s, br), 1455(w), 1160(m) cm^{-1}: NMR (220 MHz) δ 0.94 (t, J = 7 Hz, 3H), 1.27 (s, br, 18H), 1.64 (m, 4H), 2.28 (t, J = 6 Hz, 2H), 2.42 (t, J = 6 Hz, 2H), 4.06 (t, J = 6 Hz, 2H), 9.76 (s, 1H).

Analysis: calculated for $C_{17}H_{32}O_3$: C, 71.79; H, 11.34; found: C, 71.86; H, 11.36.

3-Nonyn-1-yl Triphenyl Phosphonium Bromide. A solution of 1.0 g. of 1-bromo-3-nonyne and 1.42 g of triphenylphosphine in 8 ml of chlorobenzene was heated at reflux for 24 hr. The solvent was removed in vacuo, and the residue was triturated with ethyl acetate at 0° to afford 1.44 g. (63%) of 3-nonyn-1-yl triphenyl phosphonium bromide. Recrystallization from ethyl acetate containing approx. 1% of methanol provided pure 3-nonyn-1-yl triphenylphosphonium bromide: mp 144–145° C.

Analysis: calculated for $C_{27}H_{30}BrP$: C, 69.68; H, 6.50; found: C, 69.60; H, 6.47.

13-Docosen-16-yn-1-yl Butyrate (27a). Ylide (26) was generated by adding 0.4 ml of a 2.5 M solution of *n*-butyllithium in hexane to a stirring suspension of 465 mg of 3-nonyn-1-yl triphenyl phosphonium bromide in 10 ml of dry tetrahydrofuran under nitrogen at 0° C. After stirring for 30 min at 0° C, a solution of 125 mg of 13-oxotridecan-1-yl butyrate in 2 ml of dry tetrahydrofuran was added. Stirring was continued for 1 hr while the reaction was allowed to warm to room temperature. The mixture was poured into water to quench the reaction and was extracted into hexane. The hexane solution was washed four times with water, once with saturated brine solution, dried, and concentrated in vacuo to a volume of about 5 ml. Precipitated triphenyl phosphonium oxide was removed by filtration and the filtrate was passed through 5 g. of silica gel eluting with 60 ml of 5% ether in hexane. Removal of the solvent in vacuo provided 159 mg (92%) of 13-docosen-16-yn-1-yl butyrate (27a) as an oil. An analytical sample was prepared by chromatography on silica gel eluting with hexane-ether: IR 3010(w), 2930 (s, br), 2850(m), 1740(m), 1460(w) cm^{-1}; NMR (220 MHz) δ (0.94 (m, 6H), 1.26 (s, br, 24H), 1.59–1.72 (m, 4H), 2.02 (m, br, 2H), 2.14 (t, J = 6 Hz, 2H), 2.28 (t, J = 7 Hz, 2H), 2.90 (s, br, 2H), 4.06 (t, J = 7 Hz, 2H), 5.42 (s, br, 2H).

Analysis: calculated for $C_{26}H_{46}O_2$: C, 79.94; H, 11.87; found: C, 79.72; H, 11.87.

(Z,Z)-13,16-Docosadien-1-yl Butyrate (14). Using the same procedure described for the preparation of 20a, 78 mg of 13-docosen-16-yn-l-yl butyrate (27a), 1.6 mg of palladium on barium sulfate, and 3.6 mg of synthetic quinoline in 0.6 ml of ethanol afforded 74 mg of a mixture of isomers (see text). The desired (*Z,Z*)-13,16-docosadien-1-yl butyrate (14) was the

predominant product (47%) and exhibited the same chromatographic and spectral properties as a sample of natural material.

1,1-Dicarbethoxynonadeca-10,13-diene (24a). A solution of 26.8 g of (*Z,Z*)-9,12-octadecadienoic acid (linoleic acid, Nu-Chek Prep, Inc., Elysian, Minnesota) in 50 ml of ether was added dropwise to a stirred suspension of 7.34 g of lithium aluminum hydride in 600 ml of ether under nitrogen at a rate which maintained a gentle reflux. The reaction was heated at reflux for 4 hr, cooled to room temperature, and the excess $LiAlH_4$ was consumed by adding sodium sulfate decahydrate. The solution was filtered and the residue was rinsed several times with ether. The combined ether solutions were washed with 5% sodium hydroxide and saturated brine solution and dried. Removal of the solvent in vacuo gave 24.3 g (96%) of (*Z,Z*)-9,12-octadecadien-1-ol (22a). This alcohol was converted directly to its mesylate by slowly adding 71.1 g of alcohol 22a to a stirring solution of 36.9 g of methanesulfonyl chloride in 800 ml of pyridine (dried by distilling from barium oxide) protected by a drying tube. After 3 hr the reaction was complete (TLC, silica gel, hexane–ether 1:1). The solution was poured into 800 ml of ice water and extracted twice with hexane. The combined hexane extracts were washed successively five times with water, once with saturated brine solution and dried. Removal of the solvent in vacuo afforded 78.5 g (85%) of (*Z,Z*)-9,12-octadecadien-1-yl mesylate (23a) which should be used immediately for the next reaction. To this end 8.55 g of sodium metal was dissolved by heating in 1000 ml of dry ethanol at reflux (distilled from sodium) under nitrogen atmosphere. The solution was cooled to room temperature, 81.2 g of diethyl malonate was quickly added, and the mixture was stirred for 30 min. The freshly prepared mesylate, 78.5 g, was then added dropwise at room temperature and the reaction heated at reflux for 4 hr. After cooling to 0°C, 1000 ml of water was added, and the reaction was made acidic with concentrated hydrochloric acid. The reaction was extracted three times with 300 ml of hexane. The combined hexane extractions were washed three times with water, once with saturated brine solution, and dried. Evaporation of the solvent in vacuo gave 83.8 g (90%) of 1,1-dicarbethoxynonadeca-10,13-diene (24a). An analytical sample was prepared by chromatography on silica gel using hexane–ether: IR 3010(w), 1750(m), 1730(s) cm^{-1}; NMR (220 MHz) δ 0.86 (t, br, J = 7 Hz, 3H), 1.27 (s, br, 24H), 1.85 (m, 2H), 2.01 (m, 4H), 2.74 (m, 2H), 3.27 (t, J = 6 Hz, 1H), 4.15 (q, J = 7 Hz, 4H), 5.30 (m, 4H).

Analysis: calculated for $C_{25}H_{44}O_4$: C, 73.48; H, 10.85; found: C, 73.45; H, 10.78.

(Z,Z)-11,14-Eicosadienyl Butyrate (13). A solution of 55.5 g of crude 1,1-dicarbethoxynonadeca-10,13-diene (24a) in 500 ml of 10% methanolic potassium hydroxide was heated at reflux for 1 hr. The reaction was cooled and slowly poured into 2000 ml of water, agitating to dissolve all solids. This aqueous solution was washed four times with ether. The aqueous solution was

cooled to ice temperature, acidified to pH 3 using concentrated hydrochloric acid, and extracted three times with ether. The combined ether layers were washed twice with water, once with saturated brine, dried, and the solvent removed in vacuo to provide 36.3 g (76%) of 1,1-dicarboxynonadeca-10,13-diene. A mixture of 31.8 g of this diacid with 64 ml of pyridine and 320 ml of toluene was heated vigorously at reflux for 2 hr. The solvents were removed in vacuo and the residue was taken up in hexane. The hexane solution was washed five times with water, once with saturated brine, dried, and the solvent was removed in vacuo. The residue was chromatographed on silica gel eluting with hexane-ether to provide 26.1 g (94%) of pure *Z,Z*-11,14-eicosadienoic acid (21b) which was identical in all respects (GC, IR, NMR) to an authentic sample (Nu-Check Prep, Inc.). This acid was reduced with $LiAlH_4$ to its alcohol (22b) using the same procedure described for the preparation of alcohol 22a. The (*Z,Z*)-11,14-eicosadien-1-ol (22b) was then esterified with butyric acid as outlined in the general esterification procedure to afford synthetic *Z,Z*-11,14-eicosadienyl butyrate (13) which was identical in all respects (IR, NMR, MS) to the naturally occurring butyrate.

1,1-Dicarbethoxyheneicosa-12,15-diene (*24b*). Using the procedure described for the preparation of 24a, 11,14-eicosadienoic acid (21b) was converted successively to the alcohol (22b), the mesylate (23b), and finally to the diester (24b) in an overall 78% yield. An analytical sample of 24b displayed the following spectroscopic properties: IR 3010(w), 1750(s) cm^{-1}; NMR (220 MHz) δ 0.86 (t, br, J = 7 Hz, 3H), 1.28 (s, br, 28H), 1.86 (m, 2H), 2.01 (m, 4H), 2.74 (m, 2H), 3.27 (t, J = 6 Hz, 1H), 4.15 (q, J = 7 Hz, 4H), 5.31 (m, 4H).

Analysis: calculated for $C_{27}H_{48}O_4$: C, 74.26; H, 11.08; found: C, 74.17; H, 11.27.

(*Z,Z*)-*13,16-Docosadienyl Butyrate* (*14*). Using the procedure described for the preparation of butyrate 13, 1,1-dicarbethoxyheneicosa-12,15-diene (24b) was hydrolyzed, decarboxylated, reduced, and esterified in an overall yield of 48% to provide synthetic *Z,Z*-13,16-docosadienyl butyrate (14) which was identical in all respects (IR, NMR, MS) to the naturally occurring material.

1,1-Dicarbethoxytricosa-14,17-diene (*24c*). Using the procedure described for the preparation of 24a, *Z,Z*-13,16-docosadienoic acid (21c) was converted successively to the alcohol 22c, the mesylate 23c and finally to the diester 24c in an overall 70% yield. An analytical sample of 24c displayed the following spectroscopic properties: IR 3010(w), 1750(m), 1730(s) cm^{-1}; NMR (220 MHz) δ 0.87 (t, br, J = 7 Hz, 3H), 1.27 (s, br, 32H), 1.84 (m, 2H), 2.00 (m, 4H), 2.74 (m, 2H), 3.27 (t, J = 6 Hz, 1H), 4.15 (q, J = 7 Hz, 4H), 5.30 (m, 4H).

Analysis: calculated for $C_{29}H_{52}O_4$: C, 74.95; H, 11.28; found: C, 75.05; H, 11.30.

(*Z,Z*)-*15,18-Tetracosadienyl Butyrate* (*15*). Using the procedure de-

scribed for the preparation of butyrate 13, 1,1-dicarbethoxytricosa-14,17-diene (24c) was hydrolyzed, decarboxylated, reduced, and esterified in an overall yield of 56% to provide synthetic *Z,Z*-15,18-tetracosadienyl butyrate (15) which was identical in all respects (IR, NMR, MS) to the naturally occurring material.

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