Oxidation products of arachidonic acid. V. The synthesis of 8*R*,11*R*,15(*R* and *S*)-trihydroxy-9*S*,12*S*-oxyeicosa-5*Z*,13*E*-dienoic acids

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The synthesis of the title compounds is described. It is shown that β-nitro ketals are versatile intermediates for the synthesis of prostaglandin-type C-13 – C-20 side-chains.

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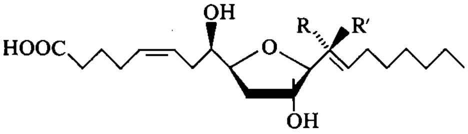
La synthèse des composés sus-mentionnés est décrite et l'utilité des β-nitrocétales en tant qu'intermédiaires dans l'introduction de chaînes aliphatiques correspondantes au segment C-13 – C-20 des prostaglandines a été démontrée.

We wish to report the synthesis of title compounds **1** and **2** (1), which confirm the structure proposed for an oxidation product of arachidonic acid by Pace-Asciak and Wolfe (2), without, however, specifying its stereochemistry, since the R_f-values of **1** and **2** are different from that of the natural product.[1]



1 R = H, R′ = OH
2 R = OH, R′ = H

The strategy involved in the synthesis was to condense a readily available and suitably protected aldehyde such as **6***a* with fragment **17**. The nitro function of **17** not only serves to generate the anion which adds to the aldehyde to give a nitro alcohol, but, after dehydration, it also serves as part of a nitro olefin which functions as Michael-acceptor for the tetrahydrofuran formation. Finally, being β to a potential ketone, its β-elimination then gives an α,β-unsaturated ketone, the reduction of which, followed by deblocking of protecting groups, provides title compounds **1** and **2**.

As a model compound, we used the readily available furanose **3** (3), which was transformed by the action of ethanethiol – zinc chloride to dithioacetal **4**, and hence to the corresponding isopropylidene compound **5**. Mercuric ion mediated hydrolysis then gave aldehyde **6***a* in 75% yield, based on **3**.

Condensation of β-nitro ketal **7** and aldehyde **6***a* in DMF (4), using diisopropylamine as base, gave a mixture of nitro alcohols **8** and **10** which were separable as their acetates **9** and **11**. Both acetates **9** and **11** were treated with anhydrous potassium carbonate and dicyclohexyl-18-crown-6 in benzene to give nitro olefin **12**. Selective hydrolysis of the isopropylidene group of **12** under various acidic reaction conditions failed because of the instability of dimethyl ketal to acid.

Treatment of nitro acetate **9** with methanolic *p*-toluenesulfonic acid gave bicyclic ketal **15**, probably via monocyclic ketal **13**. In contrast, the same acid treatment of the isomeric nitro acetate **11** gave a more polar product (tlc), which probably had the monocyclic ketal structure **14**, and which gave **16** upon reaction with triethylamine or during work-up ($NaHCO_3$). The structures of **15** and **16** were proven by their ^{1}Hmr, ir, and mass spectra.

These results can best be rationalized in the following manner. It is quite likely that the two nitro alcohols **8** and **10** have the two *threo*-configurations, since the addition **6***a* + **7** → **8** + **10** is probably reversible, so that the most stable configurations permitting hydrogen bonding of the OH and NO_2 groups should be as depicted.

If these representations are correct, then the acid treatment of acetate **9** derived from **8** should give a mixture of conformers in which conformer **13** is populated to a considerable extent. Extrusion of the methoxy group at C-15, followed by cyclization, would then give **15**. In the case of acetate **11** derived from nitro alcohol **10**, a similar acid catalyzed cyclization would lead to a tetrahydropyran in which all secondary ring-substituents are equatorial. The other conformation being of little importance, no further acid-catalyzed cyclization takes place. Base treatment then results in elimination of the elements of acetic acid and formation of a nitro olefin which then cyclizes to bicyclic ketal **16**. Attempts to transform **16**, which has the carbon frame-work of the desired final product, to **23***a*, failed. Whereas the stereochemical assignments of **10**, **11**, **14**, and **16** are probably correct, is it quite

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[1] We wish to thank Dr. C. Pace-Asciak for the chromatographic comparisons.

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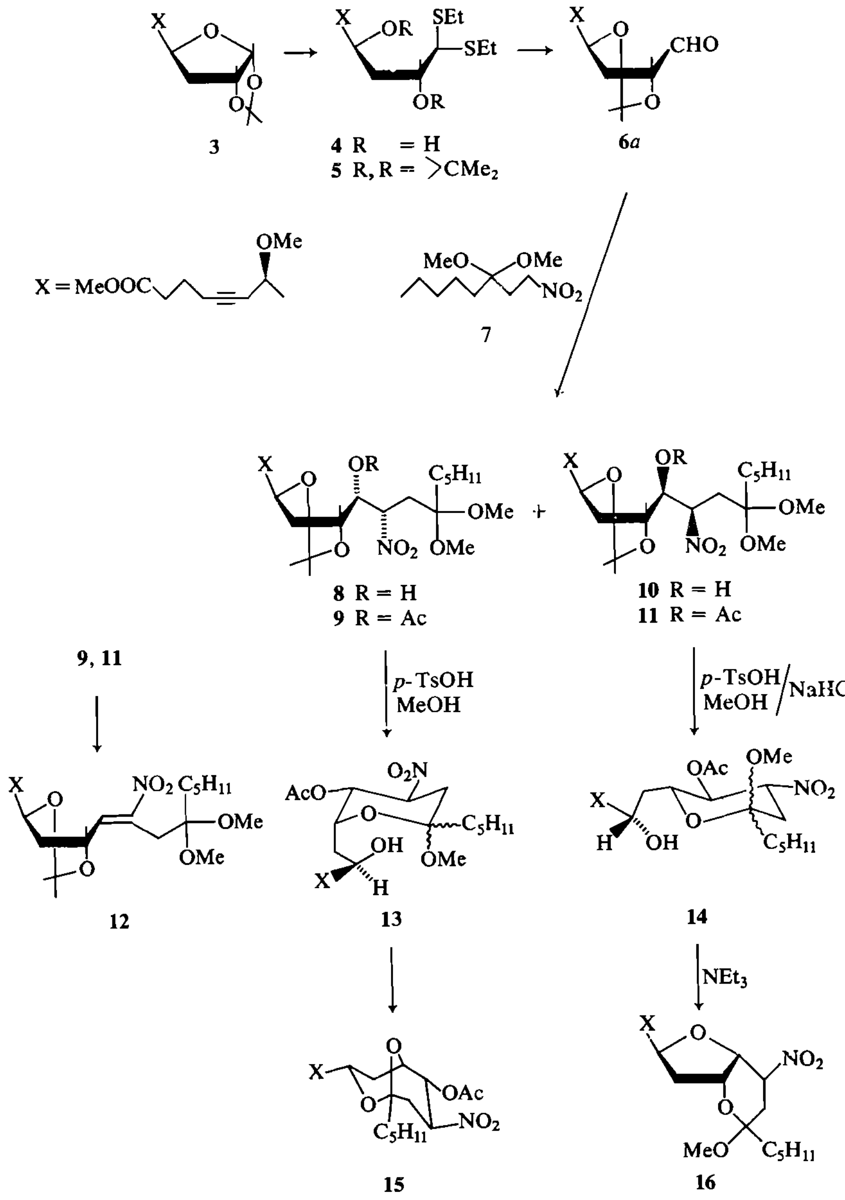
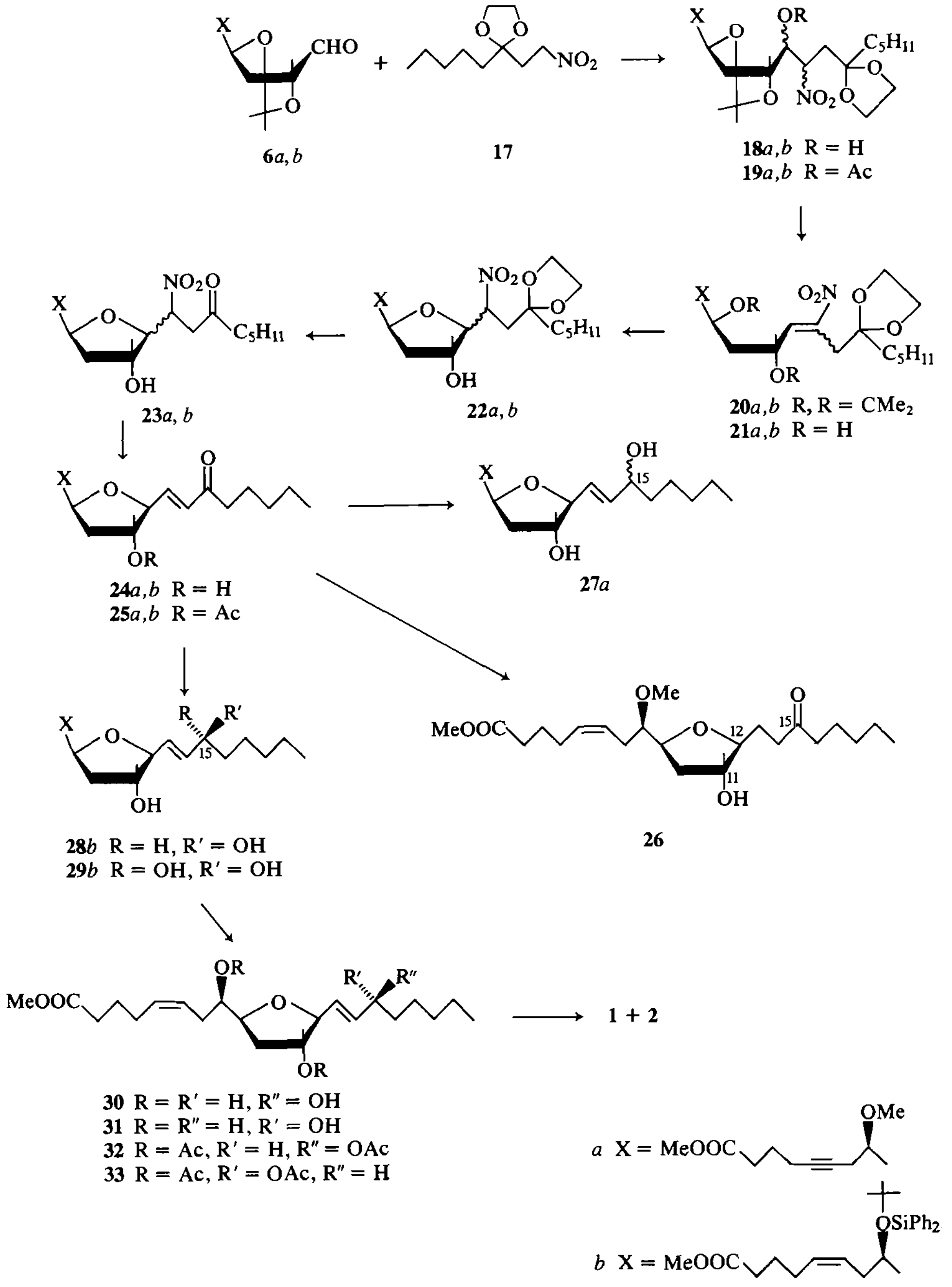


SCHEME 1

possible that the nitro and hydroxyl or acetate groups of **8**, **9**, **13**, and **15** have one of the *erythro*-configurations. A search of the literature revealed that little is known on the configuration of nitro alcohols derived from condensation of nitroalkanes with aldehydes (5).

Since we could not cleave the isopropylidene group in the presence of a dimethyl ketal in compounds of type **12**, the condensation of **6***a* was repeated with β-nitro ketal **17**. The resulting nitro alcohol **18***a* was acetylated, and nitro acetate **19***a* treated with anhydrous potassium carbonate and dicyclohexyl-18-crown-6 to give nitro olefin **20***a*. Mild acid hydrolysis of **20***a* gave the corresponding diol **21***a*, which, upon treatment with triethylamine, gave tetrahydrofuran **22***a* as a mixture of isomers. Acid hydrolysis of the ethylene ketal function gave nitro ketones **23***a*. Upon treatment with triethylamine, both isomers of **23***a* were transformed to one α,β-unsaturated ketone having structure **24***a*, which was characterized as its acetate **25***a*. This leads one to suspect that **23***a* was a mixture of isomers at C-13. Had the isomers of **23***a* differed because of difference of stereo-



SCHEME 2

chemistry at C-12, or C-12 and C-13, then acid treatment of **22***a* should have led to compounds of type **16**. In order to establish unambiguously the stereochemistry at C-12, **24***a* was hydrogenated with H_2/5% Pd–C to give **26**, which was treated under the same reaction conditions (*p*-TsOH/MeOH, 20°C) as for the transformation of **10** to **16**. No cyclic ketalization between the hydroxyl and the free carbonyl groups was observed, thus proving unambiguously that the structure assigned to **24***a* is correct.

Sodium borohydride reduction of **24***a* gave **27***a*, contaminated with products of 1,4-reduction, as a mixture of isomers at C-15, which were not separable.

Having accomplished the conversion of **6***a* to

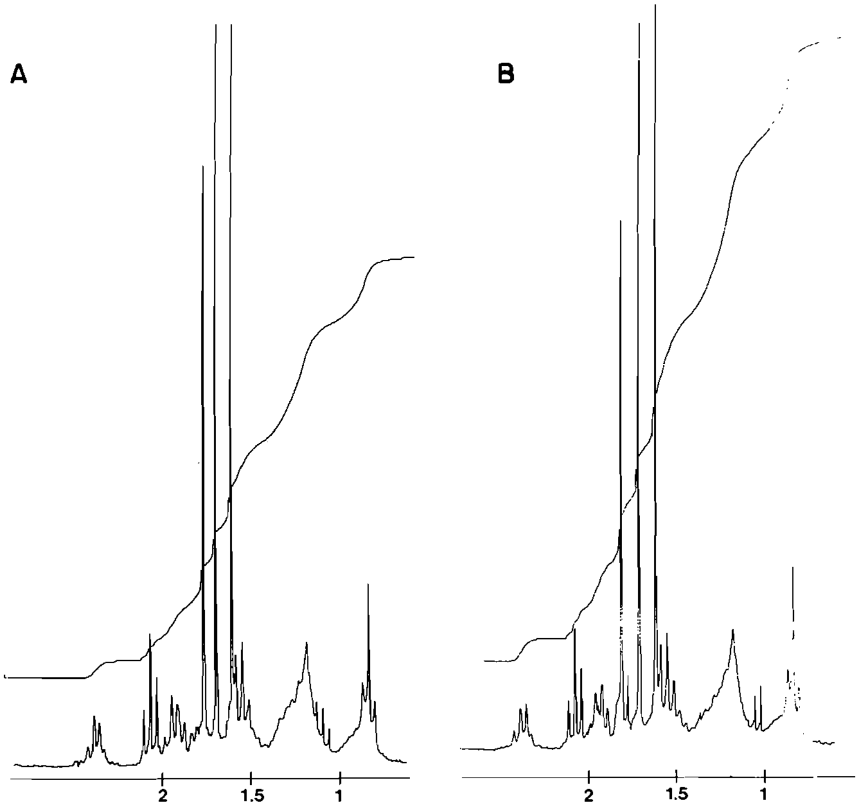


FIG. 1. 200 MHz ^{1}Hmr spectra of 8*R*,11*R*,15*S*-triacetate **32** (A) and 8*R*,11*R*,15*R*-triacetate **33** (B), betwen 0.6 and 2.6 ppm, in benzene-d_6.

27*a*, the sequence was repeated with aldehyde **6***b* (3). Except for minor details and the fact that **22***b* appeared to be one isomer only, the sequence of **24***b* paralleled the one discussed, and is the only one described in the Experimental.

Reduction of **24***b* by diisobornyloxyaluminum isopropoxide (6) gave **28***b* and **29***b* as a mixture of isomers, without contamination by 1,4-reduction products. They were cleanly separable by flash chromatography (7). Removal of the silyl protecting group of both isomers **28***b* and **29***b* by tetra-*n*-butylammonium fluoride gave the corresponding trihydroxy methyl esters **30** and **31**, respectively. They were virtually indistinguishable by mass spectrometry, ir, or ^{1}Hmr. However, the ^{1}Hmr spectra of their acetates **32** and **33** were clearly different and are reproduced in Fig. 1.

Using the method developed in our laboratory (8), the more polar fraction **30** was shown to have the *S*, and the less polar **31** the *R* configuration at C-15. Gas chromatography – mass spectra of tris-trimethylsilyl ether methyl esters of **30** and **31** showed mass spectra identical to that reported by Pace-Asciak and Wolfe (2), except for some minor differences in intensity of some peaks. The ^{1}Hmr (200 MHz) and ir spectra were all consistent with the structure proposed.

Base hydrolysis of trihydroxy methyl ester **30** gave the corresponding trihydroxy carboxylic acid **1**. Here again, the gc – mass spectrum of its tris-trimethylsilyl ether trimethylsilyl ester was identical to that of the natural product isolated by Pace-Asciak and Wolfe (2). This synthesis therefore proves the structure of **1** proposed by Pace-Asciak and Wolfe.

Experimental

Thin-layer chromatography (tlc) was performed on Merck Silica Gel 60 F_{254} aluminum-backed plates. Flash chromatography was done on Woelm Silica (32–63 μ). Melting points (mp) were measured on a Gallenkamp block and are uncorrected, unless specified otherwise. The ^{1}Hmr spectra were recorded on Varian T-60, T-60A, and where noted, XL-200 spectrometers. Infrared (ir) spectra were recorded on Perkin Elmer 257 and 297 spectrophotometers. Mass spectra (ms) were obtained on HP 5984A or LKB 9000 spectrometers, in the direct inlet mode unless indicated otherwise. Elemental analyses were performed by Midwest Microlab Ltd., Indianapolis.

Dihydroxy Dithioacetal 4

A solution of acetonide **3** (0.978 g, 3 mmol) in ethanethiol

(3.5 mL) was cooled to −15°C in an ice–salt bath. To this was added anhydrous $ZnCl_2$ (1.4 g, 10 mmol). The flask was stoppered and allowed to stand for 30 min at −15°C. The ethanethiol was removed under diminished pressure, keeping temperature below 0°C, and the foamy residue was dissolved in ethyl acetate (30 mL). To this was added 5% aqueous $NaHCO_3$ solution (20 mL), and the white precipitate was filtered off. After separation of the organic layer, the aqueous layer was saturated with NaCl and further extracted with ethyl acetate (2 × 15 mL). The combined extracts were dried ($MgSO_4$) and concentrated to give dihydroxy dithioacetal **4** as a yellowish oil in quantitative yield; $[\alpha]_D^{23}$ −2.6° (*c* 2.65, $CHCl_3$); ir (film) ν_{max}: 3440 (OH), 2920, 1730 ($COOCH_3$) cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 1.27 (t, 6H, J = 7 Hz, 2 SCH_2CH_3), 1.50–2.60 (m, 10H, 5 CH_2), 2.70 (q, 4H, J = 7 Hz, 2 SCH_2), 3.07–4.20 (m, 4H, 3 CH—O, SCHS), 3.44 (s, 3H, OCH_3), 3.67 (s, 3H, $COOCH_3$) ppm; ms (70 eV, 40°C), *m/e* (rel. int. %): 374 (0.3, $M^{+\cdot} - H_2O$), 345 (2.0, $M^{+\cdot} - CH_3OH - CH_3^{\cdot}$), 313 (3.8, 374 − $SC_2H_5^{\cdot}$), 257 (56.5, $M^{+\cdot} - 135$), 239 (36.4, 257 − H_2O), 221 (7.4, 257 − $2H_2O$), 135 (86.2, $CH(SC_2H_5)_2^{+}$), 75 (100).

Isopropylidene Dithioacetal 5

A solution of dihydroxy dithioacetal **4** (588 mg, 1.5 mmol) and 2,2-dimethoxypropane (2 mL) in acetone (40 mL) containing a catalytic amount of *p*-toluenesulfonic acid was stirred for 30 min at room temperature. The acetone was evaporated under reduced pressure and the residual oil was dissolved in ether (20 mL). The ether solution was washed with 5% aqueous $NaHCO_3$ (2 × 20 mL), water (2 × 10 mL) and brine, dried ($MgSO_4$), and evaporated *in vacuo* to give isopropylidene dithioacetal **5** as a colorless oil in quantitative yield; ir (film) ν_{max}: 2930, 1740 ($COOCH_3$), 1437, 1380 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 1.25 (t, 6H, J = 7.5 Hz, 2 SCH_2CH_3), 1.38 and 1.43 (s and s, 6H, CMe_2), 1.62–2.63 (m, 10H, 5 CH_2), 2.74 (q, 4H, J = 7.5 Hz, 2 SCH_2), 3.02–4.29 (m, 4H, 3 CH—O, SCHS), 3.44 (s, 3H, OCH_3), 3.65 (s, 3H, $COOCH_3$) ppm; ms (70 eV, 52°C), *m/e* (rel. int. %): 432 (1.1, $M^{+\cdot}$), 371 (1.0, $M^{+\cdot} - SC_2H_5^{\cdot}$), 357 (7.8, $M^{+\cdot} - CH_3COOCH_3$), 297 (96.3, $M^{+\cdot} - 135$), 293 (2.9, $M^{+\cdot} - CH_2C{\equiv}C(CH_2)_3COOCH_3^{\cdot}$), 265 (3.8, 297 − CH_3OH), 239 (34.6), 207 (44.8), 147 (60.8), 135 (32.7, $CH(SC_2H_5)_2^{+}$), 45 (100).

*Aldehyde 6*a

To a solution of dithioacetal **5** (216 mg, 0.50 mmol) in acetone (20 mL) and water (2 mL) were added HgO (976 mg, 4.5 mmol) and $HgCl_2$ (406 mg, 1.5 mmol). The heterogeneous mixture was stirred for 3 h at room temperature, and was filtered into 5% aqueous $NaHCO_3$ (20 mL); the HgO cake was washed with acetone (3 × 5 mL). Filtration and concentration to about 20 mL, followed by extraction with $CHCl_3$ (3 × 20 mL), and washing with 5% aqueous KI solution (3 × 10 mL) and water (20 mL), gave, after drying ($MgSO_4$) and evaporation *in vacuo*, crude ***6a***. Purification by flash chromatography, using petroleum ether – ethyl acetate (5:3) as eluant, afforded 123 mg (75%) of aldehyde ***6a*** as a colorless oil; $[\alpha]_D^{23}$ 11.5° (*c* 5.7, $CHCl_3$); ir (film) ν_{max}: 2990, 2935, 2820, 1736 ($COOCH_3$, CH═O), 1436, 1380 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 1.47 (s, 6H, CMe_2), 1.60–2.64 (m, 10H, 5 CH_2), 3.03–3.37 (m, 1H, CH—O), 3.45 (s, 3H, OCH_3), 3.68 (s, 3H, $COOCH_3$), 3.85–4.50 (m, 2H, 2 CH—O), 9.37 (s, 1H, CH═O) ppm; ms (70 eV, 41°C), *m/e* (rel. int. %): 311 (3.4, $M^{+\cdot} - CH_3^{\cdot}$), 297 (3.1, $M^{+\cdot} - CHO^{\cdot}$), 239 (2.0, $M^{+\cdot} - CH_2CH_2COOCH_3^{\cdot}$), 183 (7.8, $CH(OCH_3)CH_2C{\equiv}C(CH_2)_3COOCH_3^{+}$), 143 (25.7), 129 (47.3), 85 (45.1), 59 (46.7, $COOCH_3^{+}$), 45 (100).

Nitro Alcohols 8 and 10

A solution of aldehyde ***6a*** (326 mg, 1 mmol), β-nitro dimethyl ketal **7** (285 mg, 1.3 mmol), and diisopropylamine (152 mg, 1.5 mmol) in dry dimethylformamide (8 mL) was stirred overnight at room temperature. Water (100 mL) was added to the reaction mixture and the product was extracted with ether (3 × 20 mL). The combined extracts were washed with water (2 × 30 mL) and brine, dried ($MgSO_4$), and evaporated under reduced pressure to give crude adducts **8** and **10**. Purification by flash chromatography, using petroleum ether – ethyl acetate (7:3) as eluant, afforded 490 mg (90%) of nitro alcohols **8** and **10**, which were not separable, as a colorless oil; ir (film) ν_{max}: 3460 (OH), 2990, 2955, 2870, 1740 ($COOCH_3$), 1555 (NO_2), 1380 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.63–2.67 (m, 29H, 10 CH_2, 3 CH_3), 2.87–4.20 (m, 4H, 4 CH—O), 3.08 and 3.12 (s and s, 6H, $C(OCH_3)_2$), 3.40 (s, 3H, OCH_3), 3.63 (s, 3H, $COOCH_3$), 4.60–5.03 (m, 1H, CH—NO_2) ppm.

Nitro Acetates 9 and 11

To a solution of nitro alcohols **8** and **10** (327 mg, 0.6 mmol) in anhydrous ether (10 mL) were added acetic anhydride (73 mg, 0.72 mmol), triethylamine (85 mg, 0.84 mmol), and 4-dimethylaminopyridine (15 mg, 0.12 mmol). After 30 min at room temperature, the solution was washed with 0.1 *N* aqueous HCl (3 mL), 5% aqueous $NaHCO_3$ (2 × 5 mL), and water (2 × 10 mL), dried ($MgSO_4$), and concentrated under reduced pressure to give a 1:1 mixture of nitro acetates **9** and **11** with R_f = 0.31 and 0.40, respectively, in petroleum ether – ethyl acetate (3:1), in quantitative yield. Their spectroscopic data were virtually identical; ir (film) ν_{max}: 2995, 2960, 1758 and 1742 ($COOCH_3$, $OCOCH_3$), 1560 (NO_2), 1370, 1220 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.67–2.60 (m, 23H, 10 CH_2, CH_3), 1.37 and 1.41 (s and s, 6H, CMe_2), 2.07 (s, 3H, $OCOCH_3$), 3.03 and 3.07 (s and s, 6H, $C(OCH_3)_2$), 3.34 (s, 3H, OCH_3), 3.61 (s, 3H, $COOCH_3$), 2.90–4.13 (m, 3H, 3 CH—O), 4.80–5.20 (m, 2H, C*H*OAc, C*H*—NO_2) ppm; ms (70 eV, 61°C), *m/e* (rel. int. %): 572 (0.8, $M^{+\cdot} - CH_3^{\cdot}$), 556 (0.4, $M^{+\cdot} - OCH_3^{\cdot}$), 540 (1.3, $M^{+\cdot} - HNO_2$), 516 (3, $M^{+\cdot} - 71$), 469 (6.3, 540 − 71), 458 (2.1, 516 − $CH_3^{\cdot}$ − $COCH_3^{\cdot}$), 448 (1.3, $M^{+\cdot} - 139$), 404 (2.8, $M^{+\cdot} - 183$), 346 (5.6, 404 − $CH_3^{\cdot}$ − $COCH_3^{\cdot}$), 314 (14.8, 404 − HNO_2 − $C_3H_7^{\cdot}$), 297 (12.7, $M^{+\cdot} - CH(OAc) - CH(NO_2)CH_2C(OCH_3)_2C_5H_{11}^{\cdot}$), 286 (2.2, 404 − HNO_2 − 71), 254 (25.5, 314 − CH_3COOH), 183 (7.0, $CH(OCH_3)CH_2C{\equiv}C(CH_2)_3COOCH_3^{+}$), 145 (100, $C(OCH_3)_2C_5H_{11}^{+}$), 139 (8.0, $CH_2C{\equiv}C(CH_2)_3COOCH_3^{+}$), 71 (32, $C_5H_{11}^{+}$), 43 (88.7, $C_3H_7^{+}$, $COCH_3^{+}$).

Nitro Olefin 12

A mixture of nitro acetates **9** and **11** (117 mg, 0.2 mmol), powdered anhydrous K_2CO_3 (138 mg, 1 mmol), and a catalytic amount of dicyclohexyl-18-crown-6 in dry benzene (3 mL) was stirred for 5 h at 75°C under N_2 atmosphere. The solid K_2CO_3 was filtered off and, after evaporation of the solvent, the residual oil was purified by flash chromatography, using petroleum ether – ethyl acetate (8:2) as eluant, to afford 95 mg (90%) of nitro olefin **12** as a mixture of *E*- and *Z*-olefins; ir (film) ν_{max}: 2990, 2950, 1740 ($COOCH_3$), 1534 (NO_2), 1200 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.67–2.63 (m, 27H, 9 CH_2, 3 CH_3), 3.10 (bs, 2H, $C(NO_2)$—CH_2), 3.14 and 3.17 (s and s, 6H, $C(OCH_3)_2$), 3.42 (s, 3H, OCH_3), 3.65 (s, 3H, $COOCH_3$), 3.73–4.37 (m, 2H, 2 CH—O), 4.76 (ddd, 1H, J = 3, 8, 11 Hz, C═CHC*H*—O), 5.72 and 6.68 (d and d, 1H, J = 8 Hz, CH═C) ppm; ms (70 eV, 69°C), *m/e* (rel. int. %): 480 (0.2, $M^{+\cdot} - HNO_2$), 456 (0.6, $M^{+\cdot} - 71$), 438 (0.3, $M^{+\cdot} - NO_2^{\cdot} - C_3H_7^{\cdot}$), 344 (0.5, $M^{+\cdot} - 183$), 286 (5.7, 344 − $CH_3^{\cdot}$ − $C_3H_7^{\cdot}$), 183 (1.7, $CH(OCH_3)CH_2C{\equiv}C(CH_2)_3COOCH_3^{+}$), 145 (100, $C(OCH_3)_2C_5H_{11}^{+}$), 139 (1.6, $CH_2C{\equiv}C(CH_2)_3COOCH_3^{+}$), 71 (8.3, $C_5H_{11}^{+}$), 43 (9.3, $C_3H_7^{+}$, $COCH_3^{+}$). *Anal.* calcd. for $C_{27}H_{45}O_9N$: C 61.48, H 8.54, N 2.66; found: C 61.70, H 8.79, N 2.39.

Bicyclic Ketal 15

A solution of more polar nitro acetate **9** (45 mg, 0.077 mmol, R_f = 0.31 in 3:1 petroleum ether – ethyl acetate) in methanol (2 mL, dried over molecular sieves) was stirred overnight at room temperature with a catalytic amount of *p*-toluenesulfonic acid. The acid was neutralized with 5% aqueous $NaHCO_3$ solution and the methanol removed under reduced pressure. The residue was taken up in ether (20 mL), which was then washed with water (2 × 10 mL). The ether layer was dried ($MgSO_4$) and concentrated under reduced pressure. Purification by flash chromatography, using petroleum ether – ethyl acetate (3:1) as eluant, gave 27 mg (73%) of bicyclic ketal **15** as a colorless oil; ir (film) ν_{max}: 2950, 2870, 1740 ($COOCH_3$ and $OCOCH_3$), 1555 (NO_2), 1440, 1375, 1230 cm^{-1}; ^{1}Hmr 200 MHz ($CDCl_3$) δ: 0.91 (t, 3H, J = 7 Hz, CH_3), 1.13–2.55 (m, 20H, 10 CH_2), 2.07 (s, 3H, $OCOCH_3$), 3.28 (dt, 1H, J = 6, 6 Hz, C*H*—OCH_3), 3.43 (s, 3H, OCH_3), 3.68 (s, 3H, $COOCH_3$), 4.02 (dt, 1H, J = 4, 12 Hz, CH—O), 4.45–4.58 (m, 1H, CH—O), 5.10–5.25 (m, 1H, CH—NO_2), 5.38–5.47 (m, 1H, C*H*OAc) ppm; ms (70 eV, 107°C), *m/e* (rel. int. %): 437 (8.8, $M^{+\cdot} - NO_2^{\cdot}$), 377 (2.4, $M^{+\cdot} - NO_2^{\cdot} - CH_3COOH$), 345 (4.4, 377 − CH_3OH), 300 (27.2, $M^{+\cdot} - 183$), 253 (9.5, 300 − HNO_2), 252 (8.8, $M^{+\cdot} - CH_3COOH - CH_3OH - 139$), 240 (8, 300 − CH_3COOH), 237 (21.7, $M^{+\cdot} - CH_3COOH - HNO_2 - 139$), 209 (16.6, 252 − $C_3H_7^{\cdot}$), 196 (16.4, 253 − $C_4H_9^{\cdot}$), 193 (66.4, 253 − CH_3COOH), 183 (21, $CH(OCH_3)CH_2C{\equiv}C(CH_2)_3COOCH_3^+$), 139 (8.6, $CH_2C{\equiv}C(CH_2)_3COOCH_3^+$), 99 (100), 71 (76.8, $C_5H_{11}^+$), 43 (67.7, $C_3H_7^+$, $COCH_3^+$); CI (110°C): 484 (24.5, MH^+), 406 (100, $MH^+ - HNO_2 - OCH_3^{\cdot}$), 377 (65.5, $MH^+ - HNO_2 - CH_3COOH$).

Bicyclic Ketal 16

A solution of less polar nitro acetate **11** (45 mg, 0.077 mmol, R_f = 0.40 in 3:1 petroleum ether – ethyl acetate) in methanol (2 mL, dried over molecular sieves) was stirred overnight at room temperature with a catalytic amount of *p*-toluenesulfonic acid. After neutralization with 5% aqueous $NaHCO_3$ solution and evaporation of the methanol, the residue was partitioned between ether (10 mL) and water (10 mL). The ether layer was dried ($MgSO_4$) and to this was added triethylamine (0.5 mL). The resulting solution was stirred overnight at room temperature. After the usual work-up, the crude product was purified by flash chromatography, using petroleum ether – ethyl acetate (3:1) as eluant, to afford 17 mg (50%) of bicyclic ketal **16**; ir (film) ν_{max}: 2955, 2870, 1738 ($COOCH_3$), 1553 (NO_2), 1385, 1040 cm^{-1}; ^{1}Hmr 200 MHz ($CDCl_3$) δ: 0.92 (t, 3H, J = 7 Hz, CH_3), 1.18–2.36 (m, 18H, 9 CH_2), 2.44 (t, 3H, J = 7 Hz, $COCH_2$), 3.20 (s, 3H, OCH_3), 3.47 (s, 3H, OCH_3), 3.44–3.60 (m, 1H, CH—O), 3.68 (s, 3H, $COOCH_3$), 4.21–4.30 (m, 1H, CH—O), 4.36–4.50 (m, 1H, CH—O), 4.52–4.62 (m, 1H, CH—O), 4.86–5.02 (m, 1H, CH—NO_2) ppm; ms (70 eV, 85°C), *m/e* (rel. int. %): 377 (8.2, $M^{+\cdot} - HNO_2 - OCH_3^{\cdot}$), 345 (2.8, 377 − CH_3OH), 337 (5.9, $M^{+\cdot} - HNO_2 - 71$), 269 (9.9, $M^{+\cdot} - HNO_2 - 139$), 252 (3.1, $M^{+\cdot} - CH_2{=}CHNO_2 - C_5H_{11}COOCH_3$), 237 (21.7, 269 − CH_3OH), 225 (3.4, $M^{+\cdot} - HNO_2 - 183$), 223 (7.6, 269 − $OCH_3^{\cdot} - CH_3^{\cdot}$), 194 (9.3, 225 − $OCH_3^{\cdot}$), 193 (9.6, 225 − CH_3OH), 183 (64.2, $CH(OCH_3)CH_2C{\equiv}C(CH_2)_3COOCH_3^+$), 181 (100, 269 − $OCH_3^{\cdot} - C_4H_9^{\cdot}$), 151 (37.7, 183 − CH_3OH), 139 (16.3, $CH_2C{\equiv}C(CH_2)_3COOCH_3^+$), 71 (38, $C_5H_{11}^+$); CI (80°C): 456 (27.8, MH^+), 377 (100, $MH^+ - HNO_2 - CH_3OH$).

β-*Nitro Ethylene Ketal 17*

A solution of 1-nitro-3-octanone (3.46 g, 0.02 mol), ethylene glycol (1.49 g, 0.024 mol), and *p*-toluenesulfonic acid (20 mg) in benzene (20 mL) was refluxed overnight using a Dean-Stark apparatus. The resulting solution was washed with 5% aqueous $NaHCO_3$ (15 mL) and brine, dried, and evaporated under reduced pressure. Distillation gave 3.34 g (77%) of β-nitro ethylene ketal **17** as a colorless oil (bp 88–90°C/0.02 Torr); ir (film) ν_{max}: 2950, 2870, 1552 (NO_2), 1380 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.67–1.80 (m, 11H, 4 CH_2, CH_3), 2.40 (t, 2H, J = 7 Hz, $CH_2CH_2NO_2$), 3.92 (s, 4H, OCH_2CH_2O), 4.40 (t, 2H, J = 7 Hz, CH_2NO_2) ppm.

Nitro Alcohol 18b

A solution of aldehyde ***6b*** (1.66 g, 3 mmol), β-nitro ethylene ketal **17** (0.847 g, 3.90 mmol), and diisopropylamine (0.455 g, 4.50 mmol) in dry dimethylformamide (25 mL) was stirred overnight at room temperature. Water (250 mL) was added to the reaction mixture and the product was extracted with ether (3 × 60 mL). The combined extracts were washed with water (2 × 100 mL) and brine, dried ($MgSO_4$), and concentrated under reduced pressure to yield crude adduct. Purification by flash chromatography, using petroleum ether – ethyl acetate (2:1) as eluant, afforded 2.08 g (90%) of nitro alcohol ***18b*** as a colorless oil; ir (film) ν_{max}: 3450 (OH), 3060, 3040, 2930, 2850, 1730 ($COOCH_3$), 1545 (NO_2) cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.67–3.10 (m, 23H, 10 CH_2, CH_3), 1.08 (s, 9H, *t*-Bu), 1.30 (s, 6H, CMe_2), 3.60 (s, 3H, $COOCH_3$), 3.87 (bs, 4H, OCH_2CH_2O), 3.40–4.04 (m, 4H, 4 CH—O), 4.63–5.10 (m, 1H, CH—NO_2), 5.12–5.40 (m, 2H, CH=CH), 7.13–7.80 (m, 10H, 2 C_6H_5) ppm; ms (20 eV, 95°C), *m/e* (rel. int. %): 608 (0.7, $M^{+\cdot} - 143 - H_2O$), 495 (26.5, $CH(CO)(OSi(t\text{-}Bu)Ph_2)CH_2CH{=}CH(CH_2)_3COOCH_3^+$), 409 (12.7, $CH(OSi(t\text{-}Bu)Ph_2)CH_2CH{=}CH(CH_2)_3COOCH_3^+$), 381 (64.2, $CH(CHO)(OSiPh_2)CH_2CH{=}CH(CH_2)_3COOCH_3^+$), 353 (7.3, 381 − CO), 199 (17.3, 381 − $SiPh_2^{\cdot}$), 143 (100, $C(OCH_2CH_2O)C_5H_{11}^+$), 141 (8.9, $CH_2CH{=}CH(CH_2)_3COOCH_3^+$), 71 (10, $C_5H_{11}^+$).

*Nitro Acetate 19*b

To a solution of nitro alcohol ***18b*** (1.02 g, 1.33 mmol) in anhydrous ether (20 mL) were added acetic anhydride (0.163 g, 1.60 mmol), triethylamine (0.188 g, 1.86 mmol), and 4-dimethylaminopyridine (0.033 g, 0.27 mmol). After 30 min at room temperature, the solution was washed with 0.1 *N* aqueous HCl (20 mL), 5% aqueous $NaHCO_3$ (2 × 10 mL), and water (1 × 10 mL), dried ($MgSO_4$), and evaporated *in vacuo* to give nitro acetate ***19b*** as a colorless oil in quantiative yield; ir (film) ν_{max}: 3060, 2950, 2850, 1753 and 1735 ($COOCH_3$, $OCOCH_3$), 1550 (NO_2) cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.67–2.90 (m, 23H, 10 CH_2, CH_3), 1.07 (s, 9H, *t*-Bu), 1.35 (s, 6H, CMe_2), 2.01 (s, 3H, $OCOCH_3$), 3.67 (s, 3H, $COOCH_3$), 3.92 (bs, 4H, OCH_2CH_2O), 3.50–4.10 (m, 3H, 3 CH—O), 4.80–5.60 (m, 4H, CH=CH, C*H*OAc, CH—NO_2), 7.27–7.94 (m, 10 H, 2 C_6H_5) ppm; ms (70 eV, 76°C), *m/e* (rel. int. %): 811 ($M^{+\cdot}$), 796 (2.6, $M^{+\cdot} - CH_3^{\cdot}$), 740 (0.4, $M^{+\cdot} - C_5H_{11}^{\cdot}$), 696 (24.4), 693 (1.7, 740 − HNO_2), 682 (9.3), 637 (9.2, $M^{+\cdot} - 143 - OCH_3^{\cdot}$), 636 (9.5, $M^{+\cdot} - 143 - CH_3OH$), 437 (20.5, $CH(CO)(OSi(t\text{-}Bu)Ph_2)CH_2CH{=}CH(CH_2)_3COOCH_3^+$), 409 (10.1, 437 − CO), 381 (22.8, $CH(CHO)(OSiPh_2)CH_2CH{=}CH(CH_2)_3COOCH_3^+$), 199 (5.1, 381 − $SiPh_2^{\cdot}$), 143 (100, $C(OCH_2CH_2O)C_5H_{11}^+$). *Anal.* calcd. for $C_{44}H_{65}O_{11}NSi$: C 65.10, H 8.01, N 1.73; found: C 64.91, H 8.30, N 1.90.

*Nitro Olefin 20*b

A mixture of nitro acetate ***19b*** (1.90 g, 2.34 mmol), powdered anhydrous K_2CO_3 (1.61 g, 11.7 mmol), and a catalytic amount of dicyclohexyl-18-crown-6 was stirred in dry benzene (25 mL) for 6 h at 75°C under a N_2 atmosphere. The solid K_2CO_3 was filtered off and after evaporation of the benzene, the residual oil was purified by flash chromatography, using petroleum ether – ethyl acetate (8:1) as eluant to give 1.67 g (95%) of nitro olefin ***20b*** as an oil; ir (film) ν_{max}: 3060, 2950, 2925, 2850, 1735 ($COOCH_3$), 1525 (NO_2), 1423, 1106 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.67–2.40 (m, 21H, 9 CH_2, CH_3), 1.07 (s, 9H, *t*-Bu), 1.37 and 1.40 (s and s, 6H, CMe_2), 3.10 (bs, 2H, $C(NO_2)$—CH_2), 3.62 (s, 3H, $COOCH_3$), 3.80 (bs, 4H, OCH_2CH_2O), 3.60–4.00 (m, 2H, 2 CH—O), 4.36–4.90 (m, 1H, C=CHC*H*—O), 5.20–5.50 (m, 2H, CH=CH), 6.74 (d, 1H, J = 8 Hz; $C(NO_2){=}CH$), 7.17–7.80 (m, 10H, 2 C_6H_5) ppm; ms (70 eV, 119°C), *m/e* (rel. int. %): 409 (1.1, $CH(OSi(t\text{-}Bu)Ph_2)CH_2CH{=}CH(CH_2)_3COOCH_3^+$), 381 (3.6, $CH(CHO)(OSiPh_2)CH_2CH{=}CH(CH_2)_3COOCH_3^+$), 199 (7.6, 381 − $SiPh_2^{\cdot}$), 143 (100, $C(OCH_2CH_2O)C_5H_{11}^+$).

*Dihydroxy Nitro Olefin 21*b *and Hydroxy Tetrahydrofuran 22*b

A solution of isopropylidene nitro olefin **20*b*** (975 mg, 1.30 mmol) in 2 *N* aqueous HCl (8 mL) and methanol (80 mL) was stirred for 2 h at room temperature. To this 5% aqueous $NaHCO_3$ solution was added until the solution became neutral and the methanol was removed under reduced pressure. The residue was partitioned between ethyl acetate (40 mL) and saturated salt solution (20 mL), and the aqueous layer was further extracted with ethyl acetate (2 × 20 mL). The combined extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give a mixture of dihydroxy nitro olefin **21*b*** and hydroxy tetrahydrofuran **22*b***. Purification by flash chromatography, using petroleum ether – ethyl acetate (3:1) as eluant, afforded 138 mg (15%) of dihydroxy nitro olefin **21*b*** and 555 mg (60%) of hydroxy tetrahydrofuran **22*b***.

A solution of dihydroxy nitro olefin **21*b*** (138 mg, 0.194 mmol) and triethylamine (24 mg, 0.234 mmol) in dry THF (3 mL) was stirred overnight at room temperature. The THF was removed under reduced pressure and the residue was taken up in ether (10 mL). The ether solution was washed with 0.1 *N* aqueous HCl (5 mL), 5% aqueous $NaHCO_3$ (5 mL), dried ($MgSO_4$), and concentrated *in vacuo* to give hydroxy tetrahydrofuran **22*b*** in quantitative yield.

The separation of **21*b*** and **22*b*** proved to be unnecessary, and, in general, the mixture of **21*b*** and **22*b*** was submitted directly to the action of triethylamine.

Dihydroxy nitro olefin **21*b***; ^{1}Hmr ($CDCl_3$) δ: 0.67–3.30 (m, 23H, 10 CH_2, CH_3), 1.07 (s, 9H, *t*-Bu), 3.60 (s, 3H, $COOCH_3$), 3.81 (bs, 4H, OCH_2CH_2O), 3.50–3.97 (m, 2H, 2 CH—O), 4.30–4.76 (m, 1H, C═CHC*H*—O), 5.13–5.40 (m, 2H, CH═CH), 6.78 (d, 1H, *J* = 8 Hz, $C(NO_2)$═CH), 7.17–7.77 (m, 10H, 2 C_6H_5) ppm.

Hydroxy tetrahydrofuran **22*b***; ir (film) ν_{max}: 3460 (OH), 3065, 3040, 2950, 2925, 2850, 1737 ($COOCH_3$), 1550 (NO_2), 1423, 1105 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.63–2.93 (m, 23H, 10 CH_2, CH_3), 1.06 (s, 9H, *t*-Bu), 3.61 (s, 3H, $COOCH_3$), 3.84 (bs, 4H, OCH_2CH_2O), 3.53–4.80 (m, 5H, 4 CH—O, CH—NO_2), 5.06–5.43 (m, 2H, CH═CH), 7.17–7.83 (m, 10H, 2 C_6H_5) ppm; ms (70 eV, 96°C), *m*/*e* (rel. int. %): 711 ($M^{+\cdot}$), 654 (1.2, $M^{+\cdot}$ − *t*-Bu$^\cdot$), 640 (3.9, $M^{+\cdot}$ − $C_5H_{11}{}^\cdot$), 607 (3.9, 654 − HNO_2), 593 (2.3, 640 −HNO_2), 437 (3.3, $M^{+\cdot}$ − *t*-Bu$^\cdot$ − $O_2NCH_2CH_2C(OCH_2CH_2O)C_5H_{11}$), 409 (2,6, $CH(OSi(t\text{-}Bu)Ph_2)CH_2CH{=}CH(CH_2)_3COOCH_3{}^+$), 199 (25.6), 143 (100, $C(OCH_2CH_2O)C_5H_{11}{}^+$).

*Methyl 8*R-tert-*Butyldiphenylsilyloxy-11*R-*hydroxy-13-nitro-15-oxo-9*S,*12*S-*oxyeicosa-5*Z-*enoate 23*b

A solution of β-nitro ketal **22*b*** (426 mg, 0.6 mmol) in acetone (8 mL) containing a catalytic amount of *p*-toluenesulfonic acid was stirred overnight at room temperature. The acetone was removed under reduced pressure and the residue was dissolved in ether (30 mL). The ether solution was washed with 5% aqueous $NaHCO_3$ (2 × 15 mL), water (15 mL) and brine, dried ($MgSO_4$), and concentrated to give crude product. Purification by flash chromatography, using petroleum ether – ethyl acetate (3:1) as eluant, afforded 320 mg (80%) of β-nitro ketone **23*b*** as a colorless oil; ir (film) ν_{max}: 3460 (OH), 3065, 3045, 2950, 2930, 2855, 1735 ($COOCH_3$), 1720 (C═O), 1550 (NO_2), 1423, 1107 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.70–3.33 (m, 23H, 10 CH_2, CH_3), 1.07 (s, 9H, *t*-Bu), 3.60 (s, 3H, $COOCH_3$), 3.77–4.40 (m, 4H, 4 CH—O), 4.66–5.03 (m, 1H, CH—NO_2), 5.10–5.40 (m, 2H, CH═CH), 7.17–7.83 (m, 10H, 2 C_6H_5) ppm; ms (70 eV, 85°C), *m*/*e* (rel. int. %): 620 (1.1, $M^{+\cdot}$ − HNO_2), 610 (3.4, $M^{+\cdot}$ −*t*-Bu$^\cdot$), 593 (3.6, $M^{+\cdot}$ − CH_3COOCH_3), 563 (9.3, 610 − HNO_2), 545 (10.2, 563 − H_2O), 461 (1.0, 620 − H_2O − $CH_2CH{=}CH(CH_2)_3COOCH_3{}^\cdot$), 437 (5.6, 610 − $O_2NCH_2CH_2C(O)C_5H_{11}$), 409 (10.2, $CH(OSi(t\text{-}Bu)Ph_2)CH_2CH{=}CH(CH_2)_3COOCH_3{}^+$), 381 (15.3, $CH(CHO)(OSiPh_2)CH_2CH{=}CH(CH_2)_3COOCH_3{}^+$), 199 (83.1, 381 − $SiPh_2{}^\cdot$), 99 (32.8, $C(O)C_5H_{11}{}^+$).

*Methyl 8*R-tert-*Butyldiphenylsilyloxy-11*R-*hydroxy-15-oxo-9*S,*12*S-*oxyeicosa-5*Z,*13*E-*dienoate 24*b

A solution of β-nitro ketone **23*b*** (180 mg, 0.264 mmol) and triethylamine (40 mg, 0.396 mmol) in chloroform (5 mL) was stirred overnight at room temperature. The resulting solution was washed with water (2 × 5 mL) and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residual oil was purified by flash chromatography, using petroleum ether – ethyl acetate (2:1) as eluant, to give 138 mg (85%) of α,β-unsaturated ketone **24*b*** as a colorless oil; $[\alpha]_D{}^{23}$ −16.2° (*c* 1.75, $CHCl_3$); ir (film) ν_{max}: 3440 (OH), 3060, 3035, 2940, 2918, 2842, 1730 ($COOCH_3$), 1670 and 1626 (C═C—C═O), 1420, 1105 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.67–2.60 (m, 21H, 9 CH_2, CH_3), 1.07 (s, 9H, *t*-Bu), 3.62 (s, 3H, $COOCH_3$), 3.77–4.37 (m, 4H, 4 CH—O), 5.13–5.40 (m, 2H, CH═CH), 6.20 (dd, 1H, *J* = 1.5, 16 Hz, CH═C*H*—C═O), 6.72 (dd, 1H, *J* = 4.5, 16 Hz, C*H*═CH—C═O), 7.20–7.87 (m, 10H, 2 C_6H_5) ppm; ms (70 eV, 76°C), *m*/*e* (rel. int. %): 620 (2.1, $M^{+\cdot}$), 602 (1.1, $M^{+\cdot}$ − H_2O), 563 (19.9, $M^{+\cdot}$ − *t*-Bu$^\cdot$), 545 (19, 563 − H_2O), 531 (1.2, 602 − $C_5H_{11}{}^\cdot$), 409 (14.1, $CH(OSi(t\text{-}Bu)Ph_2)CH_2CH{=}CH(CH_2)_3COOCH_3{}^+$), 381 (20, $CH(CHO)(OSiPh_2)CH_2CH{=}CH(CH_2)_3COOCH_3{}^+$), 199 (100, 381 − $SiPh_2{}^\cdot$), 135 (80.5), 99 (38.1, $C(O)C_5H_{11}{}^+$). *Anal.* calcd. for $C_{37}H_{52}O_6Si$: C 71.62, H 8.39; found: C 71.34, H 8.37.

*Methyl 11*R-*Acetoxy-8*R-tert-*butyldiphenylsilyloxy-15-oxo-9*S,*12*S-*oxyeicosa-5*Z,*13*E-*dienoate 25*b

A solution of alcohol **24*b*** (42 mg, 0.068 mmol), acetic anhydride (8.4 mg, 0.082 mmol), triethylamine (9.0 mg, 0.088 mmol), and a catalytic amount of 4-dimethylaminopyridine in anhydrous ether (3 mL) was stirred for 30 min at room temperature. The resulting solution was partitioned between ether (10 mL) and 0.1 *N* aqueous HCl (3 mL). The ether layer was washed with 5% aqueous $NaHCO_3$ (5 mL), water (5 mL) and brine, dried ($MgSO_4$), and evaporated under reduced pressure to afford 40 mg (90%) of acetate **25*b*** as a colorless oil; $[\alpha]_D{}^{23}$ −25.1° (*c* 1.85, $CHCl_3$); ir (film) ν_{max}: 3060, 2945, 2920, 2845, 1735 ($COOCH_3$, $OCOCH_3$), 1670 and 1630 (C═C—C═O), 1420, 1230, 1104 cm^{-1}; ^{1}Hmr 200 MHz ($CDCl_3$) δ: 0.90 (t, 3H, *J* = 7 Hz, CH_3), 1.06 (s, 9H, *t*-Bu), 1.16–2.37 (m, 14H, 7 CH_2), 2.09 (s, 3H, $OCOCH_3$), 2.21 (t, 2H, *J* = 7 Hz, CH═CHCOC*H*$_2$), 2.47 (t, 2H, *J* = 7 Hz, CH_2—COO), 3.65 (s, 3H, $COOCH_3$), 3.98 (td, 1H, *J* = 4,8 Hz, CH—O), 4.06–4.20 (m, 1H, CH—O), 4.39 (ddd, 1H, *J* = 1.8, 3.5, 4.7 Hz, C*H*—CH═CH—C═O), 4.92–5.04 (m, 1H, C*H*OAc), 5.26–5.48 (m, 2H, CH═CH), 6.26 (dd, 1H, *J* = 1.8, 16 Hz, CH═C*H*—C═O), 6.72 (dd, 1H, *J* = 4.7, 16 Hz, C*H*—CH—C═O), 7.32–7.82 (m, 10H, 2 C_6H_5) ppm; ms (70 eV, 79°C), *m*/*e* (rel. int. %): 662 (0.4, $M^{+\cdot}$), 631 (2.0, $M^{+\cdot}$ − $OCH_3{}^\cdot$), 605 (45.7, $M^{+\cdot}$ − *t*-Bu$^\cdot$), 563 (5, $M^{+\cdot}$ − 99), 545 (33, 605 − CH_3COOH), 521 (1.4, $M^{+\cdot}$ − 141), 461 (11, 521 − CH_3COOH), 409 (17.2, $CH(OSi(t\text{-}Bu)Ph_2)CH_2CH{=}CH(CH_2)_3COOCH_3{}^+$), 381 (52.7, $CH(CHO)(OSiPh_2)CH_2CH{=}CH(CH_2)_3COOCH_3{}^+$), 199 (94.4, 381 − $SiPh_2{}^\cdot$), 141 (8, $CH_2CH{=}CH(CH_2)_3COOCH_3{}^+$), 135 (78.9), 99 (35.6, $C(O)C_5H_{11}{}^+$), 71 (20.5, $C_5H_{11}{}^+$), 43 (100, $C_3H_7{}^+$, $COCH_3{}^+$).

*Methyl 11*R-*Hydroxy-8*R-*methoxy-15-oxo-9*S,*12*S-*oxyeicosa-5*Z-*enoate 26*

A solution of α,β-unsaturated ketone **24*a*** (64 mg, 0.163 mmol) in absolute ethanol (2 mL) containing 5% Pd–C (13 mg) was hydrogenated for 30 min at atmospheric pressure until hydrogen uptake stopped. After filtration, the ethanol was removed under reduced pressure to give ketone **26** in quantitative yield; ir (film) ν_{max}: 3440 (OH), 2950, 2920, 1730 ($COOCH_3$), 1705 (C═O), 1430 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.67–2.77 (m, 25H, 11 CH_2, CH_3), 3.33 (s, 3H, OCH_3), 3.58 (s, 3H, $COOCH_3$), 3.0–4.33 (m, 4H, 4 CH—O), 5.20–5.46 (m, 2H, CH═CH) ppm.

*Methyl 8*R-tert-*Butyldiphenylsilyloxy-11*R,*15(*S *and* R*)-dihydroxy-9*S,*12*S-*oxyeicosa-5*Z,*13*E-*dienoates 28*b *and 29*b

To a solution of α,β-unsaturated ketone **24*b*** (102 mg, 0.165 mmol) in dry toluene (4 mL) was added a solution of 0.3 *M* diisobornyloxyaluminum isopropoxide (5) in toluene (1.12 mL, 0.336 mmol). The reaction mixture was stirred under a nitrogen atmosphere for 2 h at room temperature and partitioned between ethyl acetate (15 mL) and 5% aqueous KH_2PO_4 (pH = 4.1–4.5, 10 mL). The organic layer was separated and the aqueous layer further extracted with ethyl acetate (10 mL). The combined extracts were washed with water (10 mL) and brine, dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography, using petroleum ether – ethyl acetate (1:1) as eluant, afforded 82 mg (80%) of allylic alcohols as an approximately 5.5 : 4.5 isomeric mixture at C-15 (**28*b*** $R_f = 0.23$ and **29*b*** $R_f = 0.33$). The two isomers were cleanly separated by hplc, using petroleum ether – ethyl acetate (2:1) as eluant. Allylic alcohol **28*b*** with $R_f = 0.23$; $[\alpha]_D^{23}$ −16.2° (*c* 2.1, $CHCl_3$); ir (film) ν_{max}: 3395 (OH), 3070, 3050, 2950, 2930, 2855, 1736 ($COOCH_3$), 1585, 1423, 1106 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.67–2.53 (m, 21H, 9 CH_2, CH_3), 1.06 (s, 9H, *t*-Bu), 3.62 (s, 3H, $COOCH_3$), 3.73–4.38 (m, 5H, 5 CH—O), 5.11–5.45 (m, 2H, *Z* CH=CH), 5.48–5.78 (m, 2H, *E* CH=CH), 7.20–7.84 (m, 10H, 2 C_6H_5) ppm; gc–ms (1.5% OV-101, 280°C, 70 eV, di-trimethylsilylated **28*b***), *m/e* (rel. int. %): 766 (0.6, $M^{+\cdot}$), 751 (0.9, $M^{+\cdot} - CH_3^{\cdot}$), 709 (0.8, $M^{+\cdot}$ − *t*-Bu˙), 676 (2.1, $M^{+\cdot} - Me_3SiOH$), 625 (1.3, $M^{+\cdot}$ − 141), 619 (30.6, 676 − *t*-Bu˙), 586 (1.1, $M^{+\cdot} - 2Me_3SiOH$), 535 (6.7, 676 − 141), 503 (1.9, 676 − 173), 477 (1.3, 676 − 199), 409 (9, CH(OSi(*t*-Bu)Ph_2)CH_2CH=CH$(CH_2)_3$-$COOCH_3^+$), 381 (60.5, CH(CHO)($OSiPh_2$)CH_2CH=CH$(CH_2)_3$-$COOCH_3^+$), 199 (38.1, CH=CHCH($OSiMe_3$)$C_5H_{11}^+$), 173 (12, CH($OSiMe_3$)$C_5H_{11}^+$), 141 (4.4, CH_2CH=CH$(CH_2)_3$-$COOCH_3^+$), 135 (63.9), 73 (100, $SiMe_3^+$).

Allylic alcohol **29*b*** with $R_f = 0.33$; $[\alpha]_D^{23}$ −23.4° (*c* 2.5, $CHCl_3$); its ^{1}Hmr, ir, and ms data were virtually the same as compound **28*b*** described above.

*Methyl 8*R,*11*R,*15*S-*Trihydroxy-9*S,*12*S-*oxyeicosa-5*Z,*13*E-*dienoate 30*

To a solution of silyl ether **28*b*** (50 mg, 0.081 mmol) in dry THF (2 mL) was added a solution of 1 *M* *n*-Bu_4NF in dry THF (0.12 mL, 0.12 mmol) via a syringe, and the resulting solution was stirred for 7 h at 65°C under a N_2 atmosphere. The THF was removed under reduced pressure and the residue was taken up in ethyl acetate (10 mL). The solution was then washed with brine and the aqueous layer was further extracted with ethyl acetate (5 mL). The combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash chromatography, using ethyl acetate as eluant, to give 26 mg (85%) of trihydroxy methyl ester **30** as a white solid (mp 44–45.5°C); $[\alpha]_D^{23}$ −16.4° (*c* 0.95, $CHCl_3$); ir (film) ν_{max}: 3400 (OH), 2955, 2930, 2860, 1735 ($COOCH_3$), 1436 cm^{-1}; ^{1}Hmr 200 MHz ($CDCl_3$) δ: 0.89 (t, 3H, *J* = 7 Hz, CH_3), 1.18–2.46 (m, 18H, 9 CH_2), 3.68 (s, 3H, $COOCH_3$), 3.74–4.28 (m, 5H, 5 CH—O), 5.40–5.60 (m, 2H, *Z* CH=CH), 5.66 (dd, 1H, *J* = 8, 16 Hz, *E* C*H*=CH), 5.83 (dd, 1H, *J* = 7, 16 Hz, *E* CH=C*H*) ppm; gc–ms (1.5% OV-101, 220°C, 70 eV, tris-trimethylsilylated **30**), *m/e* (rel. int. %): 600 (2.0, $M^{+\cdot}$), 510 (13.8, $M^{+\cdot} - Me_3SiOH$), 495 (3.4, 510 − $CH_3^{\cdot}$), 479 (2.8, 510 − $OCH_3^{\cdot}$), 459 (7.6, $M^{+\cdot}$ − CH_2CH=CH$(CH_2)_3COOCH_3^{\cdot}$), 439 (5.9, 510 − $C_5H_{11}^{\cdot}$), 420 (2.6, $M^{+\cdot}$ − 2 Me_3SiOH), 369 (53.4, 459 − Me_3SiOH), 357 (6.8, $M^{+\cdot}$ − 243), 337 (14, 510 − 173), 279 (17.6, 459 − 2 Me_3SiOH), 267 (11.7, 510 − 243), 243 (77.3, CH($OSiMe_3$)CH_2CH=CH$(CH_2)_3COOCH_3^+$), 211 (11.8, 243 − CH_3OH), 199 (10.2, CH=CHCH($OSiMe_3$)$C_5H_{11}^+$), 173 (23, CH($OSiMe_3$)$C_5H_{11}^+$), 147 (20.1), 129 (46.8), 73 (100, $SiMe_3^+$).

Compound **31** was prepared from the corresponding silyl ether **29*b*** as described above for the preparation of compound **30** in 90% yield (mp 52–53.5°C); $[\alpha]_D^{23}$ −28.6° (*c* 1.4, $CHCl_3$). Its ^{1}Hmr, ir, and ms data were virtually the same as compound **30**.

*8*R,*11*R, *15*S-*Trihydroxy-9*S,*12*S-*oxyeicosa-5*Z,*13*E-*dienoic acid 1*

To a solution of trihydroxy methyl ester **30** (18 mg, 0.047 mmol) in methanol (0.5 mL) was added 0.5 *N* aqueous methanolic NaOH (CH_3OH–H_2O = 7:3, 0.4 mL) and the resulting solution was stirred overnight at room temperature. NaOH was neutralized with glacial acetic acid. After evaporation of the solvent, the residue was dissolved in ethyl acetate (5 mL). The solution was washed with brine (3 mL) and the aqueous layer was further extracted with ethyl acetate (2 × 3 mL). The combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give 15 mg (85%) of trihydroxy carboxylic acid **1**; ir (film) ν_{max}: 3370 (OH), 2960, 2930, 2860, 1710 (C=O) cm^{-1}; ^{1}Hmr 200 MHz ($CDCl_3$) δ: 0.88 (t, 3H, *J* = 7 Hz, CH_3), 1.18–2.50 (m, 18H, 9 CH_2), 3.58–4.44 (m, 5H, 5 CH—O), 5.34–5.94 (m, 4H, 2 CH=CH) ppm; gc–ms (1.5% OV-101, 240°C, 70 eV, fully trimethylsilylated **1**), *m/e* (rel. int. %): 658 (0.9, $M^{+\cdot}$), 643 (1.7, $M^{+\cdot} - CH_3^{\cdot}$), 568 (10.5, $M^{+\cdot} - Me_3SiOH$), 553 (4.4, 568 − $CH_3^{\cdot}$), 497 (2.7, 568 − $C_5H_{11}^{\cdot}$), 478 (3.1, $M^{+\cdot}$ − 2 Me_3SiOH), 459 (4.3, $M^{+\cdot}$ − CH_2CH=CH$(CH_2)_3COOSiMe_3^{\cdot}$), 395 (6.6, 568 − CH($OSiMe_3$)$C_5H_{11}^{\cdot}$), 369 (34.6, 459 − Me_3-SiOH), 357 (4,6 $M^{+\cdot}$ − 301), 301 (49.3, CH($OSiMe_3$)CH_2-CH=CH$(CH_2)_3COOSiMe_3^+$), 279 (12.1, 459 − 2 Me_3SiOH), 272 (30.6), 267 (12.0, 357 − Me_3SiOH), 211 (22.9, 301 − Me_3SiOH), 199 (9.7, CH=CHCH($OSiMe_3$)$C_5H_{11}^+$, CH_2CH=CH$(CH_2)_3COOSiMe_3^+$), 191 (22.9), 173 (20.0, CH($OSiMe_3$)-$C_5H_{11}^+$), 147 (29.1), 129 (47.8), 75 (63.0), 73 (100, $SiMe_3^+$).

General Micromethod for the Determination of the Absolute Chemistry at C-15 of 30

Trihydroxy methyl ester **30** (1 mg, 2.6 μmol) was acetylated using a standard method. Ozone was bubbled into a solution of triacetate **32** in dry CH_2Cl_2 (35 mL) at a rate of 8 mmol/h at −78°C for 5 min. After excess ozone was removed by flushing with N_2 at −78°C, dimethylsulfide (2 mL) was added and stirred overnight at room temperature. The residue, after evaporation of the solvent, was taken up in ether (5 mL) and washed with water (2 × 10 mL) and brine. Concentration under reduced pressure gave crude 2-acetoxyheptanal. A solution of 2-acetoxyheptanal thus obtained and excess l-ephedrine in CH_2Cl_2 (2 mL) was stirred for 1 h at room temperature. It was then diluted with ether (10 mL) and washed with water (3 × 5 mL) and brine. Evaporation and purification by column chromatography, using petroleum ether – ethyl acetate (9:1) as eluant, gave the oxazolidine derivative. Its R_f value (0.33, in petroleum ether – ethyl acetate 5:1) and 200 MHz ^{1}Hmr spectrum were identical with those of the authentic material with known stereochemistry (8).

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