Tetrahedron Vol. 48, No. 3, pp. 443-452, 1992
Printed in Great Britain

0040-4020/92 $3.00+.00

Access to Unsaturated Chiral Epoxides. I: Bisallylic Chiral Epoxides. Application to the Synthesis of Lepidopteran Pheromones.

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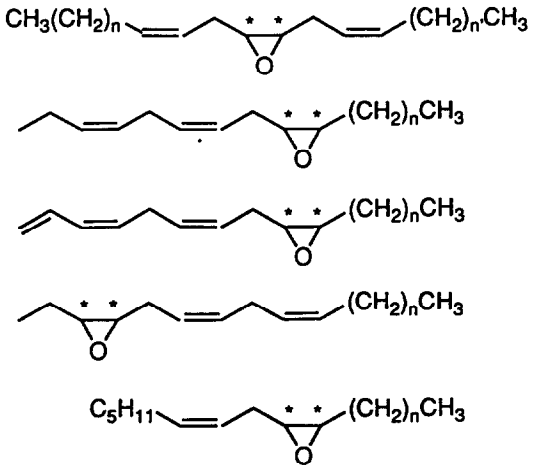
(*Received in Belgium* 21 *November* 1991)

Abstract : *A strategy useful in Lepidopteran pheromones synthesis is illustrated by the preparation of compound 1 in optically pure form. The key step relies on the opening of chiral epoxyalcohols by alkynyllithium reagents.*

Identification of insect pheromones and more generally of the various molecules involved in insect-insect and plant-insect recognition are topics of sustained interest, both from an academic viewpoint and for agrochemical applications.

As part of an ongoing program aimed at identifying sex attractants of Lepidopteran pests, we have developed the syntheses of various optically active unsaturated epoxides of types 1-5 [1-5] encountered in pheromonal secretions of these species.



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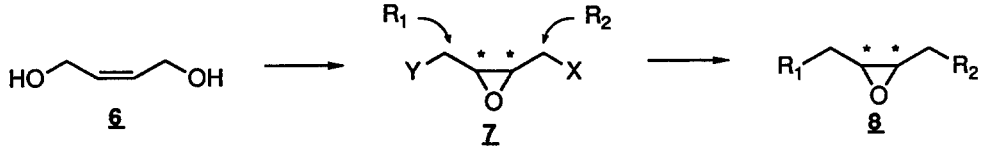
Due to the large structural variability of the target molecules and the biochemical importance of related compounds such as lipoxin[6], we tried to design a flexible strategy which is presented in this paper.

The first approach was based on the use of synthon 7, with suitable leaving groups such Tso or Br as X and Y substituents. Compound 7 is easily obtained in its two enantiomeric forms from the Z-olefin 6 by Sharpless enantiospecific epoxidation. After protection on one side (benzyloxy group) sequential substitution(X=-OTs or Br) of the other epoxide moiety was checked for the construction of an appropriate side chain (scheme 1).

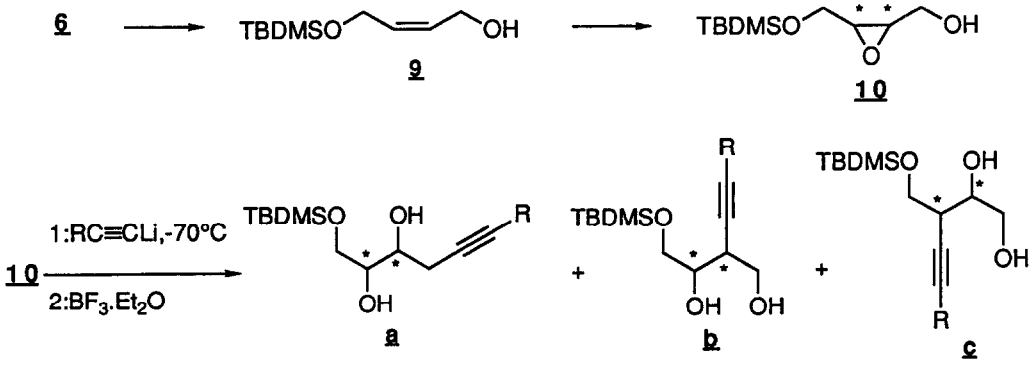


Scheme 1

However, substitution in the α-position of epoxides involving the use of Grignard reagents catalyzed by Cu^{I} proved to be very sluggish for 7 in the case of a long chain substituent (C_{10} or higher) and quite inefficient for introducing an unsaturated substituent ,even using the reverse addition technique described by Nicolaou[7].

An alternative route based on the use of acetylide derivatives as incoming nucleophiles was then explored. The triple bond could later be conveniently converted , either into a saturated chain or into part of an unconjugated system. Direct substitution of 7 (X= OTs or I) by various alkynyllithiums was also unsuccessful[8].

Substitution of 7 (X= OH) at carbon C_1 has been reported by Yamaguchi using an acetylide with activation of the epoxide by a Lewis acid[10]. This surprising result, which can be probably interpreted as a kinetic trapping by substitution of the thermodynamically disfavoured terminal epoxide (Payne rearragement), allowed us to design a simple and quite general access to the target molecules as follows : monoprotection of 6 with dimethylt.butylsilyl chloride (TBDMSCl) produced compound 9 in high yield (90%). Classical Sharpless epoxidation[9] furnished the corresponding chiral epoxy-alcohol 10 . Various alkynyllithiums were added to epoxy-alcohol 10 and afforded the regioisomer a with some amount of isomeric compound b depending up on the chain length of the alkynyl moiety. It is worthy of note that the regioisomer c resulting from attack on C_3 is never present even on trace level (scheme 2).



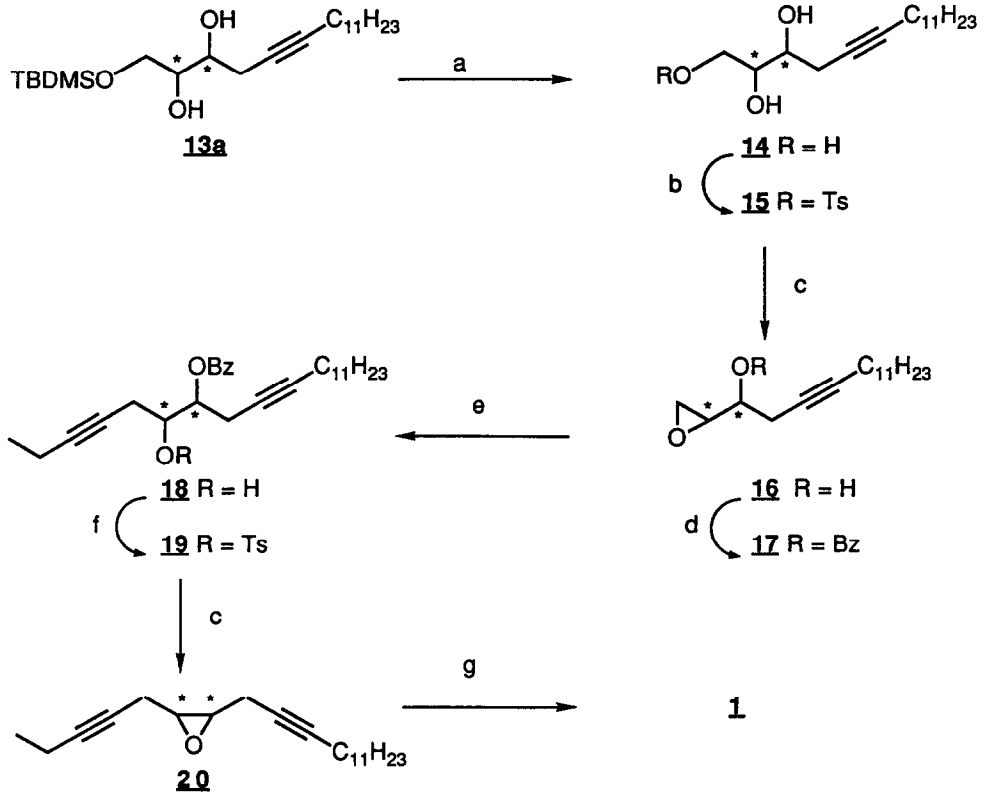
Scheme 2

Best yields are generally obtained by using a large excess of lithiated alkynes (4 eq.) as reported in table 1.

Table 1 : Opening of epoxy-alcohol 10 by alkynyllithiums

	R	a	b	total yield %
11	C_5H_{11}	50	50	80
12	C_8H_{17}	62	38	83
13	$C_{11}H_{23}$	75	25	78

The above strategy was illustrated by the synthesis of target compound 1 (n = 1 and n' = 10) . Chiral diol 13a was readily prepared by the opening of compound 10 (scheme 3).



a: n.Bu_4NF, THF; b: TsCl, -27°C, pyridine; c: K_2CO_3, dry methanol ; d: BzCl, pyridine;
e: $C_2H_5C{\equiv}CLi$, -70°C, $BF_3.Et_2O$; f:TsCl, DMAP, Et_3N; g:H_2, $Pd/BaSO_4$, quinoleine, methanol

Scheme 3

Fluoride induced desilylation gave the primary alcohol 14 which could be selectively monotosylated by operating at low temperature (–27°C, 2 days, 60 % yield). The resulting diol 15 was then converted into epoxide 16 (K_2CO_3 / MeOH), and was benzoylated to give 17. The diastereoisomeric purity was determined at this stage to be ≥ 90 % by H.P.L.C. using a chiral stationary phase [11] . The second side chain was then introduced by the action of 1-butynyllithium using the same procedure as above (92 % yield). Sequential tosylation of the resulting alcohol 18, trans-esterification of the benzoyl group (MeOH, K_2CO_3), and finally hydrogenation of the triple bonds over Pd/$BaSO_4$, afforded the desired product 1 (90 % yield from 18).

In summary, while direct substitution in the α-position of epoxides appeared to be often impossible, the reaction of chiral epoxy α-alcohols by various alkynyllithium reagents in the presence of Lewis acids appears to be a straightforward and general strategy in the preparation of disubstituted chiral epoxides. The resulting compounds allowed us to reach natural Lepidopteran pheromones or analogues, both enantiomers, in optically pure forms.

Experimental Section

General methods

NMR spectra were recorded on Bruker WP 200 and WM 400 spectrometers in $CDCl_3$. Chemical shifts (δ) are in ppm (TMS as internal standard δ = 0) . IR spectra were recorded on a Perkin-Elmer 399 instrument, using neat films on NaCl plates . Melting points were determined on a Büchi 510 apparatus and are uncorrected . Low resolution mass spectra were recorded on a Ribermag R10-10B spectrometer under chemical ionization (NH_3) conditions ; high resolution were recorded on a I.C.R.F.T. Bruker CMS 47X using electron impact. Optical rotations were measured on a Perkin-Elmer 241 polarimeter in a 1-dm cell, in dichloromethane solutions.

All reactions were carried out under an inert atmosphere. Dry solvents were freshly distilled before use . Tetrahydrofuran (THF) was distilled from sodium-benzophenone. Dichloromethane was distilled from P_2O_5 .

All reactions were monitored by thin layer chromatrography carried out on Merck silicagel plates (Ref 5549) using 5 % ethanolic phosphomolybdic acid/heat as developing agent . Merck silicagel (Ref 9384) was used for flash chromatography.

1-Tridecyne were prepared from 1-tridecene by the method of Dehmlow[12] using n.heptane as solvent .

b.p. = 60°C (0.5 mmHg) ; 70 % yield. [lit. [13] b.p. = 109°C (14 mmHg), 90 % yield].

^1H NMR (200 MHz) : 0.68 (t, 3H) ; 1.26 (m, 16H) ; 1,55 (m, 2H) ; 1.92 (t, 1H) ; 2.18 (td, 2H) .

^{13}C NMR (50.28 MHz) : 14.32 ; 18.51 ; 22.81 ; 29.74 ; 32.05 ; 68.12 ; 84.86 ·

IR ν max : 3280 ; 2120 ; 625 .

(2Z)-4-t.butyldimethylsilyloxy-2-buten-1-ol 9

To a stirred solution of 2Z-buten-1,4-diol (8.6 ml, 100 mmoles) in dry dichloromethane (50 ml) and triethylamine (16.5 ml, 120 mmoles) was added slowly a solution of t.butyldimethylsilyl chloride (15 g, 100 mmoles) in dry dichloromethane (30 ml), at ambient temperature. 30 minutes later, water (100 ml) was added and the reaction mixture extracted with ether (3 x 50 ml) . The combined organic layers were washed with water (50 ml) and dried ($MgSO_4$) . Removal of the solvents gave an oil which was distilled to give pure 9 (18.05 g, 90 % yield) . b.p. = 85°C (1 mmHg) .

^1H NMR (200 MHz) : 0.08 (s, 6H) ; 0.82 (s, 9H) ; 2.37 (s, 1H) ; 4.14 (d, 2H) ; 4.17 (d, 2H) ; 5.60 (m,

2H) .

^{13}C NMR (50.28 MHz) : - 5.23 ; 18.30 ; 25.91 ; 58.49 ; 59.64 ; 130.15; 131.02 .

IR ν max : 3400 ; 3015 ; 1650 ; 1250 ; 820 .

(2S,3R)-4-t.butyldimethylsilyloxy-2,3-epoxy-1-butanol 10

Dry methylene chloride (200 ml) was cooled to -25°C under nitrogen and titanium isopropoxide (5.95 ml, 20 mmoles) and L(+) diethyl tartrate (3.45 ml, 20 mmoles) were added sequentially . The mixture was stirred 5 min at - 25°C, and 9 was added dropwise (4.04 g, 20 mmoles). Stirring was continued for 10 min and t.butylhydroperoxide (10.5 ml of 3.6 M in toluene, 40 mmoles) was added dropwise . The resulting mixture was maintained at - 28°C for 48 h . The mixture was worked up by dropwise addition of aqueous tartaric acid (10 %, 50 ml) with vigorous stirring, keeping the temperature below - 20°C . The resulting thick slurry was stirred for a further 90 min at - 20°C, then warmed to 10°C and stirred until the aqueous layer became clear . The layers were separated and the organic layer was washed with water and dried ($MgSO_4$) . After concentration, removal of tartaric ester was accomplished by stirring the crude product with 60 ml of 1N sodium hydroxide in 150 ml of ether for 10 min, at room temperature . Usual work-up afforded crude 10 which was purified by flash chromatography (eluted with ethylacetate/cyclohexane: 1 / 1) or distilled to give a colourless oil, b.p. = 72 - 74°C (0.1 mmHg), 60 % yield . $[\alpha]_D$: - 10.5° (c =3) .

^1H NMR (200 MHz) : 0.15 (s, 6H) ; 0.96 (s, 9H) ; 2.70 (s, 1H) ; 3.20 (m, 2H) ; 3.84 (d, 2H) ; 3.90 (qd, 2H)

^{13}C NMR (50.28 MHz) : - 5.30 ; 18.24 ; 25.81 ; 56.40 ; 56.63 ; 60.53 ; 61.55

IR ν max : 3400 ; 1255 ; 1095 ; 835 .

MS m/e MH^+ : 219 (100%); $M + NH_4^+$: 236 (70%).

Anal. Calcd : $C_{10}H_{22}O_3Si$: C : 55.00 ; H : 10.15 . Found : C : 54.94 ; H : 10.41 .

(2R,3R)-4-t.butyldimethylsilyloxy-2,3-dihydroxy-5-alkynyls

The following procedure describes the synthesis of (2R,3R) 13a. The synthesis of the other alkynyl compounds were performed under identical conditions, using the appropriate alkynyl compounds .

(2R,3R)-4-t.butyldimethylsilyloxy-2,3-dihydroxy-5-heptadecyne 13a

To a solution of tridecyne (3.24 g, 18 mmoles) in anhydrous tetrahydrofuran (100 ml), was added slowly a solution of butyllithium (10.3 ml of 1.75 N in hexane, 18 mmoles) . After 10 min, the mixture was cooled to -70°C, and a solution of 10 (0.98 g, 4.5 mmoles) in anhydrous tetrahydrofuran (10 ml) was added, followed by boron trifluoride,etherate (2.75 ml, 22.5 mmoles) . The resulting mixture was maintained at - 70°C for 1 h . The mixture was worked up by dropwise addition of aqueous saturated ammonium chloride solution (80 ml) under vigorous stirring, keeping the temperature at - 70°C . The mixture was allowed to warm to room temperature and the aqueous layer was extracted with ether (3 x 100 ml) . The combined organic layers were washed with water, dried ($MgSO_4$), concentrated, flash chromatrographed, giving 13a (1 g, 60 % yield) . $[\alpha]_D$: - 0.5° (c= 1)

^1H NMR (200 MHz) : 0.07 (s, 6H) ; 0.8 (t, 3H) ; 0.9 (s, 9H) ; 1.2 (s, 18H) ; 2.1 (tt, 2H) ; 2.5 (dt, 2H); 2.6 (s, 1H) ; 3.7 (m, 4H) .

^{13}C NMR (50,28 MHz) : - 5.39 ; 14.18 ; 18.29 ; 18.84 ; 22.76 ; 24.03 ; 25.92 ; 29.03 ; 29.71 ; 31.99 ; 65.80 ; 71.13 ; 71.84 ; 75.92 ; 82.93 .

IR ν max : 3400 ; 1260 ; 1095 ; 825 .

MS m/e MH^+ : 399 (100 %) ; $M + NH_4^+$: 416 (25 %) .

and 13b (0.2 g, 17 % yield) . $[\alpha]_D$: - 7.6°(c = 1.8) .

^1H NMR (200 MHz) : 0.09 (s, 6H) ; 0.9 (s, t, 12H) ; 1.2 (s, 18H) ; 2.1 (t, d, 2H) ; 2.8 (m, 1H) ; 3.6 (q, 2H) ; 3.7 (m, 4H) .

^{13}C NMR (50.28 MHz) : - 5.39 ; 14.18 ; 18.29 ; 18.84 ; 22.76 ; 25.92 ; 29.03 ; 29.28 ; 29,44 ; 29.71 ; 31.99 ; 37.91 ; 63.88 ; 65.80 ; 71.84 ; 75.92 ; 82.93 .

I.R. ν max : 3400 ; 1250 ; 1090 ; 825.

MS m/e : MH^+ : 399 (100 %) ; $M + NH_4$: 416 (15 %).

(2R,3R)-4-t.butyldimethylsilyloxy-2,3-dihydroxy-5-tetradecyne 12a

This compound was synthesized according to the same procedure and on the same scale as used for 13a (0.8 g, 50 % yield). $[\alpha]_D$: - 0.3°(c : 0.9) .

^1H NMR (200 MHz) : 0.03 (s, 6H) ; 0.85 (s,t, 12H) ; 1.2 (s, 8H) ; 2.08 (tt, 2H) ; 2.40 (dt, 2H) ; 3 (s, 1H) ; 3.7 (m, 4H) .

^{13}C NMR (50.28 MHz) : - 5.59 ; 13.96 ; 18.10 ; 18.65 ; 22.55 ; 23.82 ; 25.74 ; 28.8 ; 31.75 ; 65.24 ; 70.65 ; 71.91 ; 75.93 ; 82.44 .

IR ν max : 3400 ; 1265 ; 1090 ; 825 .

MS m/e MH^+ : 357 (100 %) ; $M + NH_4^+$: 374 (10 %) .

(2R,3R)-4-t.butyldimethylsilyloxy-2,3-dihydroxy-5-undecyne 11a

This compound was synthesized using heptyne by the same procedure and on the same scale as 13a (0.75g, 40 % yield). $[\alpha]_D$: + 0.5°(c = 1) .

^1H NMR (200 MHz) : 0.01 (s, 6H) ; 0.85 (s,t, 12H) ; 1.4 (m, 6H) ; 2.25 (tt, 2H) ; 2.45 (dt, 2H) ; 2.85 (s, 1H) ; 3.10 (s, 1H) ; 3.8 (m, 4H) .

^{13}C NMR (50.28 MHz) : - 5.5 ; 13.95 ; 18.20 ; 18.72 ; 22.19 ; 23.94 ; 25.85 ; 28.67 ; 31.09 ; 65.55 ; 70.92 ; 71.88 ; 75.92 ; 82.68 .

IR ν max : 3400 ; 1250 ; 830 .

MS m/e MH^+ : 315 (100 %) ; $M + NH_4^+$: 332 (15 %) .

(2R,3R)-1,2,3-trihydroxy-5-heptadecyne 14

To a stirred solution of 13a (0.42 g, 1 mmole) in dry tetrahydrofuran (15 ml), at room temperature, was added dropwise a solution of tetra-n-butylammonium fluoride (1.2 ml of 1 M THF, 1.2 mmole) . The reaction mixture was diluted with a saturated aqueous ammonium chloride solution (25 ml) and extracted with ether (3 x 50 ml) . The combined organic extracts were dried ($MgSO_4$), filtered and concentrated to give a white solid . Flash chromatography (ethyl acetate) gave pure 14 (0.27 g, 90 % yield) . m.p. = 60°C . $[\alpha]_D$: - 1.5° (c =1) .

^1H NMR (200 MHz) : 0.9 (t, 3H) ; 1.3 (s, 18H) ; 1.15 (m, 2H) ; 2.1 (s, 1H) ; 2.2 (tt, 2H) ; 2.5 (dt, 2H) ; 3.8 (m, 4H) .

^{13}C NMR (50.28 MHz) : 14.19 ; 18.62 ; 22.76 ; 24.34 ; 29 ; 31.99 ; 64.64 ; 71.25 ; 72.62 ; 75.38 ; 83.74.

IR ν max : 3400 .

MS m/e MH^+ : 285 (10 %) ; $M + NH_4^+$: 302 (100 %) .

Anal. Calc. : $C_{17}H_{32}O_3$: C : 71.78 ; H : 11.33 . Found : C : 71.67 ; H : 11.17 .

(2R,3R)-1-tosyloxy-2,3-dihydroxy-5-heptadecyne 15

To a solution of 14 (0.2 g, 0.7 mmole) in dry pyridine (10 ml) at - 27°C was added p-toluenesulfonyl chloride (0.15 mg, 0.77 mmoles) . The reaction mixture was kept at - 27°C for 48 h, and then poured onto ice . The mixture was extracted with dichloromethane (3 x 50 ml) and the combined extracts were washed with 1N hydrochloric acid, dried (Na_2SO_4, K_2CO_3) and concentrated The crude product was then purified by flash chromatrography (ethyl acetate/cyclohexane : 30/70) to give 15 as a white solid (0.8 g, 63 % yield) . m.p. = 78°C . $[\alpha]_D$: + 4.5°(c= 1.4) .

^1H NMR (200 MHz) : 0.9 (t, 3H) ; 1.27 (s, 16H) ; 1.5 (m, 2H) ; 2.1 (tt, 2H) ; 2.46 (s, dt, 5H) ; 3.7 (m, 1H) ; 3.9 (m, 1H) ; 4.12 (qd, 2H) .

^{13}C NMR (50.28 MHz) : 14.24 ; 18.83 ; 21.70 ; 24.13 ; 29 ; 31.93 ; 69.38 ; 70.40 ; 71.10 ; 75.14 ; 83.74; 128.09 ; 130.01 ; 132.75 ; 145.13 .

IR ν max : 3400 ; 1620 ; 1360 .

MS m/e $M + NH_4^+$: 456 (100 %) .

Anal. Calc. : $C_{24}H_{38}O_5S$: C : 65.72 ; H : 8.73 . Found : C : 65.73 ; H : 8.85 .

(2R,3R)-1,2-epoxy 3-hydroxy-5-heptadecyne 16

To a solution of 15 (0.4 g, 1 mmole) in anhydrous methanol (20 ml) at room temperature, was added, in small portions, anhydrous potassium carbonate (5 equivalents) . After 30 min, the solvent was removed and the mixture was directly purified by flash chromatography (ethyl acetate/cyclohexane : 30/70) to give pure 16 (0.24 g, 95 % yield). $[\alpha]_D$: - 5.6°(c =0.6) .

^1H NMR (200 MHz) : 0.89 (t, 3H) ; 1.3 (s, 16H) ; 1.5 (m, 2H) ; 2.1 (tt, 2H) ; 2.5 (dt, 2H) ; 2.8 (qd 2H); 3.18 (m, 1H) ; 3.7 (s, 1H) .

^{13}C NMR (50.28 MHz) : 14.16 ; 18.79 ; 22.75 ; 25.03 ; 28.98 ; 29.22 ; 29.41 ; 29.63 ; 31.98 ; 45.01 ; 54.41 ; 70.08 ; 74.92 ; 83.41 .

IR ν max : 3400 ; 3040 ; 1260 ; 890.

HRMS calcd for $C_{17}H_{30}O_2$: 266.2240 . Found : 266.2259 .

(2R,3R)-1,2-epoxy-3-benzoyloxy-5-heptadecyne 17

To a solution of 16 (0.29 g, 1.1 mmole) in dry pyridine (15 ml), at room temperature, was added benzoyl chloride (0.17 g, 1.2 mmole) . After 20 min, the reaction mixture was diluted with water (20 ml) and extracted with methylene chloride (3 x 40 ml) . The combined organic extract was dried (Na_2SO_4), filtered and concentrated to give an oil . Flash chromatography (ethyl acetate/cyclohexane : 30/70) gave pure 17 (0.36 g, 90% yield). $[\alpha]_D$: - 7.5°(c =0.6) .

^1H NMR (200 MHz) : 0.89 (t, 3H) ; 1.26 (s, 16H) ; 1.45 (q, 2H) ; 2.14 (tt, 2H) ; 2.69 (m, 5H).

^{13}C NMR (50.28 MHz) : 14.20 ; 18.77 ; 22.10 ; 22.78 ; 28.93 ; 29.26 ; 29.44 ; 29.63 ; 29.73 ; 32.02 ; 45.24 ; 52.28 ; 72.93 ; 74.15 ; 83.39 ; 128.45 ; 129.91 ; 133.27 ; 165.7 .

IR ν max : 3050 ; 1725 ; 1270 ; 895.

MS m/e MH^+ : 371 (60 %) ; $M + NH_4^+$: 388 (100 %)

(6R,7R)-6-hydroxy-7-benzoyloxy-3,9-heneicosadiyne 18

To a solution of butyne (0.46 ml, 6 mmoles) in anhydrous tetrahydrofuran (50 ml) was added slowly a solution of butyllithium (2.5 ml of 1.6N in hexane, 4 mmoles) . After 15 min the mixture was cooled to –70°C, a solution of 17 (0.74 g, 2 mmoles) in anhydrous tetrahydrofuran (15 ml) was added, followed by boron trifluoride,etherate (0.36 ml, 3 mmoles) . The resulting mixture was maintained at - 70°C for 15 min . The mixture was worked up by dropwise addition of aqueous saturated ammonium chloride solution (30 ml) with vigorous stirring, while maintaining the temperature at - 70°C . After warming to room temperature, the aqueous layer was extracted with ether (3 x 50 ml) and the combined organic layers were washed with water, dried ($MgSO_4$) and concentrated. Purification by flash chromatography (ethyl acetate/cyclohexane : 20/80), giving 18 (0.8 g, 95 % yield) . $[\alpha]_D$: - 11.8°(c = 0.7) .

^1H NMR (400 MHz) : 0.88 (t, 3H) ; 1.06 (t, 3H) ; 1.2 (s, 18H) ; 2.0 (m, 4H) ; 2.5 (dt, 2H) ; 2.7 (qt, 2H); 4.45 (m, 1H) ; 5.25 (m, 1H) ; 7.4 - 8.2 (m, 5H) .

^{13}C NMR (100,57 MHz) : 12.49 ; 14.12 ; 14.17 ; 18.82 ; 21.36 ; 22.79 ; 24.45 ; 27.04 ; 28.97 ; 29.27 ; 29.46 ; 29.75 ; 32.04 ; 70.20 ; 74.21 ; 74.38 ; 74.76 ; 83.25 ; 85.08 ; 128.45 ; 129.91 ; 130.23 ; 133.18; 166.04 .

IR ν max : 3450 ; 1720 .

MS m/e MH^+ : 425 (100 %) ; $M + NH_4^+$: 442 (70 %) .

(6R,7R)-6-tosyloxy-7-benzoyloxy-3,9-heneicosadiyne 19

To a solution of 18 (0.42 g, 1 mmole) in dry dichloromethane (15 ml) was added, at room temperature, dry triethylamine (0.15 ml) and 4-dimethylaminopyridine (0.15 g) . The resulting mixture was cooled at 0°C, p-toluenesulfonyl chloride (0.22 g, 12 mmoles) was added. After one hour, the reaction mixture was kept at 25°C for 48 h, then poured onto ice. The mixture was extracted with ether (3 x 20 ml) and the combined extracts were washed with 1N hydrochloric acid, dried (Na_2SO_4) and concentrated. The crude product was then purified by flash chromatography (ethyl acetate/cyclohexane : 20/80) to give pure 19 (0.54 g, 94.7 % yield). $[\alpha]_D$: - 48° (c = 0.7) .

^1H NMR (200 MHz) : 0.89 (t, 3H) ; 1.1 (t, 3H) ; 1.27 (s, 18H) ; 2.09 (m, 4H) ; 2.39 (s, 3H) ; 2.55 (dt, 2H) ; 2.7 (qt, 2H) ; 4.99 (q, 1H) ; 5.5 (q, 1H) ; 7.2 - 7.97 (m, 9H) .

^{13}C NMR (50.28 MHz) : 12.47 ; 13.92 ; 14.20 ; 18.79 ; 21.11 ; 21.72 ; 22.35 ; 22.79 ; 27.02 ; 28.89 ; 28.99 ; 29.30 ; 29.46 ; 29.65 ; 29.75 ; 32.03 ; 71.57 ; 72.37 ; 73.62 ; 79.41 ; 83.71 ; 85.52 ; 127.88 - s144.70 ; 165.38 .

IR ν max : 1720 ; 1360 ; 1155.

MS m/e MH^+ : 578 (15 %) ; $M + NH_4^+$: 596 (100 %) .

(6S,7R)-6,7-epoxy-3,9-heneicosadiyne 20

To a solution of 19 (0.46 g, 0.8 mmole) in dry methanol (20 ml), at room temperature, was added, in small portions, anhydrous potassium carbonate (5 equivalents) . After 45 min, the solvent was removed and the residue was purified by flash chromatrography (ethyl acetate/cyclohexane : 15/85) to give pure 20 as a white solid (0.22 g, 95 % yield) ; m.p. : 31°; $[\alpha]_D$: - 2.5°(c =0.7) .

^{1}H NMR (400 MHz) : 0.88 (t, 3H) ; 1.12 (t, 3H) ; 1.26 (s, 18H) ; ; 2.1 - 2.5 (qd, 4H); 3.1 (m, 2H) .

^{13}C NMR (100.57 MHz) : 12.55 ; 14.21 ; 18.79 ; 22.80 ; 29.01 ; 29.28 ; 29.47 ; 29.75 ; 32.04 ; 55.44 ; 74.04 ; 74.62 ; 82.84 ; 84.08 .

MS m/e MH^+ : 303 (10 %) ; $M + NH_4^+$: 320 (100 %) .

(6S,7R,3Z,9Z)-6,7-epoxy-3,9 heneicosadiene 1

A solution of 20 (0.3 g, 1 mmole) in methanol with quinoleine (0.01ml) and Pd on $BaSO_4$ (10 mg) was stirred under a hydrogen atmosphere for 2 hours. After filtration of the catalyst and concentration, the residue was purified by flash chromatography (ethyl acetate/cyclohexane : 15/85) to give pure 1 (0.29 g, 96% yield). $[\alpha]_D$: - 1.8°(c= 0.6). [lit. [1] $[\alpha]_D$: - 1.1°(c= 6,22, CH_2Cl_2).

^{1}H NMR (400 MHz) : 0.87 (t, 3H) ; 0.97 (t, 3H) ; 1.25 (s, 18H) ; 2.05 (m, 4H) ; 2.2 (m, 2H) ; 2.4 (m, 2H) ; 2.94 (m, 2H) ; 5.4 (m, 2H) ; 5.6 (m, 2H) .

^{13}C NMR (100,57 MHz) : 14.23 ; 20.88 ; 22.81 ; 26.29 ; 29.77 ; 32.05 ; 56.65 ; 123.32 ; 123.81 ; 132.97 ; 134.48 .

IR ν max : 3020 ; 720.

MS m/e MH^+ : 307 (15 %) ; $M + NH_4^+$: 324 (90 %).

The compounds (2R, 3S) 10 (62%, $[\alpha]_D$: +10°(c = 1.3), (2S,3S) 13a (61.5 %, $[\alpha]_D$: + 0.6°(c = 0.9), (2S,3S) 14 (87 %, $[\alpha]_D$: + 1.6°(c= 0.8), (2S,3S) 15 (65 %, $[\alpha]_D$: - 4°(c = 1.4), (2S,3S) 16 (97 % ,$[\alpha]_D$: + 5°(c = 1.6), (2S,3S) 17 (88 %, $[\alpha]_D$: + 7.2°(c = 1.1), (6S,7S) 18 (96 %, $[\alpha]_D$: + 12°(c = 1), (6S,7S) 19 (94 %, $[\alpha]_D$: + 47°(c = 0.9), (6R,7S) 20 (93 %, $[\alpha]_D$: + 2.6°(c=1), (6R,7S,3Z,9Z) 1 (92 %, $[\alpha]_D$: + 1.7°(c = 0.8) were synthesized by the same procedure and on the same scale.

Acknowledgement :
We thank the I.N.R.A. (Institut National de la Recherche Agronomique) for financial support.

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