Studies on the Synthesis of Elegan-Type Linear Diterpenes: The Efficient Total Syntheses of Eleganolone, Eleganolone Acetate, Elegandiol, Eleganonal, and Epoxyeleganolone

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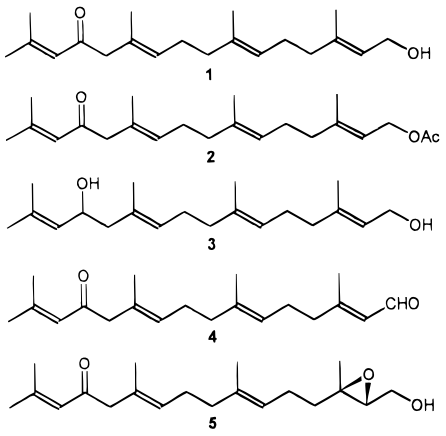
The first total syntheses of five elegan-type linear diterpenes—eleganolone (**1**), eleganolone acetate (**2**), elegandiol (**3**), eleganonal (**4**), and epoxyeleganolone (**5**)—were accomplished starting from (*E,E*)-farnesol (**6**) via four to six steps, successively, with high overall yield. The key step was the alkylation reaction of silyl cyanide with allylic iodide.

Previous studies on the pharmacological activity of *Cystoseira brachycarpa* (J. Agardh) var. *balearica* (Sauv.) Giaccone,[1] *Cystoseira elegans*, and *Bifurcaria bifurcata*[2] have found that these Mediterranean Sea algae demonstrate many significant biological activities such as antiviral and antimicrobial activities, vasodilating effects, and antihypertensive activity. For this reason, chemical studies on these marine algae have developed rapidly, and since eleganolone (**1**) was first isolated nearly 20 years ago,[3] many more such elegan-type acyclic diterpenes or sesquiterpenes have been isolated as natural products.[3−7] Five typical compounds of this kind have been isolated: eleganolone (**1**) from *C. elegans*,[3] *B. bifurcata*,[5] and *Cystoseira balearica*;[4] eleganolone acetate (**2**) from *C. balearica*;[4] elegandiol (**3**) from *B. bifurcata*;[5] eleganonal (**4**) from *C. balearica*;[6] and epoxyeleganolone (**5**) from *B. bifurcata*.[5]



The pharmacological tests indicated that these compounds exhibited significant bioactive effects, such as blocking the isoprenaline inotropic activity,[2] inhibiting the contractile activities of acetylcholine and histamine on ileum musculature. The relative pIC_{50} values of **1** were found to be 4.60 ± 0.03 and 4.84 ± 0.20, while those of **2** were 4.71 ± 0.18 and 5.18 ± 0.01, respectively. Furthermore, **1** and **2** dose dependently relaxed the same preparations precontracted with 300 mM $BaCl_2$ (pIC_{50} = 4.34 ± 0.18 for **1**, and pIC_{50} = 4.34 ± 0.02 for **2**) or with 60 mM KCl (pIC_{50} = 4.73 ± 0.18 and 4.47 ± 0.06, respectively).[1] These pharmacological results support the hypothesis of an antihypertensive activity of the brown alga *C. balearica* as found in other algae belonging to different genera. This effect could be the result of a direct relaxing effect on arterial smooth muscle together with an inhibitory activity on the cardiac inotropism stimulated by adrenergic agonists. It was further proved that these diterpenoids show a higher efficiency with respect to the previous fractions because the active principles in the crude mixture are diluted with other compounds.[2]

The geometrical configurations of these compounds have been elucidated by spectral analysis and chemical correlations, but the absolute stereochemistry of elegandiol **3** and epoxyeleganolone **5** has not yet been determined, and no synthetic work on these significant compounds has yet been reported. To verify the structures of these compounds and to determine their absolute configuration, and furthermore, to do further research on the pharmacological activities of these compounds, we explored the total synthesis of compounds **1**−**5**, and herein provide details of this work.

Our strategy started with (*E,E*)-farnesol (**6**). Acylation of **6** with Ac_2O,[8] followed by selective oxidation of the terminal *E* methyl group, gave alcohol **7**,[9] which can be transformed into iodide **8**.[10] The key step was the alkylation reaction[11] of allylic iodide **8** with silyl cyanide **9**, which was conveniently prepared from 3-methyl-2-buten-1-ol (**10**) through two steps (oxidation with active MnO_2[12] and cyanosilation with Me_3SiCN[13] in the presence of a catalytic amount of KCN/18-crown-6). Deprotection of silyl cyanide **11** with a catalytic amount of n-$Bu_4N^+F^-$ afforded the first title compound (**2**), which was hydrolyzed to obtain compound **1**. Finally, compounds **3**, **4**, and **5** were easily prepared from compound **1** by reduction with $NaBH_4$ to give **3**, oxidation with active MnO_2 to give **4**, and asymmetric Sharpless epoxidation to give **5**. In the asymmetric Sharpless epoxidation of compound **1**, we used D-(−)-DET as the chiral inducer. Therefore, the absolute configuration of

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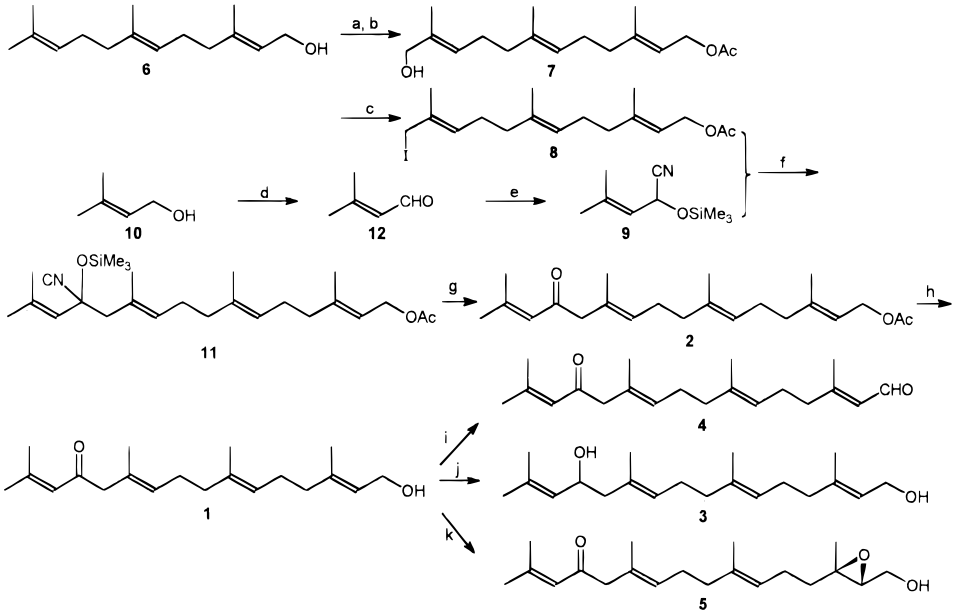
Scheme 1[a]



[a] Key: (a) Ac_2O, Py, DMAP, room temperature, 30 min, 100%; (b) SeO_2, *t*-BuOOH, room temperature, 2 h, 37%; (c) Ph_3P, imidazole, I_2, Et_2O/CH_3CN, 0 °C, 100%; (d) MnO_2, *n*-hexane, 20 h, 70%; (e) Me_3SiCN, 18-crown-6/KCN, CH_2Cl_2, 0 °C, 100%; (f) $(Me_3Si)_2NLi$, **9**, −78 °C, 40 min, then **8**, −78 °C, 2 h, 39%; (g) catalytic amount of n-$Bu_4N^+F^-$, 10% aqueous THF, Ar, room temperature, 15 h, 50%; (h) K_2CO_3, MeOH, room temperature, 2 h, 100%; (i) MnO_2, *n*-hexane, 10 h, 92%; (j) $NaBH_4$, MeOH, 80%; (k) $Ti(O^iPr)_4$, D-(−)-DET, TBHP, CH_2Cl_2, 76%.

the final product **5**, whose optical rotation has been determined as $[a]_D^{20}$ −101 (*c* 0.055, $CHCl_3$), should be (2*R*, 3*R*). See Scheme 1.

In summary, we succeeded in obtaining eleganolone (**1**), eleganolone acetate (**2**), elegandiol (**3**), eleganonal (**4**), and epoxyeleganolone (**5**) in four to six steps from (*E*,*E*)-farnesol. We have also determined that the absolute configuration of (−)-epoxyeleganolone is (2*R*, 3*R*).

Experimental Section

General Experimental Procedures. ^{1}H-NMR spectra were recorded on a Varian FT-80A or Bruker AM-400 spectrometer, and ^{13}C-NMR spectra were recorded at 100 MHz in $CDCl_3$ solution using TMS as internal reference. IR spectra were obtained as films using a FT-170SX spectrophotometer. Mass spectra were measured on a VG ZAB-HS spectrometer by direct inlet at 70 eV, and signals are given in *m*/*z* with relative intensity (%) in brackets. Optical rotation measurements were carried out on a Perkin-Elmer 141 polarimeter. All solvents were freshly purified and dried by standard techniques prior to use. All reactions were routinely carried out under an inert atmosphere of Ar and monitored by TLC. Purification of products were conducted by flash column chromatography on Si gel (200−300 mesh) purchased from Qing Dao Marine Chemical Co. (*E*,*E*)-Farnesol and 3-methyl-2-buten-1-ol were purchased from Aldrich Chemical Co. In the workup, all organic phases were washed with H_2O and brine, respectively, then dried ($MgSO_4$) and filtered prior to rotary evaporation of the solvent under reduced pressure.

3,7,11-Trimethyl-12-hydroxy-2(*E*),6(*E*),10(*E*)-dodecatrien-1-ol Acetyl Acetate (7). To a solution of (*E*,*E*)-farnesol **6** (11.1 g, 50 mmol) and a catalytic amount of DMAP in pyridine (2.15 mL), freshly distilled Ac_2O (5 mL) was added dropwise at 0 °C with vigorous stirring. Stirring was continued at room temperature for 30 min until the reaction was complete. The resulting mixture was diluted with H_2O (10 mL) and extracted with Et_2O (50 mL × 3), the combined organic layer was washed with 10% HCl aqueous solution, H_2O, and brine, then dried. Evaporation of the solvent followed by purification on Si gel afforded farnesol acetyl acetate (13 g, 100%), which was dissolved in CH_2Cl_2 (20 mL) and added dropwise to a clear solution of SeO_2 (555 mg, 5 mmol) and *t*-BuOOH (70%, 13.7 mL, 100 mmol) in CH_2Cl_2 (150 mL) at 0 °C. After being stirred at room temperature for 2 h, the reaction mixture was diluted with Et_2O (200 mL) and washed sequentially with 10% aqueous KOH, H_2O, and brine, then dried and concentrated. The resulting oil was purified by flash column chromatography on Si gel to yield alcohol **7** (4.88 g, 37%) as a colorless oil: IR (film) ν_{max} 3446 (s, OH), 1740 (s, C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 4.95−5.35 (3H, m, CH=), 4.59 (2H, d, J = 7.1 Hz, CH_2OAc), 3.98 (2H, s, CH_2O), 2.00−2.45 (8H, m, $4CH_2$), 2.04 (3H, s, CH_3-CO), 1.71 (3H, s, CH_3), 1.67 (3H, s, CH_3), 1.61 (3H, s, CH_3); *anal.* C 72.70%, H 10.10%, calcd for $C_{17}H_{28}O_3$, C 72.82%, H 10.06%.

3-Methyl-2-butenal (12). A suspension of 3-methyl-2-butenol (**10**) (2 mL, 20 mmol) and MnO_2/SiO_2 (2:1, 13 g) in *n*-hexane (50 mL) was vigorously stirred at room temperature for 20 h before being diluted with Et_2O (50 mL). The mixture was filtered through a short column on Si gel to remove MnO_2, and the resulting filtrate was concentrated and purified to give enal **12** (1.17 g, 70%) as a clear oil: ^{1}H NMR ($CDCl_3$, 80 MHz) δ 9.89 (1H, d, J = 5.6 Hz, CHO), 5.93 (1H, d, J = 8.2 Hz, =CH), 2.25 (3H, s, CH_3), 2.05 (3H, s, CH_3).

3,7,11,15-Tetramethyl-13-cyano-13-(trimethylsiloxy)-2(*E*),6(*E*),10(*E*),14-hexadecatetraen-1-ol Acetyl Acetate (11). A catalytic amount of KCN and 18-

crown-6 complex was first added to enal **12** (84 mg, 1 mmol) in CH_2Cl_2 (1 mL) with stirring, then Me_3SiCN (0.18 mL, 1.2 mmol) was added dropwise to the suspension at 0 °C under argon atmosphere. The reaction was complete within 30 min and gave silyl cyanide **9**, which was used in situ without further purification. To a stirred clear solution of **7** (280 mg, 1 mmol), Ph_3P (393 mg, 1.5 mmol) and imidazole (102 mg, 1.5 mmol) in a mixed solvent of CH_3CN (2 mL) and Et_2O (3 mL) was added iodine crystals portionwise at 0 °C (ice-water bath) until the reaction was complete. After being stirred for an additional 30 min at room temperature, the reaction mixture was diluted with Et_2O (20 mL) and washed with saturated $Na_2S_2O_3$ aqueous solution, H_2O, and brine, then dried. The solvent was removed *in vacuo* and the crude oil was purified by chromatography to afford iodide **8**, which was dissolved in anhydrous THF (2 mL) and used for the followed procedure. To a clear solution of $LiN(SiMe_3)_2$ (1.5 mmol) in anhydrous THF (5 mL) was syringed dropwise a solution of silyl cyanide **9** (183 mg, 1 mmol) in anhydrous THF (2 mL) at −78 °C under an argon atmosphere, and the reaction mixture was stirred at that temperature for a further 40 min. The above solution of allylic iodide **8** in THF (2 mL) was then added dropwise to the reaction mixture with efficient stirring. The stirring was continued for 2 h at −78 °C before the reaction was quenched by the addition of saturated aqueous NH_4Cl and Et_2O (30 mL). The organic phase was washed with H_2O and brine, then dried and concentrated. The residue was purified on Si gel to afford silyl cyanide **11** (173 mg, 39%) as a clear oil: ^{1}H NMR ($CDCl_3$, 80 MHz) δ 4.95−5.50 (4H, m, =CH), 4.62 (2H, d, J = 6.5 Hz, CH_2OAc), 1.40−2.50 (10H, m, $5CH_2$), 2.10 (3H, s, $COCH_3$), 2.17 (3H, s, CH_3), 2.09 (3H, s, CH_3), 1.75 (6H, s, $2CH_3$), 1.65 (3H, s, CH_3), 0.18 (6H, s, $2CH_3$), 0.12 (3H, s, CH_3); *anal.* C 70.29%, H 9.65%, calcd for $C_{26}H_{43}O_3SiN$, C 70.06%, H 9.72%.

Eleganolone Acetate (2). Silyl cyanide **11** (155 mg, 0.35 mmol) was dissolved in 10% aqueous THF (5 mL) and a catalytic amount of n-$Bu_4N^+F^-$ was added. The reaction mixture was stirred at room temperature under an argon atmosphere for 15 h. The resulting mixture was extracted with Et_2O (20 mL × 3), and the combined organic phases were washed with H_2O and brine, then dried. Evaporation of the solvent followed by purification by chromatography gave ketone **2** (60 mg, 50%) as a colorless oil: IR (film) ν_{max} 2965 (s), 2932 (s), 1739 (s), 1687 (s), 1620, 1449, 1380, 1232, 1024, 954 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.12 (1H, s, =CH), 5.34 (1H, t, J = 7.24 Hz, CH=), 5.25 (1H, t, J = 7.0 Hz, =CH), 5.11 (1H, m, =CH), 4.59 (2H, d, J = 7.30 Hz, CH_2O), 3.04 (2H, s, CH_2CO), 2.14 (3H, s, CH_3), 2.05 (3H, s, CH_3), 1.98−2.15 (8H, m, $4CH_2$), 1.88 (3H, s, CH_3), 1.70 (3H, s, CH_3), 1.60 (3H, s, CH_3), 1.58 (3H, s, CH_3); EIMS m/z 346 $[M]^+$ (1), 286 (1), 203 (2), 188 (3), 149 (3), 135 (3), 121 (4), 107 (3), 83 (100), 67 (5), 55 (8); *anal.* C 76.46%, H 9.83%, calcd for $C_{22}H_{34}O_3$, C 76.26%, H 9.89%.

Eleganolone (1). K_2CO_3 powder (14 mg, 0.10 mmol) was added to a solution of eleganolone acetate (**2**) (50 mg, 0.14 mmol) in dry MeOH (1 mL). The mixture was stirred at room temperature for 2 h, then extracted with Et_2O (10 mL × 3). The Et_2O layer was washed with H_2O and brine and dried. Removal of the solvent and purification of the crude residue by flash column chromatography afforded eleganolone (**1**) (42 mg, 100%) as a clear oil: IR (film) ν_{max} 3427 (s), 3382 (s), 2965 (s), 2919 (s), 1736, 1683 (s), 1618, 1442, 1380, 1004 (s), 841 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.12 (1H, s, =CH), 5.42 (1H, t, J = 7.1 Hz, =CH), 5.24 (1H, t, J = 7.1 Hz, =CH), 5.12 (1H, m, =CH), 4.16 (2H, d, J = 6.9 Hz, CH_2O), 3.03 (2H, s, CH_2CO), 2.14 (3H, s, CH_3), 1.95−2.14 (8H, m, $4CH_2$), 1.88 (3H, s, CH_3), 1.68 (3H, s, CH_3), 1.62 (3H, s, CH_3), 1.60 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 198.2, 154.6, 139.8, 135.1, 129.2, 128.4, 124.1, 123.5, 122.9, 59.4, 55.4, 39.5, 39.4, 27.8, 26.8, 26.3, 20.8, 16.3, 16.1, 16.0; EIMS m/z 304 $[M]^+$ (1), 286 (1), 205 (1), 188 (2), 149 (3), 121 (4), 83 (100), 67 (6), 55 (11); *anal.* C 79.08%, H 10.54%, calcd for $C_{20}H_{32}O_2$, C 78.90%, H 10.59%.

Eleganonal (4). A suspension of eleganolone (**1**) (15 mg, 0.05 mmol) and MnO_2/SiO_2 (2:1, 65 mg, 0.5 mmol) in n-hexane (2 mL) was stirred at room temperature for 10 h and then diluted with Et_2O. The mixture was filtered through a short column of Si gel, and the resulting filtrate was concentrated on a rotatory evaporator *in vacuo* to give the crude oil that was purified on Si gel to yield eleganonal (**4**) (13 mg, 92%) as a colorless oil: IR (film) ν_{max} 2920 (s), 1676 (s), 1620 (s), 1516, 1438, 1381, 1110, 1049, 981 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.00 (1H, d, J = 8.0 Hz, CHO), 6.11 (1H, s, =CH), 5.89 (1H, d, J = 8.1 Hz, =CH), 5.23 (1H, m, =CH), 5.10 (1H, t, J = 6.7 Hz, =CH), 3.04 (2H, s, CH_2CO), 2.17 (3H, s, CH_3), 2.15 (3H, s, CH_3), 2.00−2.45 (8H, m, $4CH_2$), 1.88 (3H, s, CH_3), 1.70 (3H, s, CH_3), 1.62 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.8, 191.3, 163.9, 156.5, 136.7, 128.7, 128.1, 127.5, 123.0, 122.9, 55.4, 40.6, 39.5, 27.8, 26.8, 25.7, 20.8, 17.6, 16.4, 16.1; EIMS m/z 302 $[M]^+$ (1), 219 (1), 186 (2), 151 (2), 121 (1), 109 (2), 91 (2), 83 (100), 67 (4), 55 (9); *anal.* C 79.21%, H 10.06%, calcd for $C_{20}H_{30}O_2$, C 79.42%, H 10.00%.

Elegandiol (3). To an ice-cooled solution of **1** (9 mg, 0.03 mmol) in dry MeOH (0.5 mL) was added $NaBH_4$ portionwise at 0 °C with stirring until the reaction was complete. The resulting mixture was diluted with H_2O and extracted with Et_2O (10 mL × 4). The organic layer was washed with H_2O and brine and dried. Evaporation of the solvent *in vacuo* gave an oily residue, which was chromatographed on Si gel to yield diol **3** (7 mg, 80%) as a clear oil: IR (film) ν_{max} 3322 (s), 2963 (s), 2923 (s), 1720, 1669, 1449, 1378, 1006, 838 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.42 (1H, m, =CH), 5.21 (1H, m, =CH), 5.11 (2H, m, 2CH=), 4.44 (1H, m, C*H*OH), 4.15 (2H, d, J = 6.9 Hz, CH_2OH), 1.99−2.11 (10H, m, $5CH_2$), 1.75 (3H, s, CH_3), 1.73 (3H, s, CH_3), 1.69 (3H, s, CH_3), 1.68 (3H, s, CH_3), 1.60 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.2, 135.2, 135.0, 131.6, 128.5, 127.4, 124.5, 123.6, 65.6, 59.4, 48.2, 39.8, 39.5, 26.4, 26.2, 25.8, 18.2, 16.2, 16.1, 16.0; EIMS m/z 222 (1), 204 (4), 189 (21), 175 (4), 161 (9), 136 (9), 121 (17), 107 (15), 93 (22), 85 (100), 68 (15); *anal.* C 78.53%, H 11.14%, calcd for $C_{20}H_{34}O_2$, C 78.38%, H 11.18%.

Epoxyeleganolone (5). To a suspension of $Ti(O^iPr)_4$ (0.01 mL, 0.03 mmol), CaH_2 (4 mg), 4-Å sieve (4 mg), and Si gel (2 mg) in anhydrous CH_2Cl_2 (1 mL) was syringed dropwise a solution of D-(−)-DET (8 mg, 0.04 mmol) in anhydrous CH_2Cl_2 (1 mL) at −20 °C with stirring. After being stirred for an additional 10 min

at −20 °C, the solution of alcohol **1** (10 mg, 0.03 mmol) in anhydrous CH_2Cl_2 (1 mL) was added dropwise to the above reaction mixture. The mixture was further stirred for 15 min at that temperature and then cooled to −40 °C, followed by the addition of a solution of TBHP in toluene (3.1 M, 0.02 mL, 0.06 mmol). The resulting mixture was stirred for a further 5 h at that temperature before being allowed to warm to −30 °C. The reaction was then quenched by the addition of 10% aqueous tartaric acid (0.1 mL). The mixture was allowed to warm to room temperature gradually and was stirred for 1 h further prior to extraction with Et_2O (20 mL × 3). The ether layer was washed with H_2O and brine and then dried. Evaporation of the solvent followed by purification on Si gel gave compound **5** (8 mg, 76%) as a colorless oil: $[\alpha]^{20}_D$ −101° (*c* 0.055, $CHCl_3$); IR (film) ν_{max} 3470 (s), 2982 (s), 2937 (s), 1744 (s), 1618, 1447, 1370, 1267 (s), 1220 (s), 1131 (s), 1031 (S), 1021, 920, 853 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.11 (1H, s, =CH), 5.23 (1H, m, =CH), 5.12 (1H, t, J = 6.9 Hz, =CH), 3.81 (1H, m, CH_2OH), 3.68 (1H, m, CH_2-OH), 3.04 (2H, s, CH_2CO), 2.98 (1H, t, J = 4.5 Hz, epoxy H), 2.14 (3H, s, CH_3), 2.02−2.17 (8H, m, 4CH_2), 1.89 (3H, s, CH_3), 1.63 (3H, s, CH_3), 1.58 (3H, s, CH_3), 1.31 (3H, s, CH_3); EIMS *m*/*z* 320 $[M]^+$ (1), 237 (1), 218 (2), 151 (2), 123 (3), 109 (3), 93 (4), 83 (100), 67 (4), 55 (7); *anal.* C 74.72%, H 10.13%, calcd for $C_{20}H_{32}O_3$, C 74.96%, H 10.06%.

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References and Notes

(1) Pieta, F. D.; Breschi, M. C.; Scatizzi, R.; Cinelli, F. *Planta. Med*. **1995**, *61*, 493−496, and references therein.
(2) Pieta, F. D.; Breschi, M. C.; Cinelli, F.; Morelli, I.; Scatizzi, R. *Planta. Med*. **1993**, *59*, 135−138, and references therein.
(3) Francisco, C.; Combaut, G.; Teste, J.; Prost, M. *Phytochemistry* **1978**, *17*, 1003−1005.
(4) Amico, V.; Oriente, G.; Piattelli, M.; Ruberto, G.; Tringali, C. *Phytochemistry* **1980**, *19*, 2759−2760.
(5) Biard, J. F.; Verbist, J. F.; Floch, R.; Letourneux, Y. *Tetrahedron Lett*. **1980**, *21*, 1849−1852.
(6) Amico, V.; Neri, P.; Piattelli, M.; Ruberto, G. *Phytochemistry* **1987**, *26*, 2637−2639.
(7) Combaut, G.; Piovetti, L. *Phytochemistry* **1983**, *22*, 1787−1789.
(8) a) Weber, H.; Khorana, H. G. *J. Mol. Biol*. **1972**, *72*, 219−221; (b) Zhdanov, R. I.; Zhenodarova, S. M. *Synthesis* **1975**, 222−245; (c) Hofle, G.; Steglich, W.; Vorbruggen, H. *Angew. Chem., Inter. Ed. Engl*. **1978**, *17*, 569−583.
(9) (a) Umbreit, M. A.; Sharpless, K. B. *J. Am. Chem. Soc*. **1977**, *99*, 5526−5528; b). Takayanagi, H.; Kitano, Y.; Morinaka, Y. *Tetrahedron Lett*. **1990**, *31*, 3317−3320.
(10) Corey, E. J.; Pyne, S. G.; Su, W. *Tetrahedron Lett*. **1983**, *24*, 4883−4886.
(11) (a) Takayanagi, H.; Kitano, Y.; Morinaka, Y. *Tetrahedron Lett*. **1990**, *31*, 3317−3320; (b) Takayanagi, H.; Kitano, Y.; Morinaka, Y. *J. Org. Chem*. **1994**, *59*, 2700−2709.
(12) Xiao, X. Y.; Prestwich, G. D. *Synth. Commun*. **1990**, *20*, 3125−3130.
(13) Evans, D. A.; Hoffman, J. M.; Truesdale, L. K. *J. Am. Chem. Soc*. **1973**, *95*, 5822−5823.

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