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THE SYNTHESIS OF (–)-KESSANE, STARTING FROM NATURAL (+)-AROMADENDRENE-II[1]

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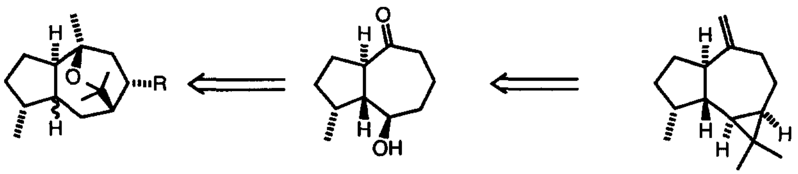
Abstract Starting from the readily available chiral synthon 5 the sesquiterpene ether (-)-kessane (1) can be synthesized in a 9 steps reaction sequence in an overall yield of 43%

(–)-Kessane (1), a guaiane sesquiterpene with an unique oxido-framework, occurs in several plants, e g *Valeriana officinalis*[2], *Heracleum dissectum*[3], and *Bothriochloa intermedia*[4] The synthesis of (±)-kessane[5], its *cis*-fused C5 epimer 2[6], and (±)-kessanol (3)[7] have been reported in the literature No syntheses of chiral kessane or its chiral derivatives are known

In our previous report on (+)-aromadendrene (4) as an attractive starting material for the synthesis of natural products, we described the large-scale preparation of keto alcohol 5 [8] This chiral synthon is a highly suitable starting material for the synthesis of guaianes, as demonstrated in this paper in the synthesis of (–)-kessane



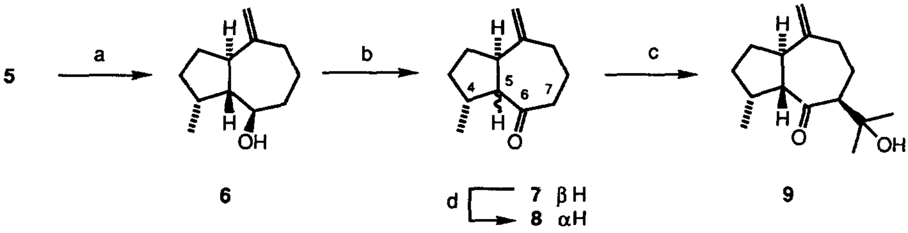
1 βH, R = H
2 αH, R = H
3 βH, R = OH

5

4

The first step in our synthetic approach to (–)-kessane was the introduction of an isopropyl group at C7 For this purpose the keto alcohol **5** was converted into the ketone **7** in high overall yield via a Wittig condensation with methylenetriphenylphosphorane in dimethyl sulfoxide followed by Jones oxidation (Scheme I) During these reactions a small percentage (~3%) of the C5 epimerized *cis*-fused compound **8** was formed In contrast, treatment of **7** with sodium methoxide in methanol gave **8** in almost quantitative yield

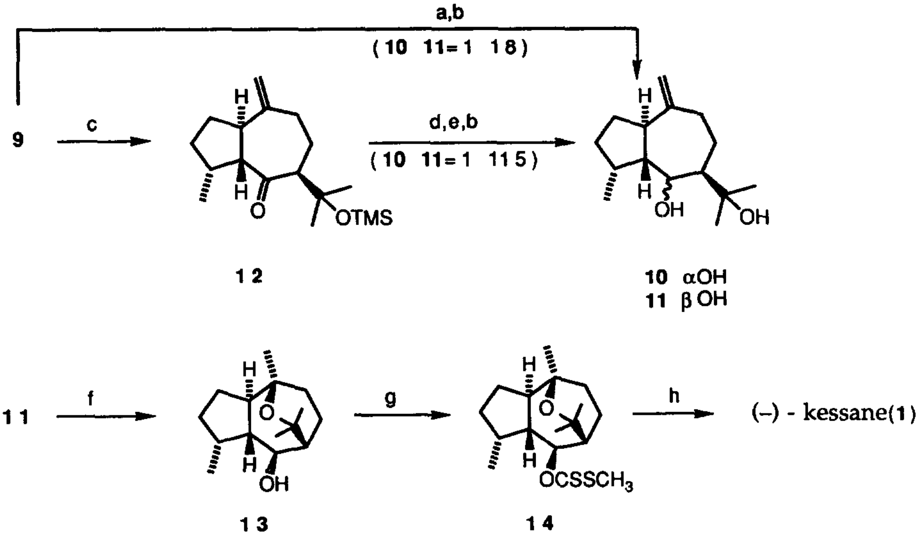
Scheme I[a]



[a](a) $Ph_3P=CH_2$, DMSO, (b) Jones oxidation, (c) LDA, $ZnCl_2$, acetone, (d) $NaOCH_3$, CH_3OH

The ketone **7** now possesses a suitable functional group for the introduction of the isopropyl substituent at C7 A zinc chloride assisted aldol condensation[9] of **7** with acetone afforded **9** in 85% yield as a single stereoisomer To avoid an undesired epimerization at C5 in transformations further in the synthesis, the carbonyl function of **9** had to be reduced[6] Furthermore, a sp^3 hybridized C6 atom will make the 7-membered ring more flexible, so that the cyclic ether formation can proceed more easily Reduction of **9** with sodium borohydride gave a mixture of the α-alcohol **10** and its β-epimer **11** in a ratio of 1 1 8, respectively When, after separation, both alcohols were subjected to oxymercuration conditions, only the β-alcohol **11** showed a smooth reaction The α-alcohol **10** reacted very slowly and mainly the starting material was recovered This behaviour of **10** can be explained by assuming a strong 1,3-diaxial steric hindrance between the methyl group at C4 and the α-hydroxyl group at C6 after ring closure Therefore, it is necessary to reduce the ketone **9** in a more selective way The best result was obtained by reduction of the trimethylsilyl ether **12**[10] with lithium aluminum hydride[11] After cleavage of the trimethylsilyl ether function with tetrabutylammonium fluoride (TBAF) the β-alcohol **11** was obtained in 92% yield together with a small quantity (8%) of its α-epimer **10** (Scheme II)

Schema II[a]



[a](a) $NaBH_4$, (b) separation, (c) TMSCl, HMDS, pyridine, (d) $LiAlH_4$, (e) TBAF, (f) $Hg(OAc)_2$, $NaBH_4$, NaOH, (g) NaH, CS_2, CH_3I, (h) Bu_3SnH, AIBN

As mentioned above the ring closure of **11** to the cyclic ether **13** proceeded in a satisfactory yield (66%) To complete the synthesis of (–)-kessane, the hydroxyl group of **13** had to be removed The best way to do this is given by Barton et al[12] Thus, conversion of **13** into its xanthate **14** and subsequent reduction of the dithiocarbonate group with tributyltin hydride in the presence of α,α'-azoisobutyronitril (AIBN) afforded (–)-kessane in an overall yield of 91%

Starting from the readily available chiral synthon **5** (–)-kessane has been synthesized in a 9 steps reaction sequence in an overall yield of 43%

Experimental section

Melting points were determined on an Olympus HSA melting point apparatus and are uncorrected Optical rotations were obtained from $CHCl_3$ solutions on a Perkin-Elmer 241 polarimeter ^1H NMR and ^{13}C NMR spectra were recorded at 200 MHz and 50 MHz, respectively, on a Bruker AC-E 200 spectrometer Chemical shifts are reported in parts per million (δ) relative to tetramethylsilane (δ 0 0) as an internal standard in chloroform-d as the solvent Mass spectral data were determined on an AEI MS 902 spectrometer equipped with a VG ZAB console Elemental analyses were determined on a Carlo Erba elemental analyzer 1106 GC analyses were carried out on a Varian Vista 6000 gaschromatograph with a flame ionization detector and a DB-17 fused silica capillary column, 30 m x 0 25 mm i d , film thickness 0 25 µm Peak areas were integrated electronically with a Spectra-Physics integrator SP 4290 Flash chromatography was performed using Merck silica gel 60 (230-400 mesh) Solvents were dried and distilled fresh by common practice For all dry reactions, flasks were dried at 150°C and flushed with dry nitrogen just before use, and reactions were carried out under an atmosphere of dry nitrogen Product solutions were dried over anhydrous magnesium sulfate prior to evaporation of the solvent under reduced pressure by using a rotary evaporator

(–)-[1R-(1β,2β,7α,10α)]-6-Methylidene-10-methylbicyclo-[5,3,0]-decanol-2 (6) To a stirred solution of 100 mL of 0 83 M dimethylsulfinylsodium in dry dimethyl sulfoxide was added 29 75 g (83 0 mmol) of methyltriphenylphosphonium bromide The mixture was stirred at room temperature for 20 min, and then a solution of 4 55 g (25 0 mmol) of 5^8 in 40 mL of dry dimethyl sulfoxide was added dropwise The reaction mixture was stirred at room temperature for 45 min, and then poured into 250 mL of water The aqueous solution was extracted with six 200-mL portions of petroleum ether (bp 40-60°C) The combined organic layers were washed with 200 mL of brine, dried, and then evaporated under reduced pressure The remaining residue was flash chromatographed on silica gel [10 1 petroleum ether (bp 40-60°C)/EtOAc] to give 4 35 g (97%) of pure **6** $[\alpha]_D$ -66°(c 1 44), ^{1}H NMR δ 0 91 (d, J = 7 0 Hz, 3H), 1 24-1 98 (m, 10H), 2 24-2 43 (m, 4H), 3 58 (dt, J = 3 9, 10 3 Hz, 1H), 4 72 (br s, 1H), 4 79 (br s, 1H), ^{13}C NMR δ 15 61 (q), 21 26 (t), 29 19 (t), 32 57 (t), 35 48 (d), 36 54 (t), 36 68 (t), 41 13 (d), 58 43 (d), 73 60 (d), 107 86 (t), 152 99 (s), mass spectrum, *m/e* (relative intensity) 180 (M^+, 0 5), 162 (67), 147 (100), 134 (26), 133 (68), 105 (32), 93 (34), 91 (34), 81 (68), 79 (37), calcd for $C_{12}H_{20}O$ (M^+) *m/e* 180 1514, found *m/e* 180 1509

(–)-[1R-(1β,7α,10α)]-6-Methylidene-10-methylbicyclo-[5,3,0]-decanone-2 (7). Jones reagent was added dropwise to a vigorously stirred solution of 3 76 g (20 9 mmol) of **6** in 120 mL of acetone The addition was continued until the characteristic orange colour of the reagent persisted The excess oxidizing agent was then destroyed by dropwise addition of isopropyl alcohol After addition of 100 mL of water, the mixture was extracted with three 100-mL portions of EtOAc The combined organic layers were washed with 100 mL of a saturated aqueous $NaHCO_3$ solution followed by 100 mL of brine, dried, and then evaporated under reduced pressure The resulting residue was flash chromatographed on silica gel [50 1 petroleum ether (bp 40-60°C)/EtOAc] to give 3 65 g (98%) of 7^{13} $[\alpha]_D$ -185° (c 1 61), ^{1}H NMR δ 0 86 (d, J = 7 0 Hz, 3H), 1 30 (m, 1H), 1 49 (m, 1H), 1 63-2 08 (m, 4H), 2 11-2 37 (m, 2H), 2 42-2 74 (m, 5H), 4 79 (s, 2H), ^{13}C NMR δ 17 53 (q), 24 58 (t), 28 80 (t), 31 77 (t), 36 46 (d), 39 86 (t), 43 83 (d), 45 13 (t), 62 79 (d), 107 92 (t), 151 15 (s), 215 41 (s), mass spectrum, *m/e* (relative intensity) 178 (M^+, 47), 163 (14), 160 (6), 149 (24), 136 (100), 123 (63), 107 (53), 94 (39), 81 (39), 79 (32), calcd for $C_{12}H_{18}O$ (M^+) *m/e* 178 1358, found *m/e* 178 1355

(+)-[1S-(1α,7α,10α)]-6-Methylidene-10-methylbicyclo-[5,3,0]-decanone-2 (8). A solution of 0 150 g (0 84 mmol) of **7** in 8 mL of 1 M sodium methoxide in methanol was stirred at room temperature for 20 min After dilution with 10 mL of water, the reaction mixture was extracted with four 10-mL portions of EtOAc The combined organic layers were washed with 15 mL of brine, dried, and then evaporated under reduced pressure The resulting residue was flash chromatographed on silica gel [50 1 petroleum ether (bp 40-60°C)/EtOAc)] to give 0 148 g (99%) of **8** mp 55-56°C [from petroleum ether (bp 40-60°C)], $[\alpha]_D$ +44° (c 0 43), ^{1}H NMR δ 0 95 (d, J = 6 6 Hz, 3H), 1 16 (m, 1H), 1 52-2 15 (m, 5H), 2 21-2 55 (m, 5H), 2 76 (dd, J = 8 4, 12 0 Hz, 1H), 3 00 (dt, J = 6 8, 10.7 Hz, 1H), 4.76 (s, 1H), 4.83 (s, 1H); ^{13}C NMR δ 19.57 (q), 22.56 (t), 29.95 (t), 34.19 (t), 34.51 (d), 36.18 (t), 41.80 (t), 46.06 (d), 61.88 (d), 111.56 (t), 148.80 (s), 212.00 (s); mass spectrum, *m/e* (relative intensity) 178 (M$^+$, 23), 163 (24), 145 (15), 135 (16), 123 (36), 107 (56), 93 (57), 81 (77), 79 (79), 41 (100), calcd for $C_{12}H_{18}O$ (M$^+$) *m/e* 178.1358, found *m/e* 178.1344.

(–)-[1R-(1β,3β,7α,10α)]-3-[1'-Methyl-1'-hydroxyethyl]-6-methylidene-10-methylbicyclo-[5,3,0]-decanone-2 (9). To a stirred solution of 21.5 mL of 1.6 M butyllithium in hexane, cooled to -78°C, was added dropwise a solution of 5.75 mL (41.0 mmol) of diisopropylamine in 25 mL of dry THF. The reaction mixture was stirred at -78°C for 40 min, and then a solution of 2.05 g (11.5 mmol) of 7 in 10 mL of dry THF was added dropwise. Stirring was continued for an additional 45 min, allowed to come to -45°C, and then a mixture of 3.06 g (22.5 mmol) of zinc chloride in 20 mL of dry THF was added. After 5 min 10 mL of dry acetone was added. The reaction mixture was stirred at -45°C for 30 min, and then diluted with 100 mL of saturated aqueous NH_4Cl solution. The aqueous solution was extracted with four 75-mL portions of EtOAc. The combined organic layers were washed with 125 mL of brine, dried, and then evaporated under reduced pressure. The remaining residue was flash chromatographed on silica gel [25:1 to 10:1 petroleum ether (bp 40-60°C)/EtOAc] to give 2.31 g (85%) of pure 9. $[\alpha]_D$ -218° (c 1.70), ^{1}H NMR δ 0.98 (d, J = 7.1 Hz, 3H), 1.16 (s, 3H), 1.22 (m, 1H), 1.24 (s, 3H), 1.45-1.73 (m, 2H), 1.82-2.11 (m, 3H), 2.16-2.88 (m, 6H), 3.64 (br s, 1H, disappears with D_2O added), 4.74 (br s, 1H), 4.79 (br s, 1H), ^{13}C NMR δ 18.14 (q), 26.35 (t), 26.51 (q), 28.97 (q), 28.97 (t), 31.85 (t), 36.97 (d), 37.93 (t), 43.35 (d), 59.29 (d), 62.33 (d), 72.01 (s), 108.75 (t), 150.28 (s), 219.45 (s), mass spectrum, *m/e* (relative intensity) 236 (M$^+$, 1), 221 (9), 218 (12), 203 (5), 193 (11), 178 (62), 135 (62), 123 (100), 109 (49), 107 (49), calcd for $C_{15}H_{24}O_2$ (M$^+$) *m/e* 236.1776, found *m/e* 236.1778.

(+)-[1R-(1β,2α,3β,7α,10α)]-3-[1'-Methyl-1'-hydroxyethyl]-6-methylidene-10-methylbicyclo-[5,3,0]-decanol-2 (10) and its 2β-isomer 11. To a stirred solution of 0.164 g (0.69 mmol) of 9 in 5 mL of methanol was added portionwise 0.045 g (1.19 mmol) of sodium borohydride over a period of 2.5 h. When the addition was complete, the reaction mixture was allowed to stand overnight at room temperature. The reaction mixture was poured into 20 mL of water, and then extracted with four 15-mL portions of EtOAc. The combined organic layers were washed with 15 mL of brine, dried, and then evaporated under reduced pressure. The remaining residue was flash chromatographed on silica gel [10:1 to 5:1 petroleum ether (bp 40-60°C)/EtOAc] to give, in order of elution, 0.045 g (27%) of pure α-alcohol **10** and 0.081 g (49%) of pure β-alcohol **11**.

10. $[\alpha]_D$ +66° (c 1.80), ^{1}H NMR δ 1.11 (s, 3H), 1.17 (d, J = 7.0 Hz, 3H), 1.29 (s, 3H), 1.20-1.85 (m, 9H), 1.96-2.29 (m, 2H), 2.57 (ddd, J = 2.3, 5.3, 14.7 Hz, 1H), 2.70-2.90 (m, 2H), 4.12 (dd, J = 2.9, 6.3 Hz, 1H), 4.62 (br s, 2H), ^{13}C NMR δ 14.89 (q), 24.19 (q), 26.72 (t), 28.73 (t), 30.59 (q), 35.31 (t), 37.18 (d), 40.51 (t), 42.93 (d), 47.54 (d), 58.31 (d), 71.10 (d), 74.92 (s), 104.19 (t), 153.21 (s), mass spectrum, *m/e* (relative intensity) 220 (M$^+$-18, 6), 187 (28), 159 (39), 146 (21), 133 (21), 105 (36), 91 (50), 79 (43), 69 (56), 59 (94), 41 (100), calcd for $C_{15}H_{26}O_2$ (M$^+$-18) *m/e* 220.1827, found *m/e* 220.1800.

11. mp 91-92°C [from petroleum ether (bp 40-60°C)], $[\alpha]_D$ + 1° (c 3.0), ^{1}H NMR δ 0.94 (d, J = 7.1 Hz, 3H), 1.21 (s, 3H), 1.23-2.17 (m, 9H), 1.38 (s, 3H), 2.21-2.41 (m, 2H), 2.55 (dt, J = 5.2, 14.0 Hz, 1H), 2.69 (br s, 1H), 3.12 (br s, 1H), 4.26 (dd, J = 3.5, 9.0 Hz, 1H), 4.66 (s, 1H), 4.68 (s, 1H), ^{13}C NMR δ 15.82 (q), 20.79 (t), 28.70 (q), 28.85 (q), 29.24 (t), 33.40 (t), 34.25 (d), 36.88 (t), 43.40 (d), 49.44 (d), 54.06 (d), 71.08 (d), 73.93 (s), 107.22 (t), 152.70 (s), mass spectrum, *m/e* (relative intensity) 220 (M$^+$-18, 4), 202 (42), 162 (69), 159 (49), 147 (100), 134 (47), 133 (43), 107 (47), 69 (83), 59 (55), calcd for $C_{15}H_{26}O_2$ (M$^+$-18) *m/e* 220.1827, found *m/e* 220.1828.

3-[1'-Methyl-1'-trimethylsilyloxyethyl]-6-methylidene-10-methylbicyclo-[5,3,0]-decanone-2 (12). To a stirred solution of 0 832 g (3 52 mmol) of **9** in 12 mL of dry pyridine were added 2 6 mL of hexamethyldisilazane (HMDS) and 1 3 mL of chlorotrimethylsilane (TMSCl) The reaction mixture was stirred at room temperature for 15 min, and then concentrated under reduced pressure The resulting residue was flash chromatographed on silica gel [100 1 petroleum ether (bp 40-60°C)/EtOAc] to give 1 060 g (98%) of pure **12** ^{1}H NMR (CDCl$_3$) δ 0 09 (s, 9H), 1 03 (d, J = 7 1 Hz, 3H), 1 18-1 76 (m, 3H), 1 26 (s, 3H), 1 27 (s, 3H), 1 78-2 19 (m, 4H), 2 25-2 62 (m, 4H), 2 77 (dd, J = 9 2, 11 9 Hz, 1H), 4 69 (br s, 1H), 4.72 (br s, 1H), ^{13}C NMR (CDCl$_3$) δ 2 42 (3 x q), 17 85 (q), 26 07 (t), 27 91 (q), 28 85 (q), 29.56 (t), 33 71 (t), 36 76 (d), 37 66 (t), 48 98 (d), 58 56 (d), 64 52 (d), 75 36 (s), 107 42 (t), 151 48 (s), 216 59 (s), mass spectrum, *m/e* (relative intensity) 293 (M$^+$-15, 4), 250 (22), 235 (4), 208 (2), 159 (2), 147 (2), 147 (2), 131 (100), 75 (10), 73 (28), calcd for C$_{17}$H$_{29}$O$_2$Si (M$^+$-15) *m/e* 293 1937, found *m/e* 293 1934

Lithium aluminum hydride reduction of 12. To a stirred solution of 0 924 g (3 00 mmol) of **12** in 18 mL of dry THF, cooled to 0°C, was added 0 140 g of lithium aluminum hydride The reaction mixture was allowed to stir for 45 min at 0°C The excess lithium aluminum hydride was then destroyed by the careful addition of a minimum amount of 25% aqueous NaOH solution The reaction mixture was stirred overnight at room temperature with anhydrous MgSO$_4$, filtered, and then concentrated under reduced pressure The remaining residue was dissolved in 5 mL of 0 5 M TBAF in THF, and this solution was stirred at room temperature for 10 min After addition of 25 mL of water and 15 mL of EtOAc, the two-phase mixture was separated, and the aqueous layer was extracted with three 25 mL-portions of EtOAc The combined organic layers were washed with 25 mL of brine, dried, and then evaporated under reduced pressure The resulting residue was flash chromatographed on silica gel [10 1 to 5 1 petroleum ether (bp 40-60°C)/EtOAc] to give, in order of elution, 0 061 g (8%) of pure α-alcohol **10** and 0 655 g (92%) of pure β-alcohol **11**

(–)-6β-Hydroxykessane (13). To a stirred solution of 0 484 g (2 03 mmol) of **11** in 5 mL of dry THF was added 1 30 g (4 08 mmol) of mercuric acetate The reaction mixture was stirred at 55°C for 16 h The mixture was allowed to come to room temperature, and then 4 mL of 3 N NaOH in water was added, followed by 4 5 mL of 0 5 M NaBH$_4$ in aqueous 3 N NaOH After stirring at room temperature for 1 5 h the reaction mixture was filtered through Celite, and the filter cake was washed with 40 mL of water and 50 mL of EtOAc The resulting two-phase mixture was separated, and the aqueous layer was extracted with three 50-mL portions of EtOAc The combined organic layers were washed with 75 mL of brine, dried, and then evaporated under reduced pressure The remaining residue was flash chromatographed on silica gel [10 1 to 5 1 petroleum ether (bp 40-60°C)/EtOAc] to give 0 320 g (66%) of pure **13** mp 130-130 5°C [from petroleum ether (bp 40-60°C)], [α]$_D$ -46°C (c 0 56), ^{1}H NMR (CDCl$_3$) δ 0 87 (d, J = 6 9 Hz, 3H), 1 09 (s, 3H), 1 26 (s, 3H), 1 34-2 42 (m, 13H), 1 42 (s, 3H), 3 75 (br d, J = 10 0 Hz, 1H), ^{13}C NMR (CDCl$_3$) δ 17 77 (q), 21 25 (t), 28 11 (t), 28 39 (q), 29 10 (q), 30 83 (d), 31 17 (t), 32 05 (q), 34 19 (t), 44 34 (d), 47 21 (d), 48 30 (d), 73 60 (s), 74 52 (s), 78 24 (d), mass spectrum, *m/e* (relative intensity) 238 (M$^+$, 32), 223 (31), 220 (15), 205 (85), 111 (71), 109 (82), 95 (69), 81 (86), 69 (72), 43 (100), calcd for C$_{15}$H$_{26}$O$_2$ (M$^+$) *m/e* 238 1933, found *m/e* 238 1932

(O-kessanyl-6)-S-methyl-dithiocarbonate (14). To a solution of 0 240 g (1 01 mmol) of **13** in 6 mL of dry THF were added a catalytic amount of imidazole and 0 050 g (1 67 mmol, as a 80% dispersion in mineral oil) of sodium hydride The mixture was heated at reflux for 3 h, after which time 0 35 mL of carbon disulfide was added After heating at reflux for an additional 30 min 0 35 mL of iodomethane was added Heating at reflux was continued for 30 min and after cooling to room temperature, 0 35 mL of acetic acid was added The reaction mixture was diluted with 25 mL of water and extracted with three 25-mL portions of CH_2Cl_2 The combined organic layers were washed successively with 25 mL of saturated aqueous $NaHCO_3$ and 25 mL of brine The organic layer was dried, and the solvent was removed under reduced pressure The crude product was flash chromatographed on silica gel [40 1 petroleum ether (bp 40-60°C)/EtOAc] to give 0 305 g (92%) of pure **14** ^1H NMR ($CDCl_3$) δ 0 78 (d, J = 7 0 Hz, 3H), 1 12 (s, 3H), 1 23 (s, 3H), 1 35 (s, 3H), 1 40-2 33 (m, 11H), 2 52 (s, 3H), 2 66 (dt, J = 8 2, 12 1 Hz, 1H), 5 55 (dd, J = 1 1, 11 6 Hz, 1H), ^{13}C NMR ($CDCL_3$) δ 18 36 (q), 18 57 (q), 20 10 (t), 28 28 (t), 28 28 (q), 28 83 (q), 30 96 (d), 31 23 (t), 31 56 (q), 33 92 (t), 40 22 (d), 45 52 (d), 47 40 (d), 73 63 (s), 74 22 (s), 89 51 (d), 214 80 (s), mass spectrum, *m/e* (relative intensity) 328 (M^+, 1), 303 (1), 295 (8), 211 (100), 203 (68), 163 (52), 147 (27), 95 (53), 91 (29), 43 (44), calcd for $C_{17}H_{28}O_2S_2$ (M^+) *m/e* 328 1531, found *m/e* 328 1528

(–)-Kessane (1). To a refluxing solution of 0 7 mL (2 60 mmol) of tributyltin hydride and a catalytic amount of AIBN in 30 mL of dry toluene was added dropwise a solution of 0 535 g (1 63 mmol) of **14** in 35 mL of dry toluene over a period of 2 25 h When the addition was complete, the reaction mixture was heated at reflux for an additional 3 h The reaction mixture was allowed to come to room temperature and then concentrated under reduced pressure The resulting residue was flash chromatographed on silica gel [petroleum ether (bp 40-60°C) to 60 1 petroleum ether (bp 40-60°C)/EtOAc] to give 0 354 g (98%) of pure **1** $[\alpha]_D$ -6 1° (c 4 40) (lit[2] -7 2°), ^1H NMR ($CDCl_3$) δ 0 76 (d, J = 6 5 Hz, 3H), 0 85-1 11 (m, 2H), 1 09 (s, 3H), 1 22 (s, 6H), 1 23-2 21 (m, 12H) ^{13}C NMR ($CDCl_3$) δ 18 50 (q), 24 16 (t), 28 20 (t), 28 20 (q), 28 36 (q), 31 09 (d), 32 05 (t), 32 81 (q), 33 24 (t), 34 69 (t), 35 67 (d), 41 46 (d), 50 13 (d), 73 87 (s), 74 82 (s), mass spectrum, *m/e* (relative intensity) 222 (M^+, 9), 207 (3), 204 (4), 189 (5), 164 (9), 161 (8), 149 (15), 126 (100), 108 (44), 81 (25), calcd for $C_{15}H_{26}O$ (M^+) *m/e* 222 1984, found *m/e* 222 1981

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10 The trimethylsilyl ether **12** was prepared from **9** according to the procedure as described See Sweely, C C ; Bentley, R , Mahita, M , Wells, W W *J Am Chem Soc* **1963,** *85,* 2497

11 When **9** was treated with lithium aluminum hydride partly a retrograde aldol reaction occurred This could be avoided by protection of the hydroxyl group as its trimethylsilyl ether

12 Barton, D H R , McCombie, S W *J Chem Soc , Perkin Trans I* **1975,** 1574

13 According to GC analysis, the purity of **7** was 96% As a by-product a minor quantity (3 5%) of **8** was formed