Synthesis of ent-9α,15α-cyclokaurene from grandiflorenic acid

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Dedicated to Prof. T. R. Govindachari on the occasion of his 85th birthday
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Abstract

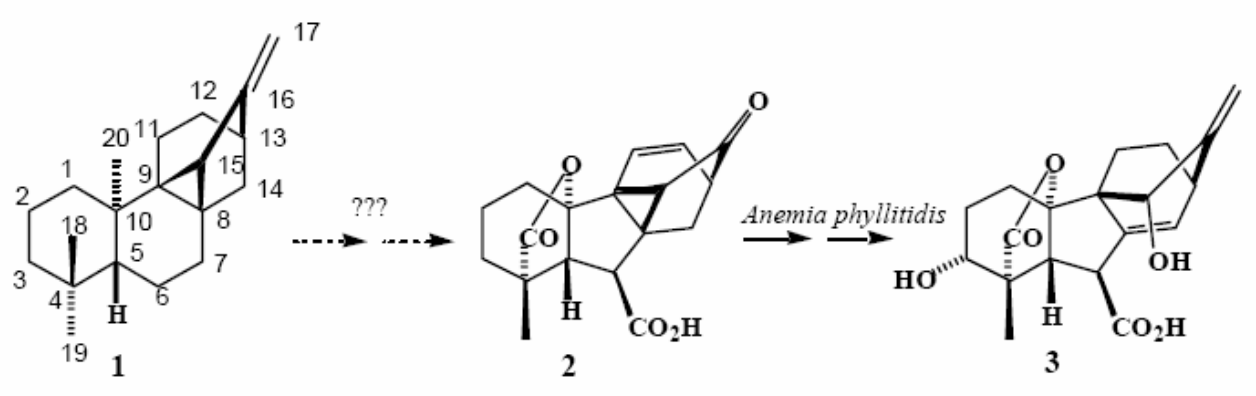
Grandiflorenic acid (*ent*-kaura-9(11),16-dien-19-oic acid) has been converted into *ent*-9,15-cyclokaurene, a speculative biogenetic precursor to 9,15-cyclogibberellin A_9 in prothallia of the fern *Anemia mexicana*. The synthetic sequence involved selective ozonolysis of the 16-ene function, allylic bromination at C-12, intramolecular alkylation by the enolate derived from the 16-one group, and Wittig methylenation; *ent*-kaura-9(11),16-ene was also prepared. In one approach to the reduction of the 19-carboxyl to a methyl group via stannane treatment of a 19-yl xanthate, the carbon skeleton was rearranged as a consequence of a presumed 1,5-hydrogen shift from C-20 to C-19. This step was followed by cylisation of the resulting homoallylic radical to a 9,20-cyclokauren-11-yl radical then fragmentation to give two 20-nor-B-homo-kaurene isomers. The alternative Wolff-Kishner reduction of a 19-al derivative proved to be satisfactory, however.

Keywords: Grandiflorenic acid, cyclokaurene, anemia mexicana, ozonolysis, allylic bromination

Introduction

A number of naturally occurring gibberellin ("GA") derivatives isolated from the prothallia of several fern species belonging to the Schizaeaceae (one of the most primitive fern families)[1,2] have been shown to promote the formation of antheridia and

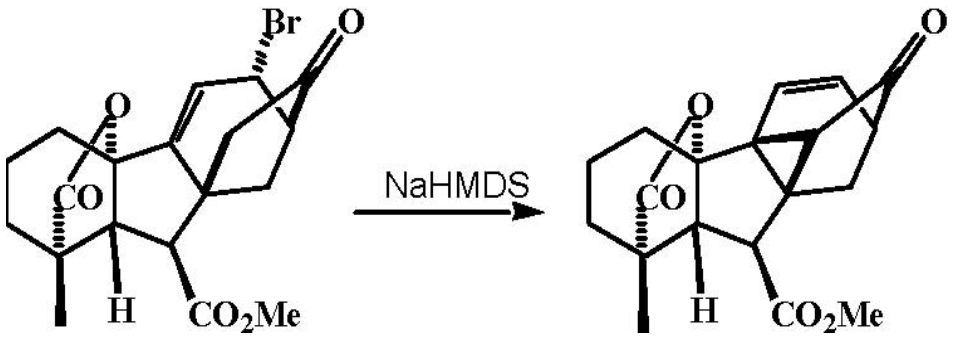
have been termed antheridiogens.[3] Among these compounds is antheridic acid **3** the major antheridiogen isolated from *Anemia phyllitidis*.[4] In a search for the biosynthetic origins of **3**, it was found from feeding studies that 17,17-d_2-cyclo-GA_9 **2** was converted into 17,17-d_2-**3** (Scheme 1).[5] While searching for biosynthetic precursors to **2**, a trace of a hydrocarbon was isolated from *A. phyllitidis* and was shown to have a molecular formula of $C_{20}H_{30}$, corresponding to a kaurene-like hydrocarbon with an additionl ring or double bond.[6] This discovery prompted the speculation that this substance possessed the 9,15-cyclokaurene structure **1** and could be implicated in the biogenesis of **2**. With no prospect of obtaining sufficient spectroscopic data with which to deduce the structure of this substance, we undertook the synthesis of **1** with a view to confirming or rejecting the putative structure assignment.



Scheme 1

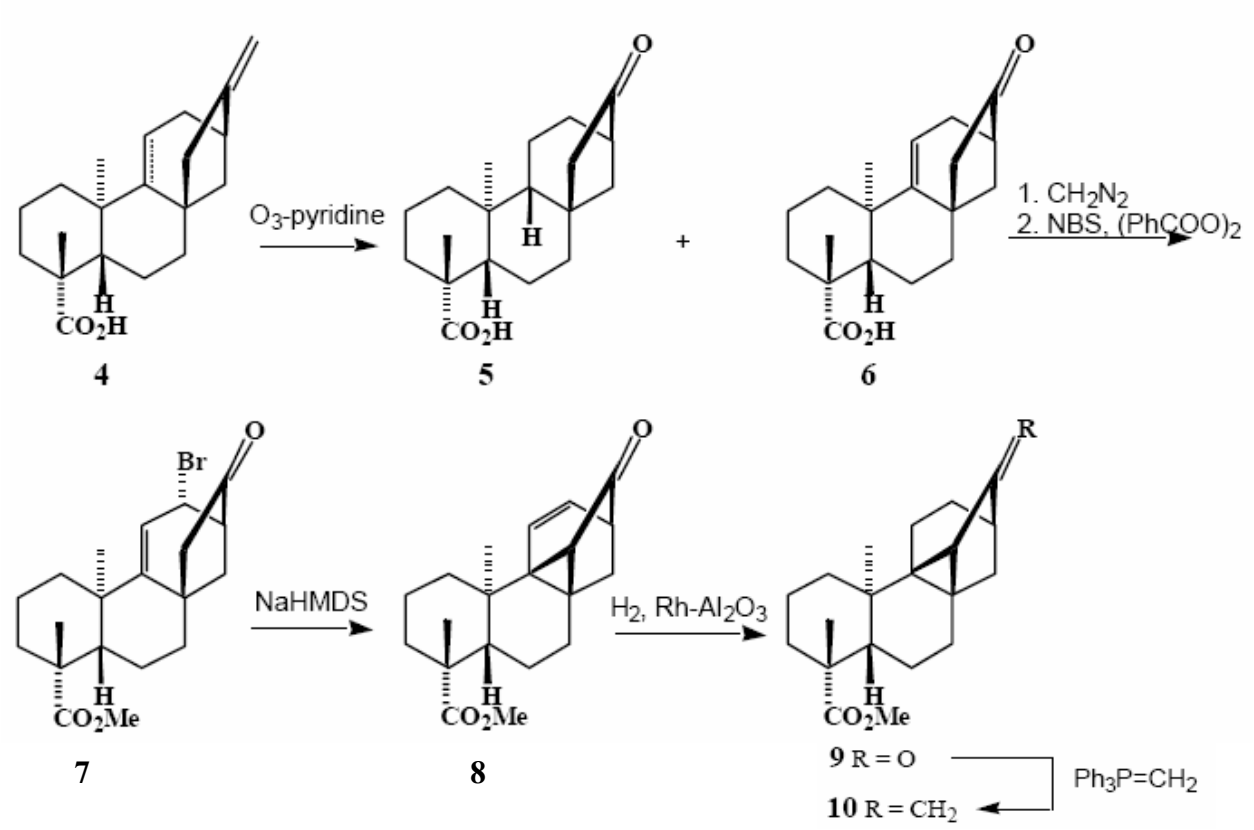
Results and Discussion

9,15-Cyclogibberellins have been assembled by three separate approaches,[7] including an intramolecular alkylation process based on the enolate anion derived from a 16-one function reacting with a 12α-bromo-9(11)-ene array (Scheme 2).[8]

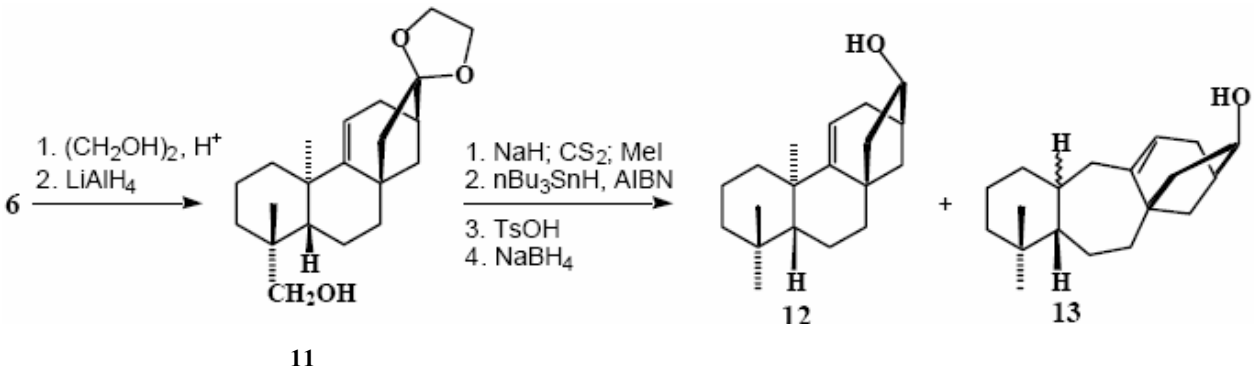


Scheme 2

The analogous intermediate **7** was therefore prepared from grandiflorenic acid **4**[9] as indicated in Scheme 3. We were unable to obtain a pure sample of the starting material, but a 1:1 mixture of **4** with kaurenoic acid was available.[10] The parent acids were not easily separated,[10] but the mixture of 17-nor-16-ones **5**[11] and **6**[9] (obtained by careful ozonolysis) could be resolved chromatographically. The rest of the planned sequence through to ester **10** by means of allylic bromination, alkylation, hydrogenation and Wittig methylenation was then executed smoothly as summarised in the Scheme. Formation of the cyclopropyl ring to give **8** was evident from the presence of a singlet at δ 1.48 for H-15 in the ^{1}H NMR spectrum and by a methine resonance for C-15 at δ 29.8 in the ^{13}C NMR spectrum. A singlet resonance for H-15 was also evident in the dihydro derivative **9** (δ 1.65), and in the methylenated product **10** (δ 1.79). Moreover, the methylene protons in the spectrum of **10** occurred characteristically at higher field (δ 4.58 and 4.61) relative to kaurenoic acid (δ 4.77);[11] *cf*. δ 4.76 and 4.74 for cycloGA9 **2**[7] vs δ 4.85 and 4.95 for the parent GA_9.[12] Ester **10** proved to be unexpectedly labile, however, and attempts to reduce the ester function in this compound through to a methyl group were not productive. The equivalent conversion was therefore executed prior to elaboration of the cyclokaurene skeleton as outlined in Scheme 4.



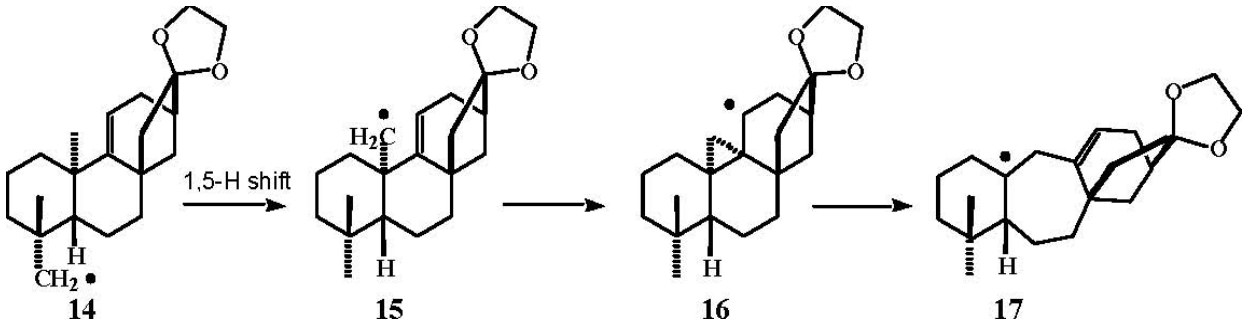
Scheme 3



Scheme 4

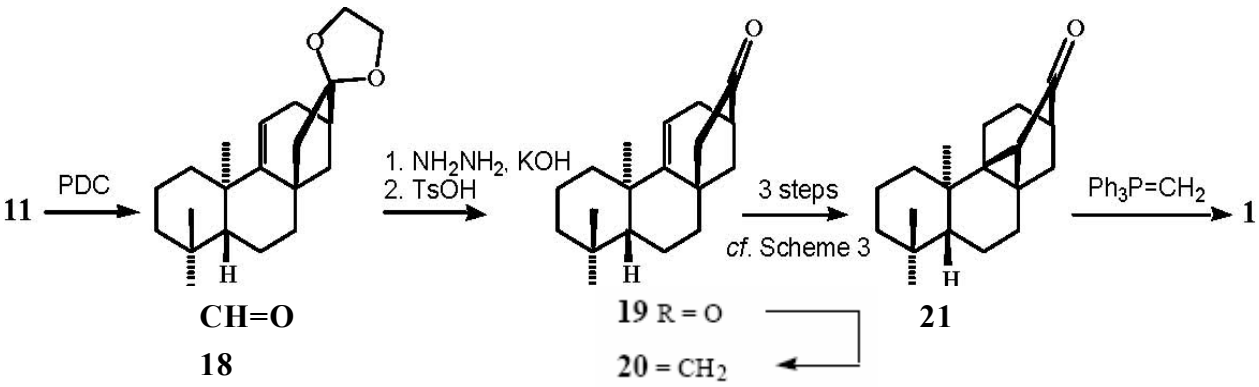
Thus, alcohol **11** was prepared and the derived xanthate treated with tri-*n*-butyl stannane with AIBN as an initiator.[13] An inseparable mixture of three products was formed, however, and removal of the acetal masking group still did not allow resolution. To facilitate separation, therefore, the mixture was reduced with sodium borohydride, and in this way alcohol **12** was obtained pure, but in only 28% yield. The

balance of material was a 3:1 mixture of isomers, the ^{1}H NMR spectrum of which showed the loss of a methyl group. Since the analogous saturated 19-chloro kaurane derivative was reduced without incident in 95% yield (see Experimental Section), we concluded that, for the 9(11)-ene, the intermediate 19-yl radical **14** had undergone a 1,5-transannular shift[14] to form the 20-yl radical **15** (Scheme 5), which then isomerised to **17** via the cyclopropycarbinyl radical **16**.[15] The 1,5 shift could also have occurred in the saturated substrate, but could not have led to rearrangement and would therefore not have been apparent.



Scheme 5

The desired enone 19 was eventually obtained in more satisfactory yield by applying the Huang-Minlon modification[16] of the Wolff-Kishner reduction to aldehyde 18, and the sequence through to the cyclokaurene 1 then completed (Scheme 6) as for the corresponding ester 7 (see above). Unfortunately, the synthetic material showed no resemblance to the natural material. In view of the occurrence of 9,11-didehydro-GA_9 in the related genus *Lygodium*,[17] diene 20 was considered also to be a possible candidate for the unknown hydrocarbon and was therefore prepared from the Wittig methylenation of 19, but again no match was obtained.



Scheme 6

Both ester **10** and hydrocarbon **1** were decomposed by brief exposure to acid, and even chromatography on silica gel afforded rearranged products. Molecules of this type are unlikely, therefore, to have survived standard isolation and purification procedures. Nevertheless, although the structure of the hydrocarbon isolated from *A. mexicana* remains unknown, the preparation of **1** and **20** narrows the options for the correct structure and one or other of these compounds may well yet prove to correspond to a natural product.

Experimental Section

General Procedures. Low resolution EI mass (l.r.m.s.) spectra (70 eV) and high resolution accurate mass measurements (h.r.m.s.) were recorded on a VG Autospec double focussing mass spectrometer. Infrared (i.r.) spectra (νmax) were recorded on a Perkin-Elmer 683 Infrared spectrophotometer in 0.25 mm NaCl solution cells or recorded on a Perkin-Elmer 1800 Fourier Transform Infrared spectrophotometer in KBr plates. ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian Gemini 300 spectrometer at 300 and 75.5 MHz, respectively. Chemical shifts are reported as δ values in parts per million (ppm) relative to tetramethylsilane or the residual peak of $CHCl_3$ (7.25 ppm) while the central peak of $CDCl_3$ (77.0 ppm) was used as the reference for carbon spectra. Distortionless enhancement by polarisation transfer (d.e.p.t.) and the attached proton test (a.p.t.) were used in the assignment of carbon spectra.

Analytical thin layer chromatography (t.l.c.) was carried out on Merck aluminum t.l.c. plates precoated with silica KG60 F_{254} and flash on Merck Kieselgel 60 silica. Tetrahydrofuran (THF), diethyl ether (ether), toluene and benzene were purified by

distillation from sodium benzophenone ketyl. Methanol, triethylamine, dichloromethane and 1,2-dichloroethane were purified by distillation from calcium hydride. Ethanol-free ethereal diazomethane was prepared from Diazald™ All moisture-sensitive reactions were conducted in flame-dried glassware under a positive pressure of dry nitrogen; reagents and starting materials were accordingly transferred via syringe or cannula as indicated.

ent-16-Oxo-17-norkaur-9(11)-en-19-oic Acid (6) and ent-16-Oxo-17-nor-kauran-19-oic Acid (5). The acid mixture **4** (1 g) in pyridine (1 ml) and dichloromethane (250 ml) was cooled to -78˚C for 5 min, then ozone was then bubbled through the solution for 9 min. The reaction mixture was immediately purged with nitrogen for 5 min before addition of triethylamine (20 ml). The resulting mixture was stirred at room temperature for 1 h then washed with 1M HCl (3×60 ml). The combined aqueous phase was extracted with dichloromethane (2×40 ml). The combined organic phase was washed with water (50 ml) and dried over Na2SO4. After filtration, the solvent was removed under reduced pressure and the residue was chromatographed on silica gel (Petroleum ether 40-60˚C/ethyl acetate, 10:1→5:1→2:1) to afford the starting material **4** (342 mg, 34.2%) and then the *9(11)-enoic acid* ***6***[10] (248 mg, 24.8%), after recrystallisation from ethyl acetate, as colourless needles, m.p. 186-187° (Found: M, 302.1885. $C_{19}H_{26}O_3$ requires 302.1882). ν_{max} ($CHCl_3$) 3500w, 3040w, 2930s, 2860s, 1730s, 1695s, cm^{-1}. ^1H NMR δ5.28, dd, $J_{11,12\alpha}$ 3.5, $J_{11,12\beta}$ 3.2 Hz, 1H, H-11; 2.50-2.62, m, 2H; 2.48, dd, $J_{15\beta,14\alpha}$ 3.4, J_{gem} 17.6 Hz, 1H, H-15β; 2.39, ddd, $J_{12\beta,11}$ 2.7, $J_{12\beta,13\alpha}$ 5.4, J_{gem} 17.5 Hz, 1H, H-12β; 2.23-2.12, m, 2H; 2.09, d, J_{gem} 17.6 Hz, 1H, H-15α; 2.04-1.75, m , 6H; 1.65-1.45, m, 4H; 1.23, s, 3H, CH_3; 1.20, m, 1H; 1.04, s, 3H, CH_3; 1.00, m, 1H. ^{13}C NMR δ 221.70, C16; 184.15, C19, COOH; 155.97, C9; 114.86, C11; 56.11, C15; 46.24, C5; 46.10, C13; 44.57, C8; 42.28, C14; 40.51, C4; 40.22, C1; 38.78, C10; 38.03, C3; 31.81, C7; 29.97, C12; 28.11, C18, CH_3; 23.47, C20, CH_3; 19.92, C6; 18.08, C2. Mass spectrum *m/z* 302 (M, 100%), 287 (46), 269 (4), 257 (40), 241 (80), 223 (6), 213 (30), 199 (42), 185 (26), 173 (15), 157 (24), 145 (40), 129 (32), 117 (43), 105 (52), 91 (74), 79 (33), 67 (24).
Further elution afforded the *saturated acid* ***5***[11] (285 mg, 28.5%) as a colourless oil. ^1H NMR δ 2.38, m, 1H, H-13; 2.29, dd, *J* 2.3, *J* 12.1 Hz, 1H; 2.17, br d, *J* 14.2 Hz, 1H; 1.98-1.40, m, 14H; 1.25, s, 3H, CH_3; 1.17, d, *J* 7.6 Hz, 1H; 1.11, dd, *J* 4.0, *J* 11.2 Hz, 1H; 1.02, m, 1H; 1.00, s, 3H, CH3; 0.84, ddd, *J* 4.0, *J* 12.1, *J* 12.1 Hz, 1H. ^{13}C NMR δ222.71, C16; 184.37, C19, COOH; 56.68, C5; 54.86, C15; 53.89, C9; 47.70, C13; 43.68, C8; 42.41, C14; 40.96, C1; 40.55, C4; 39.70, C3; 37.58, C10; 37.26, C7; 29.44, C12; 28.90, C18, CH_3; 20.66, C6; 18.93, C11; 18.71, C2; 16.02, C20, CH_3.

Methyl ent-12β-Bromo-16-oxo-17-norkaur-9(11)-en-19-oate (7). To a solution of acid (**6**) (130 mg o.43 mmol) in dichloromethane (5 ml), was added an excess of ethereal diazomethane 0˚C. After removal of solvent CCl_4 (12 ml), Nbromosuccinimide (130 mg, 0.73 mmol, 1.1 eq.) and dibenzoyl peroxide (5 mg) were added and the resulting suspension was stirred at reflux with irradiation from a tungsten lamp for 3.5 h, then cooled to room temperature, filtered and washed with anhydrous CCl_4. The solvent was removed under reduced pressure and the residue was dried under high vacuum for 30 minutes and used directly in the next step. ^{1}H NMR (300 MHz) 5.55, d, $J_{11,12\beta}$ = 4.0 Hz, H 11; 4.83, br t, $J_{11,12\beta}$ = 3.3, $J_{12\beta,13}$ = 3.3Hz H 12β; 3.67, OMe; 2.96, m, 1 H, H 13; 2.4, m, 1 H; 2.38, dd, $J_{15\beta,14\alpha}$ = 3.4, J_{gem} = 17.5 Hz, H-15β; 2.32, dd, $J_{15\beta,14\alpha}$ = 3.4, J_{gem} = 12.8 Hz, H-14α; 2.12 (1H, d, J_{gem} = 17.5 Hz, H-15;1.23, s, CH_3; 1.08, s, CH_3. ^{13}C NMR (75MHz) δ 215.2, C 16; 177.3, C 19; 159.5, C 9; 118.7, C 11; 54.3, C 5; 54.0, C 15; 51.4, OMe; 50.7, C 13; 45.7, C 12; 44.7, C 4; 41.0, C 8; 40.1, C 14; 39.2, C 1; 39.0, C 10; 38.0, C 3; 29.2, C 7; 28.0, C 18; 22.6, C 20; 19.9, C 6; 18.1, C 2.

Methyl ent-16-oxo-17-nor-9α,15α-cyclokaur-11-en-19-oate (8). Anhydrous THF (15 ml) was added to bromide **7** prepared above and the resulting solution was cooled to -78˚. Sodium bis(trimethylsilyl)amide (1M solution in THF, 0.67 ml, 0.67 mmol) was added dropwise via syringe. After addition, the reaction mixture was stirred at -78˚ for 2 h, then quenched with saturated NH_4Cl aqueous solution (1 ml). The resulting mixture was then diluted with ethyl acetate (25 ml), washed with water (2 x 8 ml) and brine (10 ml). The aqueous phase was back-extracted with ethyl acetate (8 ml). The organic phase was combined and dried over sodium sulfate. After filtration and removal of the solvent, the residue was chromatographed on silica gel (Petroleum ether 40-60˚C/ethyl acetate, 5:1) to afford *ketone **8*** (105 mg, 39%, 2 steps) as a colourless oil. Found: 314.1882 (M). $C_{19}H_{26}O3$ requires 314.1882. ν_{max} ($CHCl_3$) 1730 (s), 1715 (s), 1615 (w), 1600 (w) cm^{-1}. ^{1}H NMR (300MHz) δ 5.95, 2H, m, H 11, H 12; 3.61, OMe; 2.55, m, H 13; 1.48, s, H15; 1.12, s, CH_3; 0.94, s, CH_3. ^{13}C NMR (75MHz) δ 214.5, C16; 177.5, C 19; 127.5, 126.9, C 11, C 12; 51.3, OMe; 49.8, C 9; 47.3, C 13; 45.2, C 5; 43.4, C 4; 37.8, 37.7, C 1, C 14; 36.3, C10; 35.2, C 8; 34.6, C 3; 33.04, C4; 29.8, C 15; 28.9, C 18; 25.7, C7; 18.9, 18.8 C 2, C 6; 18.0, C 20. Mass spectrum *m/z* 314 (M, 100%), 299 (28), 286 (31), 272 (19), 255 (54), 239 (47), 227 (20), 226 (20), 213 (42), 211 (30), 197 (74), 173 (62), 159 (49), 143 (70), 133 (47), 129 (48), 105 (55), 104 (54), 91 (83).

Methyl ent-16-Oxo-17-nor -9α,15α-cyclokauran-19-oate (9). Cyclokaurenone **8** (5 mg, 0.0185 mmol) was dissolved in anhydrous THF (5 ml). To this solution, rhodium on alumina powder (5%, 2 mg) was added. The resulting suspension was degassed and purged with hydrogen (3 times), then stirred at room temperature under hydrogen for 27

hours. The reaction mixture was filtered through a short column of silica gel and washed with petroleum ether 40-60˚C/ethyl acetate, 1:1. The solvent was removed under reduced pressure to afford *ketone* ***9*** (5 mg, 100%) as a colourless solid. Found: 316.2046 (M). $C_{19}H_{28}O_3$ requires 316.2038. ν_{max} ($CHCl_3$) 1730 (S), 1700 (s) cm^{-1}. ^1H NMR (300MHz) δ3.59, s, OMe; 2.14, d, J = 13.6Hz;1.77, d, J = 11.8 Hz; 1.65, s, H 15; 1.10, s, CH_3; 0.84, s, CH_3. ^{13}C NMR (75MHz) δ 215.9, C 16; 177.6, C 19; 52.0; 51.2, OMe; 47.8; 41.9; 38.6; 38.4; 37.7; 36.9; 36.3; 4.3; 29.0; 28.6; 28.1; 19.2; 19.0; 17.5; 17.3. Mass spectrum *m/z*: 316, (M, 64%), 257 (100), 241 (53), 175 (23), 161 (30), 147 (49), 131 (18), 121 (28), 107 (42), 105 (40), 91 (47).

Methyl ent -9α,15α-Cyclokaur-16-en-19-oate (10). A suspension of methyltriphenylphosphonium iodide (72 mg, 0.18 mmol, 5 eq.) and potassium t-butoxide (20.2 mg, 0.18 mmol, 5 eq.) was purged with nitrogen for 5 minutes. Anhydrous THF (3 ml) was added and the resulting suspension was stirred at room temperature for 15 minutes. This yellow suspension was cannulated into a solution of ketone **9** (2 mg, 0.0074 mmol) in THF (2 ml). The resulting suspension was stirred at room temperature for 20 hours, then filtered through a short column of basic Al_2O_3 and washed with petroleum ether 40-60˚C (dried over K_2CO_3). The solvent was removed by a stream of dry nitrogen and the residue was chromatographed on basic Al2O3 (eluted with petroleum ether 40-60˚C, pre-dried over K_2CO_3) to afford the *product (76)* (1.9 mg, 96%) as a colourless oil. Found: 314.2242 (M). $C_{20}H_{30}$ requires 314.2246. ν_{max} ($CDCl_3$) 2940 (s), 2920 (s), 2850 (s), 1730 (s), 1650 (m), cm^1. ^1H NMR (300MHz) δ 4.61, H-17; 4.58, s, H'-17; 3.63, s, OMe; 1.79, H 15; 1.15, s, CH_3; 0.80, s, CH_3. ^{13}C NMR (75MHz) δ 178, C 19; 141.8, C16; 115.4, C17; 51.2, OMe; 47.9; 47.7; 44.0; 38.2; 36.7; 36.1; 32.9; 32.2; 29.4; 27.9; 24.5; 21.6; 20.8; 19.4; 16.3. Mass spectrum *m/z*: 314 (M, 33%), 286 (39), 255 (21), 239 (17), 211 (21), 199 (8), 183 (14), 155 (19), 131 (18), 118 (100), 105 (25), 91 (1).

Methyl ent-16,16-Ethylenedioxy-17-norkaur-9(11)-en-19-oate. To a solution of acid **6** (200 mg, 0.662 mmol) in dichloromethane (5 ml), was added an excess of ethereal diazomethane 0˚C. After 10 min, the solvent was removed and the resulting methyl ester was redissolved in benzene (50 ml). Pyridinium *p*toluenesulfonate (20 mg) was added, followed by ethylene glycol (1 ml). The resulting mixture was stirred at reflux with a Dean-Stark trap for 66 h. The reaction mixture was diluted with ethyl acetate (100 ml) and washed with saturated $NaHCO_3$ aqueous solution (2×20 ml), water (25 ml), brine (25 ml) and dried over sodium sulfate. After filtration, the solvent was removed under reduced pressure and the residue was chromatographed on silica gel (Petroleum ether 40-60˚C/ethyl acetate, 8:1) to afford the *title acetal* (230 mg, 96.6%)

as a colourless oil (Found: M, 360.2305. $C_{22}H_{32}O_4$ requires 360.2300). ν_{max} ($CHCl_3$) 3030w, 2930s, 2870s, 1714s, 1600w cm^{-1}. ^1H NMR δ 5.22, dd, $J_{11,12\alpha}$ 3.1, $J_{11,12\beta}$ 3.5 Hz, 1H, H-11; 3.75-3.95, m, 4H, 2×CH_2O; 3.63, s, 3H, $COOCH_3$; 2.40, m, 1H; 2.24, m, 1H; 2.18-2.05, m, 4H; 1.94-1.20, m, 11H; 1.14, s, 3H, CH_3; 1.05-0.90, m, 1H; 0.90, s, 3H, CH_3. ^{13}C NMR δ 177.53, C19, COO; 156.57, C9; 118.95, C16; 114.23, C11; 64.75, CH_2O; 63.24, CH2O; 54.10, C15; 50.99, OCH_3; 46.34, C5; 44.62, C8; 42.56, C4; 41.50, C13; 40.45, C10; 40.44, C14; 38.32, C1; 38.15, C3; 30.11, C7; 29.06, C12; 27.88, C18, CH_3; 23.20, C20, CH_3; 19.96, C6; 18.27, C2. Mass spectrum *m/z* 360 (M, 100%), 345 (30), 316 (4), 298 (58), 283 (13), 273 (7), 255 (15), 238 (50), 223 (17), 213 (14), 199 (46), 185 (34), 169 (31), 159 (20), 143 (43), 131 (36), 117 (32), 99 (66), 87 (69).

ent-16,16-Ethylenedioxy-17-norkaur-9(11)-en-19-ol (11). The acetal prepared above (220 mg, 0.61 mmol) was dissolved in THF (40 ml), then lithium aluminum hydride (38 mg, 1 mmol, 1.64 eq.) was added. The reaction suspension was stirred at room temperature for 20 h. Ethyl acetate (10 ml) was added dropwise to decompose the excess of $LiAlH_4$. The resulting mixture was diluted with ethyl acetate (150 ml) and washed with 10% NaOH aqueous solution (2×25 ml), water (2×30 ml) and brine (30 ml). The combined aqueous phase was extracted with ethyl acetate (30 ml). The organic phase was combined and dried over sodium sulfate. After filtration, the solvent was removed under reduced pressure and the residue was chromatographed on neutral Al_2O_3 (Petroleum ether 40-60˚C/ethyl acetate, 6:1→3:1) to afford *alcohol **11*** (178 mg, 87.6%) as a colourless oil (Found: M, 332.2351. $C_{21}H_{32}O_3$ requires 332.2351). ν_{max} ($CHCl_3$) 3620m, 3460w, 3038w, 2930s, 2865s, 1600w, cm^{-1}. ^1H NMR δ 5.16, dd, $J_{11,12\alpha}$ 3.2, $J_{11,12\beta}$ 3.2 Hz, 1H, H-11; 3.92, m, 2H, CH_2O; 3.83, d, J_{gem} 10.4 Hz, 1H, H-19_A; 3.81, m, 2H, CH_2O; 3.57, d, J_{gem} 10.4 Hz, 1H, H-19_B; 2.25, dd, $J_{12\alpha,11}$ 3.3, J_{gem} 15.6 Hz, 1H, H-12α; 2.22-2.02, m, 3H; 1.94-1.68, m, 6H; 1.60-1.22, m, 7H; 1.00, s, 3H, CH_3; 0.92, s, 3H, CH_3; 0.88, m, 1H. ^{13}C NMR δ 158.03, C9; 119.12, C16; 113.02, C11; 64.78, CH_2O; 64.15, C19, CH_2O; 63.30, CH_2O; 54.47, C15; 45.30, C5; 42.52, C14; 41.47, C13; 40.31, C8; 40.04, C1; 38.48, C10; 37.92, C4; 35.23, C3; 29.98, C7; 28.88, C12; 25.91, C18, CH_3; 25.05, C20, CH_3; 18.56, C6; 17.37, C2. Mass spectrum *m/z* 332 (M, 100%), 317 (35), 301 (44), 287 (5), 270 (45), 255 (16), 239 (18), 215 (15), 199 (12), 185 (34), 171 (26), 157 (20), 143 (34), 131 (31), 117 (22), 99 (37), 87 (34).

ent-16,16-Ethylenedioxy-17-norkaur-9(11)-en-19-ol S-Methyl Dithiocarbonate. Sodium hydride (40 mg, 60% in mineral oil, 1 mmol) was washed with THF (3 times). To this powder, a solution of alcohol **11** (133 mg, 0.4 mmol) and 4-(dimethylamino)pyridine (5 mg) in THF (12 ml) was added via cannula and washed with THF (2 ml). The resulting mixture was stirred at 75˚C (oil bath) for 3 h, followed

by addition of carbon disulphide (0.15 ml, 2.5 mmol, 6.0 eq.) via a syringe. The reaction mixture was then stirred at 75˚C (oil bath) for 4 h. Methyl iodide (0.15 ml, 2.4 mmol, 6.0 eq.) was introduced and the reaction was continued for a further 2 h at 75˚C (oil bath). The reaction mixture was then diluted with ether (100 ml), washed with water (3×25 ml) and brine (30 ml). The combined aqueous phase was extracted with diethyl ether (30 ml). The organic phase was combined and dried over sodium sulfate. After filtration, the solvent was removed under reduced pressure and the residue was chromatographed on neutral Al_2O_3 (Petroleum ether 40-60˚C/ethyl acetate,100:0→10:1→5:1) to afford the *title xanthate* (155 mg, 91.7%) as a yellow oil (Found: M, 422.1945. $C_{23}H_{34}O_3S_2$ requires 422.1949). ^{1}H NMR δ 5.18, dd, $J_{11,12\alpha}$ 3.2, $J_{11,12\beta}$ 3.0 Hz, 1H, H-11; 4.88, d, J_{gem} 11.0 Hz, 1H, H-19$_A$; 4.54, d, J_{gem} 11.0 Hz, 1H, H-19$_B$; 3.91-3.82, m, 4H, CH_2O×2; 2.54, s, 3H, SCH_3; 2.25, dd, $J_{12\alpha,11}$ 3.5, J_{gem} 15.6 Hz, 1H, H-12$_\alpha$; 2.22-2.06, m, 4H; 1.96-1.70, m, 6H; 1.60-1.40, m, 6H; 1.30, m, 1H; 1.07, s, 3H, CH_3; 1.00, m, 1H; 0.98, s, 3H, CH_3. ^{13}C NMR δ 215.75, OCSS; 157.54, C9; 119.03, C16; 113.47, C11; 76.57, C19, CH_2O; 64.83, CH_2O; 63.37, CH_2O; 54.50, C15; 45.63, C5; 42.51, C8; 41.49, C13; 40.33, C1; 39.83, C4; 37.92, C10; 37.82, C14; 36.18, C3; 29.88, C7; 28.93, C12; 26.55, C18, CH_3; 25.01, C20, CH_3; 18.65, C6; 18.60, SCH_3; 17.79, C2. Mass spectrum *m/z* 422 (M, 100%), 407 (8), 360 (10), 315 (12), 299 (14), 269 (6), 252 (28), 237 (21), 219 (12), 182 (18), 169 (15), 145 (23), 133 (37), 117 (26), 99 (54), 87 (65).

ent-16α-Hydroxy-17-norkaur-9(11)-ene (12) and 10-epimers of ent-16α-Hydroxy-B(9a)-homo-17,20-dinorkaur-9(11)-ene (13). The xanthate prepared above (147.7 mg, 0.35 mmol) and AIBN (20 mg) were dissolved in toluene (5 ml). To this solution, *n*-Bu_3SnH (0.56 ml, 2.1 mmol, 6.0 eq.) was added via syringe. The reaction mixture was then stirred at reflux with irradiation of a tungsten lamp for 2 h. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (Petroleum ether 40-60˚C/ethyl acetate, 100:0→10:1 →5:1) to afford the crude product as an oil. The crude product was then treated with *p*-toluenesulfonic acid (20mg) and water (0.01 ml) in THF (10 ml) for four h. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (Petroleum ether 40-60˚C/ethyl acetate, 100:0→10:1→5:1) to afford a mixture of three deoxygenation products (45 mg, 47%) as an oil. The mixture of ketones (20 mg) was then reduced to the corresponding alcohols by $NaBH_4$ in methanol (2ml). The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (Petroleum ether 40-60˚C:ethyl acetate, 100:0→10:1) to afford ent-*16α-hydroxy-17-norkaur-9(11)-ene* ***12*** [which was directly oxidised by pyridinium dichromate to afford the ent-*16-*

Oxo-17-norkaur-9(11)-ene ***19*** (5.6 mg, 28% overall)]. Further elution provided ent-*16α-hydroxy-B(9a)-homo-17,20-dinorkaur-9(11)-ene* ***13*** (13 mg, 65%) as a mixture of two isomers. The spectra were measured on the mixture. The ratio (major : minor = 3 : 1) of the two isomers was based on the integration of the olefinic protons in the ^{1}H NMR spectrum. The assignment of the signals in the NMR spectra was based on relative intensities. ent-*16α-Hydroxy-B(9a)-homo-17,20-dinorkaur-9(11)-ene* ***13*** (Found: M, 274.2296. $C_{19}H_{30}O$ requires 274.2296). ν_{max} (KBr) 3340m, 2920s, 2849s, 1655w cm^{-1}. *Minor product:* ^{1}H NMR δ 5.28, m, 1H, H-11; 4.42, m, 1H, H-16$_\alpha$; 2.44, m, 1H, H-13; 2.36-1.90, m, 20H; 0.89, s, 3H, CH3; 0.73, s, 3H, CH_3. ^{13}C NMR δ 150.90, C9; 120.48, C11; 74.97, C16; 56.66, CH; 51.31, 45.80, 43.50, CH; 42.24, 41.11, 40.72, 39.22, CH; 37.50, 34.14, 33.98, 31.01, CH_3; 27.80, 25.09, 22.58, 20.02, CH_3. *Major product:* ^{1}H NMR δ 5.13, m, 1H, H-11; 4.42, ddd, $J_{16\alpha,13}$ 3.1, $J_{16\alpha,15\beta}$ 6.6, $J_{16\alpha,15\alpha}$ 9.8 Hz, 1H, H-16$_\alpha$; 2.44, m, 1H, H-13; 2.36-1.90, m, 6H; 1.82, dd, *J* 9.9, *J* 13.6 Hz, 1H; 1.78-1.00, m, 13H; 0.98, s, 3H, CH_3; 0.85, s, 3H, CH_3. ^{13}C NMR δ 147.01, C9; 121.57, C11; 74.94, C16; 52.78, C5; 51.83, C14; 42.30, C8; 40.72, 39.58, CH; 39.54, 38.27, 36.83, 34.40, CH; 34.36, 30.86, CH; 27.80, 27.78, CH_3; 26.36, 22.32, 20.83. Mass spectrum *m/z* 274 (M, 32%), 256 (-H_2O, 100), 241 (10), 171 (6), 159 (10), 145 (12), 132 (24), 120 (30), 105 (23), 91 (46), 77 (11), 67 (18).

ent-16,16-Ethylenedioxy-17-norkauran-19-ol. As already described for the preparation of **11**, lithium aluminum hydride (57 mg, 1.5 mmol, 1.5 eq.) was added to a solution of the acetal derived from **5** (370 mg, 1.0 mmol) in THF (20 ml) and the reaction suspension stirred at room temperature for 20 h. The excess of $LiAlH_4$ was then decomposed by addition of ethyl acetate (10 ml). The resulting mixture was diluted with ethyl acetate (150 ml) and washed with 10% NaOH aqueous solution (2×25 ml), water (2×30 ml) and brine (30 ml). The combined aqueous phase was extracted with ethyl acetate (30 ml). The organic phase was combined and dried over sodium sulfate. After filtration, the solvent was removed under reduced pressure to afford the crude *19-ol* (322 mg) as a colourless oil. This crude product was directly used for the next step without further purification.

ent-19-Chloro-16,16-ethylenedioxy-17-norkauran and ent-19-chloro-17-norkauran-16-one. The alcohol (322 mg,~1 mmol) prepared above and triphenylphosphine (786 mg, 3.0 mmol, 3.0 eq.) were dissolved in carbon tetrachloride (30 ml) and stirred at reflux (90˚C oil bath) under nitrogen for 63 h. The resulting suspension was filtered through a short column of silica gel and washed with petroleum ether 40-60˚C/ethyl acetate, 4:1. After removal of the solvent, the residue was chromatographed on silica gel (Petroleum ether 40-60˚C/ethyl acetate, 1:0→100:1→50:1→20:1) to afford the 19-

chloro *acetal* (67 mg, 19%, 3 steps) as a colourless syrup (Found: M, Cl^{37}; 354.2142. $C_{21}H_{33}O_2Cl$ requires 354.2139. Found: M, Cl^{35}; 352.2182. $C_{21}H_{33}O_2Cl$ requires 352.2169). ν_{max} ($CHCl_3$) 2990w, 2930s, 2860m, 1735m cm^{-1}. ^1H NMR δ 3.95-3.74, m, CH_2O×2 + H-19$_A$, 5H; 3.34, d, J_{gem} 10.9 Hz, H-19$_B$, 1H; 1.98, m, 1H, H-13; 1.90, d, *J* 11.7 Hz, 1H; 1.86-1.15, m, 16H; 1.05, d, *J* 10.0 Hz, 1H; 0.99, s, 3H, CH_3; 0.97, s, 3H, CH_3; 0.92, m, 1H; 0.78, ddd, *J* 4.4, *J* 12.6, *J* 12.6 Hz, 1H. ^{13}C NMR δ 116.77, C16; 64.67, CH_2O; 63.43, CH_2O; 57.13, C5; 56.73, C9; 53.31, C15; 50.51, C8; 42.92, C13; 41.61, C14; 41.60, C10; 40.20, C4; 39.18, C1; 38.41, C3; 37.55, C7; 35.75, C19; 28.30, C18, CH_3; 26.30, C12; 19.75, C11; 18.54, C20, CH_3; 18.18, C6; 17.95, C2. Mass spectrum *m/z* 354 (M, Cl^{37}, 42%), 352 (M, Cl^{35}, 100%), 337 (60), 317 (22), 303 (80), 275 (10), 264 (75), 229 (15), 217 (47), 201 (12), 187 (14), 171 (40), 145 (30), 135 (52), 113 (82), 87 (92).

Further elution afforded the *19-chloro 16-one* (230 mg, 74.7%, 3 steps) as a white solid (Found: M, 308.1910. $C_{19}H_{29}OCl$ requires 308.1906). ν_{max} ($CHCl_3$) 2980m, 2930s, 2865s, 1730s cm^{-1}. ^1H NMR δ 3.75, d, J_{gem} 10.9 Hz, H-19$_A$, 1H; 3.31, dd, *J* 1.7, J_{gem} 10.9 Hz, H-19$_B$, 1H; 2.30, m, 1H, H-13; 2.16, br d, *J* 12.1 Hz, 1H; 1.96-1.29, m, 15H; 1.12, d, *J* 8.1 Hz, 1H; 1.06, d, *J* 12.1 Hz, 1H; 1.00, s, 3H, CH_3; 0.94, s, 3H, CH_3; 0.89, ddd, *J* 4.7, *J* 13.5, *J* 13.5 Hz, 1H; 0.75, ddd, *J* 4.4, *J* 12.6, *J* 12.6 Hz, 1H. ^{13}C NMR δ 221.79, C16; 56.75, C5; 54.92, C9; 54.65, C15; 50.10, C14; 47.59, C13; 42.10, C8; 40.91, C10; 39.97, C4; 39.07, C1; 38.20, C3; 36.99, C19; 35.50, C7; 29.25, C12; 28.14(C18, CH_3; 18.93, C11; 18.55, C20, CH_3; 18.28, C6; 17.71, C2. Mass spectrum *m/z* 310 (M, Cl^{37}, 7%), 308 (M, Cl^{35}, 18%), 293 (5), 259 (100), 241 (19), 231 (4), 203 (4), 189 (18), 177 (9), 161 (17), 151 (23), 123 (33), 109 (47), 95 (32), 81 (35), 69 (15).

ent-17-Norkauran-16-one. The chloro ketone (80.2 mg, 0.26 mmol) prepared above and azobisisobutyronitrile (10 mg) were dissolved in anhydrous benzene (5 ml) under a flow of nitrogen, followed by addition of *n*-Bu_3SnH (0.27 ml, 1 mmol, 4 eq.). The resulting solution was degassed and purged with nitrogen, then irradiated with a tungsten lamp at reflux for 120 min. The solvent was removed and the residue was chromatographed on silica gel (Petroleum ether 40-60˚C/ethyl acetate, 100:0→10:1) to afford *17-norkauran-16-one* (67.5 mg, 95%) as colourless crystals (Found: M, 274.2296. $C_{19}H_{30}O$ requires 274.2296). ν_{max} ($CHCl_3$) 2985s, 2930s, 2860s, 1730s cm^{-1}. ^1H NMR δ 2.37, m, 1H, H-13; 2.30, dd, $J_{14\alpha,15\beta}$ 2.8, J_{gem} 12.0 Hz, 1H, H-14$_\alpha$; 1.94, m, 2H; 1.85-1.32, m, 13H; 1.17, d, *J* 6.6 Hz, 1H; 1.10, dd, $J_{14\beta,13\alpha}$ 4.4, J_{gem} 12.3 Hz, 1H, H-14$_\beta$; 1.07, s, 3H, CH_3; 0.86, s, 3H, CH_3; 0.83, m, 1H; 0.82, s, 3H, CH_3; 0.74, dd, *J* 3.9, *J* 13.2 Hz, 1H. ^{13}C NMR δ 222.64, C16; 55.95, C5; 55.10, C15; 54.89, C9; 47.77, C13; 42.41, C8; 41.84, C14; 41.83, C10; 40.99, C1; 40.27, C4; 39.38, C3; 37.40, C7; 33.56,

C19, CH_3; 33.20, C12; 29.58, C11; 21.56, C18, CH_3; 19.18, C6; 18.43, C2; 17.97, C20, CH_3. Mass spectrum *m/z* 274 (M, 72%), 259 (100), 241 (14), 231 (40), 218 (12), 203 (11), 189 (27), 177 (14), 161 (27), 149 (25), 137 (37), 123 (98), 109 (43), 95 (56), 81 (52), 69 (55).

ent-16,16-Ethylenedioxy-17-norkaur-9(11)-en-19-al (18). Alcohol **11** (150 mg, 0.451 mmol) and pyridinium dichromate (376 mg,1 mmol, 2.2 eq.) were dissolved in dichloromethane (10 ml). To this suspension, one drop of pyridine was added. The resulting mixture was stirred at room temperature for 5.5 h, then filtered through a short column of basic Al_2O_3 and washed with ethyl acetate. After removal of the solvent, the residue was chromatographed on neutral Al_2O_3 (Petroleum ether 40-60˚C/ethyl acetate, 5:1) to afford *aldehyde **14** (295)* (132 mg, 88%) as a colourless oil (Found: M, 330.2196. $C_{21}H_{30}O_3$ requires 330.2195). ν_{max} ($CHCl_3$) 3040w, 2930s, 2870s, 2740w, 1709s cm^{-1}. ^1H NMR δ9.96, s, 1H, CHO; 5.21, dd, $J_{11,12\alpha}$ 3.2, $J_{11,12\beta}$ 3.3 Hz, 1H, H-11; 3.95-3.70, m, 4H, CH_2O×2; 2.25, dd, $J_{12\alpha,11}$ 3.3, J_{gem} 15.6 Hz, 1H, H-12_α; 2.22-1.80, m, 8H; 1.80-1.20, m, 8H; 1.00, m, 1H; 0.98, s, 3H, CH_3; 0.90, s, 3H, CH_3. ^{13}C NMR δ 206.65, C19, CHO; 155.72, C9; 119.10, C16; 114.52, C11; 64.93, CH_2O; 63.44, CH_2O; 54.36, C15; 48.24, C8; 45.85, C5; 42.55, C14; 41.59, C13; 40.39, C10; 39.58, C1; 38.15, C14; 35.08, C3; 29.84, C7; 29.10, C12; 24.16, C18, CH_3; 23.69, C20, CH_3; 19.06, C6; 17.46, C2. Mass spectrum *m/z* 330 (M, 100%), 315 (18), 301 (58), 287 (23), 268 (31), 258 (18), 240 (32), 225 (23), 215 (27), 201 (43), 185 (24), 169 (39), 159 (28), 145 (55), 131 (45), 117 (47), 105 (52), 91 (78), 73 (49).

ent-17-Norkaur-9(11)-en-16-one (19). Aldehyde **18** (60 mg, 0.182 mmol), potassium hydroxide (280 mg, 5 mmol) and hydrazine monohydrate (0.3 ml) were dissolved in ethylene glycol (3 ml). The resulting suspension was stirred at 100˚C (oil bath) for 2 h then stirred at 190˚C (oil bath) overnight. After cooling to room temperature, the reaction mixture was diluted with ice-water (100 ml) and extracted with diethyl ether (4×15 ml). The combined organic phase was washed with water (2×10 ml), brine (15 ml) and dried over sodium sulfate. After filtration, the solvent was removed under reduced pressure to afford the crude acetal (65 mg). This product was dissolved in THF (8 ml), one drop of water was added, followed by *p*-toluenesulfonic acid monohydrate (65 mg) and silica gel (100 mg). The resulting suspension was stirred at room temperature for 4 h, then filtered through a short column of silica gel and washed with ethyl acetate. After removal of the solvent, the residue was chromatographed on silica gel (Petroleum ether 40-60˚C/ethyl acetate, 100:0→10:1) to afford *ketone* **19** (32 mg, 64.6%, two steps) as a colourless oil (Found: M, 272.2140. $C_{19}H_{28}O$ requires 272.2140). ν_{max} ($CHCl_3$) 2990m, 2938s, 2860s, 1730s, 1600w, cm^{-1}. ^1H NMR δ 5.17, dd, $J_{11,12\alpha}$ 3.2,

$J_{11,12\beta}$ 3.3 Hz, 1H, H-11; 2.55, m, 1H, H-13; 2.53, dd, $J_{15\beta,14\alpha}$ 3.2, J_{gem} 17.4 Hz, 1H, H-15$_\beta$; 2.33, ddd, $J_{12\beta,11}$ 2.9, $J_{12\beta,13\alpha}$ 5.5, J_{gem} 17.3 Hz, 1H, H-12$_\beta$; 2.14, ddd, $J_{12\alpha,13}$ 2.2, $J_{12\alpha,11}$ 3.4, J_{gem} 17.3 Hz, 1H, H-12$_\alpha$; 2.04, d, J_{gem} 17.4 Hz, 1H, H-15$_\alpha$; 1.90, ddd, $J_{3\beta,2\beta}$ 3.2, $J_{3\beta,2\alpha}$ 13.1, J_{gem} 13.1 Hz, 1H, H-3$_\beta$; 1.85-1.70, m, 4H; 1.62-1.30, m, 5H; 1.27, dd, $J_{14\beta,13\alpha}$ 7.9, J_{gem} 11.7 Hz, H-14$_\beta$, 1H; 1.20-0.98, m, 2H; 1.04, s, 3H, CH_3; 0.87, s, 3H, CH_3; 0.79, s, 3H, CH_3. ^{13}C NMR δ 221.78, C16; 157.54, C9; 113.31, C11; 56.59, C15; 46.26, C5; 44.34, C13; 42.28, C14; 42.16, C8; 40.34, C10; 40.11, C1; 38.38, C4; 33.84, C7; 32.66, C19, CH_3; 31.66, C3; 29.96, C12; 24.34, C18, CH_3; 21.30, C20, CH_3; 19.03, C6; 18.02, C2. Mass spectrum *m/z* 272 (M, 100%), 257 (99), 239 (11), 229 (30), 215 (52), 201 (24), 187 (44), 175 (31), 159 (33), 145 (57), 133 (47), 117 (35), 105 (45), 91 (64), 81 (28), 69 (51).

ent-Kaura-9(11),16-diene (20). A suspension of methyltriphenylphosphonium iodide (36 mg, 0.09 mmol, 5 eq.) in THF (2.5 ml) was treated with potassium t-butoxide (10.1 mg, 0.09 mmol, 5 eq.) at room temperature for 30 min. A solution of ketone **19** (5 mg, 0.0184 mmol) in THF (1 ml) was added to this suspension via cannula and washed with THF (1 ml). The resulting mixture was stirred at room temperature for 20 h then diluted with water (20 ml) and extracted with diethyl ether (4×8 ml). The combined organic phase was washed with water (5 ml), brine (5 ml) and dried over sodium sulfate. After filtration, the solvent was removed and the residue was chromatographed on silica gel (Petroleum ether 40-60˚C/ethyl acetate, 1:0→4:1) to afford *diene **20*** (3.8 mg, 76%) as a colourless oil. Further elution afforded starting material (1 mg). (Found: M, 270.2342. $C_{20}H_{30}$ requires 270.2347). ν_{max} ($CDCl_3$) 2920s, 2865s, 1655w, 1600m cm^{-1}. ^{1}H NMR δ 5.16, dd, $J_{11,12\alpha}$ 3.2, $J_{11,12\beta}$ 3.4 Hz, 1H, H-11; 4.91, br s, 1H, H-17$_A$; 4.79, br s, 1H, H-17$_B$; 2.76, m, 1H, H-13; 2.67, br d, J_{gem} 15.9 Hz, 1H, H-15$_\beta$; 2.41, ddd, $J_{12\beta,11}$ 2.8, $J_{12\beta,13\alpha}$4.6, J_{gem} 16.9 Hz, 1H, H-12$_\beta$; 2.17, ddd, *J* 2.8, *J* 2.7, J_{gem} 15.8 Hz, 1H, H-15$_\alpha$; 2.02-1.70, m, 4H; 1.65-1.26, m, 7H; 1.22, dd, *J* 3.7, *J* 13.7 Hz, 1H; 1.12, dd, *J* 3.5, *J* 13.2 Hz, 1H; 1.06, s, 3H, CH_3; 0.91, s, 3H, CH_3; 0.85, m, 1H; 0.84, s, 3H, CH_3. Mass spectrum *m/z* 270 (M, 44%), 255 (100), 239 (4), 227 (8), 214 (14), 199 (15), 185 (37), 173 (22), 159 (42), 147 (27), 131 (28), 117 (25), 105 (32), 91 (38), 81 (26), 69 (39).

ent-17-Nor-9α,15α-cyclokaur-11-en-16-one. Ketone **19** (21.8 mg, 0.08 mmol), *N*-bromosuccinimide (17.3 mg, 0.09 mmol, 1.1 eq.) and dibenzoyl peroxide (1 mg) were dissolved in anhydrous carbon tetrachloride (6 ml). The resulting suspension was stirred at reflux with irradiation from a tungsten lamp for 50 min, then cooled to room temperature, filtered and washed with anhydrous carbon tetrachloride. The solvent was removed under reduced pressure and the residue was dried under high vacuum for

30 min. Anhydrous THF (8 ml) was added to the residue and the resulting solution was cooled to -78˚C for 5 min. Sodium bis(trimethylsilyl)amide (1M solution in THF, 0.12 ml, 0.12 mmol, 1.5 eq.) was added dropwise via syringe. After addition, the reaction mixture was stirred at -78˚C for 2 h, then quenched with saturated NH_4Cl aqueous solution (1 ml). The resulting mixture was then diluted with ethyl acetate (25 ml), washed with water (2×8 ml) and brine (10 ml). The aqueous phase was back-extracted with ethyl acetate (8 ml). The organic phase was combined and dried over sodium sulfate. After filtration and removal of the solvent, the residue was chromatographed on silica gel (Petroleum ether 40-60˚C/ethyl acetate, 1:0→12:1→2:1) to afford the *title ketone* (5.3 mg, 24.5%, 2 steps) as a colourless oil (Found: M, 270.1982. $C_{19}H_{26}O$ requires 270.1983). ν_{max} ($CHCl_3$) 1715s, 1615w, 1600w cm. ^{1}H NMR δ 6.03, d, $J_{11,12}$ 7.3 Hz, 1H, H-11; 5.97, dd, $J_{12,13\alpha}$ 7.0, $J_{12,11}$ 7.3 Hz, 1H, H-12; 2.57, m, 1H, H-13; 2.11, dd, *J* 4.5, *J* 9.0 Hz, 1H; 2.09, d, *J* 8.5 Hz, 1H; 2.01, dd, $J_{14\beta,13\alpha}$ 4.8, J_{gem} 11.1 Hz, 1H, H-14_β; 1.78, m, 1H; 1.66, s, 1H, H-15; 1.60-1.38, m, 5H; 1.34, d, J_{gem} 11.1 Hz, 1H, H-14_α; 1.25, m, 1H; 1.15, s, 3H, CH_3; 1.13, m, 1H,; 0.90, dd, $J_{5,6\beta}$ 4.0, $J_{5,6\alpha}$ 13.6 Hz, 1H, H-5; 0.86, s, 3H, CH_3; 0.84, s, 3H, CH_3. ^{13}C NMR δ 215.22, C16; 128.06, C11; 126.82, C12; 50.30, C9; 45.42, C5; 44.47, C13; 41.73, C14; 37.79, C1 + C8; 36.30, C10; 34.99, C3; 33.88, C19, CH_3; 33.04, C4; 29.90, C15; 29.67, C9; 24.57, C7; 21.45, C18, CH_3; 19.40, C20, CH_3; 18.42, C6; 17.08, C2. Mass spectrum *m/z* 270 (M, 77%), 255 (38), 242 (16), 227 (28), 213 (25), 201 (12), 189 (22), 173 (20), 159 (100), 143 (70), 133 (57), 117 (44), 104 (40), 91 (60), 81 (25), 69 (54).

ent-17-Nor-9α,15α-cyclokauran-16-one (21). The cyclokaurenone (5 mg, 0.0185 mmol) prepared above was dissolved in anhydrous THF (5 ml). To this solution, rhodium on alumina powder (5%, 2 mg) was added. The resulting suspension was degassed and purged with hydrogen (3 times), then stirred at room temperature under hydrogen for 27 h. The reaction mixture was filtered through a short column of silica gel and washed with petroleum ether 40-60˚C/ethyl acetate, 1:1. The solvent was removed under reduced pressure to afford *ketone **21*** (5 mg, 100%) as a colourless solid (Found: M, 272.2141. $C_{19}H_{28}O$ requires 272.2140). ν_{max} ($CHCl_3$) 1700s cm^{-1}. ^{1}H NMR δ 2.06, m, 1H, H-13; 2.00-1.86, m, 3H; 1.85, s, 1H, H-15; 1.84-1.65, m, 5H; 1.50-1.08, m, 8H; 1.08, s, 3H, CH_3; 0.84, s, 3H, CH_3; 0.82, s, 3H, CH_3; 0.75, dd, *J* 3.5, *J* 12.4 Hz, 1H. ^{13}C NMR δ216.71, C16; 52.72, C9; 44.78, C5; 42.08, C13; 41.65, C14; 38.77, C15; 38.55, C8; 36.66, C10; 36.50, C1; 34.70, C7; 34.26, C19, CH_3; 33.09, C4; 28.58, C3; 26.98, C12; 21.62, C18, CH_3; 19.22, C20, CH_3; 18.53, C11; 17.34, C6; 16.96, C2. Mass spectrum *m/z* 272 (M, 34%), 257 (100), 239 (5), 229 (14), 215 (17), 201 (11), 187 (17), 173 (12), 161 (19), 147 (24), 131 (18), 121 (24), 109 (29), 91 (28), 81 (23), 67 (19).

ent-9α,15α-Cyclokaur-16-ene (1). A suspension of methyltriphenylphosphonium iodide (72 mg, 0.18 mmol, 5 eq.) and potassium t-butoxide (20.2 mg, 0.18 mmol, 5 eq.) was purged with nitrogen for 5 min. Anhydrous THF (3 ml) was added and the resulting suspension was stirred at room temperature for 15 min. This yellow suspension was cannulated into a solution of ketone **21** (2 mg, 0.0074 mmol) in THF (2 ml). The resulting suspension was stirred at room temperature for 20 h, then filtered through a short column of basic Al_2O3 and washed with petroleum ether 40-60˚C (dried over K_2CO_3). The solvent was removed by a stream of dry nitrogen and the residue was chromatographed on basic Al_2O_3 (eluted with petroleum ether 40-60˚C, pre-dried over K_2CO_3) to afford *diene **1*** (1.9 mg, 96%) as a colourless oil (Found: M, 270.2347. $C_{20}H_{30}$ requires 270.2347). ν_{max} ($CDCl_3$) 2940s, 2920s, 2850s, 1650m, 1600w cm^{-1}. ^1H NMR δ 4.61, s, 1H, H-17_A; 4.57, d, *J* 1.7 Hz, 1H, H-17_B; 2.23, m, 1H, H-13; 1.96, ddd, *J* 2.6, *J* 8.8, *J* 14.4 Hz, 1H; 1.90-1.60, m, 5H; 1.60-1.05, m, 11H; 1.02, s, 3H, CH_3; 0.89, dd, $J_{14\beta,13\alpha}$ 3.7, J_{gem} 12.2 Hz, 1H, H-14_β; 0.84, s, 3H, CH_3; 0.83, s, 3H, CH_3. ^{13}C NMR δ 158.54, C16; 97.77, C17; 44.89, C5; 42.33, C9; 41.92, C14; 39.05, C1; 38.99, C13; 36.68, C10; 36.05, C8; 34.21, C15; 34.20, C19, CH_3; 33.15, C4; 30.08, C3; 29.72, C7; 26.27, C12; 21.76, C18, CH_3; 19.01, C20, CH_3; 18.75, C6; 17.86, C11; 17.85, C2. Mass spectrum *m/z* 270 (M, 52%), 255 (100), 242 (7), 213 (4), 199 (8), 185 (12), 173 (9), 159 (12), 148 (39), 131 (18), 118 (32), 105 (19), 91 (29), 71 (34).

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References and Notes

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