Partial Synthesis of a Trachylobagibberellin Analogue

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We have synthesized a trachylobagibberellin analogue (**14**) by rearranging a chloro-enol lactone obtained from trachinodiol (**2**). Its structure was determined by *X*-ray analysis. This implies that the stereochemistry previously given to a similar compound (**20**) obtained from epicandicandiol (**19**) by the same procedure, should be amended to (**21**).

The diterpene skeleton of trachylobane (*ent*-13*R*,16-cycloatisane) is uncommon in Nature. Trachylobanic compounds functionalized at C-18 have been isolated from *Trachylobium verrucosum* (Leguminoseae),[1] from some *Sideritis* species (Lamiaceae),[2,3] and from *Xylopia quintasii* (Annonaceae).[4] Products of this type functionalized at C-19 have been isolated from the genera *Helianthus*[5] and *Viquiera*[6] (Compositae).

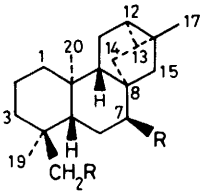
Sideritis canariensis[2,3] and *S. dendrochahorra*, two endemic species from the Canary Islands, contain trachylobanic diterpenes in high yield. Thus, we thought of transforming those compounds into trachylobagibberellins by chemical and microbiological methods. We have published some results obtained from their microbiological transformation by *Gibberella fujikuroi*.[7] Other authors[8,9] have also obtained trachylobagibberellins by feeding trachyloban-19-oic acid to a mutant of the same fungus.

The work described in this paper consisted of applying the ring-contraction of a chloro-enol lactone which we had previously developed,[10] to compounds in the trachylobane series to afford trachylobagibberellin analogues.

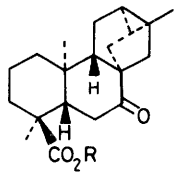
The keto acid (**3**), purified as its methyl ester (**4**), was obtained by oxidation of trachynodiol (**2**) with Jones reagent. The acid was autoxidized with oxygen in potassium t-butoxide to afford the enol-lactone (**5**) ($\nu_{max.}$ 1 790 and 1 605 cm^{-1}, $\lambda_{max.}$ 266 nm).

Several small-scale reductions of (**5**) with sodium borohydride in different solvents, for various times, and at different temperatures were carried out to optimize the reaction conditions. Those chosen are described in the Experimental section. In this reaction a mixture of compounds was obtained. The main product was the desired alcohol (**6**). The α configuration was assigned to the hydroxy group because the borohydride reduction of C-7 diterpenic ketones of the trachylobane[11] or kaurene[12] series gives the equatorial alcohol. Three other compounds were also obtained, the first two in trace amounts; the diol (**9**), the aldehyde (**10**), and the lactol (**11**). Their structures were deduced from their ^1H n.m.r. spectra. The stereochemistry at C-5 in (**9**) and (**10**) is provisionally given as α, since the reduction of other enol lactones of a similar type[13] from a *cis* A/B ring junction. Jones oxidation of the lactol (**11**) regenerated the original lactone (**5**)

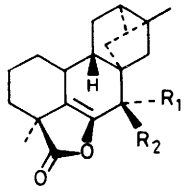
Treatment of the alcohol (**6**) with triphenylphosphine and tetrachloromethane afforded a (9:1) mixture of the two epimeric chloro derivatives (**7**) and (**8**) with similar R_F values on t.l.c. Only the major compound (**7**) could be obtained pure by dry column chromatography. The β stereochemistry given to the halogen in (**7**) is based on the fact that this type of reaction normally takes place with inversion of configuration.[14] The proton geminal to the chlorine in (**7**) has the same chemical shift as the corresponding kaurene derivative obtained stereospecifically in a similar reaction.[10]



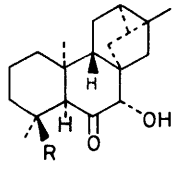
(**1**) R = H
(**2**) R = OH



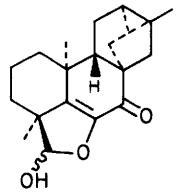
(**3**) R = H
(**4**) R = Me



(**5**) R^1 , R^2 = O
(**6**) R^1 = OH, R^2 = H
(**7**) R^1 = H , R^2 = Cl
(**8**) R^1 = Cl , R^2 = H



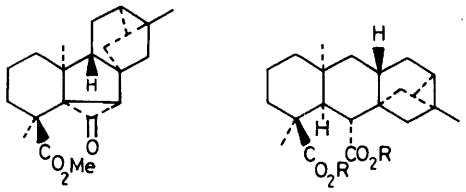
(**9**) R = CH_2OH
(**10**) R = CHO



(**11**)

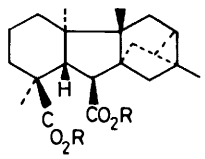
Reaction of (**7**) contaminated with (**8**) (10% determined by ^1H n.m.r.) with sodium methoxide in dimethoxyethane[15] gave the dimethyl ester of *ent*-5βH,6αH-trachylobagibberellane-7,18-dioic acid (**13**) by a Favorskii rearrangement, probably *via* the intermediate (**12**). The structure of compound (**13**) was given on the basis of the following considerations: its ^1H n.m.r. spectrum shows signals assignable to two cyclopropane hydrogens, three methyl groups, two methoxy groups, and a couple of doublets centred at 2.16 and 3.20 (*J* 10 Hz, 5α-H, 6β-H). The coupling constant could also be accommodated in a structure such as (**15**) with 5β,6α hydrogens.

Japanese authors[16] have determined unequivocally that the benzylic acid rearrangement of methyl-6,7-dioxo-5α,10α-podocarpa-8,11,13-trien-15-oate (**17**) gives the hydroxy diacid (**18**), with 5α-H,6β-H-OH stereochemistry. As in this reaction, the

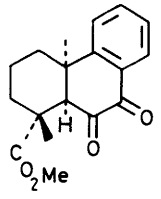


(12)

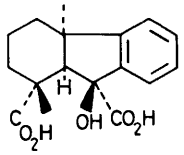
(13) R = Me
(14) R = H



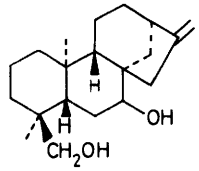
(15) R = Me
(16) R = H



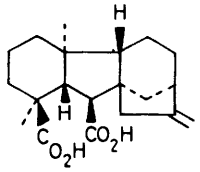
(17)



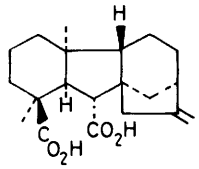
(18)



(19)



(20)



(21)

rearrangement proceeds *via* a keto-enol intermediate and the hydrogen at C-5 in (**18**) enters by the α-face; it is likely that the same occurred in our case forming compound (**13**).

The dimethyl ester (**13**) was treated with potassium t-butoxide in dimethyl sulphoxide giving the corresponding diacid (**14**). The coupling constant observed in the ^{1}H n.m.r. spectrum for 5-H,6-H was the same as in the methyl ester. The structure (**14**) was confirmed by *X*-ray analysis.

This implies that the structure given previously as (**20**) to an analogue obtained from epicandicandiol (**19**) by the same procedure described here, should be changed to (**21**).

The synthesis of this compound (**14**) with a new skeleton is potentially important from the point of view of biological application since normal C-19 trachylobagibberellins possess biological activity.[8] Moreover, other tetracyclic analogues can be obtained by opening of the cyclopropane ring in (**13**) or (**14**).

The crystal structure with its absolute configuration is shown in the Figure. The asymmetric unit contains two crystallographically independent molecules. Both have an identical conformation and no significant differences in their geometrical features can be observed. The conformational analysis has been carried out by Cremer's method[17] (Table 1), the six-membered rings of the two molecules A and B having the same conformation (twist, envelope, twist). The two molecules in the asymmetric unit are linked in pairs by hydrogen bonds. The oxygen atoms involved in this unit are related by a pseudo

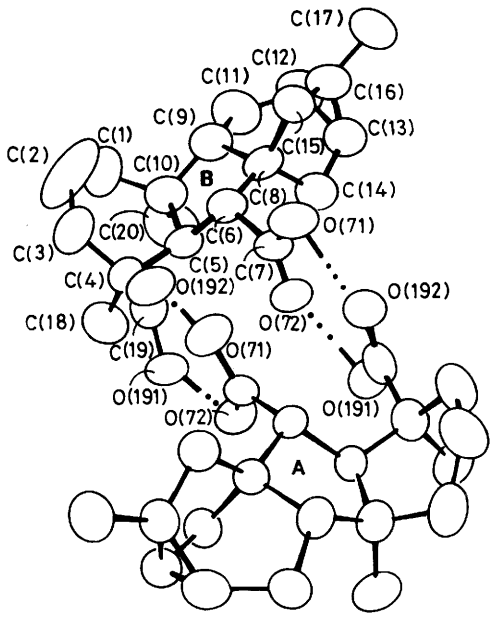


Figure. The conformation of molecules A and B in the hydrogen bonded dimer of (**14**). The atom numbering is given for molecule B. Carbons 18 and 19 in the *X*-ray Figure and Tables correspond to carbons 19 and 18 in the chemical nomenclature of (**14**)

Table 1. Conformational analysis. The θ, φ, and Q Cremer's parameters have been calculated in an anticlockwise sense.

Rings	Molecules	θ	φ	Q	Type
C(1), C(1), C(3), C(4), C(5), C(10)	A	91°	22°	0.66	$^2T_4$
a	B	99	26	0.51	$^2T_4$
C(11), C(9), C(8), C(15), C(16), C(12)	A	66°	133°	0.69	E_8
c	B	65	130	0.69	E_8
C(11), C(9), C(8), C(14), C(13), C(12)	A	100°	—29°	0.76	$^8T_{11}$
e	B	99	—27	0.77	$^8T_{11}$
C(6), C(8), C(9), C(10), C(5)	A		206°	0.44	$^6T_8$
b	B		198	0.43	$^6T_8$
C(15), C(8), C(14), C(13), C(16)	A		211°	0.42	E_8
d	B		211	0.32	E_8

Table 2. Hydrogen-bond lengths (Å), and angles (°)

X—H···Y	X···Y	X—H	H···Y	X—H···Y
O(71A)—H···O(192B)	2.65	1.05	1.62	165
O(191A)—H···O(72B)	2.62	1.09	1.56	162
O(191B)—H···O(72A)	2.65	1.09	1.57	172
O(71B)—H···O(192A)	2.64	1.17	1.50	162

centre of symmetry. Table 2 shows the geometrical features for the hydrogen bonds. The tilt of the two carboxy groups in both molecules A and B are also very similar.

Experimental

M.p.s are determined with a Kofler hot-plate apparatus and are uncorrected. I.r. spectra were taken for solution in $CHCl_3$, u.v. spectra for solution in ethanol, and ^{1}H n.m.r. spectra were determined for solutions in $CDCl_3$. Silica gel Merck (0.05—0.2 mm) was used for column chromatography.

Table 3. Atomic parameters for compound (**14**)

Atom	x/a	y/b	z/c	U(eq)
O(71A)	7 245(1)	7 353(5)	5 628(4)	69(1)
O(72A)	6 762(1)	4 938(5)	5 837(4)	62(1)
0(191A)	7 093(1)	3 025(5)	8 707(4)	69(1)
O(192A)	7 495(1)	5 642(6)	8 864(4)	71(1)
C(1A)	5 973(2)	8 147(10)	10 706(6)	86(3)
C(2A)	6 478(2)	8 629(10)	11 113(7)	90(3)
C(3A)	6 846(2)	7 069(10)	10 907(6)	79(2)
C(4A)	6 679(2)	5 552(7)	9 803(5)	57(2)
C(5A)	6 349(2)	6 361(7)	8 526(5)	49(2)
C(6A)	6 611(1)	7 577(7)	7 370(5)	45(1)
C(7A)	6 880(2)	6 483(8)	6 199(5)	48(2)
C(8A)	6 197(1)	8 664(7)	6 628(5)	46(1)
C(9A)	5 901(2)	9 198(7)	8 030(5)	54(2)
C(10A)	5 906(2)	7 491(8)	9 099(5)	59(2)
C(11A)	5 464(2)	10 028(9)	7 572(6)	67(2)
C(12A)	5 395(2)	10 585(8)	5 923(6)	64(2)
C(13A)	5 568(2)	9 205(8)	4 785(5)	57(2)
C(14A)	5 871(2)	7 675(7)	5 466(5)	52(2)
C(15A)	6 327(2)	10 445(7)	5 813(5)	54(2)
C(16A)	5 845(2)	10 978(7)	5 067(6)	57(2)
C(17A)	5 849(2)	12 492(8)	3 918(6)	72(2)
C(18A)	6 415(2)	4 026(9)	10 637(6)	77(2)
C(19A)	7 132(2)	4 732(7)	9 089(5)	55(2)
C(20A)	5 439(2)	6 311(9)	9 021(7)	85(2)
O(71B)	8 240(1)	4 590(6)	7 220(4)	82(2)
O(72B)	7 791(1)	2 110(6)	6 863(4)	71(1)
O(191B)	7 212(1)	2 738(6)	3 940(4)	75(1)
O(192B)	7 747(1)	4 995(6)	3 968(4)	78(1)
C(1B)	8 929(3)	849(14)	2 102(8)	116(4)
C(2B)	8 801(4)	2 527(16)	1 623(12)	176(5)
C(3B)	8 300(2)	3 207(10)	1 810(7)	85(2)
C(4B)	7 992(2)	2 121(8)	2 910(5)	62(2)
C(5B)	8 305(2)	1 161(8)	4 182(6)	61(2)
C(6B)	8 506(2)	2 462(8)	5 421(5)	61(2)
C(7B)	8 140(2)	3 023(9)	6 557(6)	61(2)
C(8B)	8 916(2)	1 327(8)	6 179(6)	69(2)
C(9B)	9 189(2)	494(10)	4 784(6)	81(2)
C(10B)	8 765(2)	115(8)	3 600(6)	72(2)
C(11B)	9 518(2)	−1 052(14)	5 232(8)	128(4)
C(12B)	9 657(2)	− 897(13)	6 886(8)	112(3)
C(13B)	9 250(2)	−738(12)	7 982(7)	94(3)
C(14B)	8 770(2)	−192(9)	7 290(6)	76(2)
C(15B)	9 306(2)	2 404(11)	7 084(6)	85(2)
C(16B)	9 597(2)	876(12)	7 785(7)	97(3)
C(17B)	9 975(2)	1 384(14)	8 967(8)	119(4)
C(18B)	7 694(2)	629(10)	2 060(7)	90(2)
C(19B)	7 639(2)	3 434(6)	3 652(5)	65(2)
C(20B)	8 642(3)	−1 918(10)	3 399(9)	119(3)

Table 4. Bond lengths in (Å), e.s.d. in parenthesis

O(71)–C(7)	1.304(6)	1.318(7)
O(72)–C(7)	1.217(7)	1.206(7)
O(191)–C(19)	1.298(6)	1.312(6)
O(192)–C(19)	1.221(6)	1.211(7)
C(1)–C(2)	1.474(9)	1.345(15)
C(1)–C(10)	1.525(7)	1.522(9)
C(2)–C(3)	1.539(9)	1.481(12)
C(3)–C(4)	1.545(8)	1.535(8)
C(4)–C(5)	1.564(7)	1.573(7)
C(4)–C(18)	1.534(8)	1.555(9)
C(4)–C(19)	1.536(7)	1.527(8)
C(5)–C(6)	1.554(7)	1.547(7)
C(5)–C(10)	1.569(7)	1.587(7)
C(6)–C(7)	1.523(7)	1.506(7)
C(8)–C(9)	1.560(6)	1.567(8)
C(8)–C(14)	1.541(6)	1.549(8)
C(8)–C(15)	1.538(7)	1.549(8)
C(9)–C(10)	1.573(7)	1.548(7)
C(9)–C(11)	1.548(7)	1.532(11)
C(10)–C(20)	1.551(8)	1.534(10)
C(11)–C(12)	1.532(7)	1.527(10)
C(12)–C(13)	1.516(8)	1.511(9)
C(12)–C(16)	1.498(7)	1.536(12)
C(13)–C(14)	1.518(7)	1.504(8)
C(13)–C(16)	1.523(7)	1.531(11)
C(15)–C(16)	1.525(7)	1.504(10)
C(16)–C(17)	1.512(8)	1.518(9)

ent-7-*Oxotrachyloban*-18-*oic acid Methyl Ester* (**4**).—Trachinodiol (**2**) (6.0 g) in acetone (200 ml) was oxidised with Jones reagent at room temperature for 8 h. The acetone solution was filtered and the chromic salts were washed with acetone. The combined acetone solutions were concentrated under reduced pressure to a volume of 20 ml and then poured into cold water (600 ml) and extracted with ether. Work-up gave *ent*-7-oxotrachyloban-18-oic acid (**3**), which was used in the next step without purification. Treatment with ethereal solution of diazomethane and chromatography with light petroleum–ethyl acetate (9:1) as eluant afforded the methyl ester (**4**) (5.7 g), m.p. 110—112 °C (lit.,[2] 110—111 °C), M^+ 330; δ_H (90 MHz) 0.70 and 0.85 (each 1 H, m), 1.09 (3 H, s), 1.18 (6 H, s), and 3.63 (3 H, s).

ent-7-*Oxotrachylob*-5-*en*-18-*oic Acid* 18,6-*Lactone* (**5**).—The methyl ester (**4**) (5.0 g) was dissolved in a solution of potassium t-butoxide (40 g) in t-butyl alcohol (280 ml) and the mixture stirred at room temperature in an oxygen atmosphere for 24 h. The solution was then poured into cold water, acidified with hydrochloric acid (pH 6), and extracted with chloroform. The solvent was evaporated and the residue chromatographed with light petroleum–ethyl acetate (9:1) to give (**5**) (3.5 g), m.p. 228—229 °C (Found: C, 77.1; H, 7.8. $C_{20}H_{24}O_3$ requires C, 76.89; H, 7.74%) $[\alpha]_D$ +25 (*c*, 1.41 in $CHCl_3$), $\nu_{max.}$(KBr) 2 900, 2 845, 1 790, 1 665, 1 455, 1 380, 1 285, 1 230, 1 070, and 985 cm^{-1}; $\lambda_{max.}$ 266 nm; δ_H (60 MHz) 0.74 and 1.03 (each 1 H, m), 1.23, 1.37, and 1.52 (each 3 H, s); *m/z* 312 (M^+) 297, 284, and 269.

Reduction of the Lactone (**5**).—The lactone (**5**) (1.1 g) in methanol–dimethoxyethane (1:1) (100 ml) was treated at −12 °C with portions of sodium borohydride (200 mg) for 30 min. Stirring was stopped and the reaction mixture left to stand at the same temperature for 2 h. The mixture was poured into cold water acidified with acetic acid and extracted with ether. The solvent was evaporated and the residue chromatographed with mixtures of light petroleum–ethyl acetate. The fractions eluted with light petroleum–ethyl acetate (2%) afforded ent-7β-*hydroxytrachylob*-5-*en*-18-*oic acid* 18,6-*lactone* (**6**) (770 mg), m.p. 162—163 °C (Found: M^+, 314.1845. $C_{20}H_{26}O_3$ requires M^+, 314.1881), $[\alpha]_D$ −9 (*c*, 1.81 in $CHCl_3$), $\nu_{max.}$(KBr) 3 500, 2 900, 1 770, 1 600, and 1 000 cm^{-1}; δ_H (60 MHz) 0.90 (2 H, m), 1.15, 1.23 and 1.39 (each 3 H, s), and 4.21 (1 H, s, 7-H); *m/z* 314 (M^+), 296, 281, 270, 254, and 192. Further elution with light petroleum–ethyl acetate (5%) gave ent-6-*oxo*-7β-*hydroxy*-5βH-*trachyloban*-18-*al* (**10**) (9 mg), δ_H (60 MHz) 0.93, 1.17, and 1.52 (each 3 H, s), 2.62 (1 H, s, 5-H), 4.08 (1 H, s, 7-H), and 9.31 (1 H, s, 18-H). Further elution afforded ent-6-*oxo*-7β,18-*dihydroxy*-5βH-*trachylobane* (**9**) (20 mg); $\nu_{max.}$ 3 445, 2 900, 1 700, 1 375, and 1 100 cm^{-1}; δ_H (60 MHz) 0.93 (3 H, s), 1.17 (6 H, s), 2.55 (1 H, s, 5-H), 3.05 and 3.48 (each 1 H, d, *J* 12 Hz), and 4.00 (1 H, s, 7-H). Further elution with light petroleum–ethyl acetate (10%) gave the lactol (**11**) (270 mg) as a gum (Found: M^+, 314.1874. $C_{20}H_{26}O_3$ requires M^+, 314.1882); $\nu_{max.}$ 3 400br, 2 900 and 1 640 cm^{-1}; $\lambda_{max.}$ 285 nm; δ_H (60 MHz) 0.70 and 0.90 (each 1 H, m), 1.18 (3 H, s), 1.25 (6 H, s), and 5.48 (1 H, s, 18-H); *m/z* 314 (M^+), 299, 286, 271, 203, and 168. Oxidation of compound (**11**) with Jones reagent in the usual way afforded the original lactone (**5**).

Table 5. Bond angles in (°), e.s.d. are in parenthesis.

	A	B		A	B
C(2)–C(1)–C(10)	113.9(5)	121.5(8)	C(10)–C(9)–C(11)	118.0(4)	119.2(6)
C(1)–C(2)–C(3)	114.5(6)	120.6(9)	C(5)–C(10)–C(9)	102.5(4)	104.9(4)
C(2)–C(3)–C(4)	114.8(5)	115.4(6)	C(1)–C(10)–C(9)	108.9(4)	108.6(5)
C(3)–C(4)–C(19)	108.2(4)	108.7(5)	C(1)–C(10)–C(5)	113.1(4)	111.7(5)
C(3)–C(4)–C(18)	110.3(4)	110.0(4)	C(9)–C(10)–C(20)	114.6(4)	114.1(5)
C(3)–C(4)–C(5)	110.9(4)	112.8(4)	C(5)–C(10)–C(20)	110.1(4)	109.7(5)
C(18)–C(4)–C(19)	108.5(4)	108.7(4)	C(1)–C(10)–C(20)	107.6(4)	107.9(6)
C(5)–C(4)–C(19)	108.6(4)	107.7(4)	C(9)–C(11)–C(12)	110.8(4)	110.1(6)
C(5)–C(4)–C(18)	110.8(4)	109.0(5)	C(11)–C(12)–C(16)	123.2(4)	122.9(6)
C(4)–C(5)–C(10)	114.0(4)	114.1(4)	C(11)–C(12)–C(13)	118.2(5)	117.4(5)
C(4)–C(5)–C(6)	115.5(4)	116.1(4)	C(13)–C(12)–C(16)	60.7(3)	60.3(5)
C(6)–C(5)–C(10)	107.0(4)	104.7(4)	C(12)–C(13)–C(16)	59.1(3)	60.7(5)
C(5)–C(6)–C(8)	103.4(3)	103.9(4)	C(12)–C(13)–C(14)	113.5(4)	114.3(5)
C(5)–C(6)–C(7)	113.5(4)	114.4(4)	C(14)–C(13)–C(16)	106.8(4)	107.1(5)
C(7)–C(6)–C(8)	110.0(4)	110.1(4)	C(8)–C(14)–C(13)	103.6(4)	102.6(4)
O(72)–C(7)–C(6)	122.7(4)	123.5(5)	C(8)–C(15)–C(16)	102.4(4)	101.5(5)
O(71)–C(7)–C(6)	113.8(4)	113.9(5)	C(13)–C(16)–C(15)	106.6(4)	106.9(5)
O(71)–C(7)–O(72)	123.5(5)	122.7(5)	C(12)–C(16)–C(15)	116.7(4)	118.0(6)
C(6)–C(8)–C(15)	117.8(4)	116.8(5)	C(12)–C(16)–C(13)	60.3(3)	59.0(6)
C(6)–C(8)–C(14)	118.0(4)	118.0(4)	C(15)–C(16)–C(17)	117.9(4)	117.5(7)
C(6)–C(8)–C(9)	100.3(3)	101.0(4)	C(13)–C(16)–C(17)	121.4(4)	122.1(6)
C(14)–C(8)–C(15)	102.4(4)	102.4(4)	C(12)–C(16)–C(17)	120.4(5)	119.5(6)
C(9)–C(8)–C(15)	107.5(4)	107.4(4)	O(192)–C(19)–C(4)	122.1(5)	122.6(5)
C(9)–C(8)–C(14)	110.7(4)	111.1(5)	O(191)–C(19)–C(4)	114.9(9)	115.0(5)
C(8)–C(9)–C(11)	111.1(4)	111.4(5)	O(191)–C(19)–O(192)	123.0(5)	122.4(5)
C(8)–C(9)–C(10)	107.1(4)	106.8(4)			

Treatment of the Lactone (**6**) *with Triphenylphosphine and Tetrachloromethane.*—The lactone (**6**) (750 mg) in tetrachloromethane (90 ml) and pyridine (9 ml) was mixed with triphenylphosphine (900 mg) and refluxed for 5 h. The solvent was eliminated and the residue chromatographed with light petroleum–ethyl acetate (5%) to elute ent-7α-*chlorotrachylob*-5-*en*-18-*oic acid* 18,6-*lactone* (**7**) (50 mg), m.p. 172—173 °C (Found: M^+, 322.1553. $C_{20}H_{25}ClO_2$ requires M^+, 322.1543); $\nu_{max.}$(KBr) 2 920, 1 810, 1 420, 1 000, 735, and 670 cm^{-1}; δ_H (90 MHz) 0.75 (2 H, m), 1.22, 1.21, and 1.45 (each 3 H, s), and 4.30 (1 H, s, 7-H); *m/z* 332 (M^+), 298, 292, 253, 219, 192, 174, and 168. Further elution afforded a mixture (400 mg) of (**7**) and (**8**), the latter being the minor product (10%, n.m.r.).

ent-5β-H,6α-H-*Trachylobagibberellane*-7,18-*dioic* 7,18-*Dimethyl Ester* (**13**).—The mixture of 7-chloro isomers (400 mg) dissolved in dimethoxyethane (30 ml) was treated with sodium methoxide (400 mg) under argon and stirred at room temperature for 13 h. The reaction mixture was poured into cold water and extracted with ether. The solvent was evaporated and the residue chromatographed with light petroleum–ethyl acetate mixtures affording the dimethyl ester (**13**) (220 mg) as a gum (Found: M^+, 360.2300. $C_{22}H_{32}O_4$ requires M^+, 360.2298); δ_H (90 MHz) 0.83 (2 H, m), 1.10, 1.14 and 1.20 (each 3 H, s), 2.16 and 3.20 (each 1 H, d, *J* 10 Hz), and 3.56, and 3.63 (each 3 H, s); *m/z* 360, 328, 300, 286, 268, and 226.

ent-5β-H,6α-H-*Trachylobagibberellane*-7,18-*dioic Acid* (**14**).—The dimethyl ester (**13**) (100 mg) dissolved in dimethyl sulphoxide (16 ml) was treated with potassium t-butoxide (200 mg) and stirred under argon at room temperature for 4 h. The reaction mixture was poured into water, acidified with dilute hydrochloric acid (5%), and extracted with ether in the usual way giving the *acid* (**14**) (60 mg), m.p. 257—258 °C (Found: C, 72.30, H, 8.41. $C_{20}H_{28}O_4$ requires C, 72.26, H, 8.49); δ_H (90 MHz) 1.13, 1.16, and 1.38 (each 3 H, s), and 2.18 and 2.80 (each 1 H, d, *J* 10 Hz); *m/z* 314 ($M^+ - H_2O$), 286, 271, 171, 150, and 109(100).

Crystallographic Data for Compound (**14**).—$C_{20}H_{28}O_4$, M = 332, Monoclinic, a = 27.575(7), b = 7.308(1), c = 8.956(2) Å, β = 91.14(1)°, U = 1 804.4(6) Å^3, D_c = 1.223 g cm^{-3}, $F(000)$ = 720. Space group $P2_1$, Cu-K_α radiation, λ = 1.5418 Å.

A crystal of dimensions 0.1 × 0.1 × 0.2 mm was used for data collection on an automatic four-circle diffractometer, operating in the conventional θ/2θ scan mode to the limit $\theta_{max.}$ = 60°. A total of 2 905 independent Friedel pairs were obtained; 2 718 with $I > 2\sigma(I)$ were considered as observed and were used in the refinement of the structure (full-matrix least-squares). Lorentz and polarization corrections, but not absorption corrections were made.

The structure was determined by direct methods using MULTAN program;[18] a fragment of 14 atoms could be identified. Development of this fragment into the complete structure by Fourier methods gave no further problems. The hydrogen atoms were located in difference maps, excepting the methyl groups which were positioned in their probable positions. The hydrogen atoms with the isotropic temperature factors of their attached atoms were included as fixed contributors in the full-matrix least-squares refinement. After inclusion of a weighting scheme to prevent trends in $w\Delta^2F$ *vs.* $\langle F_o \rangle$ and $\langle \sin\theta/\lambda \rangle$,[19] the final R values are R = 7.4% and R_w = 6.7%. The absolute configuration[20] of the molecule was determined comparing the 56 Bijvoet pairs with $\Delta F_c > 0.06$ and with less experimental error than in $F_o > 10\sigma(F_o)$, $10 < F_o < 30$ and $0.27 < \sin\theta/\lambda < 0.60$. The averaged Bijvoet difference was 0.498 for the right enantiomer *vs.* 0.517 for the wrong one. This little difference could be due to the pseudo-centre of symmetry existing between the eight oxygen atoms, which would minimize the observed Bijvoet differences.

Atomic co-ordinates, bond distances, and angles are given in Tables 3, 4, and 5 respectively. The thermal parameters are available as Supplementary Publication No. SUP 56084 (6 pp.).* Structure factors available from the editorial office on request.

* For details of the Supplementary Publications Scheme see Instructions for Authors (1985) in *J. Chem. Soc., Perkin Trans. 1*, 1985, Issue 1.

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Received 19*th March* 1984; *Paper* 4/431