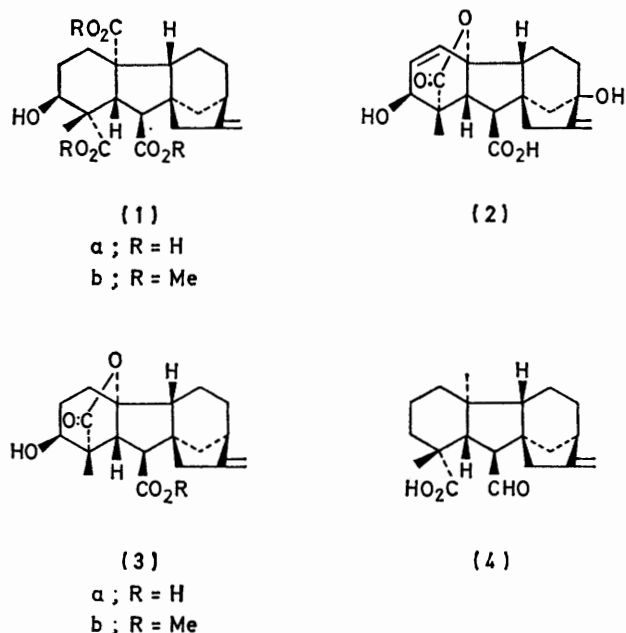


## The Molecular and Crystal Structures of Gibberellin A<sub>4</sub> and Gibberellin A<sub>13</sub> Methyl Esters

By George Ellames, James R. Hanson,\* Peter B. Hitchcock,\* and Sunday A. Thomas, The School of Molecular Sciences, University of Sussex, Brighton, Sussex BN1 9QJ

The X-ray structures of gibberellin A<sub>4</sub> methyl ester and gibberellin A<sub>13</sub> trimethyl ester have been determined. Ring A is flattened and the crowding of C(7) by C(18) and C(15) is greater in gibberellin A<sub>13</sub> trimethyl ester when compared to gibberellin A<sub>4</sub>.

THE gibberellin plant hormones may be divided into two classes; the C<sub>20</sub> compounds exemplified by gibberellin A<sub>13</sub> (1a)<sup>1</sup> and the C<sub>19</sub> compounds such as gibberellic acid (2).<sup>2</sup> There are a number of chemical differences



between the two series in, for example, the balance between the elimination and substitution reactions at C(3)<sup>3</sup> and the increased steric hindrance at C(7) in the C<sub>20</sub> gibberellins.<sup>4</sup> Furthermore the C<sub>19</sub> gibberellins are generally more biologically active than the C<sub>20</sub> compounds.<sup>5</sup> We have undertaken an X-ray study to compare gibberellins A<sub>4</sub> (3) and A<sub>13</sub> (1) which differ in the replacement of the 19,10  $\gamma$ -lactone ring by a 19,20-dioic acid. Previous X-ray studies have been performed on several derivatives of C<sub>19</sub> gibberellins.<sup>6</sup>

The molecular stereochemistry and atom numbering schemes of gibberellins A<sub>4</sub> and A<sub>13</sub> methyl esters (3b) and (1b), respectively, are shown in Figure 1. Final atom position parameters are listed in Table 1 and bond lengths and angles are given in Table 2. In both molecules the crystal structure contains intermolecular hydrogen bonds from the hydroxy-group to the C(7) carbonyl group. These are of length 1.98 Å for O(2)  $\cdots$  H(28)-O(1) in A<sub>13</sub> between molecules related by the screw axis along *b*, and 1.95 Å for O(4)  $\cdots$  H(25)-O(3)

in A<sub>4</sub> between molecules related by the screw axis along *a*, as seen in the packing diagrams (Figure 3).

The bond lengths and angles are within the expected ranges, with the ester C-O bonds averaging 1.34 Å in contrast to the other C-O bonds (av. 1.46 Å) reflecting a

small contribution of the resonance form  $R-C=O^+-R$  as seen in other structures.<sup>6</sup> The two molecules differ mainly in the conformation of ring A. In gibberellin A<sub>13</sub> trimethyl ester (1b) the two axial ester groups are arranged approximately parallel but slightly splayed

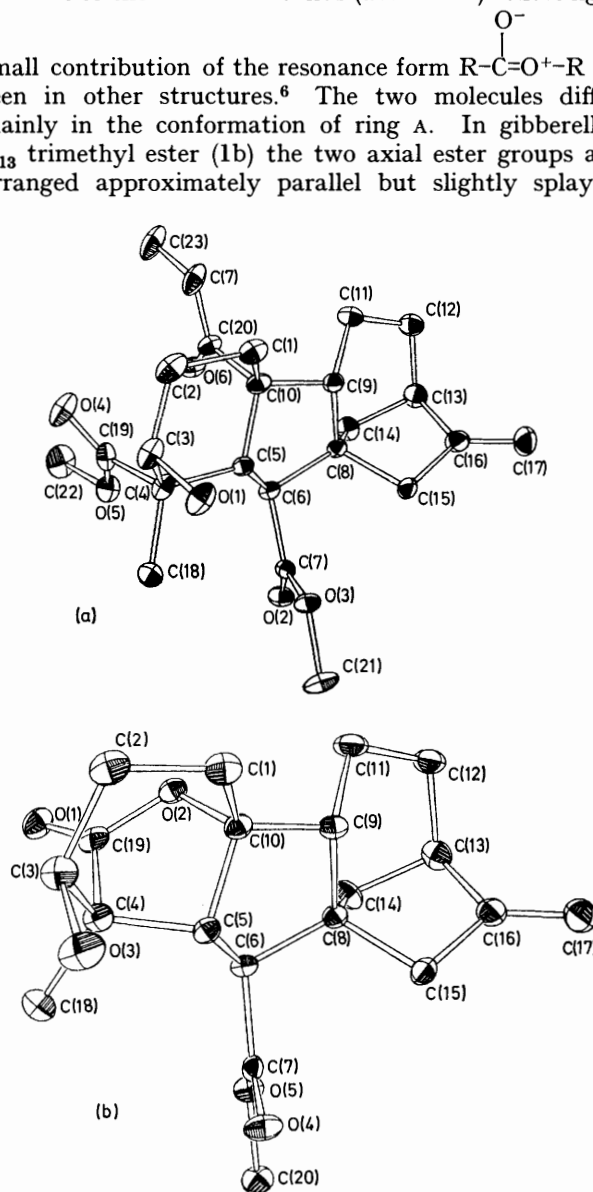


FIGURE 1 Crystal structures of (a) gibberellin A<sub>13</sub> trimethyl ester (1b) and (b) gibberellin A<sub>4</sub> methyl ester (3b)

apart to minimise steric strain as shown by the distance of 2.95 Å for C(19)···C(20) compared to 2.61 Å for C(4)···C(10). They are also rotated by 180° with respect to each other presumably to minimise interaction

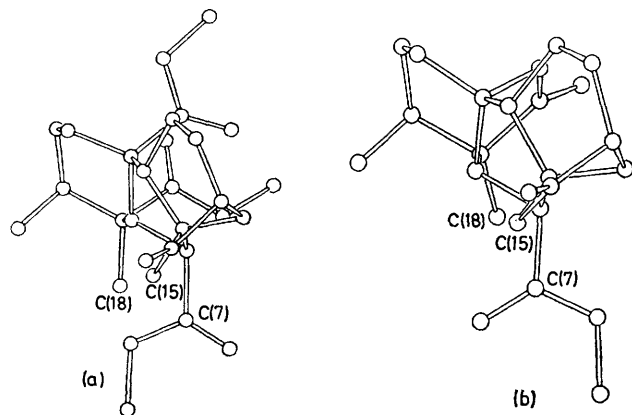


FIGURE 2 Structures viewed in projection on the plane of the C(7) ester groups: (a) gibberellin  $A_{13}$  trimethyl ester (1b); (b) gibberellin  $A_4$  methyl ester (3b)

between the carbonyl dipoles and between the methyl groups C(22) and C(23). In gibberellin  $A_4$  methyl ester (3b) the lactone bridge joining C(4) and C(10) reverses the flattening of ring A found in  $A_{13}$ , effectively moving C(19) closer to C(10). Consequently the C(18) methyl group is moved round in the same angular direction thus changing its position with respect to the C(7) ester

TABLE 1

(a) Fractional atomic co-ordinates ( $\times 10^4$ ) for gibberellin  $A_{13}$  trimethyl ester (1b) with estimated standard deviations in parentheses in the units of the last significant figure

(i) Non-hydrogen atoms

	<i>x</i>	<i>y</i>	<i>z</i>
C(1)	1 040(2)	2 178(2)	4 360(5)
C(2)	1 494(2)	1 651(2)	5 525(6)
C(3)	1 046(2)	1 669(2)	7 046(5)
C(4)	0 904(2)	2 534(2)	7 695(4)
C(5)	0 449(2)	3 041(2)	6 432(3)
C(6)	0 141(2)	3 920(2)	6 682(3)
C(7)	-0 620(2)	4 029(2)	7 738(3)
C(8)	-0 115(2)	4 215(2)	5 048(3)
C(9)	0 374(2)	3 636(2)	3 943(4)
C(10)	0 955(2)	3 067(2)	4 922(4)
C(11)	0 852(3)	4 100(3)	2 670(4)
C(12)	0 293(3)	4 768(3)	1 955(4)
C(13)	-0 311(3)	5 185(2)	3 107(4)
C(14)	0 082(3)	5 119(2)	4 694(4)
C(15)	-1 103(2)	4 206(2)	4 695(4)
C(16)	-1 149(2)	4 716(2)	3 256(5)
C(17)	-1 806(3)	4 696(4)	2 306(6)
C(18)	0 345(3)	2 465(2)	9 137(4)
C(19)	1 784(2)	2 883(2)	8 194(4)
C(20)	1 847(2)	3 491(2)	5 065(4)
C(21)	-1 918(3)	3 461(3)	8 719(6)
C(22)	2 473(3)	3 988(3)	9 410(6)
C(23)	3 292(3)	3 519(3)	4 193(9)
O(1)	0 208(2)	1 292(1)	6 920(4)
O(2)	-0 751(2)	4 644(1)	8 473(3)
O(3)	-1 158(1)	3 390(1)	7 732(3)
O(4)	2 477(2)	2 578(2)	7 959(5)
O(5)	1 682(2)	3 584(2)	8 962(3)
O(6)	1 987(2)	4 091(2)	5 817(3)
O(7)	2 435(2)	3 148(2)	4 155(4)

TABLE 1(a) (Continued)

(ii) Co-ordinates ( $\times 10^4$ ) of the hydrogen atoms

	<i>x</i>	<i>y</i>	<i>z</i>	Bonded to
H(1)	0 429	1 959	4 096	C(1)
H(2)	1 389	2 123	3 395	C(1)
H(3)	2 120	1 815	5 988	C(2)
H(4)	1 469	1 090	5 305	C(2)
H(5)	1 388	1 343	7 842	C(3)
H(6)	-0 044	2 620	6 176	C(5)
H(7)	0 627	4 299	7 056	C(6)
H(8)	-0 140	3 220	3 615	C(9)
H(9)	0 958	3 715	1 734	C(11)
H(10)	1 374	4 432	3 077	C(11)
H(11)	0 758	5 201	1 522	C(12)
H(12)	-0 095	4 589	1 099	C(12)
H(13)	-0 403	5 781	2 791	C(13)
H(14)	-0 175	5 485	5 412	C(14)
H(15)	0 667	5 280	4 841	C(14)
H(16)	-1 401	3 558	4 556	C(15)
H(17)	-1 486	4 457	5 564	C(15)
H(18)	-2 352	4 249	2 416	C(17)
H(19)	-1 762	5 105	1 423	C(17)
H(20)	0 542	2 080	9 921	C(18)
H(21)	0 178	3 007	9 585	C(18)
H(22)	-0 239	2 215	8 897	C(18)
H(23)	-1 657	3 518	9 799	C(21)
H(24)	-2 047	2 881	9 372	C(21)
H(25)	2 997	4 040	8 549	C(22)
H(26)	3 274	4 201	3 989	C(23)
H(27)	3 603	3 404	3 411	C(23)
H(28)	0 194	0 726	6 876	O(1)
H(29)	-2 282	3 054	8 402	C(21)
H(30)	2 285	4 596	9 827	C(22)
H(31)	2 868	3 514	10 210	C(22)
H(32)	3 551	3 918	5 139	C(23)

(b) Fractional atomic co-ordinates ( $\times 10^4$ ) for gibberellin  $A_4$  methyl ester (3b) with estimated standard deviations in parentheses in the units of the last significant figure

(i) Non-hydrogen atoms

	<i>x</i>	<i>y</i>	<i>z</i>
C(1)	-0 576(4)	0 243(2)	6 735(5)
C(2)	0 485(5)	0 153(2)	8 051(5)
C(3)	1 956(4)	0 372(2)	7 655(5)
C(4)	1 927(4)	0 985(1)	6 831(4)
C(5)	1 080(4)	0 930(1)	5 316(4)
C(6)	0 913(3)	1 496(1)	4 334(4)
C(7)	2 044(3)	1 579(1)	3 112(4)
C(8)	-0 592(3)	1 470(1)	3 639(4)
C(9)	-1 424(4)	1 040(2)	4 735(4)
C(10)	-0 397(4)	0 851(1)	5 997(4)
C(11)	-2 819(4)	1 297(2)	5 318(5)
C(12)	-3 683(4)	1 573(2)	3 996(6)
C(13)	-2 727(4)	1 874(2)	2 741(5)
C(14)	-1 348(4)	2 068(2)	3 544(5)
C(15)	-0 732(4)	1 254(2)	1 924(4)
C(16)	-2 233(4)	1 428(2)	1 544(5)
C(17)	-2 982(6)	1 233(3)	0 341(6)
C(18)	3 410(4)	1 240(2)	6 700(5)
C(19)	0 939(4)	1 373(1)	7 783(4)
C(20)	3 258(4)	2 279(2)	1 580(5)
O(1)	1 199(3)	1 716(1)	8 807(3)
O(2)	-0 401(3)	1 291(1)	7 278(3)
O(3)	2 676(4)	-0 007(1)	6 586(4)
O(4)	2 701(3)	1 190(1)	2 484(3)
O(5)	2 228(3)	2 144(1)	2 787(3)

(ii) Co-ordinates ( $\times 10^4$ ) of the hydrogen atoms

	<i>x</i>	<i>y</i>	<i>z</i>	Bonded to
H(1)	-0 417	-0 054	5 988	C(1)
H(2)	-1 342	0 166	7 108	C(1)
H(3)	0 539	-0 220	8 488	C(2)
H(4)	2 589	0 414	8 638	C(3)
H(5)	1 137	0 592	4 606	C(5)
H(6)	0 973	1 843	4 976	C(6)
H(7)	-1 597	0 612	4 225	C(9)
H(8)	-2 421	1 643	6 177	C(11)

TABLE 1(b) (Continued)

H(9)	-3 417	1 158	5 958	C(11)
H(10)	-4 243	1 255	3 454	C(12)
H(11)	-4 372	1 863	4 327	C(12)
H(12)	-3 225	2 216	2 191	C(13)
H(13)	-1 581	2 226	4 738	C(14)
H(14)	-0 813	2 329	2 973	C(14)
H(15)	-0 547	0 789	1 823	C(15)
H(16)	0 028	1 501	1 156	C(15)
H(17)	-4 390	1 398	0 613	C(17)
H(18)	-2 605	0 824	-0 196	C(17)
H(19)	3 403	1 587	6 056	C(18)
H(20)	3 910	1 016	5 963	C(18)
H(21)	3 681	1 326	7 589	C(18)
H(22)	3 137	2 608	1 448	C(20)
H(23)	4 190	2 202	1 911	C(20)
H(24)	2 984	2 199	0 706	C(20)
H(25)	2 445	-0 346	7 019	O(3)
H(26)	0 165	0 378	9 094	C(2)

TABLE 2(a) (Continued)

C(7)-C(6)-C(8)	109.9(2)	C(4)-C(19)-O(5)	111.0(3)
C(6)-C(7)-O(3)	112.9(2)	O(4)-C(19)-O(5)	123.3(3)
O(2)-C(7)-O(3)	124.5(4)	C(10)-C(20)-O(6)	124.7(3)
O(2)-C(7)-C(6)	122.9(3)	C(10)-C(20)-O(7)	111.6(3)
C(6)-C(8)-C(9)	105.8(2)	O(6)-C(20)-O(7)	122.1(3)
C(6)-C(8)-C(14)	115.5(3)	C(21)-O(3)-C(7)	115.6(3)
C(9)-C(8)-C(14)	110.9(3)	C(20)-O(5)-C(22)	115.5(3)
C(6)-C(8)-C(15)	115.3(2)	C(20)-O(7)-C(23)	114.7(5)
C(9)-C(8)-C(15)	109.9(3)		
C(15)-C(8)-C(14)	99.4(3)		
C(8)-C(9)-C(10)	106.8(2)		
C(8)-C(9)-C(11)	113.2(3)		
C(10)-C(9)-C(11)	115.2(3)		
C(1)-C(10)-C(5)	107.3(3)		

(b) Bond lengths (Å) and angles (°) for gibberellin A<sub>4</sub> methyl ester with estimated standard deviations in parentheses

TABLE 2

(a) Bond lengths (Å) and angles (°) for gibberellin A<sub>13</sub> methyl ester with estimated standard deviations in parentheses

## (i) Bond lengths

C(1)-C(2)	1.514(6)	C(22)-O(5)	1.440(6)
C(1)-C(10)	1.537(5)	C(23)-O(7)	1.450(5)
C(2)-C(3)	1.515(6)	C(1)-H(1)	1.03
C(3)-C(4)	1.537(4)	C(1)-H(2)	1.01
C(3)-O(1)	1.433(4)	C(2)-H(3)	1.08
C(4)-C(5)	1.557(4)	C(2)-H(4)	0.93
C(4)-C(18)	1.545(5)	C(3)-H(5)	1.03
C(4)-C(19)	1.533(5)	C(5)-H(6)	1.05
C(5)-C(6)	1.525(4)	C(6)-H(7)	1.02
C(5)-C(10)	1.549(4)	C(9)-H(8)	1.08
C(6)-C(7)	1.510(4)	C(11)-H(9)	1.05
C(6)-C(8)	1.576(4)	C(11)-H(10)	1.03
C(7)-O(3)	1.331(4)	C(12)-H(11)	1.07
C(8)-C(9)	1.554(4)	C(12)-H(12)	1.01
C(8)-C(14)	1.535(4)	C(13)-H(13)	1.02
C(8)-C(15)	1.551(4)	C(14)-H(14)	0.96
C(9)-C(10)	1.553(4)	C(14)-H(15)	0.95
C(9)-C(11)	1.545(5)	C(15)-H(16)	1.16
C(10)-C(20)	1.540(4)	C(15)-H(17)	1.05
C(11)-C(12)	1.525(6)	C(17)-H(18)	1.12
C(12)-C(13)	1.539(6)	C(17)-H(19)	1.03
C(13)-C(14)	1.534(5)	C(18)-H(20)	0.98
C(13)-C(16)	1.504(6)	C(18)-H(21)	1.00
C(15)-C(16)	1.524(5)	C(18)-H(22)	1.01
C(16)-C(17)	1.316(6)	C(21)-H(23)	1.04
C(19)-O(4)	1.194(5)	C(21)-H(24)	1.13
C(19)-O(5)	1.338(4)	C(21)-H(29)	0.91
C(20)-O(6)	1.202(4)	C(22)-H(25)	1.11
C(20)-O(7)	1.336	C(22)-H(30)	1.10
C(21)-O(3)	1.464(5)	C(22)-H(31)	1.21
C(7)-O(2)	1.211(6)	C(23)-H(26)	1.13
C(23)-H(32)	1.13		
C(23)-H(27)	0.86		
O(1)-H(28)	0.92		

## (ii) Bond angles

C(2)-C(1)-C(10)	110.6(3)	C(1)-C(10)-C(9)	115.4(3)
C(1)-C(2)-C(3)	112.7(3)	C(5)-C(10)-C(9)	102.1(2)
C(2)-C(3)-C(4)	114.6(3)	C(1)-C(10)-C(20)	119.9(3)
C(2)-C(3)-O(1)	109.4(3)	C(5)-C(10)-C(20)	112.9(3)
C(4)-C(3)-O(1)	107.1(3)	C(9)-C(10)-C(20)	107.0(3)
C(3)-C(4)-C(5)	106.3(3)	C(9)-C(11)-C(12)	112.6(3)
C(3)-C(4)-C(18)	108.8(3)	C(11)-C(12)-C(13)	112.3(3)
C(5)-C(4)-C(18)	112.5(3)	C(12)-C(13)-C(14)	109.8(3)
C(3)-C(4)-C(19)	108.3(3)	C(12)-C(13)-C(16)	110.6(3)
C(5)-C(4)-C(19)	114.1(3)	C(14)-C(13)-C(16)	102.8(3)
C(18)-C(4)-C(19)	106.3(3)	C(8)-C(14)-C(13)	100.2(3)
C(4)-C(5)-C(6)	122.2(3)	C(8)-C(15)-C(16)	102.1(3)
C(4)-C(5)-C(10)	114.2(2)	C(13)-C(16)-C(15)	108.1(3)
C(6)-C(5)-C(10)	104.8(2)	C(13)-C(16)-C(17)	127.9(4)
C(5)-C(6)-C(7)	116.2(2)	C(15)-C(16)-C(17)	123.9(4)
C(5)-C(6)-C(8)	103.4(2)	C(4)-C(19)-O(4)	125.7(3)

## (i) Bond lengths

C(1)-C(2)	1.521(6)	C(20)-O(5)	1.451(5)
C(1)-C(10)	1.520(5)	C(1)-H(1)	0.94
C(2)-C(3)	1.521(6)	C(1)-H(2)	0.81
C(3)-C(4)	1.555(5)	C(2)-H(3)	0.92
C(3)-O(3)	1.424(5)	C(2)-H(26)	1.07
C(4)-C(5)	1.525(5)	C(3)-H(4)	1.04
C(4)-C(18)	1.527(5)	C(5)-H(5)	0.98
C(4)-C(19)	1.520(5)	C(6)-H(6)	0.96
C(5)-C(6)	1.538(4)	C(9)-H(7)	1.07
C(5)-C(10)	1.529(5)	C(11)-H(8)	1.14
C(6)-C(7)	1.507(4)	C(11)-H(9)	0.85
C(6)-C(8)	1.548(5)	C(12)-H(10)	1.01
C(7)-O(4)	1.203(4)	C(12)-H(11)	0.97
C(7)-O(5)	1.319(4)	C(13)-H(12)	1.02
C(8)-C(9)	1.562(5)	C(14)-H(13)	1.10
C(8)-C(14)	1.533(5)	C(14)-H(14)	0.92
C(9)-C(10)	1.513(5)	C(15)-H(15)	1.07
C(9)-C(11)	1.530(6)	C(15)-H(16)	1.12
C(10)-O(2)	1.477(4)	C(17)-H(17)	1.40
C(11)-C(12)	1.526(6)	C(17)-H(18)	1.09
C(12)-C(13)	1.559(6)	C(18)-H(19)	0.96
C(13)-C(14)	1.541(5)	C(18)-H(20)	0.94
C(13)-C(16)	1.509(6)	C(18)-H(21)	0.82
C(8)-C(15)	1.545(5)	C(20)-H(22)	0.76
C(15)-C(16)	1.515(6)	C(20)-H(23)	0.95
C(16)-C(17)	1.322(7)	C(20)-H(24)	0.81
C(19)-O(1)	1.193(4)	O(3)-H(25)	0.88
C(19)-O(2)	1.356(4)		

## (ii) Bond angles

C(2)-C(1)-C(10)	110.6(3)	C(10)-C(9)-C(11)	115.9(3)
C(1)-C(2)-C(3)	113.7(3)	C(1)-C(10)-C(5)	111.4(3)
C(2)-C(3)-C(4)	112.0(3)	C(1)-C(10)-C(9)	118.5(3)
C(2)-C(3)-O(3)	112.8(3)	C(5)-C(10)-C(9)	106.8(3)
C(4)-C(3)-O(3)	104.9(3)	C(1)-C(10)-O(2)	107.7(3)
C(3)-C(4)-C(5)	108.5(3)	C(5)-C(10)-O(2)	101.8(2)
C(3)-C(4)-C(18)	110.7(3)	C(9)-C(10)-O(2)	109.3(2)
C(5)-C(4)-C(18)	117.1(3)	C(9)-C(11)-C(12)	112.5(3)
C(3)-C(4)-C(19)	106.6(3)	C(11)-C(12)-C(13)	111.7(3)
C(5)-C(4)-C(19)	99.9(3)	C(12)-C(13)-C(14)	108.4(3)
C(18)-C(4)-C(19)	113.0(3)	C(12)-C(13)-C(16)	110.6(3)
C(4)-C(5)-C(6)	116.5(3)	C(14)-C(13)-C(16)	103.0(3)
C(4)-C(5)-C(10)	99.9(3)	C(8)-C(14)-C(13)	99.9(3)
C(6)-C(5)-C(10)	102.1(3)	C(8)-C(15)-C(16)	101.6(3)
C(5)-C(6)-C(7)	113.9(3)	C(13)-C(16)-C(15)	108.8(3)
C(5)-C(6)-C(8)	105.7(3)	C(13)-C(16)-C(17)	125.3(4)
C(7)-C(6)-C(8)	113.5(3)	C(15)-C(16)-C(17)	125.9(4)
C(6)-C(7)-O(4)	125.9(3)	C(4)-C(19)-O(2)	109.4(3)
C(6)-C(7)-O(5)	111.1(3)	C(4)-C(19)-O(1)	129.6(4)
O(4)-C(7)-O(5)	123.1(3)	O(1)-C(19)-O(2)	121.0(3)
C(6)-C(8)-C(9)	105.3(3)	C(10)-O(2)-C(19)	108.9(3)
C(6)-C(8)-C(14)	114.8(3)	C(7)-O(5)-C(20)	116.3(3)
C(9)-C(8)-C(14)	110.1(3)		
C(6)-C(8)-C(15)	116.9(3)		
C(9)-C(8)-C(15)	108.9(3)		
C(14)-C(8)-C(15)	100.8(3)		
C(8)-C(9)-C(10)	105.9(3)		
C(8)-C(9)-C(11)	113.2(3)		

group. In gibberellin  $A_4$  methyl ester (3b), the lactone bridge increases the internal ring A torsion angles at the C(4)-C(5) and C(5)-C(10) bonds ( $70.3$ – $72.4^\circ$ ) and decreases the torsion angles at the C(1)-C(2) and C(2)-C(3) bonds ( $-42.7$ ;  $43.7^\circ$ ). It also decreases the bond angle C(10)-C(5)-C(4) to  $99.9^\circ$  and increases C(5)-C(4)-C(18) to  $117.1^\circ$ . In contrast the axial ester groups in the  $A_{13}$  ester (1b) reduce the internal ring torsion angles at the C(4)-C(5) and C(5)-C(10) bonds to  $-56.4$  and  $60.7^\circ$  and increase those at the C(1)-C(2) and C(2)-C(3) bonds ( $56.1$ ;  $-54.2^\circ$ ). The bond angle at C(10)-C(5)-C(4) is increased to  $114.2^\circ$  and C(5)-C(4)-C(18) decreased to  $112.5^\circ$ . Thus the C(18) methyl group on going from gibberellin  $A_4$  to  $A_{13}$  moves through an anti-clockwise rotation of *ca.*  $9^\circ$  about C(4) in the plane of C(4),C(19),C(10) as viewed in Figure 1. The closer approach of C(18) to C(7) in  $A_{13}$  causes C(7) to be moved closer to C(15) as seen from the decrease in the angle C(7)-C(6)-C(8) from  $113.2^\circ$  in gibberellin  $A_4$  to  $109.9^\circ$  in gibberellin  $A_{13}$ . A reflection of the different ring A torsion angles between the 3-hydroxy-group and the C(18) methyl group [ $A_4$ : O(3)-C(3)-C(4)-C(18),  $-67^\circ$ ;  $A_{13}$ : O(1)-C(3)-C(4)-C(18),  $51.6^\circ$ ] is seen in the effect of the 3-hydroxy-group on the 18-H resonances in the n.m.r. spectra: gibberellin  $A_9$ – $A_4$ ,  $\delta(C_5D_5N)$  1.30–1.55,  $\Delta\delta(OH)$  0.25;  $A_{25}$ – $A_{13}$ ,  $\delta(C_5D_5N)$  1.74–2.10,  $\Delta\delta(OH)$  0.36. The shift to lower field of the C(18) resonances in the  $C_{20}$  gibberellins may also be a reflection of the closer proximity to the C(7) carboxy-group.

The ester group at C(7) could formally adopt a variety of conformations corresponding to free rotation about the C(6)-C(7) bond. However the close proximity of C(18) and C(15) means that to avoid steric strain from short contacts of the ester group oxygen atoms with the C(18) methyl group or the C(15) methylene, the conformation with the C(7) group approximately perpendicular to a line joining C(18) to C(15) is preferred. As can be seen the crystal structures stabilise opposite conformations in gibberellins  $A_4$  and  $A_{13}$  by different arrangements of intermolecular hydrogen bonds. Different conformations, obviously arising from other features, may persist in solution in some derivatives. Thus in gibberellin  $A_{12}$  7-aldehyde (4) the H(6)-H(7) coupling constant is 6 Hz<sup>7</sup> whilst in the corresponding gibberellin  $A_4$  7-aldehyde it is 2 Hz. The difference in reactivity of the C(7) carbonyl group between gibberellins  $A_4$  and  $A_{13}$  may be a consequence of the difference in steric hindrance to an incoming nucleophile at C(7). It has been assumed by Wipke and Gund<sup>8</sup> that nucleophilic attack at a carbonyl group comes from a direction approximately along the normal to the plane of the carbonyl group at the carbon atom and that any other part of the molecule which lies close to the carbon atom in this direction will decrease the rate of attack by nucleophiles. This steric congestion has been expressed as a numerical coefficient. The work of Dunitz *et al.*<sup>9</sup> has convincingly shown that attack by a nucleophile on a carbonyl group occurs at an angle of *ca.*  $105 \pm 5^\circ$  to the C=O vector in the vertical plane containing the bisector of the angle

between the two substituents at the carbonyl group suggesting that Wipke and Gunds' congestion factor

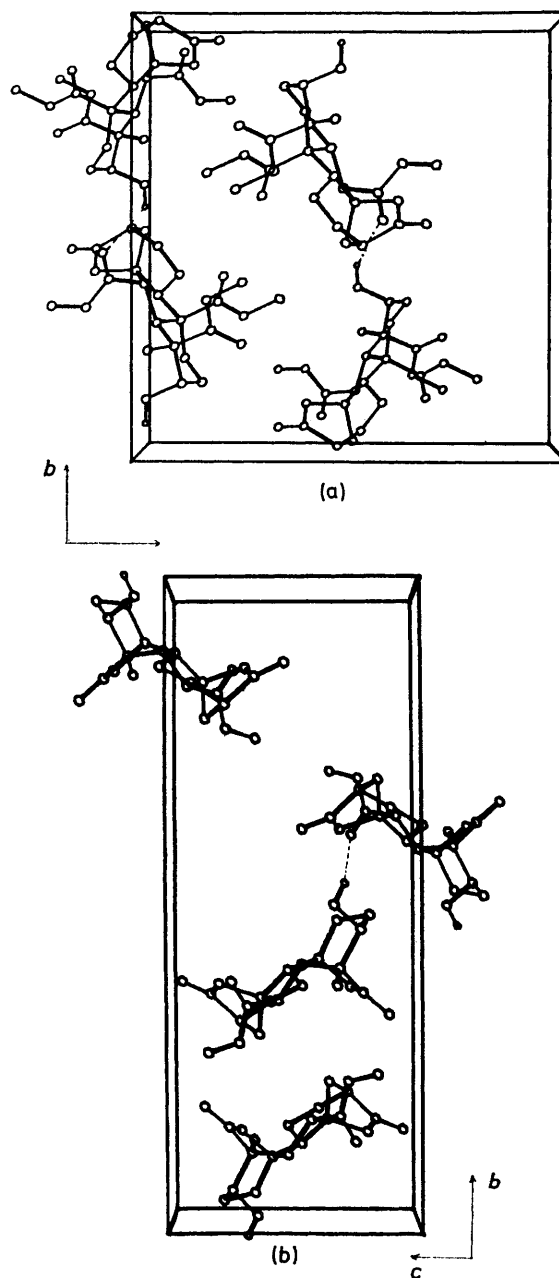


FIGURE 3 Packing diagrams for (a) gibberellin  $A_{13}$  trimethyl ester (1b); (b) gibberellin  $A_4$  methyl ester (3b)

calculation should be modified. In the case of the gibberellins  $A_4$  and  $A_{13}$  the methyl group C(18) and the methylene group C(15) would be expected to cause steric congestion at the C(7) carbonyl group. Views of the two molecules in parallel projection on the mean plane of the C(7) ester groups (Figure 2) show that in  $A_{13}$  the C(18) methyl group lies in the plane bisecting the O(3)-C(7)-C(6) angle as does C(15) on the opposite side and both are slightly behind the carbonyl group blocking the expected route of an attacking nucleophile. By

contrast, in gibberellin A<sub>4</sub> the total conformational change has moved both C(15) and C(18) away from the line C(7)–O(5) so that in the alternative conformation of the C(7) ester group, the steric hindrance is considerably reduced.

In both gibberellins ring c is in the boat conformation and, rather surprisingly, there is little difference between the torsion angles involving the C(8)–C(14) and C(14)–C(13) bonds although the nature of the C(10) substituent, with which C(14) may interact, has changed.

#### EXPERIMENTAL

*Gibberellin A<sub>13</sub> Trimethyl Ester (1b).*—Crystal data. C<sub>23</sub>H<sub>32</sub>O<sub>7</sub>, *M* = 420.6, orthorhombic, *a* = 15.384(1), *b* = 16.283(2), *c* = 8.865(1) Å, *U* = 2 220.7 Å<sup>3</sup>, *Z* = 4, *D<sub>c</sub>* = 1.26 g cm<sup>-3</sup>, *F*(000) 904, Mo-*K<sub>α</sub>* radiation, μ(Mo-*K<sub>α</sub>*) 1.0 cm<sup>-1</sup>, space group *P*2<sub>1</sub>2<sub>1</sub>2<sub>1</sub> (No. 19)<sup>10</sup> from the systematic absences *h*00 for *h* odd, *h*00 for *h* odd, 00*l* for *l* odd.

*Crystallographic Measurement.*—A crystal of dimensions ca. 0.5 × 0.25 × 0.25 mm was used for data collection. Accurate cell dimensions were determined from a least-squares treatment of setting angles for 12 reflections measured on a Hilger and Watts Y290 four-circle diffractometer. Diffraction data were collected by an ω/2θ step scan for the positive octant *hkl* in two consecutive shells θ = 2–22° and 22–25° with Mo-*K<sub>α</sub>* radiation (graphite monochromator). Each reflection was measured in 70 steps of 0.5 s each and background counts of 17.5 s were made at the end of each scan. The intensities of three standard reflections, monitored every 100 reflections, showed no significant changes. Raw data were corrected for Lorentz and polarization effects. Of 2 270 reflections measured, 1 919 having *I* > 3σ(*I*) were used in the structural analysis.

*Structure Determination and Refinement.*—All reflection data were converted into normalized structure factor magnitudes (*|E|*) and phases were derived by multiple-start tangent formula procedures<sup>11</sup> using the 207 reflections with *|E|* > 1.50. The best *E*-map gave a partial structure with rough atom positions for 17 non-hydrogen atoms taken as carbon. The remaining non-hydrogen atoms were located by tangent refinement of partial structures<sup>12</sup> using the 17 atom positions to obtain the best 30 phases. The atom positions with anisotropic temperature factors were refined by large-block-matrix least-squares using the 1 919 significant reflections with unit weight. Ambiguities between oxygen and carbon atoms were resolved on the basis of temperature factors and bond lengths. Two successive difference Fourier maps each gave the positions of the 32 hydrogen atoms. Each hydrogen atom was given the isotropic temperature factor of the carbon atom or oxygen atom to which it is bonded. A few more cycles of least squares refinement of all non-hydrogen atoms with anisotropic temperature factors and a weighting scheme defined as ω = 1.0/[σ<sup>2</sup>(*F*) + 0.001(*F*)<sup>2</sup>] gave convergence at a residual *R<sub>F</sub>* = 0.051 and *R<sub>ωF</sub>* = 0.06 when the ratio of shift to e.s.d. for any non-hydrogen parameter was less than 0.2 and a final difference Fourier map was everywhere less than 0.18 e Å<sup>-3</sup>.

\* For details see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1978, Index issue.

*Gibberellin A<sub>4</sub> Methyl Ester (3b).*—Crystal data. C<sub>20</sub>H<sub>26</sub>O<sub>5</sub>, *M* = 346.4, orthorhombic *a* = 9.500(1), *b* = 22.619(3), *c* = 8.512(1) Å, *U* = 1 829.1 Å<sup>3</sup>, *Z* = 4, *D<sub>c</sub>* = 1.26 g cm<sup>-3</sup>, *F*(000) 744; Mo-*K<sub>α</sub>* radiation, μ(Mo-*K<sub>α</sub>*) 0.96 cm<sup>-1</sup>, space group *P*2<sub>1</sub>2<sub>1</sub>2<sub>1</sub> (No. 19)<sup>10</sup> from the systematic absences *h*00 for *h* odd, *h*00 for *h* odd, 00*l* for *l* odd.

*Crystallographic Measurements.*—A crystal of dimensions ca. 0.40 × 0.35 × 0.25 mm was used for data collection as described above. However each reflection was measured in 60 steps of 0.5 s each and background counts of 15 s were made at the end of each scan. Of 1 902 reflections measured, 1 531 having *I* > 3σ(*I*) were used in the structure analysis.

*Structure Determination and Refinement.*—The structure was determined and refined as above. At convergence the final residual *R<sub>F</sub>* = 0.048 and *R<sub>ωF</sub>* = 0.055 when the ratio of shift to e.s.d. for any non-hydrogen parameter was less than 0.1 and a final difference Fourier map was everywhere less than 0.27 e Å<sup>-3</sup>.

For both structures initial data processing was done with local programmes. Data were then converted into a format suitable for the SHELX programme of G. M. Sheldrick. Scattering factors were taken from ref. 13 and no allowance was made for anomalous scattering. Final atom co-ordinates are listed in Table 1. The final structure factors together with torsion angles and thermal parameters are listed in Supplementary Publication No. SUP 22517 (24 pp.).\*

Since the absolute configuration of the gibberellins is well known no attempt was made to determine the absolute configuration in the present study. In all drawings of gibberellin A<sub>4</sub>, the configuration is inverted from the tabulated co-ordinates to make it comparable to gibberellin A<sub>13</sub>.

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