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SYNTHESIS OF GIBBERELLINS A_8 AND A_{56} FROM GIBBERELLIN A_3

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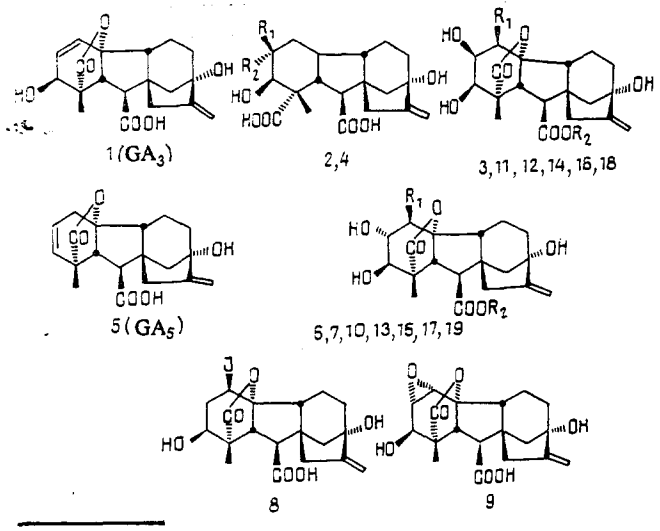
A mixture of gibberellin A_3 derivatives with 1(10)-ene-2β,3β-diol and 1(10)-ene-2α,3β-diol (2:5) groups, readily obtained from gibberellin A_3, has been used for a new and simple synthesis of gibberellin A_8 and its esters. The hydrolysis of GA_3 and the iodolactonization of a mixture of the 2-epimers was carried out in aqueous solution in a single flask, as also was a synthesis of GA_{56} from GA_3 by a method that we have modified. The mixture of 1β-iodides of GA_8 and GA_{56} was separated by chromatography on SiO_2 in the form of methyl or p-bromophenacyl esters which were then deiodinated and the methyl or p-bromphenacyl ester of GA_8 was isolated. Free GA_8 was obtained by the dephenylation of the latter ester. By two-dimensional NMR spectroscopy we succeeded in assigning all the signals in the ^{13}C and ^1H NMR spectra of the methyl esters of GA_8 and GA_{56}. In an attempt to obtain GA_5 methyl ester by the action of trimethylchlorosilane/sodium iodide on the 2α,3β-diol system in GA_{56} methyl ester, the 8,13-epimer of the latter was formed, the structure of its molecule being established from the results of X-ray structural analysis.

At the present time, 86 gibberellin phytohormones are known [1], of which only one is readily available — gibberellin A_3 (GA_3) (1), which explains its use as the starting material for the synthesis of other, less accessible, gibberellins. We have reported a simple synthesis of the new diacid (2) from GA_3 (1) [2]. This diacid (2) contains in ring A the 2β,3β-diol grouping that is characteristic for GA_8 (3) isolated from plants and another 11 gibberellins. We have investigated the possibility of synthesizing GA_8 (3) from the diacid (2), which is complicated by the fact that (2) is formed in a mixture with the main diacid (4) in a ratio of 2:5, respectively.



2. R_1=OH; R_2=H
3. R_1=R_2=H (GA_8)
4. R_1=H; R_2=OH
6. R_1=R_2=H (GA_{56})
7. R_1=I; R_2=H
10. R_1=H; R_2=$SnBu_3$
11. R_1=I; R_2=H
12. R_1=I; R_2=CH_3
13. R_1=I; R_2=CH_3
14. R_1=H; R_2=CH_3
15. R_1=H; R_2=CH_3
16. R_1=I; R_2=BPA*
17. R_1=I; R_2=BPA
18. R_1=H; R_2=BPA
19. R_1=H; R_2=BPA

*BPA — arbitrary designation of the β-bromophenacyl group.

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GA_8 (3) has previously been obtained by only one method — by treating GA_5 (5) with osmium tetroxide [3]. Product (3) was isolated from the four-component reaction mixture with a yield of 27%. A three-stage synthesis of GA_5 (5) with a yield of 18% has been described [4], and the overall yield in the synthesis of GA_8 (3) and GA_3 (1) will not exceed 4.9%.

We assumed that it would be possible to use the diacid (2) for the synthesis of GA_8 (3) just as was done in the three-stage synthesis of GA_{56} (6) from GA_3 (1) via the diacid (4) [5]. The method of synthesizing GA_{56}(6) that has been described included the alkaline hydrolysis of GA_3 (1) to (4), its isolation and purification, iodolactonation with the production of compound (7), and deiodination of the latter to GA_{56} (6).

We have found that it is possible to eliminate the laborious stages of extracting and purifying the diacid (4) in the synthesis of GA_{56} (6) and to obtain the iodolactone (7) without the isolation of the diacid (4) and the use of THF and CH_2Cl_2 (see [6]), which is important in preparative syntheses. For this, we performed a total alkaline hydrolysis of GA_3 (1) in an aqueous solution of KOH in the cold, acidified the solution with hydrochloric acid to pH 3-4, and then added an excess of sodium bicarbonate to the solution, followed by an aqueous solution of iodine and potassium iodide and obtained a quantitative yield of 1β-iodogibberellin A_{56} (7).

It is known that 1β-iodogibberellin A_4 (8) is smoothly deiodinated under the action of $NaBH_4$ in DMSO [7] but Japanese chemists did not succeed in obtaining the reduction product of 1β-iodoGA_{56} (7) under these conditions. On investigating the reaction mixture by the HPLC method, we found that in this case, as well, the iodination takes place completely with the formation of GA_{56} (6) but it is impossible to isolate the GA_{56} from aqueous DMSO by extraction. It was found that the reduction of the iodide (7) in DMSO not subjected to absolutization is accompanied by the side reaction of the formation of the epoxide (9), for which better conditions of formation have been found [8].* For the deiodination of (7) we used tri-*n*-butylstannane, and not di-*n*-butylstannane [5], and obtained a quantitative yield of the crystalline stannyl ester of A_{56} (10), from which the acid (6) was obtained by treatment with glacial acetic acid [9]. The formation of a stannyl ester of the type of (10) was suggested in the 13-deoxygenation of GA_3 (1) [10] but it could not be purified, and the free acid was isolated from the ester during chromatography on silica gel.

It is interesting to note that the synthesis of GA_{56} (6) and GA_3 (1) could be simplified and performed in aqueous solution in three stages in one flask if in the last stage the new water-soluble tri(methoxyethoxypropyl)stannane, working in weakly alkaline aqueous solutions [11], was used for the reduction of the iodide (7).

We used the two-stage method of synthesizing the iodide (7) from (1) in one flask described above for the synthesis of GA_8 (3). For this purpose, we boiled GA_3 (1) in aqueous Na_2CO_3, and the resulting mixture of the diacids (2) and (4) was relactonized, giving quantitatively a mixture of the iodides (7) and (11) in a ratio of 2:5, respectively. The mixture of acids (7) and (11) was methylated with diazomethane, the mixture of methyl esters (12) and (13) was separated by chromatography on SiO_2, and the pure iodides (12) and (13) were reduced with tri-*n*-butylstannane in a mixture of THF and benzene, giving the esters (14) and (15). The yield of GA_8 methyl ester (14) was 97% on the diacid (2) and 26% on the (1).

The GA_{56} Me ester (15) was readily hydrolyzed in 0.2 M aqueous methanolic alkali, while the hydrolysis of GA_8 Me ester (14) was accompanied by the formation of a complex mixture. In this connection, we have performed the synthesis of free GA_8 (3) by the procedure described above, replacing the methylation stage by a phenacylation stage, for which the mixture of acids (7) and (11) was treated with triethylamine and *p*-bromophenacyl bromide in acetone [12]. The phenacyl esters (16) and (17) were separated by chromatography on SiO_2 and were deiodinated to (18) and (19), after which the phenacyl group in (18) was eliminated under conditions that we had modified, giving GA_8 (3) with a yield of 64% on the diacid (2) and 17% on the initial GA_3 (1).

The conversion of the *cis*-diols into alkenes under the action of Me_3SiCl and NaI in acetonitrile has been described [13]. We attempted to use this reaction for the conversion of GA_{56} (6) into GA_5 (5), and from GA_{56} Me ester (15) we obtained a well-crystallizing product having, according to XSA, the structure of the ketone (20). The *cis*-diol system proved to be resistant to the action of Me_3SiCl/NaI, and compound (20) was formed by a rearrangement known for 13-hydroxygibberellins under the action of the acid [1] liberated on the silylation of the hydroxy group of ring *A* in (15). The molecular structure of

*In a paper by N. A. Pankrushina et al., "1α,2α-Epoxygibberellin A_3: Partial synthesis, NMR spectra, biological activity, and crystal structure of its methyl ester," published in this Journal (No. 4, 549 (1993)), in Table 1 the chemical shifts for H-1 and H-2 (2.56 and 2.62) should be replaced by 3.57 and 3.64, respectively.

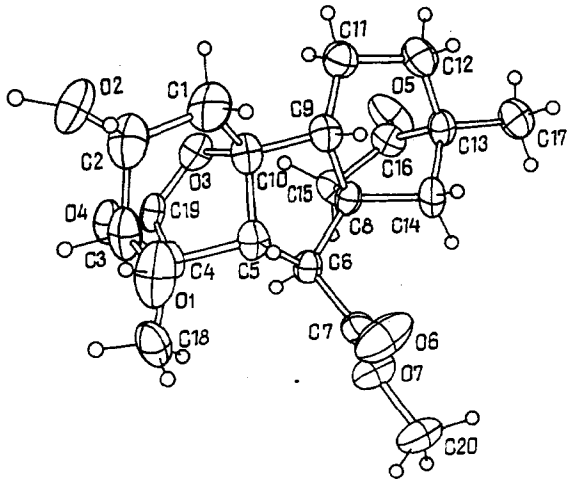
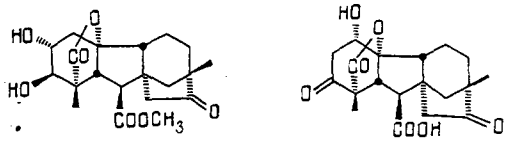


Fig. 1. Crystal structure of the diol (20).

the diol (20) is shown in Fig. 1. On comparing the form of the rings of (20) with the conformations of the analogous rings of the diketone (21) [14] it is possible to see their closeness.



Using the methods of two-dimensional ^{1}H-^{1}H NMR (COSY) and ^{13}C-^{1}H NMR (COSY, COLOC), we have interpreted the previously undescribed ^{13}C NMR spectra of 1β-iodogibberellin A_{56} [7] and the methyl esters of GA_8(14) and GA_{56} (15) (Table 1). A complete interpretation of the ^{13}C NMR spectrum in a similar way has been made for GLC (1) by Preiss et al. [15], and their results are included in Table 1.

On considering the ^{1}H NMR spectra of the esters (14), (15), and (17) it is possible to note two features common for them — the appearance of spin-spin coupling (SSC) through the four σ-bonds between the diequatorial H-1α and H-3α protons (0.8 Hz) and the complex forms of the signals for H-2 and H-3 resulting from the SSC of these protons with the protons of the hydroxy groups geminal to them. This interaction is easily excluded if the OH groups are replaced by adding heavy water to the sample, and a direct measurement of the SSCCs $J_{1,2}$, $J_{2,3}$, and $J_{1,3}$ is possible when the spectra are recorded with narrowing of the spectral lines. For the iodolactone (7), Murofushi et al. [5] described the H-2 and H-3 signals as singlets, while for the *p*-bromophenacyl ester of the same lactam that we are considering the protons gave (after the addition of D_2O) signals in the form of a doublet of doublets with $J_{1,2} = J_{2,3} = 1.5$ Hz and $J_{1,3} = 0.8$ Hz.

EXPERIMENTAL

For general observations, see [8].

Preparation of the Iodolactone (7). A solution of 3.0 g of GA_3 (1) in 45 ml of 1 M KOH was left at room temperature for two days and was then acidified with conc. HCl to pH 3-4. With stirring, 3 g of $NaHCO_3$ was carefully added to the solution, and then a solution of 4.4 g of I_2 and 6.0 g of KI in 25 ml of water in portions, and the mixture was stirred for another 60 min. The consumption of the reactants and the formation of products were determined by the HPLC method. A saturated aqueous solution of $Na_2S_2O_3$ was added to the reaction mixture until it was decolorized. Then it was acidified by the action of HCl (1:1) to pH 3, and the product was extracted with ethyl acetate (7 × 50 ml) after the aqueous layer had been saturated with NaCl. The extract was dried over $MgSO_4$, filtered, and evaporated to dryness. The crude product was

TABLE 1. Details of the ^{13}NMR Spectrum of 1β-IodoGA$_{56}$ [7] and the Methyl Esters of GA$_8$ (14), GA$_{56}$ (16), and 8,13-epi-GA$_{56}$ (20) (in pyridine-d_5, c = 0.02 M)

C_i	δC_i(7)	δC_i(14)	δC_i(15)	δC_i(20)	δC_i(GA$_3$) [15]
1	29.03 d	37.01 t	36.28 t	34.95 t	131.9
2	79.62 d	67.91 d	71.65 d	71.56 d	133.8
3	77.80 d	73.17 d	77.02 d	77.64 d	85.9
4	53.06 s	54.29 s	52.84 s	51.94 s	54.0
5	49.47 d	52.25 d	52.78 d	54.53 d	53.0
6	52.21 d	51.27 d	51.65 d	51.00 d	51.6
7	175.04 s	173.26 s	173.55 s	174.19 s	174.4
8	49.81 s	50.71 s	50.31 s	49.69 s	50.1
9	52.79 d	52.75 d	53.09 d	53.24 d	51.1
10	95.22 s	93.90 s	93.09 s	91.99 s	90.8
11	17.48 t	17.73 t	17.93 t	19.68 t	17.1
12	39.64 t	39.77 t	39.90 t	35.75 t	39.4
13	77.80 s	77.72 s	77.82 s	51.10 s	77.3
14	46.33 t	45.82 t	45.95 t	47.64 t	45.0
15	43.45 t	43.77 t	43.93 t	50.63 t	43.5
16	158.55 s	158.81 s	158.98 s	217.77 s	158.5
17	106.67 t	106.83 t	106.76 t	19.83 q	106.5
18	15.93 q	15.52 q	16.08 q	15.78 q	15.1
19	177.66 s	178.21 s	178.00 s	177.97 s	179.3
OMe	—	51.66 q	51.94 q	51.85 q	—

*The numbering of the carbon atoms for compound (20) is shown in Fig. 1.

TABLE 2. Coordinates (× 10^4, in fractions of the cell) and Equivalent Thermal Factors (U, Å^2) of the Nonhydrogen Atoms of Ketone (20)

Atom	x	y	z	U	Atom	x	y	z	U
C1	5084(7)	3631(4)	6394(2)	55	C2	5697(7)	3312(4)	5744(2)	57
C3	5881(7)	4284(4)	5295(2)	50	C4	4234(6)	5105(3)	5362(2)	36
C5	4353(5)	5539(3)	6037	35	C6	3009(6)	6455(3)	6227(2)	33
C7	4072(6)	7519(3)	6300(2)	36	C8	1973(6)	6070(3)	6833(2)	32
C9	2933(6)	4996(3)	7003(2)	37	C10	3629(6)	4535(3)	6388(1)	37
C11	1767(8)	4329(3)	7448(2)	46	C12	1295(7)	5033(3)	8021(2)	47
C13	579(7)	6173(3)	7851(2)	40	C14	2037(7)	6772(3)	7433(2)	39
C15	-195(6)	5990(3)	6733(2)	36	C16	-1024(6)	5984(3)	7384(2)	39
C17	-1(9)	6779(4)	8436(2)	57	C18	4236(7)	5955(4)	4841(2)	54
C19	2387(5)	4489(3)	5399(2)	34	C20	3866(9)	9410(3)	6195(2)	59
O1	7570(5)	4869(4)	5397(2)	71	O2	4348(6)	2546(2)	5481(2)	67
O3	2012(4)	4190(2)	5991(1)	37	O4	1286(4)	4285(2)	4978(1)	45
O5	-2662(5)	5839(4)	7520(1)	72	O6	5672(5)	7613(3)	6473(2)	78
O7	2975(5)	8351(2)	6159(1)	49					

reprecipitated twice from EtOAc/hexane. Yield 4.01 g (94.4%); amorphous powder the PMR spectrum of which corresponded to that described in the literature [5]. For the ^{13}C NMR spectrum, see Table 1. Mass spectrum, m/z (%): 490 (M^+, 0.6), 414 (26.9), 284 (14.9), 264 (64.2), 240 (13.4), 238 (91), 220 (17.9), 219 (100).

Preparation of a Mixture of the Iodolactones (7) and (11). A solution of 1.05 g of GA$_3$ (1) in 11 ml of a 2 M aqueous solution of Na_2CO_3 was held at 95-97°C for 6 h, after which it was cooled and was then worked up as described above for the iodolactone (7). This gave 1.40 g (94.2%) of a mixture of (7) and (11). (72:28 according to HPLC).

Methyl Esters of Gibberellins A$_8$ (14) and A$_{56}$ (15). An excess of an ethereal solution of diazomethane was added to a solution of 1.00 g of the mixture of iodolactones (7) and (11) in 5 ml of MeOH. After 1 h, the solution was evaporated, and the products were separated by column chromatography, giving 0.30 g of (12) with mp 169-170°C (EtOAc/hexane); PMR: 1.43 (3H, s, Me-4), 3.00 (1H, d, J = 10.0 Hz, H-6), 3.54 (3H, s, MeO-7), 3.88 (1H, dd, J = 4.0 Hz and 6.0 Hz, H-2), 4.21 (1H, d, J = 4.0 Hz, H-3), 4.50 (1H, d, 10.0 Hz, H-5), 5.00 (1H, br.s, H-17a), 5.09 (1H, d, J = 6.0 Hz, H-1), 5.54 (1H, br.s, $W_{1/2}$ = 6.0 Hz, H-17b), and 0.60 g of (13) with mp 144-146°C (EtOAc/hexane) [according to the literature; 118-120°C],

the PMR spectrum of which corresponded to that described in [5], the eluents being $CHCl_3$ with 30-40% and 45-60% of ethyl acetate, respectively.

Argon was bubbled through a solution of 0.10 g of (12) in a mixture of THF and benzene (1:1) in flask fitted with a reflux condenser for 20 min, and then a few small crystals of 2,2-azobis(2-methylpropionitrile) and 0.7 ml of $(n\text{-}Bu)_3SnH$ were added. The bubbling of argon was continued while the solution was held at 70°C for 25 min, and then the solvent was distilled off from it. The product was dissolved in 3 ml of MeCN, and the resulting solution was washed with hexane (5 × 5 ml) and was evaporated to dryness. The residue was dissolved in 2 ml of acetone and the desired product was precipitated with hexane. The yield of the ester (14) was 0.07 g (93%), mp 221-222°C; according to the literature: 221-224°C [16].

Mass spectrum (see [17]), m/z (%): 378 (M^+, 60), 360 (9), 347 (28), 346 (100), 332 (9), 328 (8), 321 (23), 320 (8), 319 (33), 318 (27), 314 (8), 304 (12), 303 (11), 301 (9), 276 (10), 275 (10). PMR: 1.51 (3H, s, Me-4), 2.03 (1H, d, J = 10.5 Hz, H-14a), 2.05 (1H, dd, J = 10.0 and 13.0 Hz, H-1a), 2.23 (1H, dd, J = 1.5 and 10.5 Hz, H-14b), 2.61 (1H, dd, J = 6.0 and 13.0 Hz, H-1b), 2.99 (1H, d, J = 10.0 Hz, H-6), 3.59 (3H, s, MeO-7), 3.85 (1H, d, J = 10.0 Hz, H-5), 4.16 (1H, d, J = 4.0 Hz, H-3), 4.31 (1H, ddd, J = 4.0, 6.0, and 10.0 Hz, H-2), 5.02 (1H, s, H-17a), 5.58 (1H, s, H-17b).

Analogously, 0.10 g of (13) yielded 0.07 g (78%) of (15), mp 211-212°C (acetone—hexane); according to the literature: mp 217-219°C; the mass spectrum corresponded to that described in [5]; $[\alpha]_{578}^{26}$ +28° (c 2.49; MeOH). PMR: 1.57 (3H, s, Me-4), 1.94 (1H, m, H-9), 2.05 (1H, d, J = 11.0 Hz, H-14a), 2.25 (1H, dd, J = 5.0 and 15.0 Hz, H-1a), 2.29 (1H, d, J = 11.0 Hz, H-14b), 2.54 (1H, d, J = 15.0 Hz, H-1b), 3.10 (1H, d, J = 11.0 Hz, H-6), 3.59 (3H, s, MeO-7), 3.85 (1H, s, J = 11.0 Hz, H-5), 4.31 (1H, d, J = 4.0 Hz, H-3), 4.62 (1H, d, J = 5.0 Hz, H-2), 5.04 (1H, br.s, $W_{1/2}$ = 6.0 Hz, H-17a), 5.58 (1H, br.s, $W_{1/2}$ = 6.0 Hz, H-17b).

Stannyl Ester of Gibberellin A_{56} (10). By the method described above for the deiodination of the iodolactone (12), 130 mg of (10) was obtained from 110 mg of (7), a yield of 98%. Crystals with mp 74-75°C (acetone—hexane). Mass spectrum: 597, 3810 ($M^+ - C_4H_9$); calculated for $C_{27}H_{41}O_7Sn$ — 597, 3774: m/z (%): 597 (100), 596 (43), 595 (74), 594 (74), 593 (39), 581 (47), 580 (23), 579 (54), 578 (22), 577 (32), 291 (14), 289 (10), 287 (5), 177 (23), 175 (16). PMR: 0.80-1.40 (27H, n-Bu), 1.78 (3H, s, Me-4), 3.25 (1H, d, J = 10.0 Hz, H-6), 3.97 (1H, d, J = 10.0 Hz, H-5), 4.38 (1H, s, H-3), 4.67 (1H, d, J = 5.5 Hz, H-2), 5.09 (1H, s, H-17a), 5.61 (1H, s, H-17b).

Gibberellin A_{56} (6) from the Ester (10). A solution of 0.13 g of (10) in 5 ml of CH_3CO_2H was stirred at room temperature for 20 min and was then evaporated to dryness in vacuum. The residue was dissolved in 6 ml of MeCN, and the resulting solution was washed with hexane (6 × 10 ml). The acetonitrile solution was evaporated to dryness, and the residue was reprecipitated with hexane from acetone. This gave 0.07 g of GA_{56} (6), the PMR spectrum of which corresponded to that described in [5]. Mass spectrum, m/z (5): 364 (41), 346 (48), 345 (14), 329 (25), 328 (74), 318 (16), 302 (16), 301 (32), 300 (27), 290 (48), 289 (27), 284 (16), 283 (42), 261 (16), 241 (18), 199 (16), 189 (16), 185 (17), 171 (100).

Hydrolysis of the Methyl Ester of Gibberellin A_{56} (15). To 39.2 g of (15) was added 7 ml of a 0.2 M solution of KOH in a mixture of methanol and water (1:1), and the reaction mixture was kept at room temperature. After 2 days, the solution was partially evaporated, and the residue was acidified with conc. HCl to pH 3 and extracted with ethyl acetate (2 × 5 ml). After drying over $MgSO_4$, filtration, and evaporation to dryness, 37.0 mg (98%) of (6) was obtained, its PMR spectrum coinciding with the spectrum of the product obtained from the ester (10).

Preparation of Gibberellin A_8 (3). At room temperature, 0.18 ml of triethylamine and 0.50 g of *p*-bromophenacyl bromide were added to a solution of 0.980 g of a mixture of the iodolactones (7) and (11) in 7 ml of acetone. After 12 h, the reaction mixture was evaporated to dryness. The products were separated by column chromatography, and from the mixture was obtained 0.326 g of the ester (16) (23.7%) with mp 104-106°C. UV spectrum: $\lambda_{max}^{C_2H_5OH}$, nm: 259 (lg ε 4.27). PMR: 1.72 (3H, s, Me-4), 3.33 (1H, d, J = 10.0 Hz, H-6), 3.98 (1H, dd, J = 4.0 and 5.5 Hz, H-2), 4.31 (1H, d, J = 4.0 Hz, H-3), 4.65 (1H, d, J = 10.0, H-5), 5.12 (1H, H-17a), 5.18 (1H, d, J = 5.5 Hz, H-1), 5.64 (1H, s, H-17b), 5.65 (1H, d, J_{AB} = 14.0 Hz, CH_2COAr), 5.76 (1H, d, J_{AB} = 14.0 Hz, CH_2 COAr), 7.60-7.90 (4H, C_6H_4Br).

The deiodination of 0.20 g of the ester (16) by the procedure described above in the preparation of GA_8 Me ester (14) yielded 0.13 g (79.6%) of the *p*-BPA ester of GA_8 (18) with mp 90-92°C ($CHCl_3$—hexane). PMR: 1.67 (3H, s, Me-4), 2.59 (1H, dd, J = 7.0 Hz and 13.0 Hz, H-1a), 3.19 (1H, d, J = 10.0 Hz, H-6), 3.86 (1H, d, J = 10.0 Hz, H-5), 4.15 (1H, m, H-3), 4.29 (1H, m, H-2), 4.96 (1H, br.s, H-17a), 5.48 (1H, d, J_{AB} = 17.0 Hz, CH_2COAr), 5.55 (1H, br.s, H-17b), 5.60 (1H, d, J_{AB} = 17.0 Hz, CH_2COAr). To 50 mg of (18) in 3.5 ml of MeOH were added 80 mg of NH_4Cl, 61 mg of zinc dust, and 0.1 ml of CH_3CO_2H. The mixture was stirred for 2 h and was filtered, the residue was washed with MeOH, and the combined filtrate was evaporated to dryness. The residue was shaken with 1 ml of 3% HCl, and the product was extracted with ethyl acetate (2 × 2 ml).

The ethyl acetate solution was washed with a 10% solution of $NaHCO_3$ (3 × 1.5 ml), and the combined aqueous soda solution was acidified with HCl to pH 3 and extracted with ethyl acetate (2 × 5 ml). The extract was dried, filtered, and evaporated to dryness. The residue was reprecipitated with hexane from acetone, giving 31 mg of GA_8 (3) (95.5%), $[\alpha]_{578}^{28}$ +8.9° (c 1.12; MeOH), lit. [16]. PMR: 1.64 (3H, s, Me-4), 2.09 (1H, dd, J = 11.0 and 13.5 Hz, H-1a), 2.67 (1H, dd, J = 7.0 and 13.5 Hz, H-1b), 3.18 (1H, d, J = 10.5 Hz, H-6), 4.01 (1H, d, J = 10.5 Hz, H-5), 4.20 (1H, d, J = 4.5 Hz, H-3), 4.34 (1H, ddd, J = 4.5, 7.0 and 11.0 Hz, H-2), 5.00 (1H, s, H-17a), 5.57 (1H, s, H-17b).

Interaction of the GA_{56} Me Ester (15) with Me_3SiCl. A solution of 0.08 g of NaI in 1 ml of MeCN was added to a solution of 0.09 g of (15) in 1 ml of dry MeCN. After it had been stirred at 20°C for 10 min, the reaction mixture was treated with 0.05 ml of Me_3SiCl. After this, the solution was stirred for another 20 min and evaporated to dryness, 2 ml of a saturated aqueous solution of $Na_2S_2O_3$ was added to the residue, and it was then acidified with HCl to pH 3 and extracted with ethyl acetate (5 × 4 ml).

After drying, elimination of the desiccant, and evaporation, the product was purified by column chromatography. A mixture of $CHCl_3$ and ethyl acetate (40-50%) eluted 0.07 g of compound (20) with mp 219-220 (acetone—hexane), PMR: 1.01 (3H, s, Me-13), 1.61 (3H, s, Me-4), 2.24 (1H, dd, J = 5.0 and 15.0 Hz, H-1a), 2.36 (1H, d, J = 19.0 Hz, H-15a), 2.51 (1H, d, J = 15.0 Hz, H-1b), 3.14 (1H, d, J = 7.5 Hz, H-6), 3.32 (1H, dd, J = 4.0 and 19.0 Hz, H-15b), 3.73 (3H, s, MeO-7), 3.85 (1H, d, J = 7.5 Hz, H-5), 4.32 (1H, br.s, $W_{1/2}$ = 4.0 Hz, H-3), 4.63 (1H, d, J = 5.0 Hz, H-2). For the ^{13}C NMR spectrum, see Table 1.

X-Ray Structural Experiment with the Ketone (20). For the general conditions, see [8]. Crystallographic characteristics: a = 7.041(1), b = 12.365(2), c = 21.459(3) Å, V = 1868.3(6) Å^3, space group $P2_12_12_1$, $C_{20}H_{26}O_7$, Z = 4, d_{calc} = 13.4 g/cm^3, $2\theta_{max}$ = 114 deg, number of reflections 1394, R = 0.061, R_W = 0.058, S = 0.3. The atomic coordinates obtained are given in Table 2.

REFERENCES

1. L. N. Mander, Chem. Rev., **92**, 573 (1992).
2. A. G. Druganov and N. A. Pankrushina, Khim. Prir. Soedin., 693 (1990).
3. N. Murofushi, R. C. Durley, and R. P. Pharis, Agric. Biol. Chem., **41**, 1075 (1977).
4. É. P. Serebryakov, Izv. Akad. Nauk SSSR, Ser. Khim., 2596 (1980).
5. N. Murofushi, M. Sugimoto, and K. Itoh, Agric. Biol. Chem., **43**, 2179 (1979).
6. M. Penny, C. L. Willis, A. S. Batsanov, and J. A. K. Howard, J. Chem. Soc., Perkin Trans. I, 541 (1993).
7. N. Murofushi, I. Yamaguchi, H. Ishigooka, and N. Takahashi, Agric. Biol. Chem., **40**, 2471 (1976).
8. N. A. Pankrushina, A. G. Druganov, I. Yu. Bagranskaya, Yu. V. Gatilov, V. A. Raldugin, M. M. Shakirov, E. V. Evtushenko, and V. A. Saprykin, Khim. Prir. Soedin., 549 (1993).
9. M. H. Beale, J. MacMillan, C. R. Spray, D. A. Taylor, and B. O. Phinney, J. Chem. Soc. Perkin Trans. I, 541 (1984).
10. M. H. Beale and J. MacMillan, J. Chem. Res., "M", 3536 (1980).
11. J. Light and R. Breslow, Tetrahedron Lett., **31**, 2957 (1990).
12. A. G. Druganov, L. I. Demenkova, I. E. Maksimov, V. A. Raldugin, and V. A. Pentegova, Khim. Prir. Soedin., 228 (1980).
13. N. C. Barua and R. P. Sharma, Tetrahedron Lett., **23**, 1365 (1982).
14. E. Hohne, L. Seidel, G. Adam, and P. D. Hung, Tetrahedron, **31**, 81 (1975).
15. A. Preiss, G. Adam, D. Saman, and M. Budesinsky, Magn. Reson. Chem., **25**, 239 (1987).
16. J. MacMillan, J. C. Seaton, and P. J. Suter, Tetrahedron, **18**, 349 (1962).
17. R. Binks, J. MacMillan, and R. J. Pryce, Phytochemistry, **8**, 271 (1969).