It is suggested that the correlation of the C-1' chemical shifts with the vicinal spin-spin coupling constants of the H-1' and H-2' protons is a consequence of a 1,2-eclipsing interaction between O-2' and the nitrogen atom of the heterocyclic base with the ribose ring in the S type of conformation.

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CORRECTED STRUCTURE OF THE REACTION PRODUCT OF GIBBERELLIN A_3 WITH ACETIC ANHYDRIDE AND ZINC AND ITS CRYSTALLINE STRUCTURE. RARE CASE OF THE DIELS—ALDER REACTION

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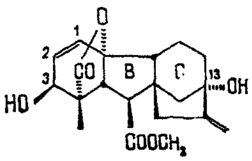
The correct structure has been established for the compound obtained on the treatment of the methyl ester of gibberellin A_3 with zinc in boiling acetic anhydride, to which the erroneous structure (II) was previously assigned. A mechanism of the formation of compound (II) is suggested which includes an intramolecular diene condensation between an acetate carbonyl group and the conjugated diene system in the intermediate mixed anhydride (V).

In the process of investigating derivatives of gibberellin A_3, we obtained a product of the interaction of the methyl ester of gibberellin A_3 (I) with zinc in boiling acetic anhydride which has been described by Jones, Growe, and MacMillan [1] and to which these authors ascribed structure (II). The corresponding acid (III) was obtained under the same conditions from gibberellin A_3 itself [1].



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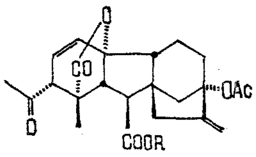

II. $R = CH_3$
III. $R = H$

Under the reaction conditions, the acetylation of the hydroxy groups first takes place [1] and the further transformation of the compound at ring A has a more complex nature, which Jones et al. [1] interpreted as a new reaction in which an acetoxy group was replaced

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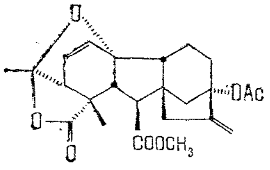
by an acetyl group. A feature of the NMR spectrum of compound (II) is the considerable upfield shift of the signal of the methyl protons of the 3-C acetyl group (1.4 ppm), which Jones et al. [1] explained by a strong screening influence on these protons of the rigidly fixed lactone ring. However, such a unique case of the appearance of intramolecular electronic effects required a more reliable basis. With this aim, we have analyzed the spectral characteristics for the compounds formed on the reaction of the methyl ester of gibberellin A_3 with zinc in boiling acetic anhydride [1] which, as was found, contradicts structural formula (II) suggested for it by Jones et al. [1].

The UV spectrum of compound (II) lacks the absorption maximum at 290-300 nm with an extinction of the order of 100 that is characteristic for β γ-unsaturated ketones [2]. No β,γ-enol system (or any ketone system) appears, either, on the optical rotatory dispersion curve, which is smooth and positive (for a solution in ethanol) as far as 280 nm. The IR spectrum of compound (II) shows three strong bands at 1780, 1740, and 1730 cm^{-1} with practically the same intensities, which can be assigned to the carbonyls of a γ-lactone and of acetoxy and methoxy carbonyl groups. The presence of a fourth carbonyl group (3α-acetyl group) in the IR spectrum was not confirmed. Finally, in the ^{13}C NMR spectrum of this compound there are no signals in the 180-240 ppm region that is characteristic for the carbon atoms of a keto group [3].

On the basis of these facts, it may be concluded that the compound under investigation does not contain a 3α methyl ketone group and structure (II) suggested for it by Jones et al. [1] is erroneous, as also is that of the corresponding acid (III). This compound has a different nature of the substitution in ring A of the 20-norgibberellane carbon skeleton. For it we suggest the new structure (IV), which agrees well with all the spectral characteristics. To check the correctness of this hypothesis and to determine the absolute configuration of the substance under investigation, we have made an x-ray structural analysis of it using a single crystal grown from solution in hexane—benzene (1:1). The results of this experiment confirmed formula (IV) and the configurations of all the asymmetric centers shown in it.



IV

The structure of the molecule (IV) is shown in Fig. 1. Below we give the bond lengths in the molecule:

Bond	Length, Å	Bond	Length, Å
$C_1—C_2$	1,318	$C_{12}—C_{13}$	1.541
$C_1—C_{10}$	1,499	$C_{13}—C_{14}$	1 544
$C_2—C_3$	1,507	$C_{13}—C_{16}$	1.529
$C_3—C_4$	1,570	$C_{15}—C_{16}$	1.508
$C_3—C_{1'}$	1,514	$C_{16}—C_{17}$	1,313
$C_4—C_5$	1.556	$C_{21}—C_{22}$	1,504
$C_4—C_{18}$	1,529	$C_{1'}—C_{2'}$	1 506
$C_4—C_{19}$	1,518	$C_7—O_1$	1.176
$C_5—C_6$	1,540	$C_7—O_2$	1.335
$C_5—C_{10}$	1,553	$C_{10}—O_5$	1.462
$C_6—C_7$	1.521	$C_{13}—O_3$	1,460
$C_6—C_8$	1 559	$C_{19}—O_6$	1,358
$C_8—C_9$	1.532	$C_{19}—O_7$	1.193
$C_8—C_{14}$	1,539	$C_{20}—O_2$	1.452
$C_8—C_{15}$	1.557	$C_{21}—O_3$	1.352
$C_9—C_{10}$	1.515	$C_{21}—O_4$	1,196
$C_9—C_{11}$	1.539	$C_{1'}—O_5$	1,408
$C_{11}—C_{12}$	1.541	$C_{1'}—O_6$	1.469

The lactone ring E is cis-linked with ring A at the $C_3—C_4$ bond. The O_5 atom joins the $C_{1'}$ and C_{10} atoms, forming the rigid ring F in the molecule. Its formation sharply changes the conformation of ring A (boat) as compared with the form of this ring in 3-dehydrogibberellin A_3 [4] and in 16α,17-dibromogibberellin A_3 [5] (half-chair with departure of the C_5 atom from the plane).

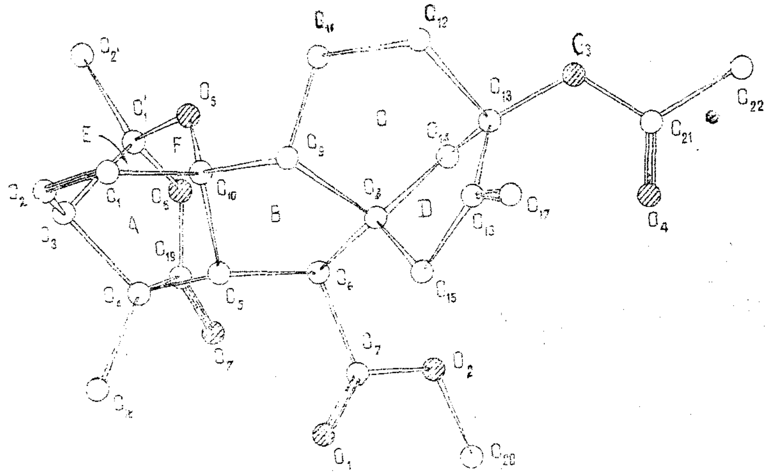


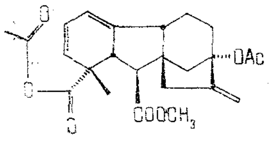
Fig. 1. Molecular structure of compound (IV).

The conformations of the rings are conveniently compared by making use of the Cremer—Popple parameters [6]. These parameters for the molecule (IV), calculated from the torsional angles [7], are given in Table 2. The comparison shows that the forms of rings B, C, and D of the molecule of (IV) that are identical for the molecule of 3-dehydrogibberellin A_3 [4] and differ from the conformations of these fragments in the molecule of 16α,17-dibromogibberellin A_3 [5]. Thus, the formation of the new ring F does not affect the geometry of rings B, C, and D.

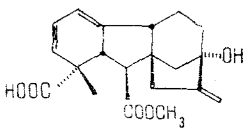
The orientation of the 13-O-acetyl group relative to ring C is characterized by a C_{12}-C_{13}-O_3-C_{21} torsional angle of 178°. The carboxylic ester grouping C_7, C_{20}, O_1, O_2 is planar. The O_1-C_7-C_6-C_5 and O_1-C_7-C_6-C_8 torsional angles are, respectively, −21 and 98°. The strain of the molecule is expressed in a lengthening of the C_3—C_4, C_4—C_5, C_5—C_{10}, C_6—C_8, and C_8—C_{15} bonds, the lengths of which are, respectively, 1.570, 1.556, 1.553, 1.559, and 1.557 Å, and also in a shortening of the $C_{1'}$—O_5 bond (1.408 Å).

In the crystal, the molecules are bound by Van der Waals interactions. It is possible to observe slightly shortened contacts [8] between molecules connected by a twofold axis of symmetry — $H_{2'-2} \ldots H^{i}_{2'-2}$ (x, −y, −z) 2.148 Å and $H_{18-3} \ldots H^{i}_{18-3}$ (x, 1 − y, −z) 2.203 Å.

Thus, product (II) described by Jones et al. [1] actually has the formula (IV) and is (−)-13-acetoxy-3α-(1'-hydroxyethyl)-7-methoxycarbonyl-1',10-epoxy-20-norgibberella-1,16-dien-19-oic acid 19,1'-lactone. We have assumed that the key stage in the formation of product (IV) from the methyl ester of the diacetic of gibberellin A_3 is an intramolecular Diels-Alder reaction between the conjugated diene system and the acetate carbonyl group in the mixed anhydride (V) which is apparently formed from the initial compound in two stages. In the initial stage, under the action of the zinc the elimination of the 3-acetoxy group and the opening of the lactone ring take place in a similar manner to what has been observed in the reaction of palladium salts with 3-O-formylgibberellin A_3 [9]. The dienic acid (VI) formed, at the expense of the large excess of acetic anhydride, gives the mixed anhydride (V), which then cycles intramolecularly to compound (IV).



V



VI

In order to check the proposed mechanism, we obtained the dienic acid (VI) by Corey's method [10] and caused it to react with acetic anhydride. The reaction was complete after the mixture had been boiled for 1 h and it led quantitatively to product (IV), identical in melting point, TLC behavior, and IR and PMR spectra with the sample of the same compound obtained by Jones et al. [1] from the methyl ester of gibberellin A_3. In this reaction, likewise, in the first stage the corresponding mixed anhydride may be formed which, apparently, because of the elevated temperature, undergoes an intramolecular diene condensation. The high regio-

TABLE 1. Coordinates of the Atoms (× 10^4; for H, × 10^3) of Compound (IV)

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
C_1	+3832(8)	1865(6)	—6754(3)	C_{14}	2303(7)	1387(3)	1945(3)
C_2	+2727(9)	2076(4)	−1021(3)	C_{15}	4618(8)	2488(4)	1811(3)
C_3	+0747(8)	2274(4)	—0809(3)	C_{16}	5561(9)	1743(4)	2168(3)
C_4	+0655(8)	2969(4)	—0225(3)	C_{17}	7278(8)	1697(4)	2403(3)
C_5	+2133(8)	2700(4)	0319(3)	C_{18}	0868(10)	3902(4)	—0471(3)
C_6	+1530(8)	2620(3)	1073(3)	C_{19}	—1275(9)	2781(4)	0062(3)
C_7	+1321(9)	3498(4)	1415(3)	C_{20}	—0039(14)	4232(5)	2333(4)
C_8	+3039(7)	2025(3)	1404(3)	C_{21}	3743(9)	0918(5)	3396(3)
C_9	3971(8)	1525(3)	0786(3)	C_{22}	3955(9)	0311(4)	3992(3)
C_{10}	2855(7)	1776(4)	0157(3)	C_1'	—0087(8)	1518(4)	—0394(3)
C_{11}	4132(9)	0544(4)	0903(3)	C_2'	—0830(9)	0776(4)	—0799(3)
C_{12}	4801(9)	0312(3)	1630(3)	O_1	2007(8)	4147(3)	1227(2)
C_{13}	4186(8)	0987(4)	2164(3)	O_2	0256(7)	3424(3)	1972(2)
O_3	4173(6)	0505(3)	2807(2)	H_{14-2}	132(7)	093(3)	179(2)
O_4	3282(6)	1660(3)	3431(2)	H_{15-1}	561(7)	283(3)	152(2)
O_5	1218(5)	1217(2)	0089(2)	H_{15-2}	401(7)	294(3)	217(2)
O_6	1645(5)	1928(3)	—0028(2)	H_{17-1}	812(7)	216(3)	242(2)
O_7	—2343(6)	3252(3)	0345(2)	H_{17-2}	774(7)	106(3)	253(2)
H_1	530(7)	161(3)	— 056(2)	H_{18-1}	218(7)	398(3)	— 075(2)
H_2	322(6)	214(3)	— 153(2)	H_{18-2}	—029(8)	412(3)	— 084(3)
H_3	— 011(7)	247(3)	— 126(2)	H_{18-3}	093(6)	430(3)	— 012(3)
H_5	336(7)	311(3)	027(2)	H_{20-1}	—100(7)	468(3)	203(2)
H_6	029(7)	231(3)	114(2)	H_{20-2}	062(8)	412(3)	277(3)
H_9	532(7)	174(3)	071(2)	H_{20-3}	123(7)	457(3)	235(2)
H_{11-1}	290(7)	028(3)	084(2)	H_{22-1}	542(7)	000(3)	399(2)
H_{11-2}	524(7)	0,29(3)	056(2)	H_{22-2}	364(7)	061(3)	447(2)
H_{12-1}	433(7)	— 028(3)	179(2)	H_{22-3}	287(7)	—016(3)	393(2)
H_{12-2}	632(7)	024(3)	161(2)	$H_{2'-1}$	—198(7)	098(3)	— 111(2)
H_{14-1}	162(7)	167(3)	235(2)	$H_{2'-2}$	—142(7)	033(3)	— 048(2)
				$H_{2'-3}$	015(8)	051(3)	— 110(3)

TABLE 2. Cremer—Popple Parameters [6] for the Rings of the Molecule of (IV)

Ring	Atoms forming the ring	q_2	φ_2°	Q	θ°	Form of the ring
A	C_1, C_2, C_3, C_4, C_5, C_{10}	0,947	156,0	0,951	95,4	Boat
B	C_5, C_6, C_8, C_9, C_{10}	0,579	277,7	—	—	Envelope, C_5 atom outside the plane
C	C_8, C_9, C_{11}, C_{12}, C_{13}, C_{14}	0 938	258,0	0,997	70,3	Intermediate between twist form and boat
D	C_8, C_{13}, C_{14}, C_{15}, C_{16}	0,683	68,0	—	—	Half-chair, C_8 and C_{14} above below plane, respectively
E	C_3, C_4, C_{19}, O_6, C_1'	0,627	272,7	—	—	Envelope, C_3 outside plane
F	C_1, C_2, C_3, C_1', O_5, C_{10}	0,895	94,1	0,903	82,4	Boat

and stereospecificity of the reaction (no by-products whatever were detected) is in harmony with the proposed mechanism. The fact that here the acetate carbonyl takes the unusual role for it of a dienophile can be explained by its convenient location with respect to the cisoid diene system and also by its activation as a dienophile by the second carbonyl group, at C_{19}.

The reaction found may have general value for obtaining similar hexacyclic gibberellin derivatives.

EXPERIMENTAL

The x-ray structural experiment was performed on a Syntex $P2_1$ diffractometer in Mo radiation with a graphite monochromator, using the single crystal of substance (IV) with dimensions of approximately 0.2 × 0.3 × 1.0 mm. Crystals of the rhombic system, space group $P_22_12_1$: $a = 7.154(2)$, $b = 15.476(4)$, $c = 19.537(5)$ Å; $z = 4$; $d_{calc} = 1.32$ g/cm^3; mp 183-184°C; $C_{24}H_{28}O_7$.

The intensities of 1968 independent reflections were measured (weak reflections were not taken into account) by the ω-scanning method in the $2\theta < 55$ degree region. In all the calculations 1542 reflections with $I > 2\sigma$ were used, the absorption of the beam in the crystal not being taken into account ($\mu = 1.0$ cm^{-1}). The structure was interpreted by the direct method using a modified [11] MOULTAN-XTL program. The correct variant of the phases of the reflections was the best according to the criterion NQEST = −0.32 and average according to the ABSFOM criterion. The structure was refined by the method of least squares in the isotropic approximation and then in the anisotropic full-matrix approximation (the hydrogen atoms found from a D-synthesis were refined isotropically separately) to $R = 0.051$ and $R_W = 0.046$, where $w^{-1} = \sigma_F^2 + (0.005F)^2$.

The coordinates of the atoms of the molecule of IV are given in Table 1 and the lengths of the interatomic bonds in Table 3.

Compound (IV) was obtained by the method of Jones et al. [1] from the methyl ester of gibberellin A_3. It had mp 183-184°C [from hexane–benzene (1:1)]. Mass spectrum: m/z 428 (M^+). The PMR spectrum corresponded to that given by Jones et al. [1].

Preparation of Compound (IV) from the Dienic Acid (VI). The dienic acid (VI) (0.14 g), obtained by the method of Corey et al. [10] was dissolved in 15 ml of acetic anhydride, and this solution was kept at 140°C for 1 h, after which it was evaporated in vacuum to dryness. This led to 0.16 g of compound (IV), homogeneous on TLC, the IR and PMR spectra of which coincided with those for a sample of compound (IV) obtained by the method of Jones et al. [1]. After it had been passed through a column of silica gel (with benzene as eluent) crystals of substance (IV) with mp 183-184°C were obtained.

SUMMARY

1. It has been established that the product of the interaction of the methyl ester of gibberellin A_3 with zinc in boiling acetic anhydride has the structure of (−)-13-acetoxy-3α-(1'-hydroxyethyl)-7-methoxycarbonyl-1',10-epoxy-200-norgibberella-1,16-dien-19-oic acid 19,1'-lactone.

2. The key stage in the reaction of the methyl ester of gibberellin A_3 with zinc in boiling acetic anhydride is an intramolecular Diels–Alder reaction with the participation of the carbonyl of the acetoxy group of the intermediate compound

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