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GIBBERELLINS

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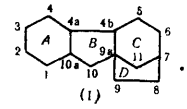
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This review is devoted to the gibberellins — a new class of natural compound, the ever increasing interest in which is due to their high physiological activity as phytohormones.

The present article will be concerned with the chemical and biochemical aspects of the problem of the gibberellins. For a detailed analysis of the various physiological changes which can be observed in higher plants under the action of gibberellins, the reader is referred to several papers which have appeared in Soviet scientific literature [1-8].

I. GIBBERELLINS — NATURAL PHYTOHORMONES

The gibberellins, tetracyclic carboxylic acids, the structure of which is based on the hydrocarbon gibbane (I), were discovered by Japanese scientists investigating the reasons for the "bakanae" disease of rice ("foolish seedling disease"):



(I)

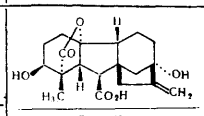
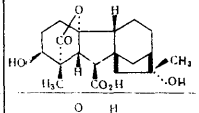
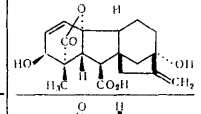
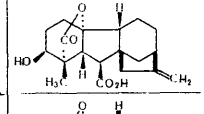
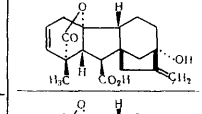
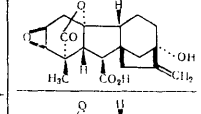
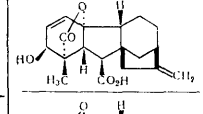
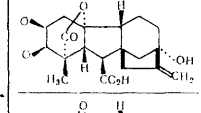
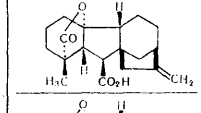
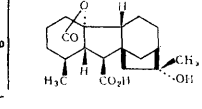
As long ago as 1898, Hori [9] established that the hypertrophic growth of the vegetative organs of rice seedlings which is typical of "bakanae" is caused by a fungus, the conidial stage of which was later named *Fusarium moniliforme* Sheld., the ascomycetous stage being named *Gibberella fujikuroi* Saw. In 1926, Kurosawa showed [10] that a similar physiological effect was produced by treating the seedlings with a culture medium of the fungus, free from mycelia, and in 1938 Yabuta and Sumiki [11] isolated as a crystalline material the active principles of the culture liquid of *Gibberella f.*, which they named gibberellin A and gibberellin B.

Subsequently the Japanese biochemists intensively studied the chemical structure and physiological properties of the preparations isolated, but their work only became known outside Japan in the 'fifties, when it gave an impetus to the development of studies in the field of gibberellins in other countries.

The first success in these investigations was the development of methods for the chromatographic purification of the crude preparation of gibberellin, which allowed Curtis and Cross [12] and also Stodola and coworkers [13] to isolate a pure substance with a high physiological activity, which was named gibberellic acid (GAc) or gibberellin A_3 (GA_3). The methods of fermentation and isolation which were developed out of Cross and Stodola's studies formed the basis of the industrial method of making GAc and made it an available substance [14,15]. Somewhat later, two other pure, physiologically active substances were isolated from the crude gibberellin preparation: gibberellins A_1 [16-18] and A_2 [17-19] (GA_1 and GA_2)†, and from the culture liquid of new strains of *Gibberella f.* the gibberellins A_4 (GA_4) [19-21], A_7 (GA_7) [22], A_9 (GA_9) [22], and A_{10} (GA_{10}) [23] were obtained (see Table 1).

† The numbering of the first three gibberellins is determined by the order of their elution from columns during chromatography on a Celite 545 : Norite A mixture (1 : 1). The numbering of the other gibberellins (see below) was determined by the sequence in which they were isolated from natural sources.

TABLE 1. Physicochemical properties of the C_{19} gibberellins.

Name	Structural formula	M.p., °C	$[\alpha]_D$* (°C)	M.p. of methyl ester	$[\alpha]_D$ (°C) of methyl ester	pK_{a_1} (25°) from Ref. 33	Ref.
Gibberellin A_1		255	+36 (20)	234	+46 (20)	3.97	16
Gibberellin A_2		235 255**	+11,7 (20)	190	+25 (26)	4.09	16,18,19
Gibberellin A_3 (gibberellic acid)		233	+92 (20)	209	+75 (20)	4.21	12,16
Gibberellin A_4		216 255**	−3 (20)	175	0±3 (20)	4.21	21
Gibberellin A_5		260	−77 (22)	191	—	4.09	30
Gibberellin A_6		206	−20 (26)	136	—	4.03	35
Gibberellin A_7		169 202**	+20 (24)	152 168**	+33 (23)	4.11	22
Gibberellin A_8		210	+13 (23)	221 231**	+14.8 (23)	4.04	35
Gibberellin A_9		208	−22 (22)	136	−15 (17)	4.26	22
Gibberellin A_{10}		245	+3	157	—	—	23

* Measured in ethanol for GA_1, GA_3, GA_7, and GA_9 and in methanol for GA_2, GA_5, GA_6, and GA_8.

** Polymorphic modifications.

The initial assignment of all these new substances to the gibberellin group was based on their common source in nature and the similarity of their spectra and physiological action on higher plants. Many investigations published in the 'fifties showed that the gibberellins are able to interfere actively in almost all the growth and development processes of plants. Thus, treatment with gibberellins stops the hibernation of seeds and stimulates their germination, accelerates the growth of seedlings, and "heals" the dwarf form of growth of dwarf mutants of higher plants. The last property is not possessed by any known chemical preparation. The ability of gibberellins to influence the photoperiodic reaction of flowering plants (long-day plants flower under short-day conditions after treatment with gibberellins) and their ability to alter the action of low temperatures (plants which need vernalisation flower normally and bear fruit without vernalisation after treatment with gibberellins) is extremely characteristic and specific.

Generalisation of the experimental results on the physiological activity of gibberellins led Chailakhyan[2,24] and, independently, Brian[25,26] to a hypothesis about the phytohormonal nature of the gibberellins. According to this hypothesis, the higher plants are capable of producing substances similar in properties to the gibberellins of fungal manufacture. These substances (endogenic gibberellins) play an important part in regulating the normal growth and the development of plants, and a shortage of them in the plant organism is responsible for the appearance of mutants with a dwarf form of growth, and also for the inability of plants which need vernalisation or a long day to develop normally in the absence of the appropriate external conditions.

Convincing confirmation of this hypothesis was given by recent investigations which showed that extracts of the epigeal parts of higher plants exhibit a gibberellin-like physiological activity and the substances present in them are almost indistinguishable from the fungal gibberellins in paper chromatography[4,27,28]. The chromatography of such extracts on a mixture of Celite 545 and Norite A permitted the separation — in addition to the known GA_1,[29-32] GA_3,[34,35] GA_4, and GA_7[23] — of three new individual substances: gibberellins A_5 (GA_5),[30,34] A_6 (GA_6),[35] and A_8 (GA_8)[35] (see also Table 1), the physiological activity of which is close to the activity of the fungal gibberellins‡.

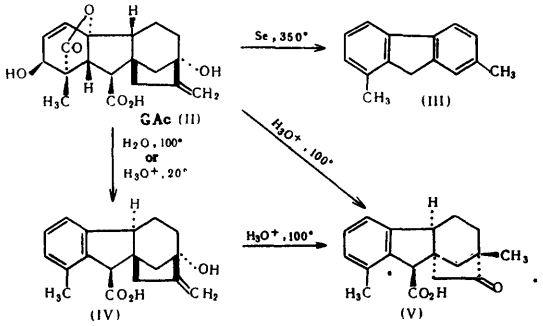
II. STRUCTURE AND CHEMICAL FEATURES OF THE GIBBERELLINS

In parallel with the work on the isolation of new gibberellins and study of the spectrum of their physiological activity, the investigation of the chemical structure of the compounds isolated was undertaken on a wide front. It was started by a group of Japanese chemists headed by Sumiki[41-46], who developed methods of degrading the gibberellins. However, up to 1955 these investigators worked with a preparation of gibberellin A, which was shown subsequently to be a mixture of GA_1, GA_2, and GA_3, therefore the characteristics which they obtained for the degradation products and also several conclusions about their structure needed checking. This task was completed by a group of English chemists headed by Cross, Grove, and McMillan, and as a result of their work the structure of the gibberellins which is now generally accepted was established and the peculiarities of the chemical conversions of this new class of natural compound were revealed.

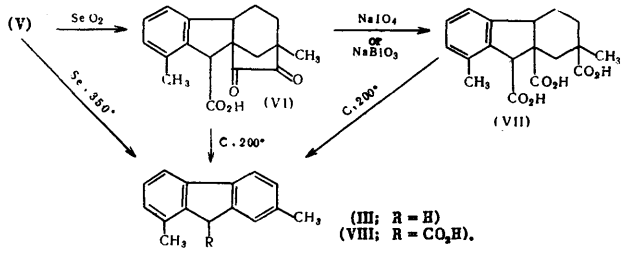
‡ Note that as well as the gibberellins substances more polar than the gibberellins and which exhibit gibberellin-like physiological activity were also separated chromatographically from the tissues of higher plants[36-40]. It was initially suggested that such substances are peptide complexes[36] or glucosides[37] of the known gibberellins and this received confirmation in the work of Sembdner and coworkers[38]. They showed that the highly polar neutral substance which they isolated from bean seeds is converted under acid hydrolysis conditions into a physiologically active organic acid comparable in polarity with known gibberellins. In addition to this acid, at least two other substances of carbohydrate type and three of peptide type were observed in the hydrolysate. Similar results were obtained by Sembdner and Schreiber[40] in studying tobacco seed gibberellins and also by Maksimov and coworkers in studying kale [*Brassica oleracea* var. *acephala* DC (Ed. of Translation)] gibberellins[36].

The key substance in the investigations to establish the structure of the gibberellins was GAc§, which is readily accessible. In this connection it is necessary to dwell in detail on the methods of determining the structure of GAc, particularly as the elucidation of the structure of this complex and very labile substance can serve as a good illustration of the enormous possibilities of contemporary organic chemistry and of the fruitfulness of a combination of chemical and physicochemical methods in studying natural products.

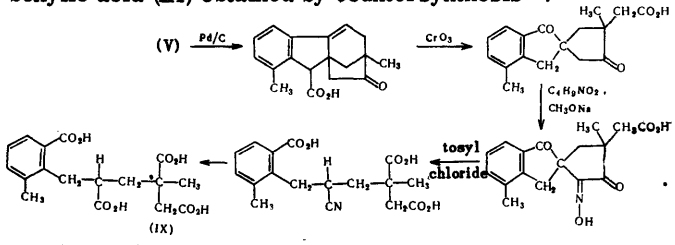
On the basis of the results of elemental and functional analyses, molecular weight determinations, and ultraviolet and infrared spectroscopic data, it was established that GAc has the empirical formula $C_{19}H_{22}O_6$, and is a tetracyclic, doubly-unsaturated dihydroxylactone-acid containing a methyl and a terminal methylene group[48]. It was shown that dehydrogenation of GAc with selenium at 350° [49] leads to 1,7-dimethylfluorene (III), which is evidence of the presence of the dimethylfluorene nucleus in its molecule. Subsequent stages of the work were connected with the revealing of the structure of the two main products of the degradation of GAc under acid conditions — allogibberic (IV) and gibberic (V) acids:



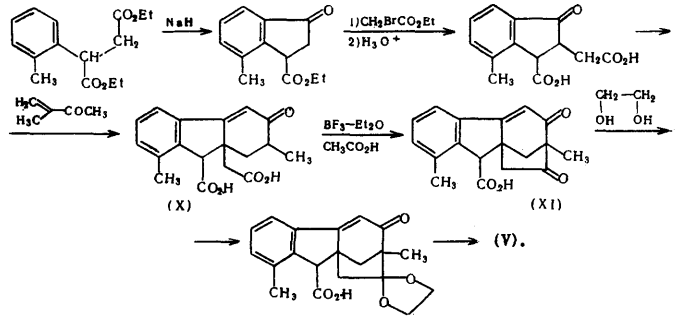
The analytical and spectroscopic data indicated that gibberic acid (V) is a tetracyclic dimethyl-substituted keto-acid of empirical formula $C_{18}H_{20}O_3$, in the skeleton of which there are an aromatic ring and a cyclopentane ring bearing a carbonyl group. The oxidation of gibberic acid with selenium dioxide leads to gibberdionic acid (VI) which under the action of sodium bismuthate or periodate is readily converted into a tricarboxylic acid (VII). The dehydrogenation of the latter, like the dehydrogenation of gibberic acid itself with selenium at 350°, leads to 1,7-dimethylfluorene (III):



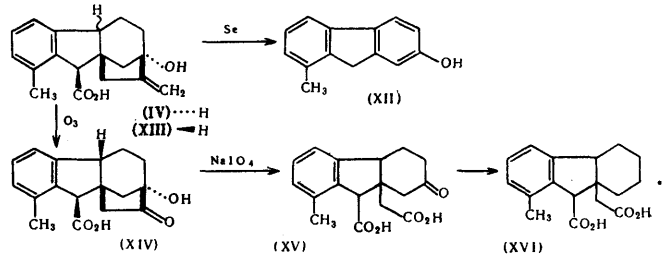
From these results it was concluded that the dehydrogenation of gibberic acid with selenium takes place without rearrangement of the skeleton and is accompanied by the breaking of the $-CH_2-CO-$ bridge connected to the flurorene nucleus at two quaternary carbon atoms. These facts, in conjunction with the formation of 1,7-dimethylfluorene-9-carboxylic acid (VIII) on the dehydrogenation of methyl gibberdionate, allowed gibberic acid to be given formula (V).[48,50] Its correctness was confirmed[51] by the oxidative degradation according to the scheme below to a tetracarboxylic acid (IX) obtained by countersynthesis[52]:



The final work in establishing the structure of gibberic acid was its synthesis, effected in 1960 by Loewenthal and Malhotra[53] by the scheme given below. The most interesting stage in this synthesis was the cyclisation (X) → (XI) in acetic acid in the presence of boron trifluoride–diethyl ether which enabled the tetracyclic diketo-acid (XI) to be obtained in ~ 80% yield:



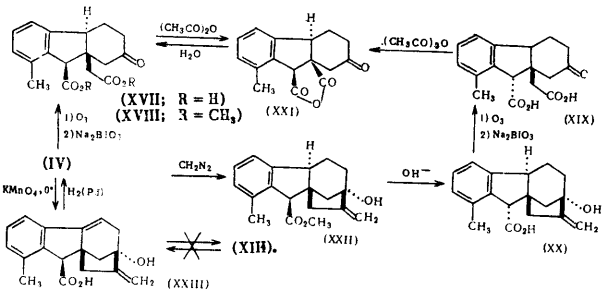
The other product of the degradation of GAc — allogibberic acid (IV) — is a tetracyclic carboxylic acid containing an aromatic ring, a tertiary hydroxyl group, and a terminal methylene group situated at the five-membered ring[48,50]. Since the dehydrogenation of allogibberic acid with selenium leads to 1-methylfluoren-7-ol (XII),[54] and when it is heated with dilute acids gibberic acid is formed (V), allogibberic acid was given formula (IV), and this was then confirmed by oxidative degradation as follows[52]:



As is seen from this scheme, the ozonation of epiallogibberic acid (XIII) — the epimer of (IV) at the $C_{(4b)}$ hydrogen atom — leads to the norketone (XIV) which in accordance with its α-ketol structure is readily cleaved by the action of sodium periodate or bismuthate. The reduction of the ketodicarboxylic acid (XV) thus obtained by the Kishner method leads to an acid (XVI), the structure of which was confirmed by countersynthesis[55,56]. A study of the stereochemistry of the conversions of the oxidative degradation products of allogibberic acid allowed its relative

§ In the fermentation of *Gibberella f.*, up to 1 g GAc,[47] 12 mg GA_1,[16] 0.3 mg GA_4,[21] 25 mg GA_7,[22] and 3–4 mg GA_9[22] are isolated from 1 litre of culture liquid. 2 mg GA_1,[28] 1 mg GA_5,[30] 8 mg GA_6,[35] and 16 mg GA_8[35] are isolated on extracting 1 kg of *Phaseolus multiflorus* seeds.

configuration to be found[57]. This problem was solved after the elucidation of the configuration of the carboxylic group at $C_{(10)}$ relative to the ethylene bridge at $C_{(7)}$–$C_{(9a)}$ and also the stereochemistry of the junction of rings *B* and *C*. The first part of the problem was solved by studying the formation of anhydrides by the dicarboxylic acids (XVII) and (XIX), which are epimeric at $C_{(10)}$ and were obtained in the oxidative degradation of allogibberic acid (IV) and its $C_{(10)}$ epimer (XX):



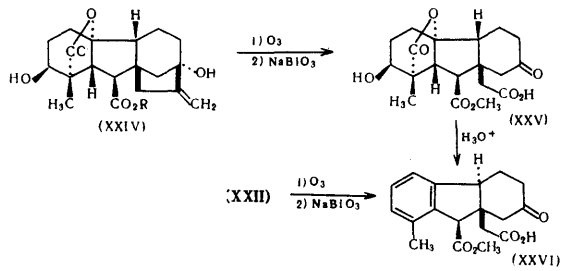
On heating with acetic anhydride, both isomeric acids give the same *cis*-anhydride (XXI), the saponification of which with water leads only to the *cis*-acid (XVII). Since this acid was identical with the degradation product of allogibberic acid (IV) the safe conclusion was drawn that in the latter there is a *cis* arrangement of the $C_{(10)}$ carboxyl group and the ethylene bridge.

The stereochemistry of the junction of the rings *B* and *C* was found by studying the stereochemistry of the hydrogenation of dehydroallogibberic acid (XXIII), formed on treating allogibberic acid (IV) with an aqueous solution of potassium permanganate at 0°. It is well known that in the catalytic hydrogenation of a double bond the addition of hydrogen proceeds from the least hindered side of the molecule. Therefore the formation of allogibberic acid (IV), uncontaminated with epiallogibberic acid (XIII) in the catalytic hydrogenation of acid (XXIII) indicated the *trans*-orientation of the hydrogen atom at $C_{(4b)}$ relative to the ethylene bridge and relative to the carboxyl group at $C_{(10)}$.

Analogous conversions in the gibberic acid (V) series showed that its carboxyl group is *trans*-oriented relative to the ethylene bridge and that rings *B*/*C* are *cis*-fused[41].

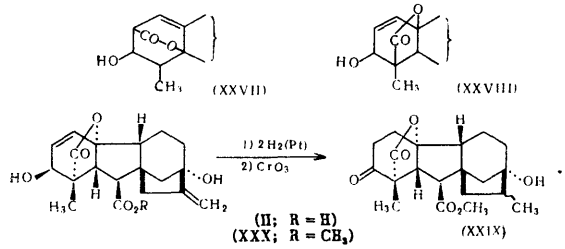
The examination of the chemical conversions still did not give the possibility of establishing the absolute configuration of gibberic and allogibberic acids. To solve this problem the method of optical rotatory dispersion was applied. With its aid Klyne[21,59], and independently of him Stork and Newman[58], showed that gibberic acid has the (7-*R*, 9a-*R*, 10-*R*)- and allogibberic acid the (7-*S*, 9a-*S*, 10-*R*)-configuration. However, this method did not allow the absolute configuration of the $C_{(4b)}$ asymmetric centre to be determined reliably, since it appeared that the rotatory dispersion curves of the compounds epimeric at $C_{(4b)}$ of this series are almost identical[59]. The problem was solved by using the method of circular dichroism, with the aid of which the (4b-*S*) absolute configuration of both acids was established[60].

The elucidation of the structure of gibberic and allogibberic acids allowed the next step to be taken in the proof of the structure of gibberellic acid — to introduce the hypothesis that the structure of rings *B*, *C*, and *D* in allogibberic and gibberellic acids is identical[61]. Confirmation of this was obtained by studying the oxidative degradation of the methyl ester of GA_1 (XXIV; R = CH_3) — the dihydro-derivative of the methyl ester of GAc. The ozonation of (XXIV) and the subsequent treatment of the resulting norketone with sodium bismuthate leads to the ester (XXV). On treatment with mineral acid the latter is converted into ester (XXVI) — the oxidative degradation product of methyl allogibberate (XXII)[61,62]:



The conclusion about the identity of the absolute configuration of rings *B*, *C*, and *D* in allogibberic and gibberellic acids, made in the same work on the basis of the optical rotatory dispersion results, seemed, however, inaccurate (see above). Use of the method of circular dichroism[60] showed that the absolute configurations of the centres $C_{(7)}$, $C_{(9)}$, and $C_{(10)}$ in these acids are identical but those of the $C_{(4b)}$ centre are contrary, that is, the system of rings *B*, *C*, and *D* in GAc has the (4b-*R*, 7-*S*, 9a-*S*, 10-*R*) absolute configuration.

The most complex step in determining the structure of GAc was elucidating the structure of ring *A*, for which in 1958 Japanese chemists proposed the partial formula (XXVII),[63] and English chemists formula (XXVIII)[64]:



Many conversions of GAc carried out by both groups of investigators showed that the (XXVIII) was the more probable formula. The final choice in its favour was made, however, only after employing the NMR method[65,66], which showed that GAc contains a hydrogen atom at $C_{(10a)}$ and four olefinic protons. Later, formula (XXVIII) was also confirmed by X-ray diffraction[60,67].

Many difficulties were encountered in proving the configuration of ring *A* of gibberellic acid. In 1959 Cross and coworkers[68] proposed formula (II) for GAc, in which the $C_{(2)}$ hydroxyl, which is readily epimerised by the action of 0.01 *N* alkali, was given the axial β configuration and the *A*/*B* ring junction was given the so-called *trans*-unnatural¶ (4a-α, 10a-β) configuration. The correctness of this formula was confirmed by nuclear magnetic resonance studies which showed the *trans*-fusion of the *A*/*B* rings in gibberellic acid. It was also demonstrated that ketone (XXIX) obtained by hydrogenation of the methyl ester of GAc (XXX) and subsequent oxidation of the OH group at $C_{(2)}$ exhibits a

¶ The name arises from the fact that most natural terpenes and steroids exhibit the antipodal fusion of rings *A* and *B*.

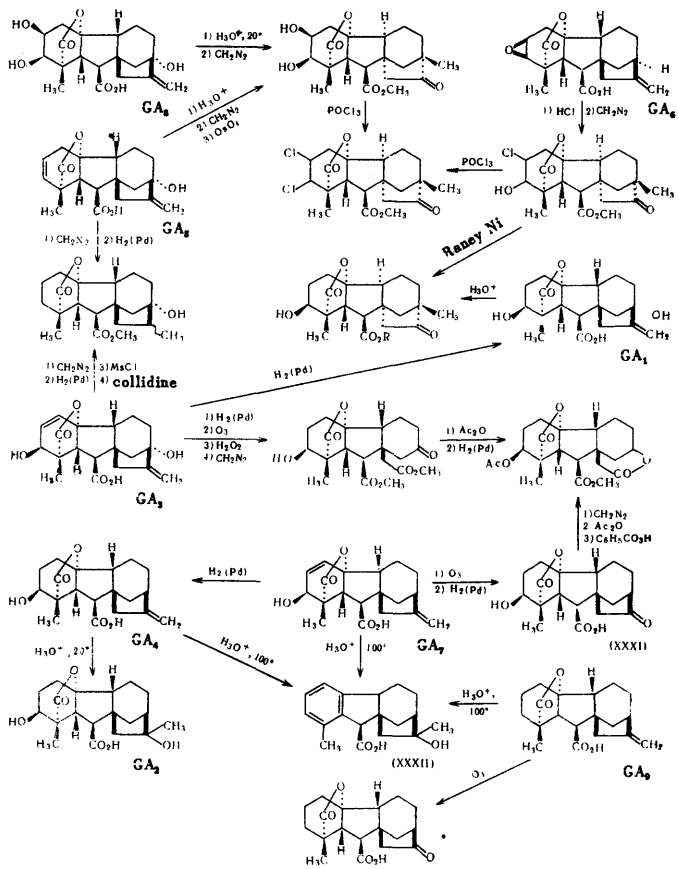
negative Cotton effect. This allowed, by application of the Octant Rule, a conclusion to be drawn about the β configuration of the hydrogen atom at $C_{(10a)}$.

In 1960 the Hudson–Klyne Lactone Rule[69] was applied to determine the stereochemistry of ring *A* of gibberellic acid; it enabled a decision to be made concerning the configuration of the lactone rings on the basis of the change in sign of the molecular rotation accompanying the opening of this ring. Stork and Newman[70] compared the changes in molecular rotation observable in the opening of steroid lactones with an α-configuration of the lactone ring on the one hand and of gibberellic acid on the other and concluded there was α-orientation of the lactone ring in GAc. Somewhat later Whalley and coworkers[71] investigated the regularities in the change in molecular rotation of lactones of the diterpene series with α- and β-configurations of the lactone ring and by applying the results obtained to the GAc system they concluded that a β-orientated lactone ring is present in ring *A* of GAc. However, this conclusion could not be considered to be firmly based as in both instances compounds with "natural" (that is, opposite to gibberellin) fused *A/B* rings were taken for comparison. The other chemical papers of 1960–1962 also did not give an unambiguous solution to the problem although detailed investigation of the stereochemistry of ring *A* made by Grove and coworkers[72] yielded a weighty argument in support of formula (II). Conclusive confirmation of it was obtained by X-ray diffraction[60] which demonstrated the α-orientated lactone ring in GAc.

Hence the structure of gibberellic acid is now reliably proved. It is expressed by formula (II) in complete agreement with which are the data obtained in studying the path of its biosynthesis.

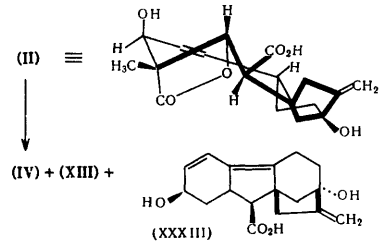
The structure of the other gibberellins† was found by referring them to the derivatives and degradation products of GAc.[19,21,22,30,35] It transpired that one group of gibberellins (GA_1, GA_5, GA_6, and GA_8) differ from GAc only in certain modifications of ring *A*. On treatment with hot solutions of mineral acids the gibberellins of this group are converted into gibberellic acid (V). The gibberellins of the other group (GA_2, GA_4, GA_7, and GA_9) differ from GAc more significantly. They do not contain a hydroxyl group at $C_{(7)}$ and thanks to this on ozonation they form norketones — for example, (XXXI) — which neither sodium bismuthate nor sodium iodate can cleave. Under the action of hot solutions of mineral acids the gibberellins of this group give aromatic acids — for example, (XXXII). The only change which occurs in the system of rings *C* and *D* during this treatment is the hydration of the terminal methylene group.

The chemical reactions which allow the structure of all the C_{19}-gibberellins at present known to be demonstrated are given schematically below:



During the elucidation of the structure of the gibberellins a series of chemical reactions was observed which are characteristic for these polycyclic compounds. We will consider the most interesting of them in detail.

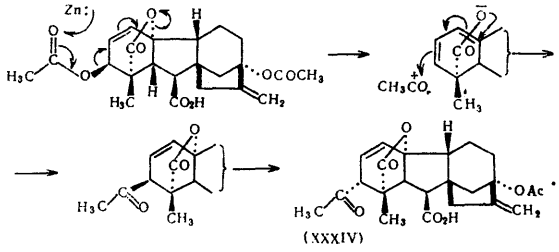
1. As mentioned above, gibberellins are extremely labile compounds, which undergo changes in aqueous solutions even at room temperatures. In this the most reactive centres of their molecules are the lactone ring, the $C_{(2)}$ hydroxyl group, and the $C_{(4b)}$ hydrogen. The opening of the lactone ring, which is accompanied by the formation of polyene and partly aromatised compounds, proceeds especially readily in gibberellins with a double bond in ring *A* (GA_3 and GA_7). In aqueous solutions it is observed even at room temperature. At elevated temperatures the process is complicated by epimerisation of the hydrogen atom at $C_{(4b)}$ and the principal reaction products are allogibberic (IV), epiallogibberic (XIII), and gibberellenic (XXXIII) acids:



The ease of formation of acids (IV) and (XXXIII) is due to the stereochemistry of the gibberellin molecules. According to the X-ray analyses[60], ring *C* of the gibberellins has a boat-shaped conformation, thanks to which there

† While this review was being prepared for publication Cross and Norton[108] isolated, from the culture liquid of *Gibberella f.*, a group of C_{20} di- and tri-carboxylic acids which are biogenetic precursors of the gibberellins. They proposed to name these compounds C_{20}-gibberellins. For more detailed information about these compounds see p. 858. The same authors reported[23,108] the isolation of a new C_{19} gibberellin, giberellin A_{11}; however, information concerning its structure and physicochemical properties has not been published yet.

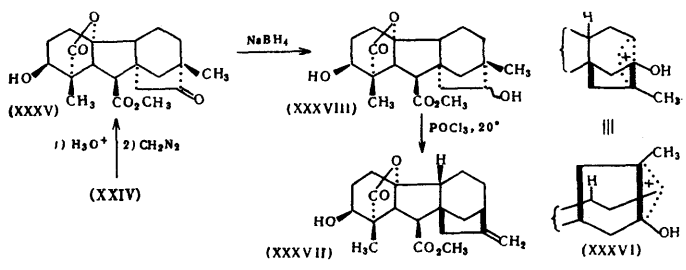
is considerable interaction of the spatially close axial hydrogen atom at $C_{(4b)}$ and carboxyl group at $C_{(10)}$ and with the ethylene bridge. Therefore the processes of epimerisation and dehydrogenation at $C_{(4b)}$, which remove this interaction, are energetically favourable. The instability of the lactone ring of gibberellins A_3 and A_7 is also due to steric reasons: the allyl lactone grouping formed by participation of the quaternary $C_{(4a)}$ atom is considerably strained and in consequence is readily opened under the influence of even such weak acids as the gibberellins themselves. The lability of the lactone ring of the gibberellins introduces several significant limitations into the chemistry of these compounds. For example, it is impossible to change from the compounds of the gibberellic acid series to the corresponding 7-deoxy-compounds with the aid of zinc and acetic acid anhydride. As McMillan and coworkers showed[73], under these conditions formation of an acetyl derivative (XXXIV) occurs, probably by the following mechanism:



2. Under conditions of catalytic hydrogenation under neutral and acid solvents the lactone ring of the gibberellins undergoes partial hydrogenolysis. The proportion of hydrogenolysis products in the reaction mixture is especially high for GA_3 and GA_7.[74-78]

3. The treatment of gibberellins containing a hydroxyl group at $C_{(7)}$ with hot dilute solutions of acids is accompanied — in addition to the opening of the lactone ring considered above and the epimerisation at $C_{(4b)}$ — by rearrangement of the carbon skeleton of rings *B*, *C*, and *D*, leading to gibberic acid (V).

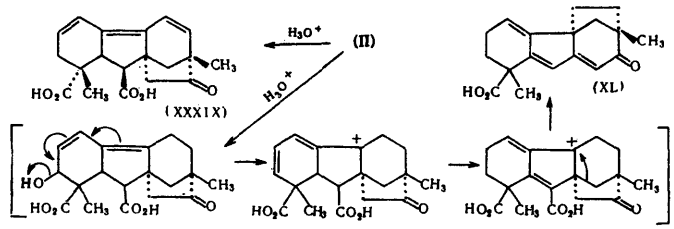
For gibberellins with a saturated ring *A* such a rearrangement takes place more readily than the opening of the lactone ring, so that it is possible to go, for example, from GA_1 (XXIV; R = H) to the ketone (XXXV). An analogous rearrangement is known for other natural compounds containing a fragment similar to rings *C* and *D* of the gibberellins (the diterpenes of the phyllocladene group, the diterpene alkaloids of the atisine group, etc.; see below). Its mechanism was studied in detail by Grove and Mulholland[57] and also by Birch and coworkers[79] who showed by the tracer method that a conversion analogous to the formation of (V) from GAc takes place by the mechanism of the Wagner–Meerwein rearrangement through a non-classical ion (XXXVI). This rearrangement of the gibberellin skeleton was used by Cross and coworkers[80] for going from derivatives of GA_1 to 7-deoxy-compounds of the GA_4 series:



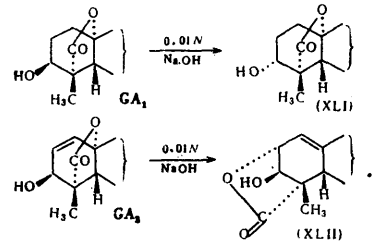
As the scheme shows, the methyl ester of GA_4 (XXXVII) was obtained by these investigators from the methyl ester of GA_1 (XXIV; R = CH_3) as the result of a double Wagner–Meerwein rearrangement: (XXIV) → (XXXV), (XXXVIII) → → (XXXVII). The low yield in this reaction is attributed to steric causes: on converting (XXXVIII) into (XXXVII) — in distinction from the conversion of (XXIV) into (XXXV) — the chair form of ring *C* becomes boat-shaped.

It is interesting to note that in gibberellins which do not contain a hydroxyl group at $C_{(7)}$ such a rearrangement is not observed. Under the conditions considered these compounds undergo only hydration of the terminal methylene group (see p. 854).

When gibberellins with an unsaturated ring *A* (GA_3, GA_7) are treated with an alcoholic solution of sulphuric acid, rearrangement of the carbon skeleton also occurs. However, unlike the reaction in an aqueous medium, the action of alcoholic sulphuric acid on these gibberellins is not accompanied by aromatisation of ring *A* and the main products of the reaction are the acids (XXXIX) and (XL)‡. A mechanism proposed for the formation of (XXXIX) includes a single, and that for the formation of (XL) a double, Wagner–Meerwein conversion[81] in accordance with the scheme:



4. Under weakly alkaline conditions the most "vulnerable" place of the gibberellins is again ring *A*. Treatment of the gibberellins possessing a saturated ring *A* (for example, GA_1) with 0.01 *N* NaOH is accompanied by epimerisation of the hydroxyl group at $C_{(2)}$ and leads to the lactone (XLI). Under similar conditions the gibberellins with an unsaturated ring *A* (GA_3 and GA_7) undergo an allyl rearrangement[82] and give lactones of type (XLII), which contain, like the original gibberellins, a hydroxyl group at $C_{(2)}$§:

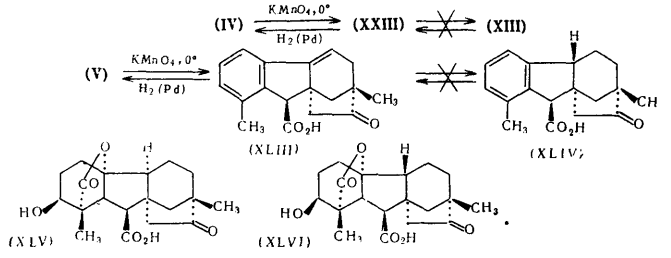


5. The complex stereochemistry of the gibberellins suggests that they should exhibit a variety of reactions of the free groups. As a rule, the information about such

‡ Note that the formation of (XXXIX) and (XL) is connected with the appearance of a dark red coloration accompanied by a blue fluorescence which is observed during the treatment of GA_3 and GA_7 with alcoholic solutions of sulphuric acid.

§ Note that epimerisation at $C_{(2)}$ and the conversion of (II) into (XLII) are accompanied by complete loss of physiological activity.

reactions is still very limited. As an example may be mentioned the difference in reactivity of compounds which are epimeric at $C_{(4b)}$, those studied in greatest detail being the degradation products of GAc containing an aromatic ring *A*.



Thus it has been found that allogibberic (IV) and gibberic (V) acids, for which the hydrogen atom at $C_{(4b)}$ has *trans*-orientation relative to the carboxyl group at $C_{(10)}$, are readily dehydrogenated under the action of potassium permanganate and even at 0° give the corresponding dehydro-acids (XXIII) and (XLIII). Contrary to this, the epimeric acids (XIII) and (XLIV), in which the hydrogen atom at $C_{(4b)}$ has *cis*-orientation relative to the carboxyl group at $C_{(10)}$, are stable to the action of potassium permanganate at 0° and do not form dehydro-acids (XXIII) and (XLIII) on hydrogenation.

The interaction of the carboxyl group at $C_{(10)}$ with the $C_{(4b)}$ hydrogen atom which is *cis*-oriented in relation to it is also apparent in the NMR spectra. Thus whereas in the spectrum of methyl gibberellate the signal of the proton at $C_{(4b)}$ is at $\tau = 7.7$, and in the norketone (XLV) it is at $\tau = 7.61$, in the norketone (XLVI) it occurs at $\tau = 7.2$.[59]

Yet another example of the sterically adjacent groups in the gibberellin molecule is provided by the interaction of the Δ^2 double bond and the carbonyl group of the lactone ring in GA_5 and its derivatives, which can be observed from the appearance of an anomalous absorption peak in the ultraviolet spectra of the corresponding compounds[30].

In examining the chemical features of the gibberellins it is impossible to avoid discussing the methods of analysing mixtures of these compounds of great structural similarity, particularly as these methods now form the basis for the identification of new gibberellin-like substances.

Although the first gibberellins were isolated as pure compounds by chromatography on columns packed with Celite 545 as long ago as the 'fifties, a reliable method of complete analysis of their mixtures did not exist until recently. The use of paper chromatography for this purpose allowed GA_8 and GA_9 to be determined reliably, but it was impossible to separate GA_1–GA_3 mixtures, or GA_4 and GA_7, by this method, although many chromatographic systems were tried[18,22,34,83,84]. Table 2 gives the R_f values of the gibberellins in the most convenient systems of solvents.

Satisfactory separation of a mixture of GA_1 and GA_3 was achieved by using centrifugal paper chromatography[85], and also thin-layer chromatography on aluminium oxide[85] and silica gel[86,87].

McMillan and Suter[88] made a complete analysis of a mixture of gibberellins by comparing the results of chromatography in a thin layer of silica gel G and kieselguhr G (see Table 3).

TABLE 2. Chromatography of gibberellins on Whatman No. 1 paper at 20°.[84]

Gibberellin	Value of R_f^*			
	system 1	system 2	system 3	system 4
GA_6	0.15	0.40	0.25	0.35
GA_5	0.29	0.50	0.40	0.48
GA_1	0.31	0.52	0.40	0.49
GA_6	0.33	0.51	0.42	0.51
GA_8	9.45	0.59	0.49	0.56
GA_4	0.60	0.72	0.57	0.72
GA_7	0.61	0.71	0.57	0.71
GA_9	0.725	0.77	0.65	0.78

* System 1: n-butanol–1.5 *N* ammonia (3 : 1); descending. System 2: propan-2-ol–water (4 : 1); ascending. System 3: n-butanol–t-pentanol–acetone–ammonia–water (5 : 5 : 5 : 2 : 3); descending. System 4: propan-2-ol–7 *N* ammonia (5 : 1); ascending.

TABLE 3. Thin-layer chromatography of the gibberellins.

Gibberellin	R_f^*			
	on silica gel G		on kieselguhr G	
	system 1**	system 2	system 2**	system 3**
GA_6	0.04	0.00	0.28	0.06
GA_5	0.11	0.00	0.42	0.18
GA_1	0.11	0.00	0.54	0.26
GA_2	0.04	0.00	0.64	0.30
GA_6	0.25	0.21	0.95	0.76
GA_8	0.31	0.35	1.00	0.88
GA_7	0.37	0.70	1.00	1.00
GA_4	0.37	0.82	1.00	1.00
GA_9	0.75	1.00	1.00	1.00

* System 1: di-isopropyl ether–acetic acid (95 : 5). System 2: benzene–acetic acid–water (8 : 3 : 5). System 3: benzene–propionic acid–water (8 : 3 : 5).

** The upper phase of the system is used.

TABLE 4. Fluorescence of the gibberellins on thin-layer chromatograms.

Gibberellin	Colour of the fluorescing spot	Induction period of fluorescence, min	Gibberellin	Colour of the fluorescing spot	Induction period of fluorescence, min
GA_1	blue	30—40	GA_6	blue	10—20
GA_2	purple	4—8	GA_7	yellow	1—2
GA_3	blue-green	1—3	GA_8	blue	10—20
GA_4	purple	4—8	GA_9	purple	4—8
GA_5	blue	10—20			

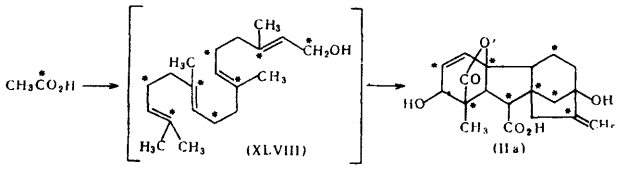
During thin-layer chromatography the gibberellins are observed by treatment of the plate with sulphuric acid and then heating. Spots which fluoresce in ultraviolet light appear, the colour and conditions of appearance of which (see Table 4) are important characteristics of the gibberellins[32].

This method allowed Jones and coworkers[31,32,87] to identify the known gibberellins in plant tissues at negligibly low concentrations (3–5 γ kg^{-1}).

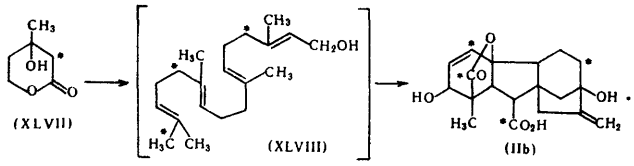
A rapid and reliable analysis of mixtures of the known gibberellins can be made also by gas–liquid chromatography[89]. Finally, very recently it was shown[90] that fragmentation mass spectrometry can be used for the analysis of mixtures and identification of individual gibberellins.

III. BIOGENESIS OF THE GIBBERELLINS AND THEIR PLACE AMONG OTHER NATURAL POLYCYCLIC COMPOUNDS

Even before the final elucidation of the structure of the gibberellins the study of the biosynthesis paths of GAc with the enzyme systems of *Gibberella fujikuroi* had begun. The first investigation of this problem was published by Birch and coworkers[91] who suggested that GAc is built by the fungus by the normal path of biosynthesis of cyclic diterpenes¶, that is, from molecules of acetic acid or the most characteristic precursor of the terpenes — mevalonolactone (XLVII). During this, the structural units are linked in accordance with the Ruzicka isoprene rule (by the head-to-tail principle), and the synthesis proceeds through a stage of formation of a normal acyclic precursor of the geranylgeraniol diterpenes (XLVIII). Cyclisation and slight transformation of the latter leads to GAc. This hypothesis could be easily checked by the use of labelled atoms. Actually, if it is true, then in GAc synthesised by fungi on a culture medium containing $^{14}CH_3CO_2H$, or mevalonolactone with ^{14}C in the $C_{(2)}$ position, the ^{14}C tracers should be distributed according to formulae (IIa) and (IIb):



(XLVIII) (IIa)

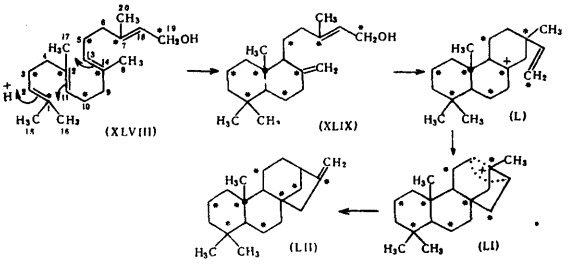


(XLVII) (XLVIII) (IIb)

Birch and his coworkers succeeded in showing that the tracer distribution corresponds strictly with the prediction.

Very recently[95], it was shown experimentally that the incubation of radioactive geranylgeraniol with *Gibberella f.* does not lead to the formation of radioactive gibberellic acid, and the precursor of the gibberellins is, as might have been expected, not this diterpene itself, but its pyrophosphate.

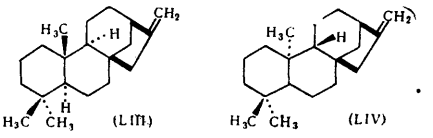
A detailed study of the reactions leading from the acyclic precursor of type (XLVIII) to GAc was not carried out in this work of Birch. However, it was assumed that the first stage in this conversion is the anti-*trans*-cyclisation at the Δ^{11} double bond to form a bicyclic product (XLIX) in which rings *A*/*B* are *trans*-fused. Subsequently there is the stage of dehydration of (XLIX) accompanied by closure of ring *C* and the formation of a carbonium ion (L), in which attack of the double bond by the cationic centre at $C_{(14)}$ passes through the stage of the non-classical ion (LI) to the tetracyclic precursor (LII):



(XLVIII) (XLIX) (L) (LII) (LI)

The first confirmation of this hypothesis was obtained even in the work of Birch and coworkers[91], since the distribution of the radioactive tracers in rings *C* and *D* of the gibberellic acid which is formed during fermentation in the presence of labelled acetic acid agreed well with the proposed scheme — compare formulae (LII) and (IIa).

Developing this hypothesis concerning the biogenesis of the gibberellins, Birch and Winter[96] suggested that the tetracyclic precursor of GAc of type (LII) is the well-studied diterpene phyllocladene (LIII).[97] However, their attempt to convert phyllocladene into GAc with the aid of the enzyme systems of *Gibberella f.* were unsuccessful: on incubation with phyllocladene labelled with ^{14}C, the fungus produced only non-radioactive GAc. In the light of contemporary ideas about the stereochemistry of the gibberellins this result does not seem unexpected, since phyllocladene exhibits the "natural" configuration at the fusion sites of rings *A* and *B*, contrary to the gibberellin configuration:



(LIII) (LIV)

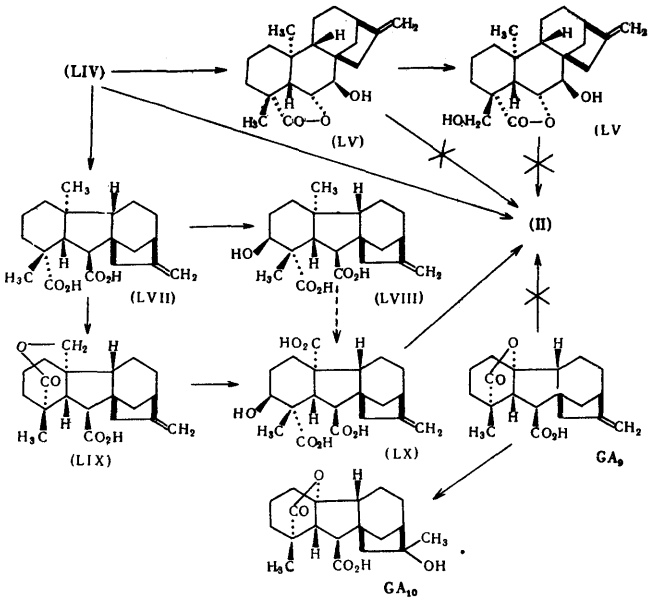
The true tetracyclic precursor of the gibberellins was found by Cross and coworkers[23,98] who showed that the culture liquid of *Gibberella f.* contains a tetracyclic diterpene (-)-kaurene (LIV),[99,100] which is easily converted into GAc under the action of fungal enzymic systems.

Extensive work carried out by the Cross group on the identification of the metabolites of various strains of *Gibberella f.* under different fermentation conditions[23,101–104] allowed the sequence of biosynthetic stages leading from kaurene to GAc to be noted. Until the publication of the results of these investigations it was thought[91,105] that the contraction of the six-membered ring *B* on going from the tetracyclic precursor to GAc precedes the introduction of the oxygen-containing functions into this ring. However, experimental verification showed[23] that neither hydroxykaurenolide (LV) nor dihydroxykaurenolide (LVI), which are isolated from the culture liquid of *Gibberella f.*, are converted by the fungus into GAc†.

¶ A discussion of the biosynthesis paths of the cyclic terpenes goes beyond the bounds of the present review. The reader should consult Refs. 92–94.

† GA_9 is also not a precursor of GAc. With the aid of the method of labelled atoms it was shown that under fermentation conditions GA_9 is converted into a new gibberellin, GA_{10}.[106]

Cross and his coworkers assume that the contraction of ring *B* is brought about in unoxidised kaurene, which is converted by acids (LVII)–(LX) into gibberellic acid:



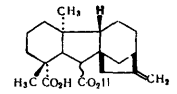
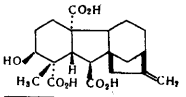
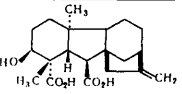
A detailed investigation of these last stages in the biosynthesis of GAc is now being made in Cross's laboratory. In the latest communications from this laboratory[107] the isolation of the acids (LVII)–(LX) from the *Gibberella f.* culture liquid has been described, and also the conversion of acid (LVII) labelled with ^{14}C at the $C_{(8)}$ methylene group into gibberellic acid (II) and the acid (LX). In both compounds the radioactive marker was found only in the terminal methylene group. On the basis of the results, Cross and Norton propose to call the acids (LVII), (LX), and (LVIII) — which are precursors of the gibberellins and exhibit gibberellin-like physiological activity — gibberellins A_{12}, A_{13}, and A_{14} respectively[108] (see Table 5). These compounds therefore disclose a new group of C_{20} gibberellins, which differ markedly from the C_{19} gibberellins considered above in the structure of ring *A*.

The investigation of the biosynthesis paths for the gibberellins in the tissues of higher plants has started only very recently. West and coworkers[95] have shown that in the incubation of a cell-fluid-free homogenate of endosperm nuclei of wild cucumber with [2-^{14}C]mevalonolactone, radioactive (-)-kaurene and (-)-kauren-19-ol are synthesised, which are converted by the enzymic systems of *Gibberella f.* into gibberellins. Hence it is quite probable that in plant tissues also the gibberellins are synthesised from (-)-kaurene.

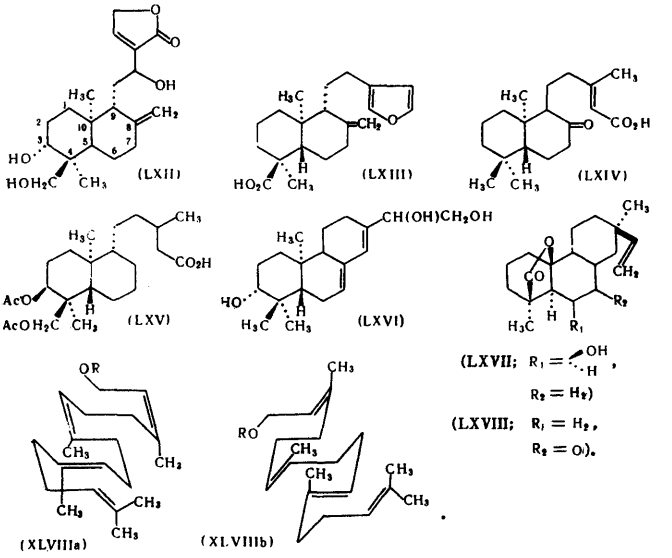
Some interesting work has been done by Lang and coworkers[109]. On incubating *Gibberella f.* with the diterpene steviol (LXI) these investigators detected the radioactive tracer in the mixture of gibberellins synthesised by the fungus. Careful chromatography of this mixture established that the tracer is concentrated in a zone free from known gibberellins but exhibiting high gibberellin-like activity.

A study of the biogenesis of the gibberellins allows us to understand the place of this unique polycyclic system among the natural compounds.

TABLE 5. Physicochemical properties of C_{20} gibberellins.

Name	Structural formula	M.p., °C	$[\alpha]_D$ (°C) n alcohol	M.p. of methyl ester, °C
Gibberellin A_{12}		245		liquid
Gibberellin A_{13}		194	−48(17)	117
Gibberellin A_{14}		232	−73	liquid

As is well known, geranylgeranyl pyrophosphate, an acyclic precursor of GAc, forms the start of a large group of natural diterpenes, which consequently are also the nearest biogenetic relatives of the gibberellins. When the cyclisation of geranylgeranyl pyrophosphate is interrupted at the stage of the GAc precursor of type (XLIX) (see p. 857), then bicyclic diterpenes are formed. In this, the transformation of the general precursor can mask the relationship of the compounds which are formed, leading to such different structures as andrographolide (LXII) [110], polyalthic (LXIII) [111], copalic (LXIV) [112], and eperuic (LXV) [113] acids‡.

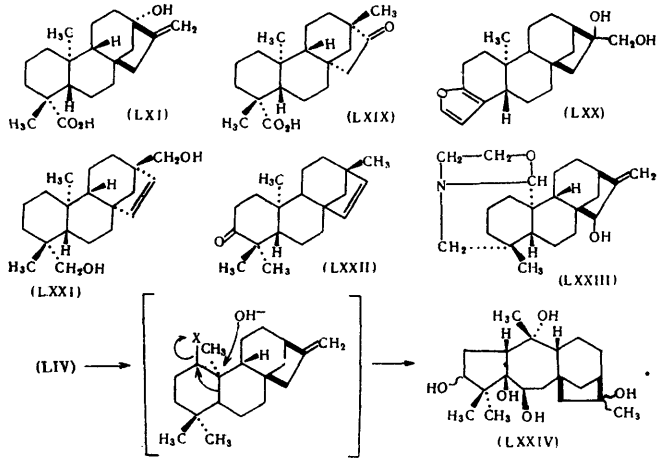


When the cyclisation of geranylgeranyl pyrophosphate is broken off at the stage of the precursor of type (L) then tricyclic diterpenes are formed. Further transformations of the precursor lead here to such substances as darutigenol (LXVI) [115], rosololactone (LXVII) [116], and rosenonolactone (LXVIII) [116,117]. Compounds (LXII)–(LXVI), like the gibberellins, possess an "unnatural" configuration of the *A/B* ring fusion and are formed, apparently, in the cyclisation of geranylgeranyl pyrophosphate in the same

‡ The configuration of these compounds at $C_{(9)}$ does not agree with the contemporary views on the stereochemistry of the diterpenes and requires verification [114]. The results of the verification have not yet been published.

"unnatural" conformation (XLVIIIa), which leads also to GAc. The lactones themselves (LXVII) and (LXVIII) have the 5α-, 10β-configuration§ usual for most terpenoids, and consequently are formed by cyclisation of geranylgeranyl pyrophosphate into conformation (XLVIIIc) antipodal to that which leads to the gibberellins. Therefore, despite the generality of the structural elements of ring *A*, lactones (LXVII) and (LXVIII) are biogenetically further from the gibberellins than darutigenol or andrographolide.

The cyclisation of geranylgeranyl pyrophosphate can lead, finally, also to a tetracyclic precursor of type (LII), to give initially the diterpenes of the phyllocladene group and their simplest derivatives. Among those closest structurally to the gibberellins there are many compounds in which the stereochemistry of the fusion of the rings *A*, *B*, and *C* is identical with the stereochemistry of the corresponding centres in GAc. Such compounds include kaurene (LIV), steviol (LXI) [118], isosteviol (LXIX) [181], cafestol (LXX) [113], beyerol (LXXI) [119], and stachenone (LXXII) [120]:



The biosynthetic transformations of the tetracyclic diterpenes can lead also to such natural compounds as the alkaloids of the atisine group — compare, for example, garryfoline (LXXIII) [121] — and the grayanotoxins — compare, for example, grayanotoxin A (LXXIV) [122]. The last is of special interest as according to its structure it can be formed from the tetracyclic precursor of the gibberellins by rearrangement of the *A*/*B* ring system by a mechanism close to the mechanism for contraction of ring *B* in the gibberellins.

IV. APPROACH TO AN EXPLANATION OF THE MECHANISM OF ACTION OF THE GIBBERELLINS ON HIGHER PLANTS

The proof of the phytohormonal nature of the gibberellins and the detailed study of the spectrum of their physiological activity (see pp. 850, 851) led in turn to the problem of explaining the mechanism of action of the gibberellins on the higher plants.

Systematic investigations in this field started only seven or eight years ago and have proceeded in two main directions: (1) study of the effect of gibberellins on the exchange of substances and the activity of the enzymic systems; (2) study of the interaction of gibberellins with other plant growth regulators.

§ Steroid numbering.

Even in the first studies devoted to investigating the influence of gibberellins on the morphological features of plants it was shown that the operation of gibberellic acid is accompanied by an increase in the dry weight of the epigeal parts of plants with only slight change (sometimes even a decrease) in the weight of the roots. Hence the growth stimulation under the influence of GAc depends not only on an increase in the general assimilation but also a redistribution of the plant material to the benefit of the epigeal part [123]. Detailed study of the changes in the exchange of substances of the epigeal parts of plants brought about by GAc allowed observation of an intensification of the photochemical [1,123,124] and dark [124] fixation of carbon and also of the stimulation of the processes of water supply in plants [125], transpiration processes [125], and processes for the biosynthesis of protein and RNA [125-128]. A large volume of material has been published about the effect of GAc on the biosynthesis of chlorophyll. As is well known, one of the distinctive features of plants treated with GAc is chlorosis However, a combination of treatment with GAc and a greater supply of mineral supplements prevents chlorosis [123]. From these results, and also from determinations of the percentage of chlorophyll in digitalis [129] and buckwheat [130] plants it followed that GAc does not suppress the biosynthesis of chlorophyll. This conclusion does not contradict the results on the reduction in the percentage of chlorophyll in the dry residue of lettuce [131], and pea [132] seedlings and also in the leaves of flowering plants [133], since when there is a sharp change in the weight of dry substance of plants under the influence of GAc it would be more correct to determine not the change in the percentage of chlorophyll in the dry residue but the change in its total quantity which can be made by the given organ of the plant.

However, the most characteristic feature of the change in materials exchange in plants under the action of GAc is the intensification of phosphorus–carbohydrate exchange. Studies by many investigators have shown that treatment with GAc brings about the utilisation of stored carbohydrates in the plants: the processes of phosphorolysis of starch and cellulose are intensified, and there is a significant increase in the level of monosaccharides [123,127,128,134-138]. The most active utilisation of stored substances under the influence of GAc occurs in germinating seeds. Detailed information on this process was obtained by studying the interaction of GAc with enzymic systems responsible for the splitting of the higher sugars. The principal objects of investigation were germinating barley seeds in which Hayashi and coworkers [139,140] observed as long ago as 1940 a sharp rise in activity of α-amylase. Subsequent work [141-146] confirmed this and also showed that, in addition to α-amylase, GAc is capable of activating other hydrolytic enzymes which participate in the splitting of starch and cellulose: diastase [147], β-amylase [141,146,148], cellulose [142], and phosphorylase [135].

In 1960 Paleg [149] showed experimentally that the activation of the α-amylase of barley grains under the influence of GAc is due to an intensification of the biosynthesis of this enzyme. Further investigation [150] established that GAc initiates the synthesis of α-amylase and the splitting of starch in seeds which have lost the ability to utilise the stored substances as a result of the removal of the germ or of γ irradiation. The results obtained enabled Paleg to develop a hypothesis that the apparatus for the control at the start of the hydrolytic processes in seeds and consequently at the start of germination is present in the germ and includes an endogenic gibberellin, which is an initiator of the biosynthesis of hydrolytic enzymes.

These studies of Paleg explained the first principles of the ability of gibberellins to interrupt the rest period of the seed and to stimulate its germination. Unfortunately, the problem of the nature of other aspects of the physiological activity of gibberellins is much less clear.

For example, despite many investigations, the problem of the mechanism of the acceleration of the growth of seedlings and the "healing" of the dwarf mutants of higher plants under the influence of gibberellins is still not solved. It has been shown reliably [1,8] that the enhanced growth after treatment with GAc stems from an increase in the cell elongation and an acceleration of their division, but the mechanism of the influence of GAc on each of these processes is not clear. To explain the action of gibberellins on the cell elongation several hypotheses have been propounded which explain the physiological activity of the gibberellins by including them in a scheme for the exchange of indolylacetic acid and other heteroauxins. The experimental basis for these hypotheses was the observation of many instances in which the level of the endogenic heteroauxins was raised [151-153] and the activity of indolylacetic acid oxidase was suppressed [154-156] after treatment of plants with gibberellins and also of the facts of the synergism of auxins and gibberellins [157-161] in their action on the plant. On the basis of these facts Galston and Warburg [162] suggested that the gibberellins are stimulators of the biosynthesis of polyphenols, which are capable of inhibiting indolylacetic acid oxidase, and consequently of raising the level of the endogenic heteroauxins in the plants. According to Galston and Warburg's hypothesis, a direct consequence of this is an intensification of cell elongation — a characteristic reaction of plants to auxins.

However, the above hypothesis is contradicted by many experimental results, including those of Kato [163] and of Brian and Hemming [164], who observed a marked difference in the reactions of the higher plants to gibberellins and heteroauxins (see Table 6).

Better agreement with the experimental results was shown by the hypothesis of Brian and Hemming [157], according to which the intensification of growth under the influence of GAc is explained by the ability of the gibberellins to suppress the biosynthesis of the polyphenolic inhibitors of the heteroauxins. Hence according to this hypothesis, just as with the Galston–Warburg hypothesis, the reason for the physiological activity of the gibberellins lay in an increase in the level of the endogenic heteroauxins, but the absence of the activity of the gibberellins in certain biosyntheses characteristic for heteroauxins was explained by the absence of the inhibitor for the auxins. However, this hypothesis also did not explain all the facts, particularly the ability of gibberellins to act in the dark and also to be cumulative in action on plants with superoptimal (inhibiting) quantities of heteroauxins.

TABLE 6. Main difference between heteroauxins and gibberellins.

Bio-test	Auxin	Gibberellin
Transport polar	+	−
Promote root initiation	+	−
Inhibit root elongation	+	−
Delay leaf abscission	+	−
Inhibit lateral buds	+	−
Induce callus formation	+	−
Promote growth of intact plants, especially of drawf mutants	−	+
Promote seed germination and breaking of dormacy	−	+
Substitute for vernalisation	−	+
Promote flowering in long-day plants under unfavourable light conditions	−	+

In recent years the main sense of the above hypotheses — the ability of the gibberellins to stimulate the biosynthesis of polyphenols — has been demonstrated experimentally by Netherlands chemists [165] by the example of ferulic, caffeic, and chlorogenic acids. However, they put forward quite another interpretation of the results obtained. Since ferulic acid can serve as the starting point for the biosynthesis of lignin, these investigators suggested, and then demonstrated by experiment, that gibberellins stimulate the biosynthesis of lignin. And since lignin plays the part of a material which strengthens the bond between cellulose fibres and gives the cell wall strength and elasticity, these investigators consider that the gibberellins play a part independent of the other growth regulators in the cell growth process: by stimulating the biosynthesis of lignin they are able to facilitate the densification of the cell walls and give them the optimal mechanical properties.

French investigators [166] also had a separate viewpoint about the action (independently of other hormones) of the gibberellins on plant growth, making clear the synergism of the auxins and gibberellins by their ability to combine with a single enzyme having two active centres, so that the adsorption of one hormone facilitates the adsorption of the other.

The stimulation of the biosynthesis of polyphenols under the influence of gibberellins can also be the key to understanding the action of these substances on the photoperiodic reaction of plants.

Actually, in recent investigations [167,168] there have been observations that the light regime has a considerable effect on the activity of oxidising enzymes taking part in the respiration processes of plants. It appeared that long-day conditions activate the so-called terminal oxidases which contain heavy metals and are capable of being poisoned by poisons of the potassium cyanide and sodium azide type (for example, polyphenoloxidase and ascorbinase), but short-day conditions activate residual respiration oxidases (including peroxidases). As it was also found reliably [167,168] that the activation of polyphenoloxidase in a long day is due to the improvement in the supply of this enzyme by polyphenols, it is easy to see that the ability of gibberellins to stimulate the biosynthesis of polyphenols can be the biochemical basis for their action on a long-day plant under short-day conditions.

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Summing up all the results of the investigations in the field of the chemistry and biochemistry of gibberellins which have been considered, something must be said about the future development of this field of bio-organic chemistry.

Whereas in the 'fifties the central task of the problem of the gibberellins was the establishment of the structure of this group of natural compounds and revealing the spectrum of their physiological activity, the centre of investigation has now shifted to the field of studies of the biogenesis of the gibberellins and the mechanism of their action on the plant. In this connection there is great interest in studying the metabolism of GAc in plants, and also the isolation and study of the structure of new endogenic growth regulators which exhibit gibberellin-like physiological activity, but differ in properties from the known gibberellins [38,169-172].

A considerable part in future investigations of the problem of gibberellins will evidently be played by work on the full synthesis of these compounds and their chemical conversions [173-176], since in this way it is possible to find not only the connection between structural and physiological activity in this group of compounds but also to observe new forms of biological activity of gibberellin-like substances.

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GLYCOSPHINGOLIPIDS: ESTABLISHMENT OF STRUCTURE, SYNTHESIS, BIOLOGICAL ROLE

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The present review considers lipids that are grouped together under the name glycosphingolipids. In addition to structural similarities, these compounds have at least one property in common in that they are capable of taking part in specific immunological reactions, the study of which may open a new approach to the understanding of the fine structural differences in animal and human tissues in normal and pathological states.

I. NOMENCLATURE

The term "sphingolipoids" was proposed by Carter to denote those lipids that contain the aliphatic amino-glycol sphingosine (I).[1] This term may now be extended to natural derivatives of dihydrosphingosine (II), C_{20}-sphingosine (III), and C_{20}-dihydrosphingosine (IV), which are found together with derivatives of sphingosine (I) in animal tissue, and also to the compounds phytosphingosine (V) and dehydrophytosphingosine (VI) and their C_{20}-homologues, which have been isolated from plants.