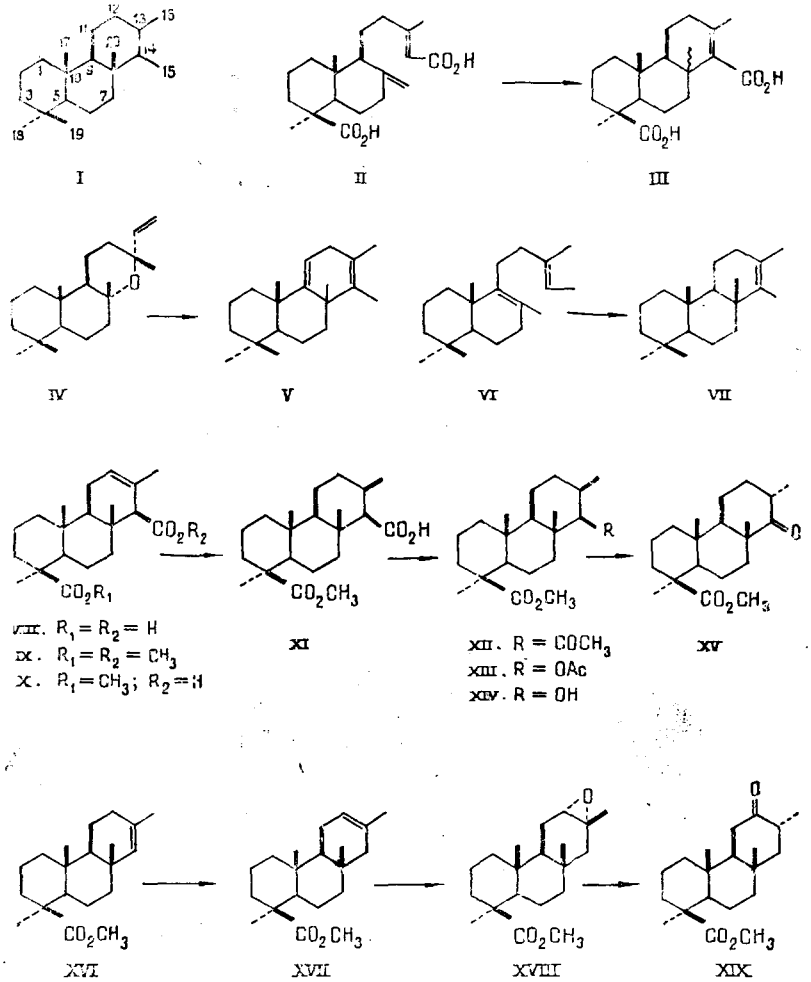
ISOAGATHANE DITERPENOIDS

P. F. Vlad and N. D. Ungur

UDC 547.596/599

The chemistry, stereochemistry and methods of synthesis, and also natural sources of isoagathane diterpenoids are discussed.

The isoagathane diterpenoids are those with the carbon skeleton (I). This is a so far not numerous but rapidly growing subgroup of diterpenoids isolated exclusively from marine organisms. The first natural isoagathane derivative was described only in 1971 [1], but substances of this structure were known as early as 1930. They were synthesized by the electrophilic cyclization of a number of labdane bicyclic diterpenoids. Thus, Ruzicka and Hosking [2], on heating agathic acid (II) with formic acid, obtained isoagathic acid, to which, on the basis of chemical transformations, especially dehydrogenation and decarboxylation, they assigned structure (III) [3]. Similarly, manoyl oxide (IV) [4] and dihydrosclarene (VI) [5] yielded the isoagathane hydrocarbons (V) and (VII), respectively. Their tricyclic structure was assumed on the basis of results of dehydrogenation but was not strictly demonstrated.



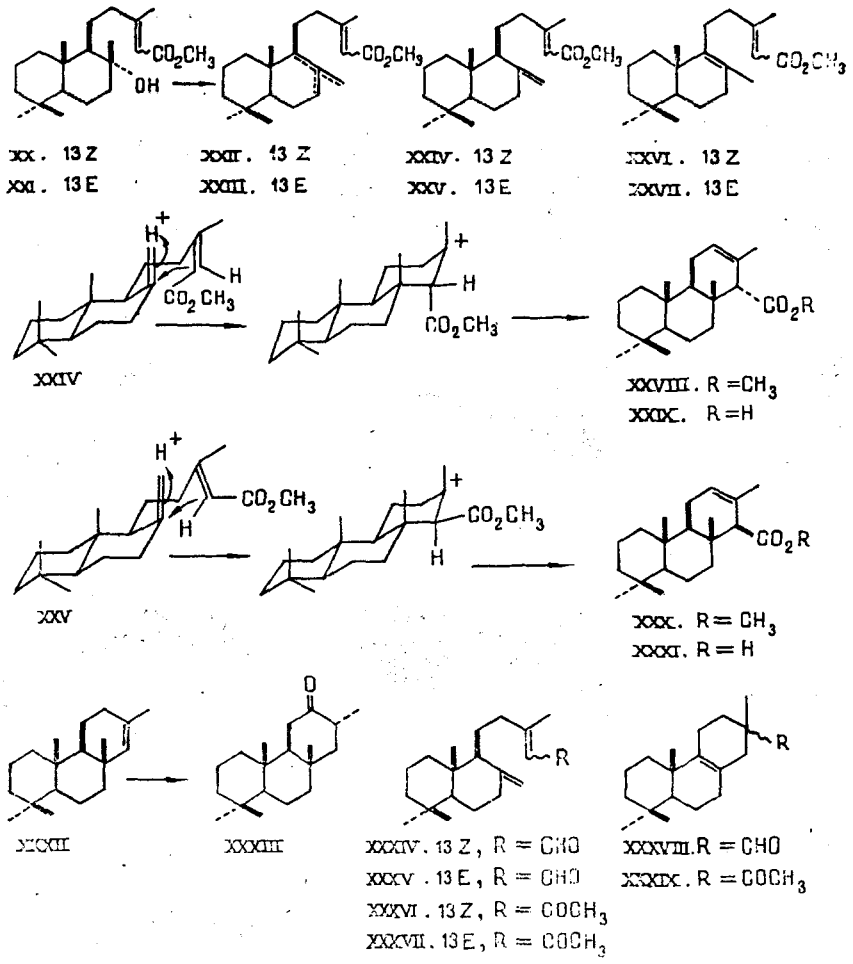
Institute of Chemistry, Academy of Sciences of the Moldavian SSR, Kishinev. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 397-410, July-August, 1986. Original article submitted October 30, 1984.

0009-3130/86/2204-0369$12.50

The stereochemistry and definitive structure of isoagathic acid – the ancestor of the isoagathane diterpenoids – were shown by French chemists [6, 7]. On investigating the IR and NMR spectra of dimethyl isoagathate they came to the conclusions that its double bond was trisubstituted and linked carbon atoms C_{12} and C_{13}. Consequently, isoagathic acid actually possesses the structure (VIII), and its diester is (IX). This conclusion was confirmed by mass spectrometry, since the main direction of fragmentation of the diester (IX) includes, as was to be expected, decomposition by a retro-Diels-Alder scheme. This course of fragmentation is common for isoagathanoids with an ethylenic bond at C_{12} [8].

When the isoagathic acid monoester (X) was hydrogenated under pressure over platinum dioxide in acetic acid, the ester-acid (XI) was obtained which was then converted by interaction with oxalyl chloride into the methyl ketone (XII); this was stable under the action of alkali, i.e., its methyl ketone group and, consequenlty, the carboxy group of the ester-acid (XI) are equatorial and the C_{14}-carboxy group of isoagathic acid is pseudoequatorial. The methyl ketone (XII) is oxidized by trifluoroperacetic acid to the diester (XIII), which is saponified by alkali to the hydroxy ester (XIV), which, in its turn, is oxidized by chromium trioxide to the keto ester (XV). Under the oxidation conditions epimerization takes place at C_{13} with the formation of the more stable keto ester with an equatorial methyl group at this center. The keto ester (XV), like 1-keto-5α-steroids, gives a weak negative Cotton effect showing the trans-linkage of rings B and C and the β configuration of the methyl group at C_8 in all the isoagathane compounds studied (an equatorial methyl group makes no contribution to the Cotton effect).

The following route also led to the same conclusion. On being heated, the ester-acid (X) underwent decarboxylation, giving the unsaturated ester (XVI), which was readily isomerized by acid to the ester (XVII). p-Nitroperbenzoic acid converted the latter into the α-epoxy ester (XVIII), isomerized by boron trifluoride etherate into a mixture of two carbonyl compounds one of which possessed the structure (XIX). The ester ketone (XIX), like 3-keto-5α-steroids, gave a strong positive Cotton effect showing that its rings B and C had the trans linkage, and the methyl group at C_8 the β orientation. Finally, the stereo-



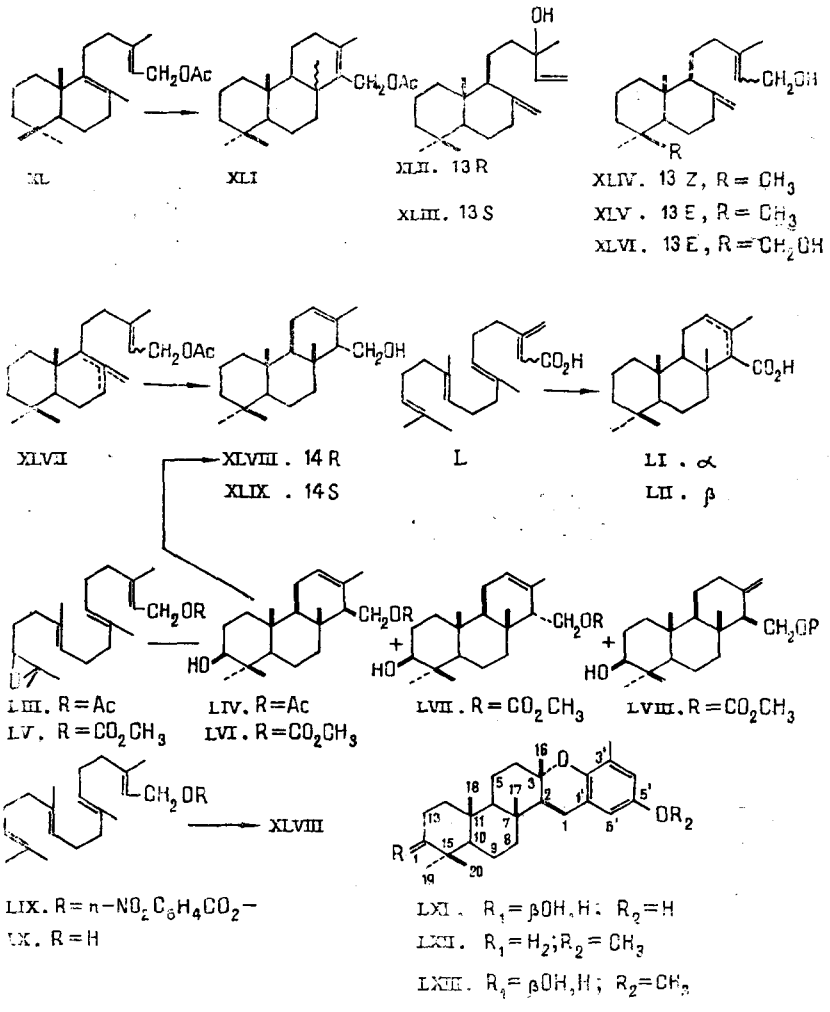
chemistry of isoagathic acid shown in formula (VIII) was confirmed by the PMR spectra of its derivatives [7].

Using as examples the methyl esters of 13Z- and 13E-8α-hydroxylabd-13-en-15-oic acid (XX) and (XXI), the products (XXII) and (XXIII) of their dehydration with phosphorus oxychloride in pyridine, and the methyl esters of 13Z- and 13E-labd-8(20),13-dien-15-oic acids (XXIV) and (XXV) and of 13Z- and 13E-labd-8(9),13-dien-15-oic acids (XXVI) and (XXVII), it has been shown [6, 9] that on cyclization with formic acid, all 13Z- esters give methyl 14S-isoagath-12-en-15-oate (XXVIII), and all compounds of the 13E series gives its epimer at C_{14} (XXX). Thus, their cyclization induced by the protonation of the double bond in ring B is stereospecific and takes place by the mechanism shown in the scheme with conformational formulas (the hydroxy esters (XX) and (XXI) first undergo dehydration).

The fact that the esters (XXVIII) and (XXX) are epimeric at C_{14} followed from the fact that they were epimerized by alkali and the acids corresponding to them, (XXIX) and (XXXI), were decarboxylated with the formation of one and the same hydrocarbon (XXXII). By analogy with the transformation of compound (XVI) this substance was converted into the ketone (XXXIII), the positive Cotton effect of which showed the trans linkage of rings B/C and the β configuration of the methyl group at C_8 in the esters (XXVIII) and (XXX). The configurations of the latter at C_{14} were established by PMR spectroscopy.

In contrast to the α,β-unsaturated acids and esters of the labdane series considered above, the aldehydes (XXXIV) and (XXXV) and the methyl ketones (XXXVI) and (XXXVII) corresponding to them were converted under the action of formic acid into a mixture of the pimaro-8(9)-enic compounds (XXVIII) and (XXXIX), epicmeric at C_{13}; i.e., in this case cyclization was initiated as the result of the protonation of the carbonyl group [10].

In 1938, Ruzicka et al. [5] studied the cyclization of the dienic acids (XL) under the action of formic acid. On the basis of the results of dehydrogenation they assigned structure (XLI) to the reaction product. However, neither the structures nor the stereo-



chemistries of the initial compounds and the reaction products were strictly demonstrated. Subsequently, in a whole series of investigations [11] the interaciton of manool (XLII) and its epimer (XLIII), their allyl isomers (XLIV) and (XLV), and also the agathenediol (XLVI) with acids, but no isoagathane compounds were obtained. However, it must be mentioned that in some of these investigations the oxygen-containing part of the cyclization products either was not investigated or was investigated only partially.

We [12, 13] have investigated the cyclization of the mixture of acetates (XLVII) and of its individual components with a mixture of sulfuric and formic acids and have shown that under these conditions acetates with a $\Delta^{8(20)}$ double bond give a small yield (~5%) of a mixture of isoagathic alcohols epimeric at C_{13} (XLVIII) and (XLIX), identical, respectively with the products of the reduction of the esters (XXX) and (XXVIII) [14] (compare with [5]). It was found that these alcohols are formed in small amount under the action of protonic acids on a whole series of labdane diterpenoids (manool, sclareol, manoyl oxide, etc.).

It follows from the investigations that have been mentioned that isoagathane diterpenoids can be obtained in vitro from labdanoids. However, because of the absence of biochemical information it is impossible to draw any conclusions whatever concerning their biosynthesis, since aliphatic diterpenoids may also be precursors of the isoagathanoids. The basic possibility of obtaining isoagathane diterpenoids in vitro from aliphatic compounds has also been demonstrated, although this route for their synthesis has so far been feebly developed. Thus, the cyclization of geranylgeranic acid (L) with a mixture of sulfuric and formic acids gave a mixture of α- and β-tricyclogeranylgeranic acids (LI) and LII) [15]. However, the stereochemistries of the initial compound and the reaction products were not established, and the structures of the latter were not shown sufficiently strictly.

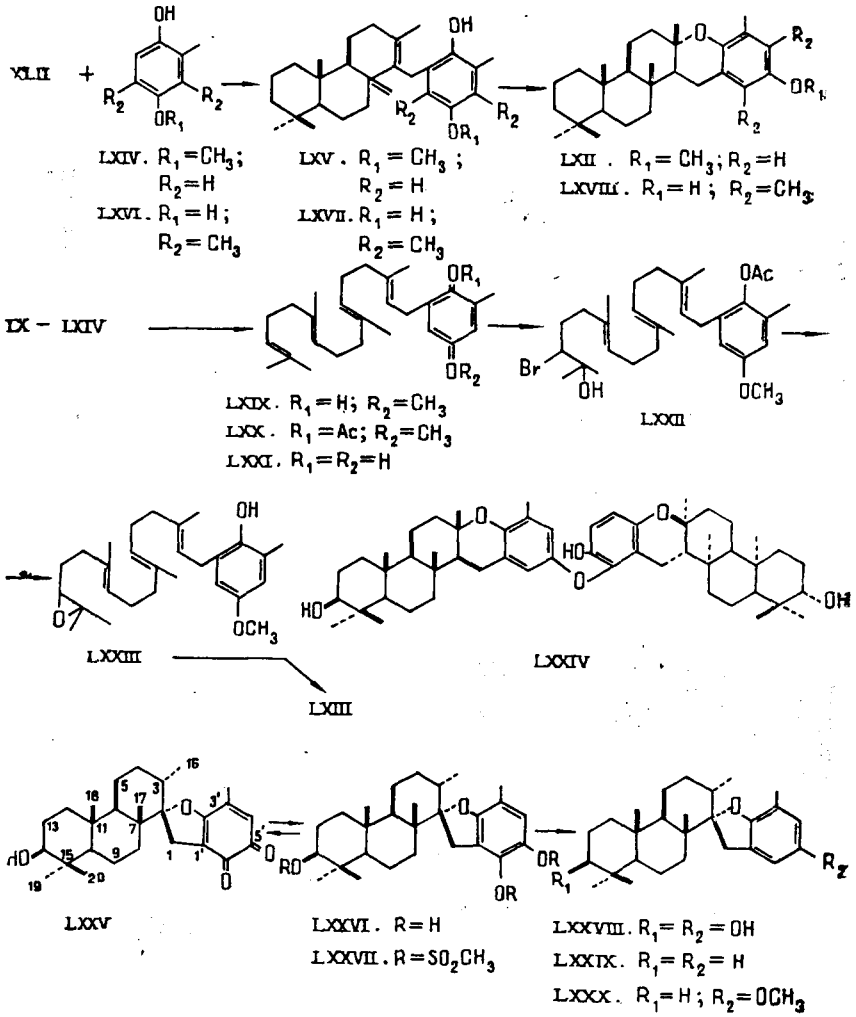
Later [16], the cyclization of the terminal epoxide of all-trans-geranylgeranyl acetate (LIII) was carried out with tin tetrachloride. The reaction product proved to be a complex mixture of substances from which the 15-monoacetate (±)-isoagath-12-ene-3β,15-diol (LIV) with a pseudo-equatorial hydroxymethyl group at C_{14} was isolated with a yield of 10%. It was identified by a four-stage conversion into the (±)-alcohol (LVIII). Thus, in this case, as well, the cyclization process proved to be stereospecific and, as the authors showed, uninterrupted, but its structural selectivity was low. The yield of isoagathane compounds was higher in the cyclization of all-trans-epoxygeranylgeraniol methyl carbonate with boron trifluoride etherate in nitromethane [17]. The main reaction product (36%) was the 15-(methyl carbonate) of (±)-isoagath-12-ene-3β,15-diol (LVI). In this case, the formation of a small amount (8.5%) of (LVII), the epimer of compound (LVI) at C_{14}, showed the partial isomerization of the initial compound (LV) before cyclization. Finally, this is the only case in which cyclization yielded an isoagathane product (LVIII) with a semicyclic double bond (yield 8.5%). The reaction of the p-nitrobenzoate of all-trans-geranylgeranoil has also been investigated [18]. When the reaction product was treated with sodium chloride and then with sodium tetrahydroborate, the (±)-alcohol (XLVIII) (22%) was isolated.

In all cases, apart from [17], the cyclization of bicyclic and aliphatic diterpenoids formed only isoagathane compounds with their double bond at C_{12} (α isomers). According to Bory et al. [7], this is due to the fact that with such a position of the double bond with the trans-linkage of rings B/C and the presence of a β-methyl group at C_8 the spatial interactions in the tricyclic system are smallest and it is the most stable thermodynamically [19, 20].

Thus, by the moment of the detection of isoagathanoids in natural sources, the chemistry, stereochemistry, and methods of synthesizing these compounds has been fairly well studied, which substantially facilitated their identification.

The first of the isoagathanoids to be described was taondiol, isolated from the marine alga Taonia atomaria [1]. Taondiol is a meroterpenoid, the terpene moiety of which has an isoagathane structure. Spectral characteristics showed that it was an analogue of tocopherol containing an 8-methylchroman-6-ol grouping and an isoagathane fragment with an equatorial hydroxyl at C_3. The relative configuration of taondiol and, finally, its structure were established by x-ray structural analysis [21], and its absolute configuration as the result fo the synthesis of the methyl ether of dioxytaondiol (LII) from manool (XLII) [21, 22]. The interaction of the latter with the monoethyl ether of toluhydroquinone (LXIV) in the presence of boron trifluoride etherate led to the labdadienylphenol (LXV), which was cyclized by formic acid to the methyl ether of deoxytaondiol (LXII), also obtained from

the methyl ether of taondiol (LXIII) on its oxidation by the Jones reagent followed by the reduction of the resulting ketone via the ethylene thioketal. The deoxytaondiol analogue (LXVIII) was synthesized similarly from manool and trimethylhydroquinone (LXVI) via the manoylhydroquinone (LXVII) [23]].

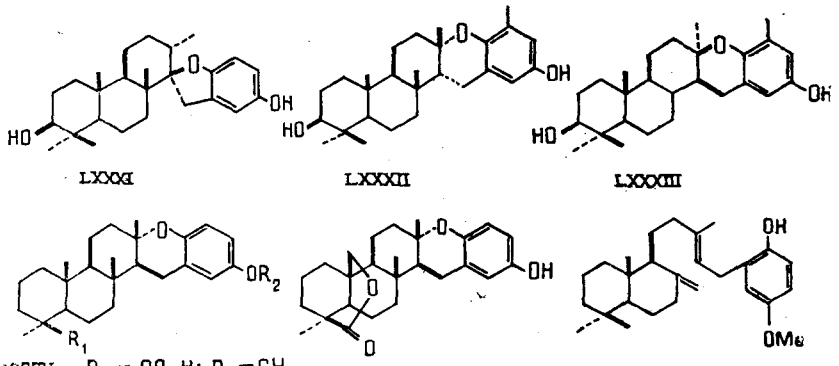


The total synthesis of the methyl ether ((±)-taondiol (LXIII)) has also been described [24, 25]. By alkylating compound (LXIV) with all-trans-geranylgeraniol (LX) in the presence of boron trifluoride etherate, the prenylphenol (LXIX) was obtained, and the acetate of this (LXX) gave with N-bromosuccinimide the bromohydrin (LXXII), which was converted under the action of potassium acetate into the epoxide (LXXIII). The cyclization of the latter by tin tetrachloride led to the ether of (±)-taondiol (LXIII).

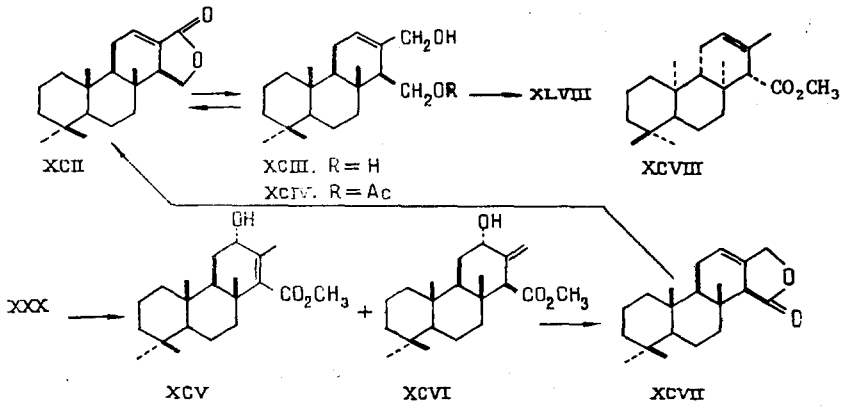
Taondiol (LXI) has also been found in the brown marine alga Stypopodium zonale [26]. Judging from the sign of its specific rotation, the authors concerned considered that this alga contained an enantiomer of taondiol, although the absolute value of its specific rotation was substantially smaller than that of taondiol. It is difficult to explain the presence of ent-taondiol in Stypopodium zonale from the biogenetic point of view, as well, since all the other related meroterpenoids isolated from these algae (see below) belong to the same stereochemical series as taondiol (LXI). A partially oxidized dimer of taondiol (LXXIV) has also been detected in the brown alga Taonia atomaria [27].

A group of meroditerpenoids related to taondiol has been isolated from the alga Stypopodium zonale [26, 28] (the number of the atoms in the meroditerpenoids is given in accordance with [26]). Predominating among them were stypoldione (LXXV) and stypotriol (LXXVI). The triol (LXXVI) was readily oxidized by atmospheric oxygen to the quinone (LXXV), which in its turn, was reduced to the triol (LXXVI) by sodium hydrosulfite. Their structures and relative stereochemistries followed from their spectral characteristics and were confirmed by an x-ray analysis of the quinone (LXXV). Stypodiol (LXXVIII) proved to be the 6'-deoxy

derivative of stypotriol, as was established spectrally and by its formation together with the ether (LXXIX) on the reduction of stypotriol trimesylate (LXXVII) with lithium in liquid ammonia. 2-Epistypodiol (LXXXI) has also been isolated from the algae mentioned, its stereochemistry following unambiguously from a comparison of its ^1H and ^{13}C NMR spectra with those of stypodiol. In the alga Stypopodium zonale collected at great depths, 2-epitaondiol (LXXXII) has also been detected. Its spectral characteristics were close to those for taondiol (LXI) and showed that they were epimeric. As it differed from 3-epitaondiol (LXXXIII) – the product of the isomerization of taondiol by alkali [23] – it could only be 2-epitaondiol, since it followed from a consideration of molecular models that in 2,3-diepitaondiol ring C should be in an unstable boat configuration and, because of this, be readily epimerized at C_3 under the action of alkali, which was not in fact observed.



LXXXIV. $R_1 = CO_2H$; $R_2 = CH_3$
LXXXVI. $R_1 = CO_2H$; $R_2 = H$
LXXXVII. $R_1 = CO_2CH_3$; $R_2 = CH_3$
LXXXVIII. $R_1 = CH_2OH$; $R_2 = CH_3$
LXXXIX. $R_1 = CH_2OTs$; $R_2 = CH_3$
XC. $R_1 = R_2 = CH_3$

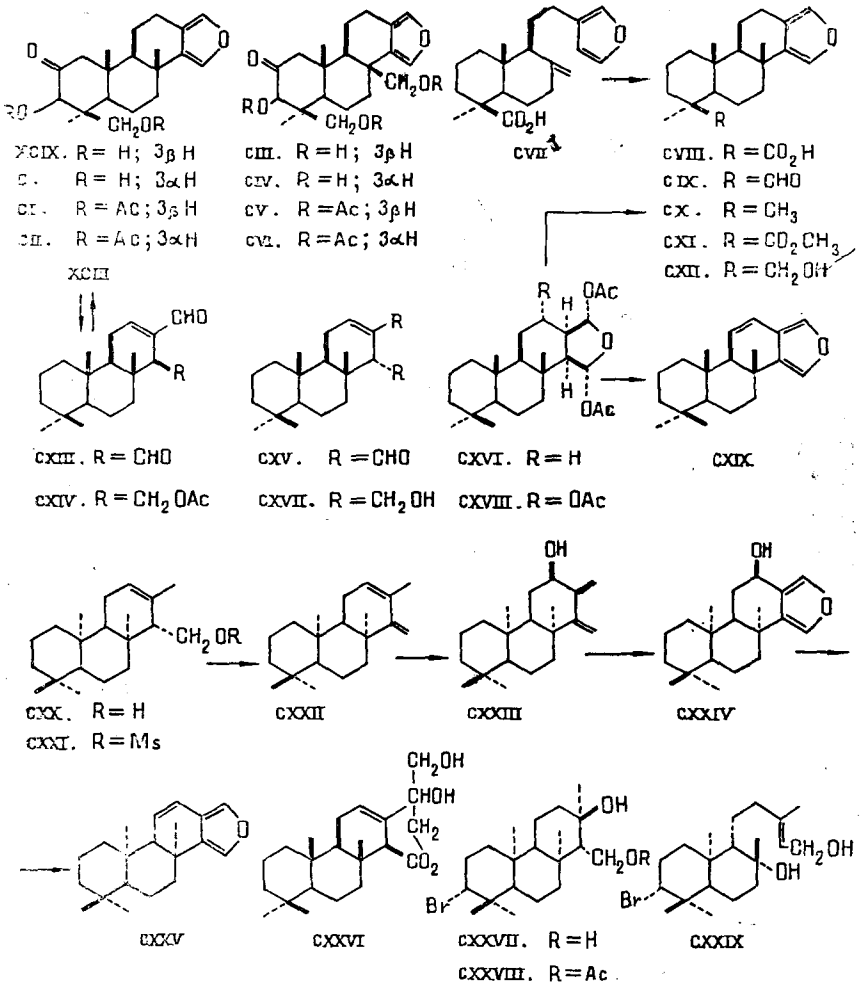


The absolute configuration of the meroditerpenoids from Stypopodium zonale was established as the result of the production on the cyclization of the mannoylphenol (LXV) of, together with compound (LXII), a small amount of the methyl ether of 14-deoxystypodiol (LXXX) [29], which was also synthesized from stypodiol (LXXVIII) by the oxidation of one of its hydroxy groups to a keto group and the reduction of the latter through the ethylene thioketal. The facts given above show that the taon- and the stypo-meroditerpenoids must have one and the same biogenetic precursor. Such precursor may be all-trans-geranylgeranylhydroquinone (LXXI), which has also been isolated from the alga Stypopodium zonale [26].

Substances related to taondiol have been detected in the marine sponge Strongylophora durissima [30]. These are strongylophorins 1-3 (LXXXIV)-(LXXXVI). The structure and relative stereochemistry of stronglyophorin-2 (LXXXV) have been established by x-ray structural analysis, and those of substances (LXXXIV) and (LXXXVI) on the basis of spectral characteristics and chemical transformations. The methylation of compounds (LXXXIV) and (LXXXVI) formed one and the same ether-ester (LXXXVII), reduced by lithium tetrahydroaluminate to the alcohol (LXXXVIII), the tosylate of which (LXXXIX) was reduced by zinc and sodium iodide

to the ether (XC). The latter compound was synthesized from manool (XLII): When the monomethyl ether of hydroquinone was alkylated with manool in the presence of boron trifluoride etherate, the manoylphenol (XCI) was formed, and this was cyclized by formic acid to the ether (XC). This correlation also established the absolute configuration of the strongylophorins.

A rich source of "true" isoagathane diterpenoids is represented by marine sponges of the genus Spongia. The first of them was isoagathalactone (XCII) isolated from S. officinalis collected in the Mediterranean sea [14]. Its structure and stereochemistry were shown by spectral methods and were confirmed by chemical transformations. On reduction with lithium tetrahydroaluminate, it gave the glycol (XCIII) which, on hydrogenation over platinum in acetic acid, was converted into the alcohol (XLVIII). Several syntheses of isoagathalactone have been described. When the ester (XXX) was subjected to photolysis in the presence of Methylene Blue and the product was reduced with trimethyl phosphite, a mixture of the hydroxy esters (XCV) and (XCVI) was formed. Isomerization of the latter with sulfuric acid led to the lactone (XCVII), which was reduced with lithium tetrahydroaluminate to the diol (XCIII), which was reduced with lithium tetrahydroaluminate to the (XCII) [31]. Brazilian chemists [32] synthesized an enantiomer of isoagathalactone similarly starting from the enantiomeric ester (XCVIII), while other authors [33, 34] have synthesized (±)-isoagathalactone. We [35] obtained the glycol (XVIII) – the key product in the synthesis of isoagathalactone – together with other compounds by the oxidation of the alcohol (XLVIII) with selenium dioxide in ethanol, although a previous attempt to perform this conversion [32] had been unsuccessful.

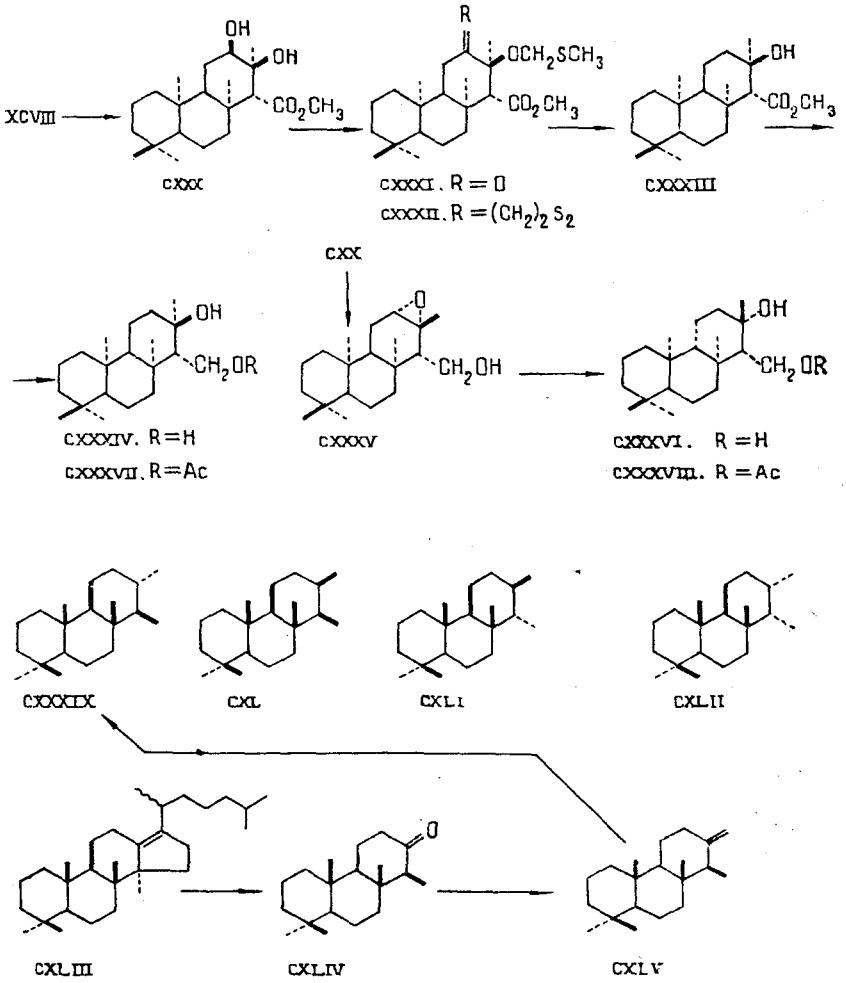


Kazlauskas et al. [37] had isolated from unidentified species of the genus Spongia collected at various points in the waters to the south of Australia spongiadiol (XCIX), epispongiadiol (C), their diacetates (CI) and (CIII), spongiatriol (CIII), and epispongiatriol (CIV) and their triacetates (CV) and (CVI). Their structures followed from spectral characteristics and, in particular, from a comparative analysis of the ^{1}H and ^{13}C NMR spectra

of the acetates (CI) and (CVI) and were confirmed by an x-ray analysis of the triacetate (CIII). The latter method showed that ring A of compound (CIII) had the boat conformation which, according to the PMR spectrum, is also retained in solution. Its absolute configuration was established by ORD and CD methods. It must be mentioned that the qualitative and quantitative compositions of sponge metabolites vary with the site and depth from which they were collected.

Belgian chemists [38] isolated three related diterpenoids (CVIII)-(CX) from the sponge Spongia officinalis collected near New Guinea. The structure and stereochemistry of the acid (CVIII) were established by ^{1}H and ^{13}C NMR spectroscopy (by comparison with compounds (XCIX)-(CVI)). When the methyl ester of this acid and the aldehyde (CXI) were reduced with lithium tetrahydroaluminate, one and the same alcohol (CXII) was formed, the mesylate of which, on reduction with zinc dust and sodium iodide, gave the furan (CX). The structure of substances (CVIII)-(CX) was shown definitively through the synthesis of the ester (CXI) by the cyclization of the lambertianic ester (CVII) with fluorosulfonic acid or 100% sulfuric acid [35]. Compounds (CVIII)-(CX) possess antifungal activity.

Some years after the identification of isoagathalactone, Cimino et al. [39] isolated the isoagathane metabolites (CXIII)-(CXVI), as well, from the Mediterranean sponse Spongia officinalis. The structure and stereochemistry of the dialdehyde (CXIII) were shown by its formation on the lithium tetrahydroaluminate reduction of the known diol (CXIII), which was oxidized by dimethyl sulfoxide and oxalyl chloride reversibly to the dialdehyde (CXII) [35, 36]. According to its spectral characteristics, compound (CXIV) contained and α,β-unsaturated aldehyde group and an acetoxymethyl group. On reduction with lithium tetrahydroaluminate, it also was converted into the diol (CXIII), which is a proof of its structure. The aldehydoacetate (CXIV) has been synthesized [35] from the acetate of the alcohol (XLVIII). On oxidation with selenium dioxide, it gave, together with other substances, the hydroxy acetate (XCIV), the further oxidation of which by the chromium trioxide/pyridine complex



led to the aldehydo acetate (CXIV). The racemic hydroxy acetate (XCIV) has been synthesized from the (±)-diol (XCIII) by the selective protection of the C-hydroxy group with a tert-butyldimethylsilyl group, acetylation of the C_{15}-hydroxy group, and elimination of the silyl protective group by acid hydrolysis [36]. The structure of the dialdehyde (CXV) followed from its formation by the isomerization of the dialdehyde (CXIII) with alkaline alumina. Its synthesis was achieved by the oxidation of the glycol (CXVII) with the chromium trioxide/pyridine complex [35]. The glycol (CXVII) is the product of the interaction of the alcohol (XLIX) with selenium dioxide.

The structure and stereochemistry of the metabolite (CXVI) were determined on the basis of its transformation on heating in benzene in the presence of silica gel into the isoagathofuran (CX) and the closeness of the values of the chemical shifts of the same atoms in the ^{13}C NMR spectrum of aplysillin (CXVIII), a diterpenoid isolated from the sponge Aplysilla rosea [40], the structure and stereochemistry of which have been shown by x-ray structural analysis. On pyrolysis, aplysillin was converted into the vinylfuran (CXIX), an enantiomer of which has been synthesized from the ester of (CXVIII) [32]. Under the action of sodium ethanolate, the mesylate (CXXI) of the product of its reduction – the alcohol (CXX) – gave the diene (CXXII). When this was subjected to photolysis in the presence of Rose Bengal and the product was reduced with trimethyl phosphite, the dienol (CXXIII) was formed. Photolysis of the latter under the same conditions and reduction of the photolysate with ferrous sulfate led to the hydroxyfuran (CXXIV), which was dehydrated by toluenesulfonic acid to the vinylfuran (CXXV). However, the absolute configuration of aplysillin (CXVII) remained unelucidated, since the specific rotation of the vinylfuran (CXIX) was unknown.

In the nudibranchiate mollusc Archidoris montereyensis [41] the isoagathane glyceride (CXXVI) has been detected. Its structure and relative stereochemistry have been determined by x-ray structural analysis, and its absolute configuration by the formation of the alcohol (XLVIII) on its reduction with diisobutylaluminum hydride.

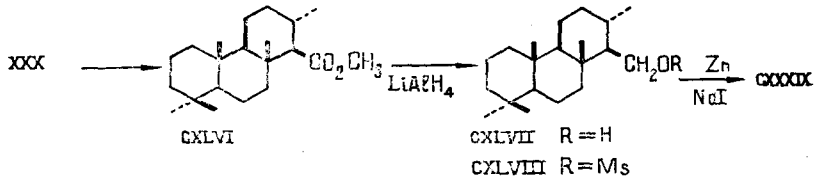
So far, a single halogen-containing agathane derivative is known. This is isoaplysin-20 (CXXVII), which has been isolated from the sea have Aplysia kurodai [42]. Its structure and relative configuration at all the chiral centers apart from C_{13} have been established on the basis of a study of the spectral characteristics of the compound itself and of its mono-acetate (CXXVIII), and a comparison of them with those of the aplysin-20 (CXXIX) isolated from the same source [43]. To determine the configuration of isoaplysin-20 at C_{13}, the epimeric diols (CXXXIV) and (CXXXVI) and their acetates (CXXVII) and (CXXXVIII) were synthesized [44]. The first of them was obtained from the ester (CXVIII) in a manner similar to that by which its enantiomer was obtained [45]. The ester (CXVIII) was hydroxylated by osmic acid to the dihydroxy ester (CXXX) which, on interaction with dimethyl sulfoxide and acetic anhydride, gave the keto ether-ester (CXXXI). Its thioketal (CXXXII) was disulfurated with Raney nickel to the hydroxy ester (CXXIII), which was reduced with lithium tetrahydroaluminate to the epoxy alcohol (CXXV) – the product of the epoxidation of the alcohol (CXX) with m-chloroperbenzoic acid. The ^1H and ^{13}C NMR spectra of the diol (CXXXIV) and its acetate (CXXXVII) were similar to the spectra of isoaplysin-20 (CXXVII) and its acetate (CXXVIII), and the changes in the chemical shifts of the protons of the C_{15}-methylene group and the C_8-methyl group on passing from the diols to their monoacetates were identical.

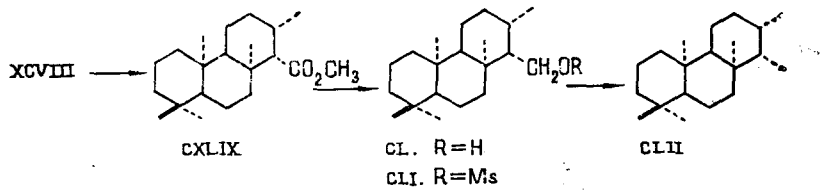
Isoaplysin-20 is the first diterpenoid of the ent-isoagathane series. However, it must be mentioned that its absolute configuration was adopted only on the basis of biogenetic considerations (isoaplysin-20 is found together with aplysin-20 in the sea hare) but has not been strictly demonstrated.

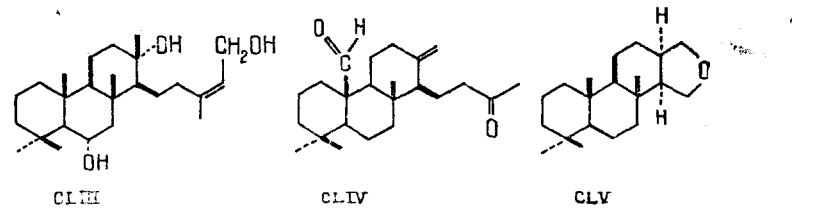
In addition to marine organisms, a number of mineral sources of isoagathane compounds is known. These are petroleum, oil-bearing sands, and other combustible minerals in which isoagathane hydrocarbons have been detected. Aquinto Neto et al. [46] have shown that in these combustible minerals the predominating diterpene is 13S,14R-isoagathane (CXXXIX), but its diastereoisomers (CXL)-(CXLII) are also present in small amounts. They were all identified by comparison with the corresponding authentic synthetic samples. However, only the synthesis, and this a fairly complex one, of the isomer (CXXXIX) is given in [46]. The starting material was the triterpene (CXLIII). On pyrolysis in the presence of alkali, the product of its oxidation by ruthenium tetroxide gave the ketone (CXLIV), which was converted in eight stages into the hydrocarbon (CXLV). This was hydrogenated over platinum oxide in acetic acid to the isoagathane (CXXXIX). 13S,14R-Isoagathane has been synthesized far more simply from the ester (XXX) [47]. On its hydrogenation in pentane over palladium

on carbon, the main product was the ester (CXLVI). It was purified by chromatography and via the alcohol (CXLVII) and its mesylate (CXLVIII) was reduced to 13S,14R-isoagathane (CXXXIX).

Ruveda et al. [32] have described the synthesis of an enantiomer of (CLII), 13R,14R-isoagathane (CXL). The ester (CXVIII) was hydrogenated stereodirectively over platinum oxide in methanol to the ester (CXLIX) [45]. It was reduced with lithium tetrahydroaluminate to the alcohol (CL), the mesylate of which (CLI) with lithium in liquid ammonia gave 13S,14S-ent-isoagathane (CLII).







The hydrocarbon (CXXXIX) is apparently a product of the cleavage of higher terpenes with an aliphatic chain at C_{14}, since its C_{19}-C_{45} homologues have been isolated from petroleum oils and oil-bearing sands [48, 49]. All these compounds are of interest as biolgoical labels of combustible minerals, although their origin has not yet been elucidated.

It can be seen from the facts presented that the subgroup of isoagathane diterpenoids is relatively few in number. However, the rate of accumulation of factual material in this series of substances is increasing with each year. A specific feature of these compounds is the fact that they have all been isolated from marine organisms, but have not yet been detected in plants. Although definite information has accumulated on the chemistry of these diterpenoids, the synthesis of the most complex of them has not been performed. Their biosynthesis has also remained completely unstudied.

The isoagathane hydrocarbon skeleton (I) is a structural fragment of several higher terpenoids – for example, the sesterterpenoid cheilanthatriol (CLIII) [50, 51], and the bisnorsesterterpenoid luteone (CLIV) [52, 53]. The isoagathane diterpenoids may therefore be considered as the initial compounds for their synthesis, just as the methods of obtaining isoagathanoids may be suitable for the synthesis of these higher terpenoids.

In conclusion, a few words on the nomenclature of the isoagathanoids described above. Although not many of them are yet known, there is already a fair amount of confusion in their nomenclature. Thus, to denote the hydrocarbon (I) in some publications [9, 14] the name "isoagathane" is used, and in other [39, 45] "ent-isocopalane," while in yet others substances in which the isoagathane skeleton includes a tetrahydrofuran ring are considered (in our view quite unjustifiably if the nomenclature in other subgroups of diterpenoids such as the labdane series is considered) as derivatives of a new heterocyclic system (CLV), for which the name "spongian" has been proposed [32, 37, 39]. We consider that the names of the diterpenoids of this subgroup should be derived from the name of its ancestor – iso-

agathic acid (VIII) – i.e., they should all be considered as derivatives of the hydrocarbon isoagathane (I) and its enantiomer.

LITERATURE CITED

1. A. G. Gonzalez, J. Darias, and J. D. Martin, Tetrahedron Lett., 2729 (1971).
2. L. Ruzicka and J. R. Hosking, Helv. Chim. Acta, 13, 1402 (1930).
3. L. Ruzicka and J. R. Hosking, Helv. Chim. Acta, 14, 203 (1931).
4. J. R. Hosking and C. W. Brandt, Chem. Ber. 68, 37 (1935).
5. L. Ruzicka, L. L. Engel, and W. H. Fischer, Helv. Chim. Acta, 21, 364 (1938).
6. C. Asselineau, S. Bory, M. Fétizon, and P. Laszlo, Bull. Soc. Chim. Fr., 1429 (1961).
7. S. Bory, M. Fétizon, and P. Laszlo, Bull. Soc. Chim. Fr., 2310 (1963).
8. H. E. Audier, S. Bory, and M. Fétizon, N. T. Anh, Bull. Soc. Chim. Fr., 4002 (1966).
9. S. Bory, Duc Do Khac Manh, M. Fétizon, M. Kone, and N. T. Anh, Bull. Soc. Chim. Fr., 2347 (1975).
10. M. Fetizon and N. Ragoussis, Tetrahedron, 34, 287 (1978).
11. P. F. Vlad, Izv. Akad. Nauk MoldSSSR, Ser. Biol. Khim. Nauk, No. 2, 67 (1977).
12. P. F. Vlad, N. D. Ungur, and M. N. Koltsa, Khim. Prir. Soedin., 581 (1979).
13. P. F. Vlad, N. D. Ungur, and M. N. Koltsa, Tetrahedron, 39, 3947 (1983).
14. G. Cimino, D. de Rosa, S. de Stefano, and L. Minale, Tetrahedron, 30, 645 (1974).
15. A. Caliezi and H. Schinz, Helv. Chim. Acta, 35, 1649 (1952).
16. E. E. van Tamelen and R. G. Nadeau, J. Am. Chem. Soc., 89, 176 (1967).
17. E. E. van Tamelen and S. A. Marson, J. Am. Chem. Soc., 97, 5614 (1975).
18. N. Nishizawa, H. Takenaka, and Y. Hayashi, Chem. Lett., 1459 (1983).
19. E. J. Corey and R. A. Sneen, J. Am. Chem. Soc., 77, 2505 (1955).
20. R. B. Turner, W. R. Meador, and R. E. Winkler, J. Am. Chem. Soc., 79, 4122 (1957).
21. A. G. Gonzalez, J. Darias, J. D. Martin, and C. Pascual, Tetrahedron, 29, 1605 (1973).
22. A. G. Gonzalez and J. D. Martin, Tetrahedron Lett., 2259 (1972).
23. A. G. Gonzalez, M. A. Alvarez, J. Darias, and J. D. Martin, J. Chem. Soc., Perkin Trans., No. 1, 2637 (1973).
24. A. G. Gonzalez, J. D. Martin, and M. L. Rodriquez, Tetrahedron Lett., 3567 (1973).
25. A. G. Gonzalez, J. D. Martin, and M. L. Rodriguez, An. Quim. Real Soc. Esp. Fis. Quim., 72, 1004 (1976).
26. W. H. Gerwick, and W. Fenical, J. Org. Chem., 46, 22 (1981).
27. A. G. Gonzalez, J. Darias, and J. D. Martin, An. Quim. Rea. Soc. Esp. Fiz. Quim., 68, 1187 (1972).
28. W. H. Gerwick, W. Fenical, N. Fritsch, and J. Clardy, Tetrahedron Lett., 147 (1974).
29. A. G. Gonzalez, M. A. Alvarez, J. D. Martin, M. Norte, C. Perez, and J. Rovirosa, Tetrahedron 38, 719 (1982).
30. J. C. Braekman, D. Daloze, G. Hulot, B. Tursch, J. P. Declerq, G. Germain, and M. van Meerssche, Bull. Soc. Chim. Belg., 87, 917 (1978).
31. P. M. Imamura, M. G. Sierra, and E. A. Ruveda, J. Chem. Soc., Chem. Commun., 734 (1981).
32. D. S. de Miranda, G. Brendolan, P. M. Imamura, M. G. Sierra, A. J. Marsaioli, and E. A. Ruveda, J. Org. Chem., 46, 4851 (1981).
33. T. Nakano, M. I. Hernandez, Tetrahedron Lett., 23, 1423 (1982).
34. T. Nakano, and M. I. Hernandez, J. Chem. Soc., Perkin Trans., No. 1, 135 (1983).
35. P. F. Vlad and N. D. Ungur, Abstracts of the 14th International Symposium on the Chemistry of Natural Productsm, Poznan, Vol. 1 (1984), p. 282.
36. M. P. Mischne, M. G. Sierra, and E. A. Ruveda, J. Org. Chem., 49, 2035 (1984).
37. R. Kazlauskas, P. T. Murphy, R. J. Wells, K. Noack, W. E. Oberhänsli, and P. Schonholzer, Aust. J. Chem., 32, 867 (1979).
38. N. Capella, J. C. Braekman, D. Daloze, and B. Tursch, Bull. Soc. Chim. Belg., 89, 399 (1980).
39. G. Cimino, R. Morrone, and G. Sodano, Tetrahedron Lett., 23, 4139 (1982).
40. R. Kazlauskas, P. T. Murphy, and R. J. Wells, Tetrahedron Lett., 903 (1970).
41. K. Gustafson, R. J. Andersen, M. H. M. Chen, J. Clardy, and J. E. Hochlowski, Tetrahedron Lett., 25, 11 (1984).
42. S. Yamamura and Y. Terada, Tetrahedron Lett., 2171 (1977).
43. S. Yamamura and Y. Hirata, Bull. Soc. Chim. Jpn., 44, 2560 (1971).
44. P. M. Imamura and E. A. Ruveda, J. Org. Chem., 45, 510 (1980).
45. Do Khae Manh Duc, M. Fétizon, and M. Kone, Bull. Soc. Chim. Fr., 2351 (1975).
46. F. R. Aquinto Neto, A. Restle, J. Connan, P. Albrecht, and G. Ourison, Tetrahedron Lett., 2027 (1982).

47. T. D. Cyr and O. P. Strausz, J. Chem. Soc., Chem. Commun., 1028 (1983).
48. M. G. Sierra, R. M. Cravero, M. de los Angeles Laborde, and E. A. Ruveda, J. Chem. Soc., Chem. Commun., 417 (1984).
49. D. Heissler, R. Ocampo, P. Albrecht, J. J. Riehl, and G. Ourisson, J. Chem. Soc., Chem., Commun. 496 (1984).
50. H. Khan, A. Zeman, G. L. Chetty, A. S. Gupta, and S. Dev. Tetrahedron Lett., 4443 (1971).
51. A. S. Gupta, S. Dev, M. Sangare, B. Septe, and G. Lukacs, Bull. Soc. Chim. Fr., 1879 (1976).
52. J. Hellou, R. J. Andersen, S. Rofli, E. Arnold, and J. Clardy, Tetrahedron Lett., 4173 (1981).
53. J. Hellou, R. J. Andersen, and J. E. Thomson, Tetrahedron, 38, 1875 (1982).

POLYSACCHARIDES OF IRIDACEAE

IV. A XYLOGLUCOGALACTAN OF THE BULBS OF Juno drepanophylla

Kh. A. Arifkhodzhaev

UDC 547.917

Polysaccharides (WSPSs, PSs, and HMCs) have been isolated from various organs of Juno Drepanophylla and their qualitative compositions have been characterized. ESPS-I from the bulbs has been studied and has proved to be a polydisperse high-molecular-weight and branched amyloid. In its physicochemical properties and composition, WSPS-I is close to amyloids of the first class known from the literature. On the basis of the results of methylation, oxidation with chromium trioxide, and IR and ^{13}C NMR spectra, it has been established that the glucopyranose residues are linked with one another by β-(1 → 4) bonds, and the xylo and galactopyranose residues by α(1 → 4) bonds with the C-6 position of the glucose residue.

Plants from the family Iridaceae of the genus Juno Tratt, are rich in polysaccharides [1]. In the present paper we give the results of investigations of the polysaccharides of the Juno drepanophylla (Aitch. et Baker) Rodion. From various organs of the plant the ethanol-soluble (ES) sugars, the water-soluble polysaccharides (WSPSs), the pectin substances (PSs), and the alkali-soluble polysaccharides (hemicelluloses – HMCs) were extracted successively. The amounts of the polysaccharides and their monosaccharide compositions are given in Table 1. The amounts of ES sugars were (%): in the bulbs with roots – 5.5; leaves – 1.2; and seeds – 2.2. The presence of monosaccharides (glucose, fructose), sucrose, and unidentified fructooligosaccharides was detected with the aid of paper chromatography.

As can be seen from Table 1, the amount of WSPSs in the bulbs with roots was the greatest, which served as an argument for their further investigation.

WSPS-I was obtained by precipitation from aqueous solution with methanol (1:4), and WSPS-II was isolated additionally from the mother solution with a mixture of methanol and acetone (3:2).

The ash content of WSPS-I was 0.23-0.3% and they contained no nitrogen or methoxy groups; $[\alpha]_{546}$ +66.7° (c 0.25; water), +56.4° (c 0.25; 0.5% KOH).

Analysis in the ultracentrifuge, gel chromatography on Sepharose-4B, and the high-pressure liquid chromatography (LC) of WSPS-I showed their inhomogeneity. For a 1% solution of WSPS-I in 0.3% sodium chloride in the ultracentrifuge, S was found to be $10.3 \cdot 10^{-13}$ sec, and D $4.6 \cdot 10^{-7}$ cm^2/sec, giving a discrete peak on the sedimentogram.

On a column containing Sephadex G-100 and on Sepharose-4B, WSPS-I emerged earlier than dextran with a molecular weight of 2 million.

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 410-415, July-August, 1986. Original article submitted February 28, 1986.

 0009-3130/86/2204-0380$12.50