RECENT ADVANCES IN THE FIELD OF THE SYNTHESIS OF JUVENILE HORMONES

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The review considers recent advances in the field of the synthesis of juvenile hormones – briefly with respect to fundamental investigations up to 1975, and in more detail in relation to studies of the last 8-10 years, including investigations by the authors.

It is well known that the life cycle of an insect is represented in the general case by a jump-like development according to the scheme egg → larva → pupa → adult individual (imago). Within this scheme its last two stages are controlled by a complex endocrine system through a series of hormonal substances of different natures. In the very first moments, the neurosecretory cells of the brain begin to secrete a polypeptide hormone, the so-called activation hormone (AH), which stimulates the whole succeeding process of this stage. Under the influence of the AH the prothoracal glands elaborate ecdysteroid hormones causing the development and growth of the larva, which is accompanied by molting. Simultaneously, the AH also penetrates into the adjacent bodies that secrete the juvenile hormone (JH), which counteracts the molting hormones and prevents metamorphosis with retention of the larval nature of development. The molting hormones and the JH act in balanced fashion only in the larval stage. In the pupal molt, the concentration of JH falls. The imaginal molt is possible only in the absence of the JH. The introduction into the insect organism of JH in the preimaginal period stops metamorphosis or causes additional molts and the appearance of gigantic forms which, as a rule, are not viable.

The brief excursion into the physiology of the important stages of the development of the insect that has been given indicates the important and hitherto far from elucidated role that the JH plays here, which, in its turn, means that it is necessary to know at least the structures of these low-molecular-weight bioregulators. However, it must be mentioned that even long before the structures of such molecules were established, a series of natural synthetic compounds with juvenile-hormonal activity were found which were subsequently given the name "juvenoids" [1]. The JHs and their analogs exert an action on insects both when injected and on local application. In view of this, the attractive prospect has recently arisen of creating basically new agents for the fight against insect pests – insecticides with a hormonal action – and this has led in the last two decades to numerous investigations on the synthesis both of the JHs themselves and of juvenoids in general, which today form some of the most important representatives of the "pesticides of the third generation." The first information on the structure and physiological action of the JHs was obtained little more than 20 years ago thanks to advances in the field of the biochemistry and endocrinology of insects, and also to the development of fine organic synthesis, including instrumental methods for it. Monographs and reviews in large number have been devoted to all these questions [1-7] but they have generalized the enormous amount of factual material existing only up to the beginning of 1975. In the present review we consider recent advances in the field of the synthesis of JHs – briefly in relation to the fundamental investigations up to 1975 and in more detail for the work of the last 8-10 years.

At the present time, four JHs have been isolated that are all derivatives of methyl farnesoate; the simplest of them is its monoepoxide – JH III (8). In addition, the corresponding mono-, bis-, and trishomo derivatives are known – JH II [9], JH I [10], and JH 0 [11], and all of which possess the 2E,6E-geometry of the C=C bonds [8, 11, 12] and the 10R,11S-configuration of the epoxide fragment [13-17].

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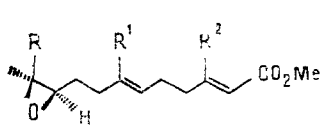


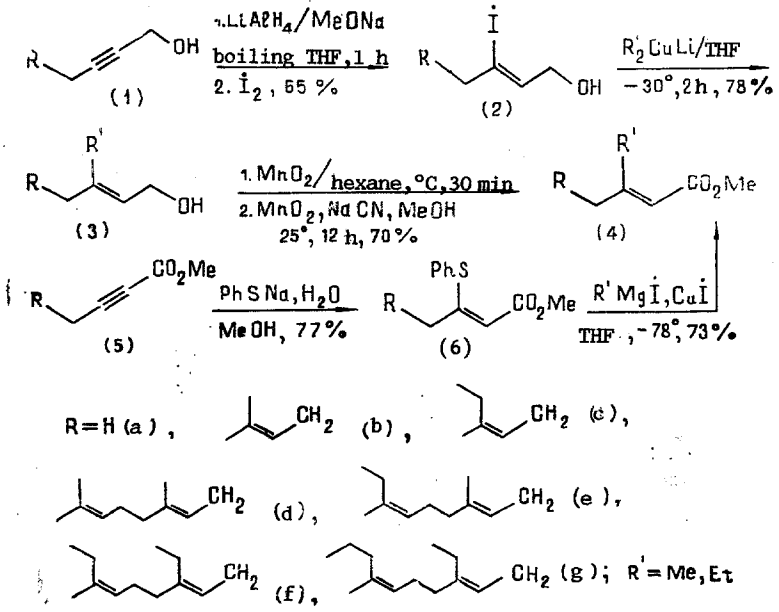
$R = R^1 = R^2 = Me$ (JH III)
$R = Et, R^1 = R^2 = Me$ (JH II)
$R = R^1 = Et, R^2 = Me$ (JH I)
$R = R^1 = R^2 = Et$ (JH 0)

Generalized results of investigations [1] of the dependence of the biological action of the JHs on the stereochemistry of their double bonds indicate that maximum activity is exhibited primarily by the 2E,6E-isomers. The first stereospecific synthesis of (±)-JH I was performed in 1968 [18]. At the present time, something like fifteen schemes have been proposed for the construction of its molecule that are suitable in some degree or other for the synthesis of the other three representatives of the JHs, all these schemes being based on various stereospecific methods of introducing a trisubstituted double bond into an already created farnesane chain. The concluding stage of the selective introduction of a terminal oxide is usually performed by van Tamelen's method via an intermediate bromohydrin [19, 20] or by the epoxidation of the corresponding triene with the aid of a selected paracid [12, 19].

SYNTHESIS OF JHs FROM ACETYLENES

The active development of the chemistry of organocuprate reagents that was observed in the middle sixties, permitting, in particular, the creation of trisubstituted olefins directly from acetylenes [21], almost immediately found application for the stereospecific synthesis of various terpanoids, including JHs.

In his pioneer study, Corey [18] proposed an approach for the stereospecific construction of a trisubstituted C=C bond starting from propargyl alcohols (1) (scheme 1). Their hydroalumination and the subsequent replacement of a C–Al bond by a C–I bond takes place strictly regio- and stereospecifically, smoothly giving the 2-vinyl iodides (2). The cuprate alkylation of the latter with retention of the geometry of the olefin is performed with high yields of the alcohols (3), which has opened up a universal route to the preparation from the disubstituted acetylenes (1a-f) of the whole set of JHs known today and some of their derivatives. The two-stage passage from the allyl alcohols (3) to the corresponding methyl esters (4) – for example, from (3f, R' = Me) to JH I, obtained with an overall yield of ∿1% [18] – includes the oxidation of the intermediate aldehydes with a mixture of MnO_2 and NaCN in MeOH by Corey's method [22].

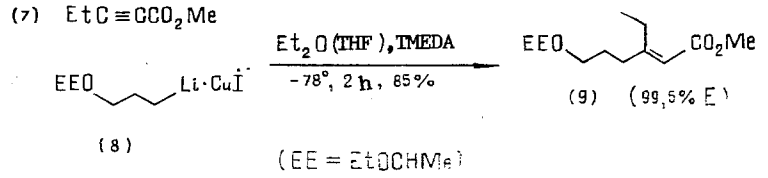


Scheme 1

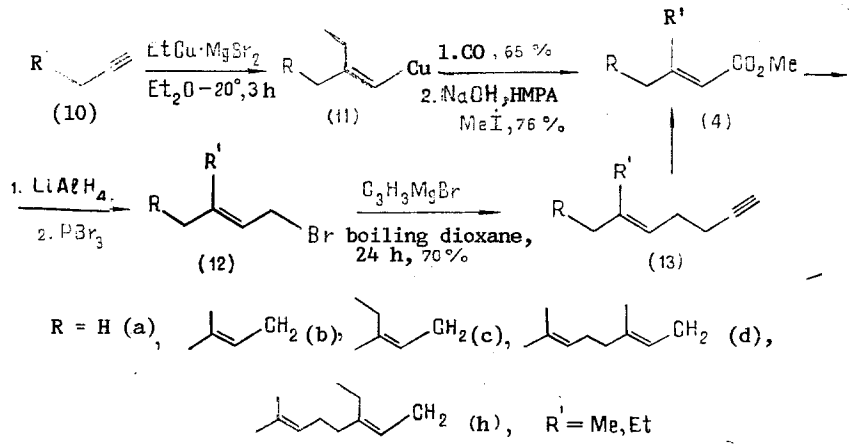
A related approach to the esters (4d-g, R' = Me) and, consequently, to the series of JHs and some of their analogs is based on the reaction of organocuprates with vinyl sulfides (6), which are readily formed by the Michael addition of a thiophenolate to substituted propiolates (5) [23, 24]. Here we must particularly emphasize the high (93-95%) stereospecifity

of all the transformations considered, leading to the formation of trisubstituted C=C bonds.

The possibility of using acetylenes and organocopper compounds in the synthesis of JHs is far from exhausted by the examples given. A stereospecific method of creating trisubstituted olefins by the syn addition of organocuprates to (un)activated C=C bonds that is extremely popular at the present time has practically always been developed in its application to these substances. Thus, the reaction of the ester (7) with the cuprate (8) stabilized by tetramethylethylenediamine (TMEDA) takes place under mild conditions giving a high yield of the E-ethoxyethyl ester (9) – an intermediate in one of the schemes (see below) for the complete synthesis of JH 0 [25].

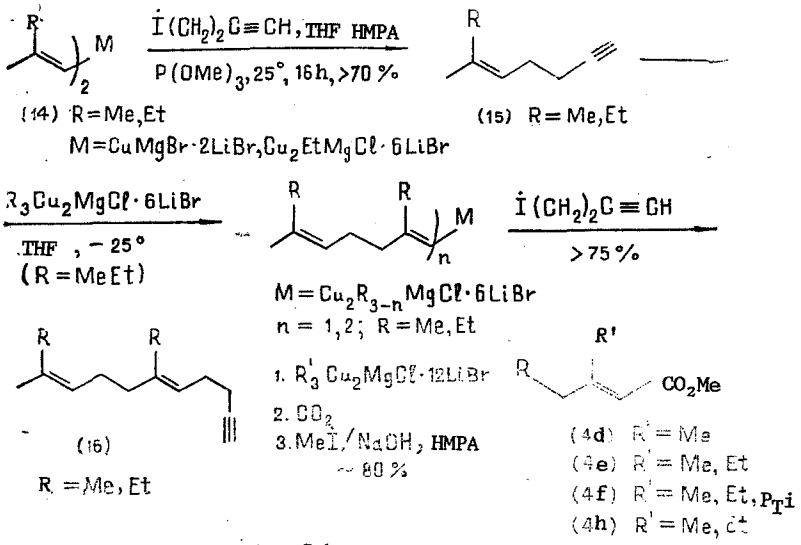


α,β-Unsaturated esters of type (4) can easily be obtained by the concerted addition of a suitable organocopper compound and CO_2 to selected monosubstituted acetylenes (10) [26] (scheme 2). As a result, the trisubstituted olefins (4, R' = Et) are smoothly formed through the stage of the vinyl cuprates (11). The passage from the latter to their (homo)prenologs. by the same scheme – for example, from (4a, R' = Et) and (4b, R' = Me, Et) to (4c) and (4d, h), respectively, includes the standard synthesis of the allyl bromides (12) and the further growth of the chain by a three-carbon fragment with the aid of propargylmagnesium bromide to form the 1,5-vinylacetylenes (13). Thus, depending on the nature of the initial (10) or intermediate (15) substances, satisfactory (20-50%) yields have been obtained of a series of α,β-unsaturated esters (4) – in particular, the methyl farnesoate derivatives (4d, h, R' = Et), and, consequently, also the corresponding JH analogs.



Scheme 2

One universal method of constructing the farnesane chain with the object of synthesizing JHs and a number of related substances has recently been proposed in connection with a study of some feature of the concerted addition of higher organocuprates to monosubstituted acetylenes [27] (scheme 3). Thus, the treatment with 4-iodobutyne, obtained in situ from propyne (10a), of the organometallic intermediates (14) leads under reported conditions with a high yield to the 1,5-enynes (15). Repetition of these operations using trialkyl dicuprates and the same electrophilic agent gives the homologous acetylenes (16). The replacement in the concerted addition to the latter of 4-iodobutyne by CO_2 leads in the final account to methyl farnesoate (4d) and to a series of derivatives given in the scheme (4e, f, h) (overall yield ~40%), which are then readily transformed into the corresponding JH I–JH III and their analogs.

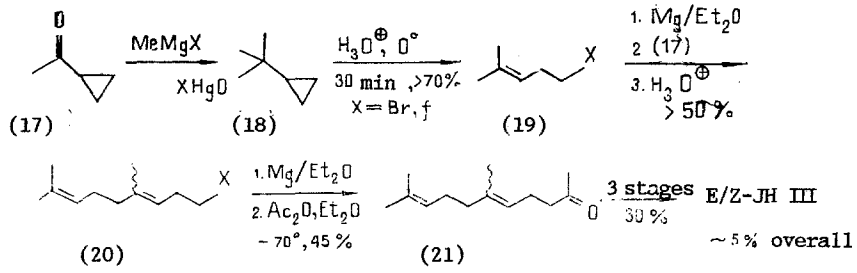


Scheme 3

Thus, the investigations considered illustrate the interest that has arisen in recent years in the use for the synthesis of JHs of various cuprate reagents the reaction of which with various acetylene derivatives permits the regio- and stereoselective creation of the farnesane skeleton of the desired molecules with good overall yields.

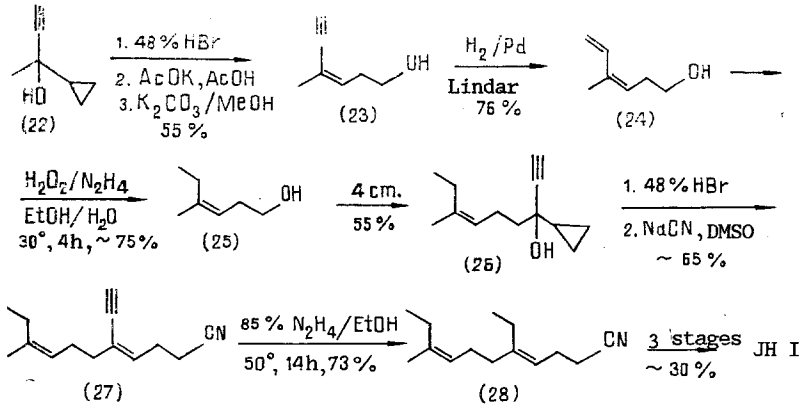
SYNTHESES OF THE JHs USING SOME SIGMATROPIC REACTIONS

The analysis of literature material on the question under discussion indicates the continuing interest in the use of various sigmatropic rearrangements for the given purpose. In particular, a modification has recently been proposed [28] of the two-stage method of obtaining homoallyl halides from the corresponding cyclopropyl ketones by the Julia-Johnson method [29, 30] used previously in investigations by these authors on the synthesis of various terpenoids, including JHs [6-7]. The proposed modification consists in decomposing with moderately dilute mineral acid the product (18) initially formed from cyclopropyl methyl ketone (17) by the Grignard reaction, which permits the reactive homoallyl halides (19) to be obtained directly and smoothly without passing through the corresponding alcohols (scheme 4). A repetition of these operations leads, via the stage of the halide (20) and the ketone (21) to JH III with an overall yield of ∿5% [31]. A disadvantage of the approach to the synthesis of JHs that has been described remains, as before, the nonstereospecificity of the key operations, including the cyclopropylcarbinyl → homoallyl rearrangement.



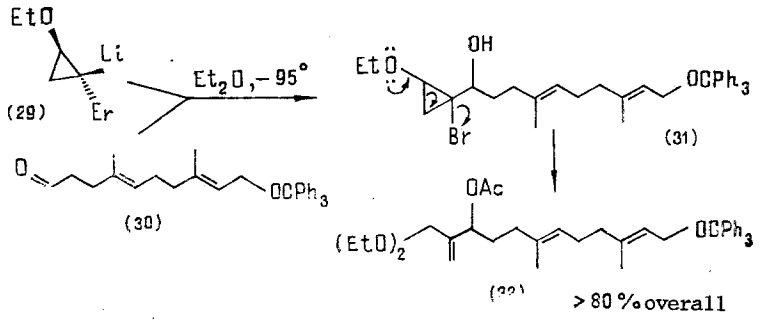
Scheme 4

Of other studies during the last 10 years on the use of this rearrangement, we must mention Mori's synthesis of JH I starting from the acetylenic alcohol (22) (scheme 5) [32, 33]. An interesting feature of this scheme was its unexpectedly high stereospecificity, leading in the final account to the Z-carbinol (23) with ∿5% of the R isomer as impurity. The selective hydrogenation of the enyne (23) to the intermediate 1,3-diene (24) and its subsequent diazene reduction gave the Z-homoallyl alcohol (25). Passage from the latter to the cyanide (27) via the stage of the carbinol (26) was effected with an overall yield of ∿35%. The obvious intermediate (28) in the synthesis of the desired JH I was obtained by the severe diazene reduction of (27), its overall yield amounting to ∿2%.



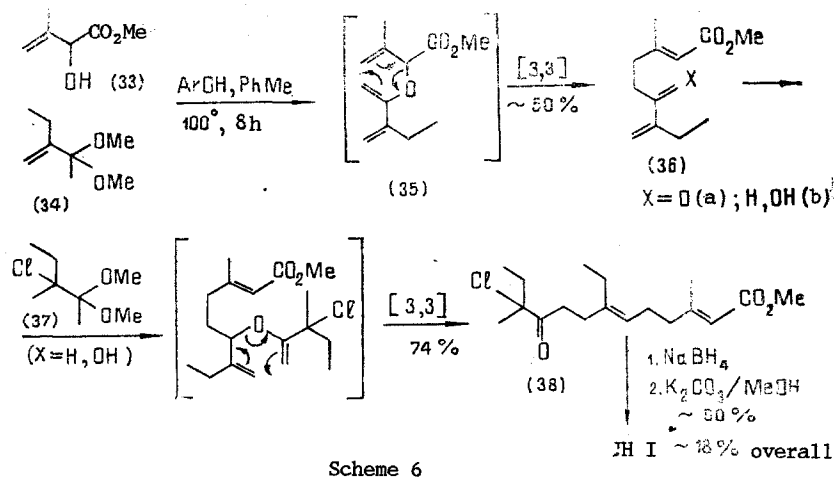
Scheme 5

We must also mention one more example of the continuing use of the isomerization of cyclopropanes in the synthesis of JHs. Thus, when the lithium derivative (29) arising on the treatment of 1,1-dibromo-3-ethoxycyclopropane with Bu^nLi was brought into reaction with the aldehyde (30), readily obtainable from the trityl ether of farnesol, the bromohydrin (31) was smoothly formed, and this was converted in two simple operations with high yield into the acetal (32) [34]. The first stage of this interesting transformation takes place with the simultaneous opening of the cyclopropane ring and the splitting out of Br^- via the intermediate allyl carbocation [35]. The passage from (32) to JH III will be discussed below.



Of other variants of the reorganization of a carbon skeleton for the purposes of the stereospecific construction of the molecules under discussion, at the present time, as previously, attention continues to be attracted by a Claisen-type rearrangement of vinyl allyl ethers [36], the possibilities of which were demonstrated by Johnson's group as early as 1970 [37, 38] for, as examples, the synthesis of JH I and its 10E isomer. It was shown then (scheme 6) that the cothermolysis of the allyl alcohol (33) and the acetal (34) catalyzed by a mild acid, such as 2,4-dinitrophenol, gave with good yield – apparently through the intermediate (35) – the vinyl ketone (36a), readily reducible to the corresponding allyl alcohol (36b). Repetition of the same operation with the latter but with the participation of the chloroacetal (37) led to the α-chloro ketone (38) – an obvious precursor of JH I. Here we must mention the very high stereospecificity of the rearrangement under discussion; in particular, the diene (38) contains > 98% of the E,E isomer.

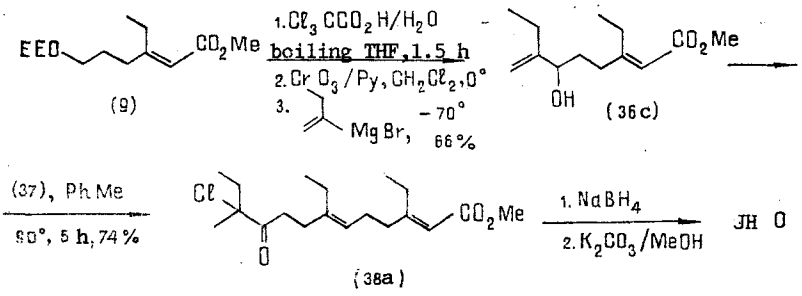
It must be emphasized that the use of just the chloroacetal (37) in the form of its antipodes enabled Johnson for the first time [14], in accordance with scheme 6, to perform the total synthesis of all four possible 10,11-oxides (JH I and its epimers) of methyl bishomofarnesoate (4f, R' = Me) by the $NaBH_4$ reduction of the R- and S-chloroketones (38) to the corresponding pairs of erythro- and threo-chlorohydrins, and these were separated by preparative TLC on Al_2O_3 with the aim of their subsequent cyclization. A little later (∿3 months) [15] it was shown that of the four substances obtained, the 10R,11S-(+) isomer corresponded to the native JH I.



Scheme 6

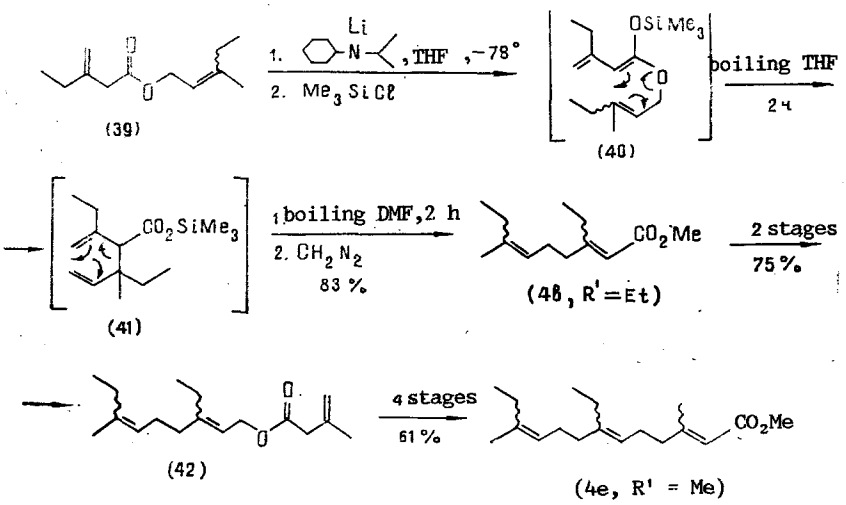
It is interesting to note that in the last eight years only one paper [39] has appeared on the synthesis of optically active forms of the JHs. In this, following a methodology developed previously [40, 41], (±)-JH III was subjected to enzymatic hydrolysis with the aid of the mycelium of the fungus Colletotrichum nicotianae, and the chiral glycols obtained were converted into the oxides corresponding to them by standard chemical methods.

In accordance with the approach described, the selective elimination of the ethoxyethyl protection in the molecule of the diether (9), the oxidation of the alcohol formed to the aldehyde, and its subsequent treatment with but-2-enylmagnesium bromide led to the allyl alcohol (36c). A subsequent rearrangement of the Claisen type using the chloroacetal (37) gave the chloroketone (38a) in high yield, and this was then converted in two obvious stages into JH 0 [25]. The latter was synthesized in this way at least five years after the identification of this hormone in the cells of developing embryos of the hawk-moth Manduca sexta.

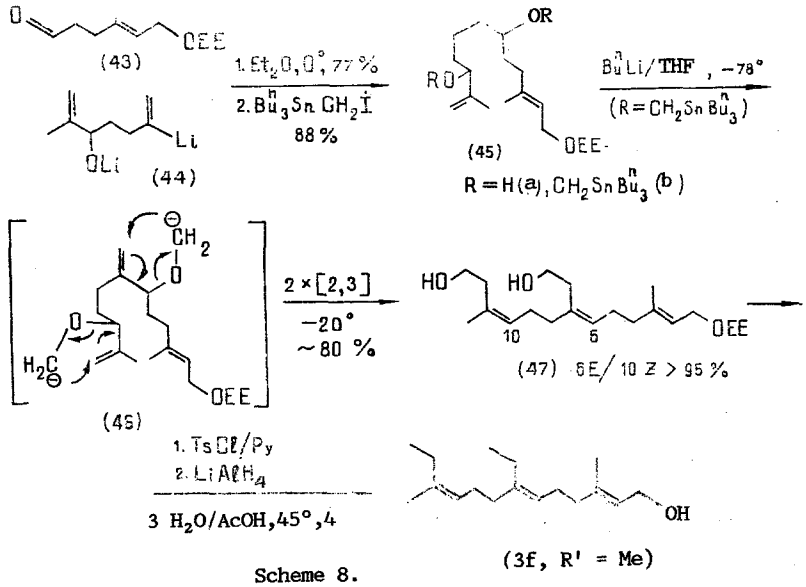


Comparatively recently [42], a nonstereospecific synthesis of JH I based on the [3,3]-sigmatropic rearrangement of allyl ethers of 3-methylenealkanoic acids has been proposed (scheme 7). For example, the protonation and the subsequent silylation of the ether (39) led to the ketene acetal (40) which, in boiling THF, underwent a rearrangement of the Claisen type to the diene (41), and this, without isolation, was subjected to a Cope rearrangement in boiling DMF. The resulting mixture of ethers (4c, R' = Et) was converted into the 3-methylenebutyrates (42) from which, by the same scheme, a mixture of all the possible geometric isomers of methyl bishomofarnesoate (4f, R' = Me) was obtained in a ratio EEE:EEZ:EZE:EZZ:ZEE:ZEZ:ZZE:ZZZ = 9:7:14:11:17:13:16:13.

Let us consider an exceptionally stereospecific method of constructing a precursor of JH I – bishomofarnesol (3f, R' = Me) – by a sigmatropic Wittig rearrangement that was first used for this purpose (scheme 8). The starting material in this case was the bisallyl alcohol (45a), obtained smoothly from the aldehyde (43) and the dilithium derivative (44). The metallation of the bis(tri-n-butylstannyl methyl ether) (45b) took place under extremely mild conditions and was accompanied by the double rearrangement mentioned, obviously with the participation of the intermediate (46). The resulting glycol (47), formed with a yield of ∿80%, was then converted in three simple operations, including the hydrogenolysis of the ditosylate and the elimination of the ethoxyethyl protection, into the desired allyl alcohol (3f, R' = Me).



Scheme 7.

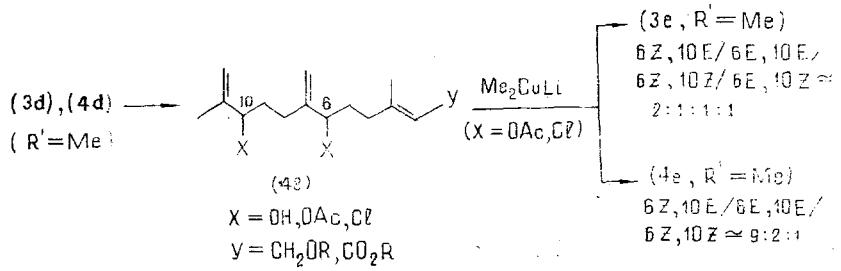


Scheme 8.

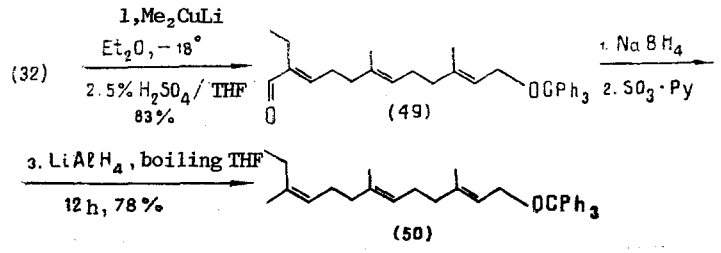
The transformations considered thus indicate the exceptional usefulness of a number of known sigmatropic rearrangements for constructing the farnesane skeleton of the JHs.

STEREOSPECIFIC HOMOLOGIZATION OF E,E-FARNESOL DERIVATIVES

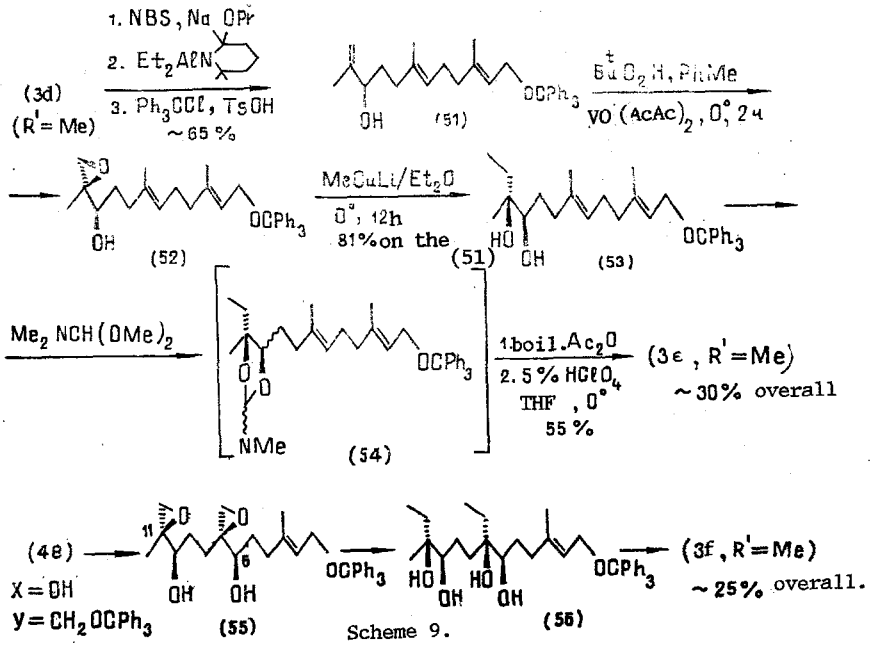
The comparatively readily accessible E,E-farnesol (3d, R' = Me) and methyl E,E-farnesoate (4d, R' = Me), which are obvious precursors of JH III, continue to be considered as extremely attractive synthons for constructing other representatives of the JHs by the most economic possible stereospecific homologization of these sesquiterpenes. The basic four-stage scheme for solving this problem was published in early papers [44-47] based on the isomerization of the 6,10-dihydroxides of the olefins (3d, 4d, R' = Me) to the allyl alcohols corresponding to them, the acetates of which or the corresponding allyl chlorides were subjected to an alkylation of the S_n2' type under the action of Me_2CuLi. However, in view mainly of the non-stereospecific nature of the first stage of the direct epoxidation of the initial trienes, the subsequent bisallyl derivatives (48) proved to be mixtures of diastereomers, and the homologs finally obtained (3f, 4f, R' = Me) consisted of mixtures of geometric isomers [44, 45].



The alkylation of the allyl acetate (32), which is free from such a limitation, gave, after selective elimination of the acetal protection, an almost quantitative yield of the unsaturated 10E-aldehyde (49). The latter was converted by standard methods for terpene chemistry into a precursor of JH II – the trityl ether of homofarnesol (50) [34].



In view of the additional lowering of the stereoselectivity of the S_N2'-type reaction for the allyl acetates and chlorides (48) on their interaction with Me_2CuLi that has been reported, the four-stage method of homologizing the farnesane skeleton that has been described was transformed in later investigations into a five-stage method [48, 49] (scheme 9). Exceptionally important points in this approach are the use of the well-known regiospecificity of the nucleophilic opening of primary-tertiary epoxides, the recently [50] found exceptional enantioselectivity of the hydroperoxide oxidation of allyl alcohols and, finally, the high selectivity of the Eastwood synthesis of olefins from vicinal glycols [51]. As a result, for example, the glycol monoether (51), obtainable smoothly in three stages from E,E-farnesol (3d, R' = Me) was converted under the conditions mentioned into the erythro-epoxyalcohol (52). Ring-opening of the latter formed the erythro-diol (53), passage from which to the corresponding trisubstituted olefin with the retention of the geometry of the initial carbon skeleton was performed without the isolation of the intermediate aminoacetal (54). The concluding elimination of the latter and of the trityl protection led in the final account to homofarnesol (3e, R' = Me) with an overall yield of ∿30% in the eight stages considered.



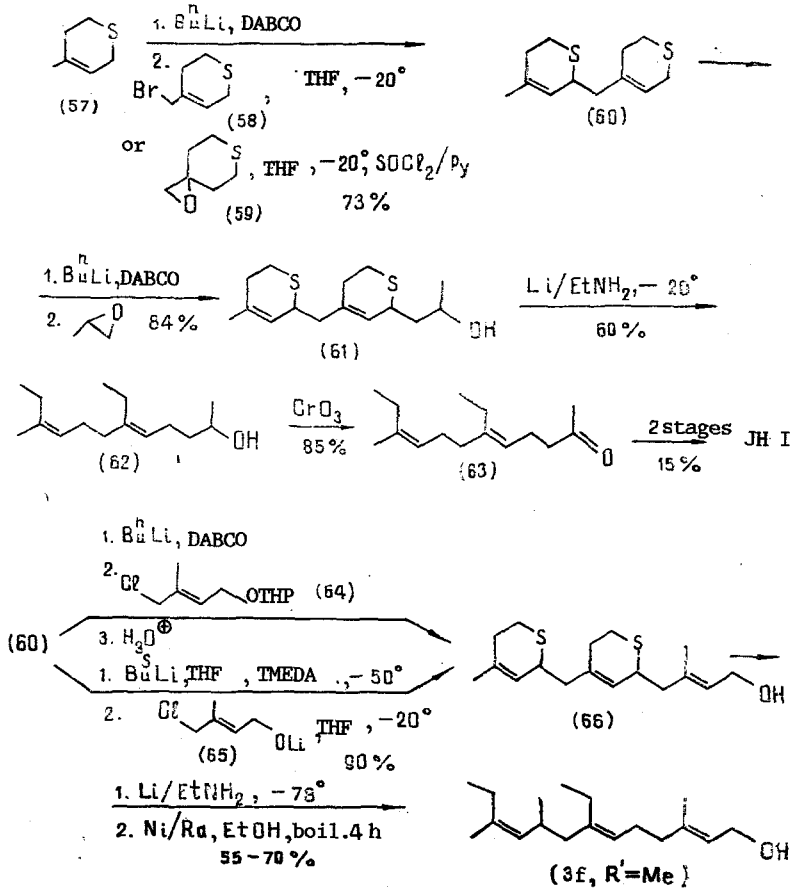
Scheme 9.

Similarly, starting from the glycol (48) in the form of a mixture of the corresponding isomers, the individual (with the erythro configuration of the C_6, C_7 and of the C_{10}, C_{11}, centers) isomer (55) was obtained, and this was converted into the tetrol (56) and then into bishomofarnesol (3f, R' = Me) with an overall yield of ∿25%.

Thus, the investigations described demonstrate the continuing multistage nature of the stereoselective homologization under consideration, which will undoubtedly prevent the use of this approach for the preparative synthesis of the JHs.

SYNTHESIS OF JHs USING SULFUR-CONTAINING COMPOUND

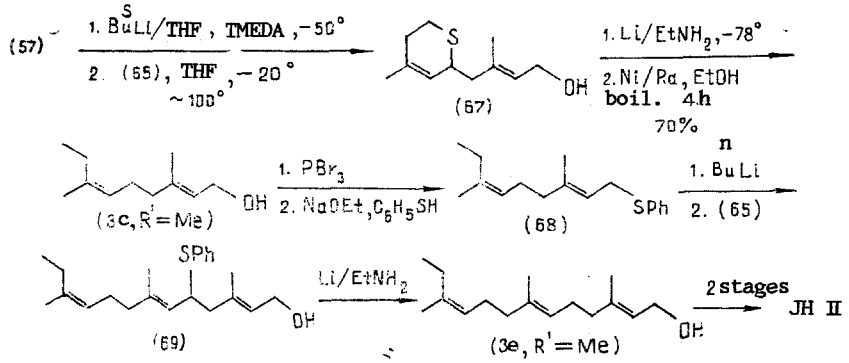
In recent years, the attention of chemists has been attracted by sulfur-containing compounds as synthons for the stereospecific construction of trisubstituted olefins, including JHs. Thus, two groups of workers [52, 53] simultaneously proposed to use for the construction of the farnesane chain a dihydrothiopyran fragment, on the reductive desulfuration of which an ethyl group arises and a cisoid geometry of the trisubstituted C=C bond is preserved. The key product in the synthesis of JH I by this method (scheme 10) is the bis-dihydrothiopyran (60) obtained by condensing the C_5-synthon (57) and its bromo (58) or epoxy (59) derivative. The introduction of the lacking C_5-olefinic bond and the reduction opening of the thiopyran ring have been effected by two routes.



Scheme 10.

According to the first of them, the carbanion generated from (60) under the action of Bu^nLi in the presence of 2,3-diazobicyclo[2.2.2]octane (DABCO) gives with propylene oxide the alcohol (61), the reductive desulfuration of which with Li in $EtNH_2$ leads with total stereospecificity to the 4E,8Z-dienic alcohol (62). The oxidation of the latter gives the ketone (63) and from this JH I is obtained by a known method with an overall yield of ∿4%.

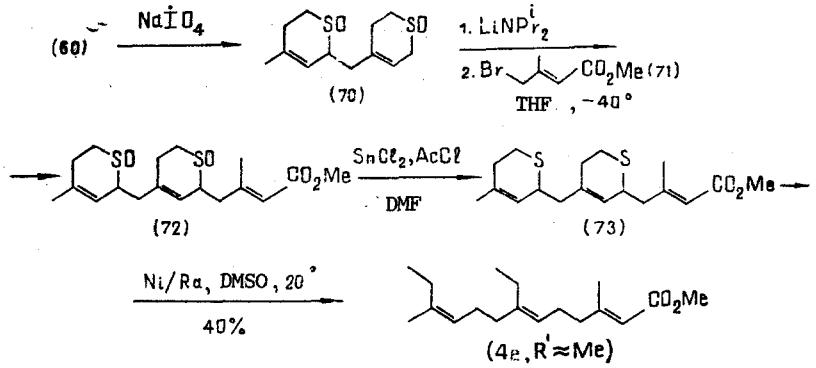
The other method consists in the direct alkylation of the disulfide (60) with the appropriate C_5 allyl halide (64) or (65) to form the alcohol (66), which by reduction with Li in $EtNH_2$ followed by desulfuration with deactivated Raney nickel (Ni/Ra) gives, completely stereospecifically, the obvious precursor (3f, R' = Me) of JH I with an overall yield of 35-45%.



Scheme 11.

The dihydrothiopyran (57) has also been used in the synthesis of JH II (scheme 11) [53]. The alkylation of (57) with the chloride (65) followed by reductive sulfuration of the intermediate alcohol (67) smoothly gave the diene (3c, R' = Me), which then, in seven stages, including the preparation of the sulfide (68) and its alkylation by the same chloride (65) to the hydroxy sulfide (69), was converted into JH II with a satisfactory overall yield.

The approach to the synthesis of JH I that has been considered was modified [54] by the use, in place of the disulfide (60), of the more readily alkylated bissulfide (70), which with the E-C_5 synthon (71) (scheme 12) gave the ester (72). The latter was first reduced to the disulfide (73) and this, in its turn, by treatment with Ni/Ra in DMSO was converted directly into the precursor (4f, R' = Me) of JH I.

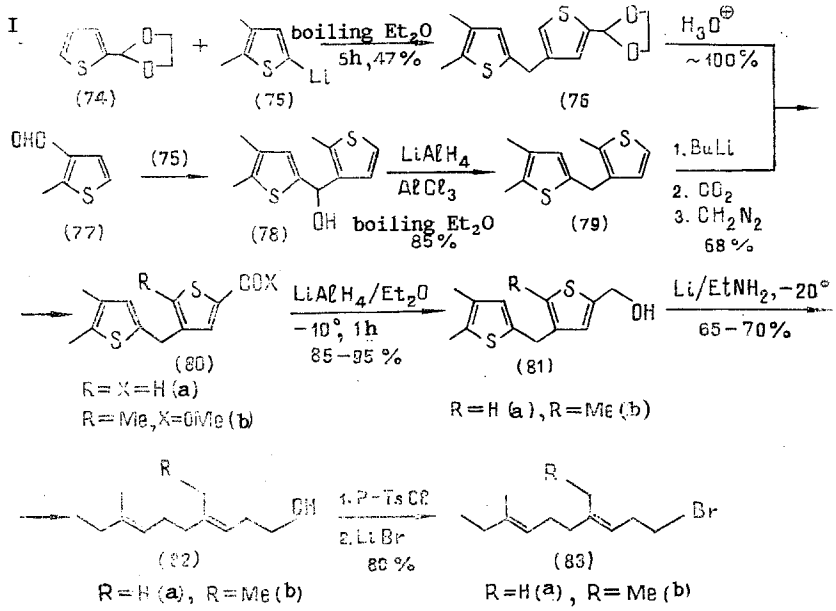


Scheme 12.

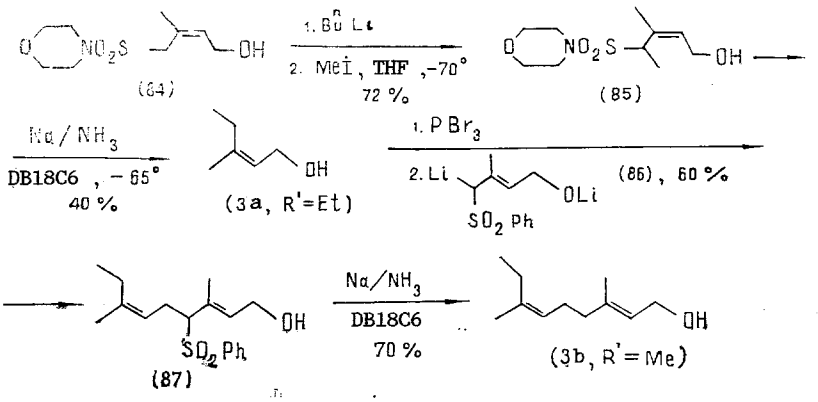
Recently, we have developed a new route to the 10E isomers of JH I and JH II starting from readily available thiophene synthons (scheme 13) [55]. Thus, when the iodide (74) was condensed with 2-lithiothiophene (75) the aldehyde (80a) was formed smoothly via the stage of the acetal (76). On the other hand, the reaction of the aldehyde (77) with (75) gave the carbinol (78), and the trimethyl-substituted dithienylmethane (79). The latter, in two simple operations involving carboxylation and acidification, was converted into the methyl ester (80b). The hydride reduction of the aldehyde (80a) and of the ester (80b) led with a high yield to the dithienylmethanols (81a and b). The key stage in the scheme under consideration is the reductive desulfuration with Li in $EtNH_2$ of the carbinols (81a, b), which takes place with a high stereospecificity giving good yields of the corresponding 3E,7E-homoallyl alcohols (82a, b) which are smoothly converted into the bromides (83a, b). Passage from the latter to the 10E isomers of JH I and JH II is effected in four simple operations with an overall yield of ∿20%, as described in [56, 57].

In conclusion, in scheme 14 is considered the basic possibility of constructing JH molecules with the aid of the readily available Z- and E-C_5-synthons (84 and 86, respectively) [58]. Thus, the successive treatment of the hydroxysulfonamide (84) with Bu^nNi and MeI gives the corresponding alkylation product (85), the Birch reduction of which takes place with high regioselectivity in the presence of catalytic amounts of dibenzo-18-crown-6 (DB18C6) with the formation of the Z-pentenol (3a, R' = Et). Its two-stage trans-C_5 homologization, including the alkylation of the E-dilithium derivative (86) with the allyl bromide obtained from (3a, R' = Et) and the reductive cleavage of the C—S bond in the sulfone

(87) leads with good yield to the dienic alcohol (3c, R' = Me) – a key product in some schemes for the total synthesis of JH II.



Scheme 13.



Scheme 14.

The studies that have been considered therefore illustrate the promising nature of the use of the methods of the chemistry of sulfur-containing compounds for the regio- and stereo-directed synthesis of JHs.

Thus, we must mention the diversity of synthetic methods used for the creation of the homofarnesane skeleton of the JHs that flow from the material presented, which, as a whole, is serving the development of general methods for the organic synthesis of unsaturated compounds. In general, the juvenile hormones are not substances suitable for practical use. Their fairly high lability and the inadequacy of the manifestation of their biological properties with respect to various species of insects, in combination with their comparative structural complexity, form obvious obstracles to their wide use. Nevertheless, the unabating interest in new syntheses of the JHs appears to be completely justified and permits at least the hope of the development of a few schemes for their reduction in the very near future.

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POLYSACCHARIDES OF Polygonatum

VIII. STRUCTURE OF A GLUCOFRUCTAN FROM Polygonatum sewerzowii

MASS-SPECTROMETRIC PROPERTIES OF PERACETATES OF FRUCTOOLIGOSACCHARIDES

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UDC 547.917

By partial hydrolysis, tetra- and pentafructooligosaccharides have been obtained from Polygonatum sewerzowii Regel. Structures of the individual tetra- and pentasaccharides have been proposed on the basis of the results of ^{13}C NMR and mass spectrometry. In the ^{13}C NMR spectrum a signal with a chemical shift of 76.5 ppm has been detected which is characteristic for the C-4 atom of a nonterminal unit. Consequently, the pentasaccharide has mixed 2 → 1 and 2 → 6 bonds in the chain. A comparative mass-spectrometric study of isomeric trisaccharide peracetates has been performed.

We have previously reported on the study by ^{13}C NMR spectroscopy of the glucofructan pseverin from Polygonatum sewerzowii consisting of β-2 → 6- and β-2 → 1-bound fructofuranose units, i.e., having a mixed type of bonds — of inulin and levan natures [1]. A determination of the amounts of monosaccharides is the polysaccharide by the methods of Bertrand and Kolthoff [2] has shown that pseverin contains 94% of fructose residues and 6% of glucose residues.

In order to study the sequence of monosaccharide residues, pseverin was subjected to partial hydrolysis. Glucose, fructose, sucrose, and tri-, tetra- (I), and penta-(II)-fructooligosaccharides were detected in the hydrolysate. The trifructooligosaccharides were identified with markers in PC. The fructooligosaccharides (I) and (II) were obtained in the individual form by preparative PC, and glucose and fructose were revealed in hydrolysates of them.

To determine the nature of the types of bonds of the monosaccharide units, fructooligosaccharides (I) and (II) were methylated by Hakomori's method [3]. The permethylates were subjected to methanolysis. In a hydrolysate of the permethylate of oligosaccharide (I) TLC revealed the presence of 2,3,4,6-tetra-O-Me-D-glucose, 1,2,4,6-tetra-O-Me-D-fructose, and 3,4,6-tri-O-Me-D-fructose. The isolation of 3,4,6-tri-O-Me-D-fructose showed the presence of a 2 → 1 bond between fructofuranose units.

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