2. To obtain unsaturated TAGs it is more desirable to use the continuous cultivation of yeast than batch cultivation.

LITERATURE CITED

1. L. V. Zaitseva, Yu. A. Sultanovich, S. L. Gramolin, and A. P. Nechaev, Khim. Prir. Soedin., 28 (1986).
2. C. Ratledge and M. J. Hall, Biotechnol. Lett., No. 1, 115 (1979).
3. M. V. Rozhdestvenskaya, Yu. A. Sultanovich, and A. P. Nechaev, "Change in the chemical composition of total, the polar and the neutral lipids of a yeast of the genus *Rhodotorula* as a function of the level of accumulation of the total lipids in the biomass" [in Russian], Moscow (1986). Dep. VNIISENTI. No. 304 mb – Dep. 86. 25. 03 (1986).
4. Catalogue of Cultures of the All-Union Collection of Non-pathogenic Microorganisms [in Russian], Nauka, Moscow (1976).
5. E. G. Bligh and W. G. Dyer, Can. J. Biochem. Physiol., 37, p. 911 (1959).
6. M. Kates, Techniques of Lipidology, North Holland, Amsterdam, American Elsevier, New York (1972) [Russian translation], Mir, Moscow (1975), p. 120].
7. H. Brockerhoff, J. Lipid Res., 6, 10 (1965).
8. H. Brockerhoff and N. K. N. Ayengar, Lipids, 14, p. 88 (1979).

PHOTOCHEMICAL ROUTE TO CEMBRANOIDS CONTAINING A cis-DISUBSTITUTED DOUBLE BOND

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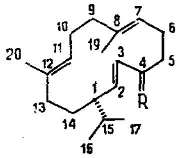
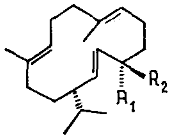
The 2-cis isomers of the natural diterpenoids isocembrol, 4-epiisocembrol, and isocembrene have been synthesized from a norcembrane ketone by the use of photochemical methods.

A large number of cembrane diterpenoids contain in their molecules a disubstituted double bond in the C-2—C-3 position [1, 2], and in all cases it has the trans (E) configuration. As examples we can give isocembrene (I) [3], isocembrol (II) [4], and 4-epiisocembrol (III) [5]. This paper is devoted to the synthesis of the 2-cis isomers of compounds (I)-(III), their preparation being of interest for the study of their biological activity in view of the fact that some 2-trans-cembranoids exhibit growth-regulating properties [6].



I. R = CH$_2$
IV. R = O



	R$_1$	R$_2$
II.	CH$_3$	OH
III.	OH	CH$_3$

As the starting compound for the synthesis of the 2-cis-cembranoids we selected the known [7] ketone (IV). Since cis-trans isomerization is a characteristic photoreaction of α-enols [8] the photolysis of ketone (IV) could be expected to form its 2Z-isomer (ketone (V)). In actual fact, when a pentane solution of ketone (IV) was irradiated with the light of a high-pressure mercury lamp a photoequilibrium mixture of ketones (IV) and (V) (~5:3, according to GLC) was rapidly formed, and these were slowly converted into three other compounds. One of them – the tricyclocembrane ketone (VI) – is described in a separate communication [9].

Ketone (V), like the other photoisomerization products, was isolated by chromatography on silica gel. The cis configuration of its disubstituted double bond was shown by the mag-

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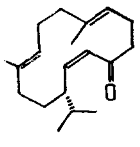
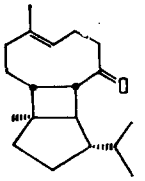
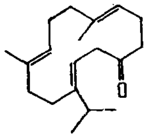
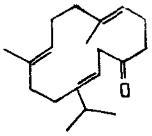
nitude $J_{2,3}$ = 11.5 Hz in its PMR spectrum, and the unchanged trans configuration of the nonconjugated double bonds by values of the chemical shifts for the signals due to the C-19 and C-20 atoms (14.86 and 15.25 ppm) and in the ^{13}C NMR spectrum [10].

The other two products had the structures expressed by formulas (VII) and (VIII). The PMR spectra of these ketones were qualitatively similar, their common features being the doublet signal of the methyls of an isopropyl group (in the PMR spectra of cembranoids having an asymmetric center at C-1 they give two doublets with an integral intensity of 3 H each) and a two-proton doublet (at 3.00 and 3.15 ppm, respectively) of the two protons at C-3 in the allyl position with respect to a methylene group. The doublet splitting of this signal is due to spin-spin interaction with the neighboring olefinic proton, as was confirmed by a double-resonance experiment.


V


VI

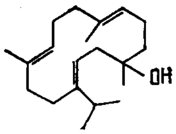

VII

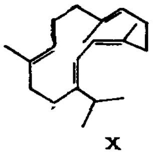

VIII

Since the photoisomerization of compound (IV) was carried out in solution in pentane, which is not a sensitizer for the cis-trans isomerization of nonconjugated double bonds, ketone (VII) and (VIII) should differ from one another only by the configuration of the double bond formed at C-1—C-2. The retention of the trans configurations of the other two, trisubstituted, double bonds was confirmed, in accordance with Bates' rule [11], by the values of the chemical shifts of the signals of the methyl groups in the PMR spectra.

The configuration of the C-1 double bond in the molecule of each of the ketones under consideration was established in the following way. The reaction of ketone (VII) with methylmagnesium iodide in diethyl ether gave the coresponding tertiary alcohol (IX). The dehydration of this alcohol could theoretically give five hydrocarbons — two with a double bond at C-3—C-4 (Z and E isomers), one with an exomethylenic double bond at C-4—C-18, and two with a double bond at C-4—C-5 (Z and E isomers). One or both hydrocarbons with a double bond at C-3-4 should prove to be identical with one or two of the three known stereoisomeric pinacenes described in [12].

On performing dehydration with the use of phosphorus oxychloride in pyridine we obtained a mixture of four hydrocarbons, GLC behavior and the IR and PMR spectra of the main one (56%) of which coincided with those of the authentic sample of β-pinacene (X). Of the other three hydrocarbons, not one was identical with known pinacenes. Thus, ketone (VII), like β-pinacene, had the 1Z configuration, and ketone (VIII), correspondingly, the 1E configuration. These ketones were the production of the deconjugation reaction that, like cis-trans isomerization, is typical for the photoreactions of α-enones [8].


IX


X

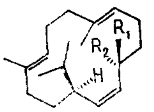
According to the results of adsorption chromatography the ratio of ketones (IV), (V), (VI), (VII), and (VIII) after irradiation for four hours was 11:7.5:2.5:1.5:1, respectively. The cis ketone (V), as the most polar, was readily isolated by chromatography on silica gel and could be used for subsequent syntheses of cembrane derivatives with a cis-disubstituted double bond at C-2—C-3 — in particular, the 2Z isomers of the natural isocembrol (II), 4-epiisocembrol (III), and isocembrene (I).

On the interaction of ketone (V) with methylmagnesium iodide in diethyl ether, four tertiary alcohols were formed; the normal products of the reaction — the alcohols (XI) and (XII) — and also isocembrol (II) and 4-epiisocembrol (III). According to the results of column adsorption chromatography their ratio was 24:12:1:8, respectively. The formation of the last two alcohols was unexpected and inexplicable from the point of view of the traditional mechanism of the nucleophilic addition of a Grignard reagent to α-enols.

In a study of the mechanism of the reaction of Grignard reagents with ketones, Ashby [13] described the isomerization of a cis-α-enol into a trans-α-enol, and he isolated the product of 1,2-addition to the trans-α-enol formed. He made use of these results as one of the proofs of the existence of one-electron transfer under the conditions of the reaction of Grignard inversion of the configuration of the double bond through the formation of a ketyl radical anion capable of cis-trans isomerization.

For the correct use of a one-electron mechanism to explain this transformation we had to perform a number of experiments. In the first place, when the reaction was performed with a large excess of the reagent and a low degree of conversion of the initial ketone (V), we isolated ketone (IV). And, in the second place, an ethereal solution of magnesium iodide isomerized ketone (V) to only a small degree (~2%). The agreement of the results of these experiments with Ashby's statements and also the identical ratio of the alcohols (II) and (III) formed from ketones (IV) and (V) permitted the assumption that the cis-trans isomerization of ketone (V) under the action of methylmagnesium iodide took place through the formation of a ketyl radical anion.

It must be mentioned that the isomerization of ketone (V) was not connected with the action of iodine that could have been formed from the magnesium iodide [14], since an ethereal solution of iodine caused practically no change in ketone (V). Further, the isomerization of ketone (V) was not connected with the action of the Grignard compound as a basic reagent, since the 4-epiisocembrol isolated from the mixture of products of the reaction of ketone (V) with methylmagnesium iodide showed no lowering of the value of $[\alpha]_D$ as compared with that of the natural compound. This shows that the hydrogen atom at C-1 in the molecule of ketone (V) was not affected in the isomerization process.

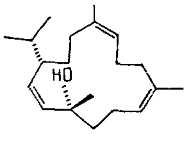


	R_1	R_2
XI	CH_3	OH
XII	OH	CH_3

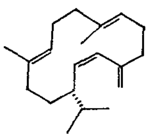
The formation of isocembrol and its epimer in the reaction under investigation is not a complicating factor in the synthetic plan, since alcohols (XI) and (XII) are highly nonpolar and are therefore readily isolated by chromatography. This property of theirs must be mentioned particularly, since in their chromatographic behavior they differ greatly from known tertiary cembrane alcohols and on silica gel are eluted in the same way as diterpene alcohols, esters, and oxides [16]. The lack of polarity of these compounds is explained by the fact that the hydroxy group in their molecules is bound almost wholly by an intramolecular hydrogen bond, identifiable from the IR spectra of dilute solutions.

A proof of the configuration of the asymmetric center at C-4 in the molecules of alcohols (XI) and (XII) was obtained on their photoisomerization in solution in acetone, which is a sensitizer of the cis-trans isomerization of nonconjugated double bonds [17]. Under these conditions, alcohol (XI) formed isocembrol and two other isomers, and alcohol (XII) formed 4-epiisocembrol and another three isomers. Thus, alcohols (XI) and (XII) were the 2Z isomers of isocembrol and of 4-epiisocembrol, respectively. It is impossible not to mention the pronounced selectivity of the photoisomerization of the alcohols (XI) and (XII) in acetone solution — the reaction systems contained, in addition to the initial compound, three and four products, respectively, instead of the seven expected in each case.

Each of the products, in addition to isocembrol, formed from alcohol (XI) had a cis-disubstituted double bond in its molecule (PMR spectra) and therefore they differed only by the configurations of the trisubstituted double bonds. In the first of them, less polar, one of these bonds had the trans, and the other the cis, configuration (the Me-8 and Me-12 signals in the PMR spectrum were located at 1.56 and 1.68 ppm [11]). In the PMR spectrum of the second alcohol the signals of the vinyl methyl groups were located at 1.66 and 1.68 ppm. The latter shows the Z configuration of the trisubstituted double bonds [11] and, thereby, the structure of this compound as (1S, 4R)-cembra-2Z,7Z,11Z-trien-4-ol (XIII), which is the Z,Z,Z-isomer of isocembrol.



XIII



XIV

TABLE 1. Values of the Chemical Shifts (ppm) and Spin-spin Coupling Constants (Hz, shown in parentheses) of the Signals in the PMR Spectra of Compounds (V), (VII), (VIII), (XI), (XII), and (XIII)

Compound	$-CH(C\underline{H}_3)_2$	Me-8, * Me-12	H-2	H-3	H-7, H-11†	Me-4	Other signals
V	0,85 d (7) 0,88 d (7)	1,45 1,58	5,67 dd (10,5; 11,5)	6,12 d (11,5)	4,66 t (~7,5) 4,95 t (~5)	—	—
VII	0,93 d (7) (6H)	1,49 1,49	4,90 t (8)	3,00 d (2H, 8)	4,77 t (~6) 4,90 t (~8)	—	2,88 septet (7) H-15
VIII	0,99 d (7) (6H)	1,53 1,55	5,29 t (7)	3,15 d (2H, 7)	4,93 t (~6) 5,03 t (~7)	—	—
XI	0,85 d (7) 0,87 d (7)	1,54 1,56	5,04 dd (12,0; ~11,5)	5,38 d (12)	4,94 t (~6) 5,22 t (~7)	1,21 s	2.89 m H-1
XII	0,88 d (7) 0,92 d (7)	1,55 1,60	5,23 t (11,5)	5,59 (11,5)	4,91 d (~10) 5,17 t (~6)	1,23 s	2,56 m H-1
XIII	0,86 d (7) 0,91 d (7)	1,66 1,68	5,25 dd (10; 12)	5,31 d (12)	5,14 t (~7) 5,18 t (~7)	1,29 s	2.97 dddd H-1 (10; 7; 5; 5)

*In all cases the signals of these methyl groups are broadened or slightly split singlets.

†In all cases the components of the multiplets for both protons are highly broadened.

While the use of a Grignard reagent gave the possibility of obtaining the 2Z-isomers of isocembrol and of 4-epiisocembrol, the methylenation of ketone (V) by the reagent obtained from zinc, methylene bromide, and titanium tetrachloride [18] led to the hydrocarbon (XIV) (the 2Z-isomer of isocembrene).

EXPERIMENTAL

^1H and ^{13}C NMR spectra were recorded on a Bruker WP-200 instrument (200.13 MHz for ^1H and 50.237 MHz for ^{13}C) for solutions in $CDCl_3$ (TMS, δ-scale). Conventional designations used in the descriptions of the PMR spectra: s — singlet; d — doublet; t — triplet; m — multiplet. IR spectra were recorded on a UR-20 instrument for solutions in CCl_4, and UV spectra on a Specord UV-VIS spectrophotometer. Specific optical rotations were measured on a Zeiss polarimeter and a Spectropol-1 polarimeter for solutions in $CHCl_3$. The mass spectra of ketone (V) were recorded on a MS-902 high-resolution spectrometer (70 eV, direct introduction).

Type L silica gel (Czechoslovakia) with a grain size of 0.100-0.160 mm was used for chromatography, the ratio of substance and sorbent being ~1:20, and the eluent petroleum ether with a rising concentration of diethyl ether.

Details of the PMR spectra for compounds (V), (VII), (VIII), (XI), and (XII) are given in Table 1.

Photoisomerization of Ketone (IV). A solution of 0.620 g of ketone (IV) in 40 ml of pentane was irradiated in an argon atmosphere with the light of a DRSh-1000 high-pressure mercury lamp for 4 h. Chromatography of the product led to the successive isolation of 0.149 g of (V), 0.056 g of (VI), 0.031 g of (VII), 0.019 g of (VIII), 0.220 g of the initial ketone (IV), and 0.140 g of a mixture of highly polar compounds. The R_f values for ketones (V), (VI), (VII), (VIII), and (IV) in the diethyl ether—petroleum ether (15:85) system were 0.64, 0.51, 0.39, 0.34, and 0.28, respectively.

(1S)-18-Norcembra-2Z,7E,11E-trien-4-one (V). Colorless crystals with mp 28-30°C (from pentane), $[\alpha]_D^{22}-21.3°$ (c 5.63). IR spectrum: 1630, 1705 cm^{-1} (C=C—C=O). UV spectrum: $\lambda_{max}^{C_2H_5OH}$ 230 nm (log ε 3.57). Mass spectrum: m/z 274.2314 (calculated for $C_{19}H_{30}O$, 274.2297). ^{13}C NMR spectrum (ppm): quartets at 15.25 and 14.86 (C-19 and C-20), 19.96 and 19.01 (C-16 and C-17); triplets at 2201, 23.99, 27.54, 36.52, 38.59, and 42.74; doublets at 40.91 (C-1), 32.85 (C-15), 124.22 and 125.14 (C-7 and C-11), 129.21 (C-3), and 150.38 (C-2); singlets at 132.88 and 134.93 (C-8 and C-12), and 200.62 (C-4). The assignment of the signals was made in the light of the observed values of their residual splitting under the conditions of incomplete suppression of spin-spin coupling with protons.

18-Norcembra-1Z,7E,11E-trien-4-one (VII). Colorless optically inactive oil with n_D^{20} 1.5100. IR spectrum: 1710 cm^{-1} (C=O). UV spectrum: λ_{max}^{hexane} 290 nm (ε 57). Mass spectrum: m/z 274.2306 (calculated for $C_{19}H_{30}O$ 274.2297).

18-Norcembra-1E,7E,11E-trien-4-one (VIII). Colorless optically inactive oil with n_D^{28} 1.5080. IR spectrum: 1715 cm^{-1} (C=O). UV spectrum λ_{max}^{hexane} 290 nm (ε 88).

Determination of the Stereochemistry of Ketone (VII). With stirring and cooling to 0°C, a solution of 0.110 g of ketone (VII) in 5 ml of absolute diethyl ether was added dropwise to 20 ml of a 0.1 N solution of methylmagnesium iodide in diethyl ether. The reaction mixture was left in the dark at +8°C for 20 h, after which it was poured into a saturated aqueous solution of ammonium chloride cooled to +5°C. The ethereal solution was separated off and was washed successively with saturated aqueous sodium bicarbonate solution and water, and was dried with sodium sulfate. After elimination of the solvent, the product was chromatographed. This gave 0.100 g of cembra-1Z,7E,11E-trien-4-ol (IX) in the form of an oil. IR spectrum: 3610 cm^{-1} (OH); PMR spectrum (ppm): 0.94 (6H, d, J = 6.5 Hz, $-CH(CH_3)_2$), 1.14 (3H, s, Me-4), 1.55 (6H, br.s, Me-8, Me-12), 4.84-5.34 (3H, m, H-2, H-7, H-11). A solution of 0.100 g of this alcohol in 5 ml of pyridine ws treated dropwise with 0.5 ml of phosphorus oxychloride, and the mixture was left at +8°C for 15 h. Then it was poured into a saturated aqueous solution of sodium bicarbonate, and the product was extracted with petroleum ether. After the usual working up, 0.09 g of a mixture of hydrocarbons was isolated that consisted of four components (56, 23, 9, and 12%; relative retention times 1.00 (β-pinacene), 0.88, 0.81, and 0.71, respectively). GLC was conducted on a Chrom-4 instrument (5% of XE-60/Chromaton N-AW (0.160-0.200), t_{col} 140°C, t_{evap} 200°C, carrier gas nitrogen). Chromatography of this mixture on silica gel impregnated with a 5% solution of silver nitrate gave β-pinacene (0.047 g), the PMR and IR spectra of which coincided with those for an authentic sample.

Reaction of Ketone (V) with a Grignard Reagent. The reaction of 0.990 g of ketone (V) in 10 ml of absolute diethyl ether with 50 ml of a 1 N ethereal solution of methylmagnesium iodide and subsequent working up were performed in a similar way to that described above for ketone (VII). Chromatography of the product yielded successively 0.535 g of (XI), 0.255 g of (XII), and 0.195 g of a mixture of (II) and (III) (eluent: petroleum ether with the addition of 3, 5, and 15% of diethyl ether, respectively).

The chromatography of 0.195 g of the mixture of (II) and (III) on silica gel impregnated with 5% silver nitrate yielded 0.02 g of isocembrol (II) and 0.175 g of 4-epiisocembrol (III), identified form their IR and PMR spectra. The specific optical rotation ($[\alpha]_D^{20}$) for (III) was +112° (c 3.1); according to the literature [5]: $[\alpha]_D^{22}$ + 110.5° (c 3.35).

The reaction of 1.17 g of ketone (V) in 10 ml of absolute diethyl ether with 50 ml of a 1 N ethereal solution of methylmagnesium iodide and subsequent working up were carried out as described above, but the reaction was stopped 3 h after the addition of the ketone (V). Chromatography of the product (1.11 g) yielded successively 0.39 g of a mixture of (V) and (X), 0.3 g of (X), 0.2 g of (XI), 0.02 g of ketone (IV), and 0.2 g of a mixture of (II) and (III).

(1S,4R)-Cembra-2Z,7E,11E-trien-4-ol (XI). Colorless oil with n_D^{18} 1.5020, $[\alpha]_D^{18}$ +6.7° (c 7.41). IR spectrum (cm^{-1}): 3550 (OH—π hydrogen bond), 3610 (OH) (recorded at a concentration of the solution of 0.06% and a cell thickness of 2 cm). The ratio of the integral intensities of the bands at 3610 and 3550 cm^{-1} was ~1:12, respectively. The transformation of the PMR signal of the H-2 proton into a doublet on suppression of the signal at 2.89 ppm was a confirmation of the assignment of the latter to the H-1 proton (see Table 1).

(1S,4S)-Cembra-2Z,7E,11E-trien-4-ol (XII). Crystals with mp 51.5-52.5°C (from a mixture of CCl_4 and acetonitrile), $[\alpha]_D^{21}$ −243° (c 2.6). The spectrum in the 3500-3700 cm^{-1} region was very close to that for the alcohol (XI). For the PMR spectrum, see Table 1.

Isomerization of Ketone (V) in Ethereal Solutions of Magnesium Iodide and Iodine. An ethereal solution (50 ml) of magnesium iodide was prepared by the method described in [14], using 2.54 g of iodine and 0.42 g of magnesium. With stirring, a solution of 0.050 g of ketone (V) in 5 ml of absolute diethyl ether was added to a portion (20 ml) of this solution.

After being kept in the dark at +8°C for 6 h, the solution was worked up in the same way as after the reaction with methylmagnesium iodide. A mixture (0.042 g) of ketones (IV) and (V) present in a ratio of 1:42 (GLC; the instrument and conditions have been described above) was isolated.

A solution of 0.03 g of ketone (V) in 5 ml of absolute diethyl ether was added to a solution of 0.3 g of iodine in 10 ml of the same solvent, and the mixture was left in the dark at +8°C. After 20 h, according to TLC, the ketone (V) has scarcely changed and the formation of only trace amounts of less polar products and of ketone (IV) was observed.

Photoisomerization of Alcohol (XI). A solution of 0.280 g of alcohol, (XI) in 30 ml of acetone in a Pyrex glass cell was irradiated with the light of a DRSh-1000 high-pressure mercury lamp, with a constant stream of argon through the solution, for 2 h. Chromatography of the product on silica gel yielded successively 0.114 g of (XI), 0.056 g of the 2Z,7E,11Z isomer of isocembrol (II), 0.015 g of (XIII), 0.01 g of isocembrol (identified by its PMR spectrum and by TLC), and 0.08 g of a mixture of highly polar compounds.

The 2Z,7E,11Z Isomer of Isocembrol (II). Colorless oil. IR spectrum: 3610 cm^{-1} (OH). PMR spectrum (ppm): 0.86 and 0.85 (3H each, d, d, J = 7 Hz each; $-CH(C\underline{H}_3)_2$); 1.20 (3H, s, Me-4); 1.56 and 1.68 (3H each, br.s, Me-8 and Me-12); 2.75 (1H, dddd, J = 11.0 and 12.5 Hz, H-2); 5.15 and 5.30 (1H each, m, m; H-7 and H-11); 5.38 (1H, d, J = 12.5 Hz; H-3).

(1S,4R)-Cembra-2Z,7Z,11Z-trien-4-ol (XIII). Colorless oil. IR spectrum: 3610 cm^{-1}. For the PMR spectrum, see Table 1.

Photoisomerization of the Alcohol (XII). This was carried out as described above for alcohol (XI). From 0.200 g of the initial compounds were obtained, after chroamtography, 0.100 g of unchanged alcohol (XII), 0.01 g of 4-epiisocembrol contaminated (~14%) with an unidentified isomer containing a trans-disubstituted double bond (PMR spectrum), 0.025 g of an irresolvable mixture (~1:1, according to the PMR spectrum) of two unidentified alcohols, and 0.065 g of a mixture of highly polar compounds.

Synthesis of (2Z)-Isocembrane (XIV). In this synthesis, the reagent and the procedure described in [18] were used. From 0.120 g of the ketone (V) was obtained 0.084 g of a mixture of hydrocarbons the chromatography of which on silica gel with 5% of silver nitrate gave 0.074 g of (2Z)-isocembrane (XIV) and 0.01 g of isocembrene (I) (eluents: petroleum ether with the addition of 7 and 12% of diethyl ether, respectively). The isocembrene was identified from its PMR spectrum and by TLC.

(2Z)-Isocembrene (XIV). Colorless oil with $[\alpha]_D^{20}$ −133° (c 5.27). IR spectrum 895 cm^{-1} ($C=CH_2$). UV spectrum: $\lambda_{max}^{C_2H_5OH}$ 235 nm (log ε 3.74). PMR spectrum (ppm): 0.86 (6H, d, J = 7 Hz; $-CH(C\underline{H}_3)_2$; 1.49 and 1.58 (3H each, s, s; Me-8 and Me-12); 4.88 and 4.92 (1H each; br.s, br. s, $C=CH_2$); 4.84-4.94 (1H, M, H-7 or H-11); 5.08 (1H, br.t, J ~ 7 Hz; H-11 or H-7); 5.23 (1H, dd, J = 11.0 and 11.5 Hz; H-2); 5.89 (1H, d, J = 11.5 Hz; H-3).

SUMMARY

1. The 2Z isomers of natural cembranoids – (2Z)-isocembrol, (2Z)-4-epiisocembrol, and (2Z)-isocembrene – have been synthesized for the first time, with the use of photoisomerization in the key stages.

2. A process of the cis-trans isomerization of a macrocyclic α-enone under the conditions of its interaction with a Grignard reagent has been detected.

LITERATURE CITED

1. A. J. Weinheimer, C. W. J. Chang, and J. A. Matson, Prog. Chem. Org. Nat. Prod., 36, 285 (1979).
2. I. Wahlberg and C. R. Enzell, Beitr. Tabakforsch. Int., 12, No. 3, 93 (1984).
3. N. K. Kashtanova, A. I. Lisina, and V. A. Pentegova, Khim. Prir. Soedin., 10 (1969).
4. V. A. Raldugin, A. I. Rezvukhin, and V. A. Pentegova, Khim. Prir. Soedin., 598 (1971).
5. V. A. Raldugin and V. A. Pentegova, Khim. Prir. Soedin., 669 (1971).
6. V. A. Raldugin, V. E. Kozlov, V. M. Chekurov, N. I. Yaroshenko, and V. A. Pentegova, Khim. Prir. Soedin., 733 (1981).
7. V. A. Raldugin and V. A. Pentegova, Khim. Prir. Soedin., 174 (1976).

8. J. A. Barltrop and J. D. Coyle, Excited States in Organic Chemistry, Wiley-Interscience, New York, 1977 [Russian translation: Mir, Moscow (1978), p. 246].
9. A. V. Vorob'ev, V. A. Raldugin, S. A. Shevtsov, and Yu. V. Gatilov, Khim. Prir. Soedin., 295 (1986).
10. P. Crews and E. Kho-Wiseman, J. Org. Chem., 42, 2812 (1977).
11. R. B. Bates and D. M. Gale, J. Am. Chem. Soc., 82, 5749 (1960).
12. V. A. Raldugin and V. I. Mamatyuk, Izv. Sib. Otd. Akad. Nauk SSSR. Ser. Khim. Nauk, Series No. 6, Issue No. 17, 71 (1984).
13. E. C. Ashby and T. L. Wieseman, J. Am. Chem. Soc., 100, No. 10, 3101 (1978).
14. R. Stewart and A. Ubbelohde, J. Chem. Soc., No. 10, 2649 (1949).
15. V. Franzen and H. Krauch, Chem. Ztg., 79, 137 (1955).
16. V. A. Raldugin, V. A. Khan, Zh. V. Dubovenko, and V. A. Pentegova, Khim. Prir. Soedin., 609 (1976).
17. J. A. Barltrop and J. D. Coyle, Excited States in Organic Chemistry, Wiley Interscience, New York, 1977 [Russian translation: Mir, Moscow (1978), p. 283].
18. L. Lombardo, Tetrahedron Lett., 23, 4293 (1982).

OBTUSIFOLIN – A NEW COUMARIN FROM ROOTS OF *Haplophyllum obtusifolium*

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From the neutral fraction of a methanolic extract of the roots of *Haplophyllum obtusifolium* Ledeb. (family Rutaceae) have been isolated the lignan diphyllin, the alkaloids skimmianine and γ-fagarine, and a new coumarin with mp 179-180°C the structure of which has been established as 3-(α,α-dimethylallyl)-7-methoxy-8-(3-methylbuta-1,3-diethyl)coumarin.

The isolation of furanoquinoline alkaloids from the basic fraction of a methanolic extract of the roots of *Haplophyllum obtusifolium* Ledeb. (family Rutaceae) has been reported previously [1]. Continuing these investigations, we have studied the neutral fraction obtained from the same methanolic extract. Chromatography of the neutral fraction led to the isolation of a substance with mp 179-180°C (I), the lignan diphyllin, and the alkaloids simmianine and γ-fagarine.

Substance (I) – $C_{20}H_{22}O_3$ – was new, and has been called obtusifol. It dissolved readily in chloroform, less readily in methanol and ethanol, crystallized from ether and acetone, and was revealed by the Dragendorff reagent and in UV light.

The UV spectrum of obtusifolin contained absorption bands of an α-pyrone carbonyl (1710 cm^{-1}) and of aromatic and aliphatic C=C bonds (1624, 1610, 1600, 1569 cm^{-1}). Its UV spectrum had maxima at (nm) 220, 265* (inflection), 276*, 302, 319* (log 4.30, 4.11, 4.19, 4.44 [sic]), which are characteristic for 7-O-substituted coumarins [2].

In the PMR spectrum of obtusifolin three one-proton signals from the protons of the coumarin nucleus appeared at 6.77, 7.20, and 7.42 ppm. According to the literature [2-4], the singlet at 7.42 ppm belonged to a proton at C-4. Its singlet nature indicated the presence of a substitutent at C-3. The other two signals, doublets, at 7.20 and 6.77 ppm were the signals of the protons of a benzene ring present in the ortho-position to one another, as was shown by their spin-spin coupling constant (J = 9 Hz).

The facts given above showed that the coumarin nucleus of obtusifolin has three substituents. One of them is a methoxy group, the protons of which resonated at 3.88 ppm, while the other two were represented by isoprene units. The proton signals observed in the regions of (ppm) 1.42 (6H, singlet; two methyl groups at a quaternary carbon atom); 1.96 (3H broadened

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