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¹³C NMR SPECTRA AND STRUCTURE OF BUNGEIDIOL AND ITS TRANSFORMATION PRODUCTS

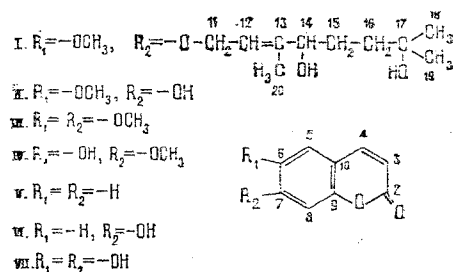
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The results are given of a study of the ¹³C NMR spectra of the new terpenoid coumarin bungeidiol (I) and of the products of its transformation (II) and (III) and some model compounds (IV-VII). On the basis of the results obtained from these ¹³C NMR spectra and with the use of additive contributions depending on the nature and positions of various substituents (hydroxy and methoxy groups) in the aromatic ring, the structure (I) has been confirmed and a complete assignment of the signals of all the carbon atoms both in the coumarin ring and in the aliphatic part of the molecule of (I) has been made.

Previously, in a study of the coumarin composition of *Haplophyllum bungei* Trautv., we isolated a new terpenoid coumarin with the composition C₂₀H₂₆O₆, mp 108-109°C, [α]_D²⁰ +42.8° (c 3.55, ethanol). On the basis of a detailed study of the proton magnetic resonance spectra and its chemical transformations, structure (I) was established for it.

In the present paper we give the results of an investigation of the ¹³C NMR spectra of compound (I), and its transformation products (II and III), and some model compounds (IV-VIII) with the aim of confirming the proposed structure (I) and elucidating the correlation between the ¹³C chemical shifts and additive contributions depending on the natures and positions of various substituents (hydroxy and methoxy groups) in the aromatic ring of the coumarin nucleus [1, 2]. The ¹³C NMR spectra of compounds (V-VII) have been studied previously by other authors [1, 3, 4].



As can be seen from the chemical shifts and spin-spin coupling constants in the ¹³C NMR spectra of the substances investigated (I-VII) (Table 1 and Figs. 1-5), the signals of all the carbon atoms appear clearly and in number and multiplicity they correspond completely to structures (I-VII). The assignment of the signals in the ¹³C NMR spectra was made in the light of the degree of hybridization of the carbon atoms, the number of protons attached to the corresponding carbon atoms [5], and literature information on ¹³C NMR spectra of analogs of the compounds under investigation (V-VII) [1, 3, 4]. To determine the chemical shifts of the signals, the spectra of compounds (I-VII) were taken in the regime of complete decoupling

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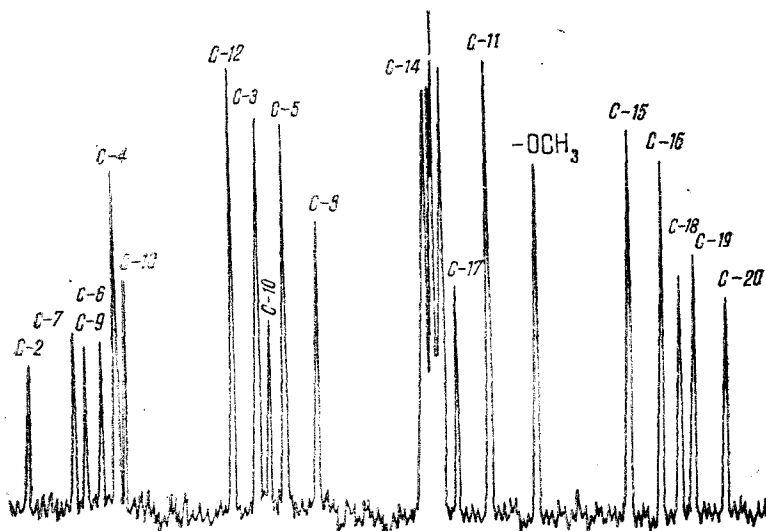


Fig. 1. ^{13}C NMR spectrum of bungeidiol with complete suppression of spin-spin coupling with protons.

from protons, and the spin-spin coupling constants were determined from the spectra obtained in the pulsed scanning regime. This considerably shortened the time of accumulation through the action of the Overhauser effect [5, 6]. The numbers of protons attached to the carbon atoms were measured in spectra taken under the conditions of stationary off-resonance decoupling, and the positions of the quaternary carbon atoms and the multiplicities of the protonated carbon atoms were confirmed in the spectra taken at a low proton-decoupling power.

In the ^{13}C NMR spectra of bungeidiol (I), the signals of all 20 carbon atoms appear clearly (see Table 1 and Fig. 1), and the majority of them were readily assigned with the aid of literature information on the ^{13}C NMR spectroscopy of analogous structures [3, 7]. Thus, quartets in the strong field at 18.8, 23.3, and 26.4 ppm belong to the methyl carbons C-20, C-19, and C-18 in the aliphatic part of the molecule, respectively, and a quartet at 56.1 ppm corresponds to the carbon atom of a methoxy group attached to the aromatic ring in position 6. The triplets observed in the strong-field part of the spectrum at 29.4 and 36.5 ppm are due to the C-15 and C-16 carbon atoms. The signals from the C-11 methylenic carbon, attached to the aromatic ring through oxygen appears in a weaker field at 66.2 ppm. A doublet at 118.5 ppm corresponds to the region of the chemical shifts of sp^2 -hybridized carbon atoms and it may therefore be considered that this signal is due to the C-12 carbon atom [8]. Singlets at 141.5 and 72.9 ppm are assigned, respectively, to the sp^2 -hybridized C-13 carbon atom and to an sp^3 -hybridized carbon with oxygen attached, C-17. A doublet at 77.7 ppm is due to the C-14 carbon. Figure 2 shows the ^{13}C NMR spectrum of (I) taken in the pulsed scanning regime. The multiplicities of the signals of the carbon atoms were confirmed in spectra taken under the conditions of incomplete decoupling from protons, fragments of which contain the characteristic doublets, triplets, and quartets shown above the spectrum in Fig. 2.

The ^{13}C NMR spectrum of (I) (Fig. 1) has in the weak-field regime (160-140 ppm) a group of signals due to quaternary carbon atoms of the coumarin nucleus in (I) the assignment of which presents certain difficulties because of the presence of two substituents simultaneously in the aromatic part of the molecule — a methoxy group and a terpenoid radical. For the accurate assignment of these signals we made use of the principles of additive contributions to the change in the chemical shifts of the carbon atoms of the coumarin series that depend on the natures and positions of the various substituents in the aromatic ring [1, 2].

To confirm the correctness of the use of the principle of additivity when a methoxy group is present in a coumarin nucleus, we made a comparison of the positions of the signals of the carbon atoms in the ^{13}C NMR spectrum for (IV) obtained experimentally and calculated empirically (Table 2 and Fig. 3). In view of the fact that the chemical shifts of the C-3 and C-5 signals are very close ($\Delta\delta = 0.7$ ppm) the unambiguous assignment of their signals presents some difficulty. Consequently, for an accurate assignment of the signals of these carbon atoms, in addition to the chemical shifts we measured the spin-spin coupling constants of all the compounds studied. We assigned the C-3 and C-5 signals on the basis that $J_{\text{C}_3-\text{H}} >$

TABLE 1. Chemical Shifts and Spin-Spin Coupling Constants of the ^{13}C -H Carbon Atoms in the ^{13}C NMR Spectra of the Compounds under Investigation

Carbon atom	I		II		III		IV		V		VI		VII	
	δ , ppm	J, Hz	ppm Δ	J, Hz	δ , ppm	J, Hz	δ , ppm	J, Hz	δ , ppm	J, Hz	δ , ppm	J, Hz	δ , ppm	J, Hz
C-2	161.0	*	160.5	*	160.4	†	160.6	†	160.1	*	160.8	*	161.0	*
C-3	112.9	173	111.6	171	112.5	171	112.5	173	116.2	173	111.6	173	111.8	172
C-4	143.1	161	141.3	161	144.2	164	144.1	167	143.0	161	144.3	163	144.5	164
C-5	107.8	158	109.6	160	109.0	161	111.8	156	127.5	160	130.0	163	112.6	160
C-6	146.2	*	145.6	*	145.8	†	143.3	†	124.0	164	113.4	168	143.1	*
C-7	151.6	*	150.8	*	152.4	†	151.6	†	131.4	163	161.7	*	150.5	*
C-8	100.9	161	102.7	161	99.9	163	99.9	161	116.2	164	102.8	163	102.9	161
C-9	149.3	*	149.3	*	149.1	**	148.2	†	153.5	*	155.9	*	148.8	*
C-10	111.1	*	110.5	*	111.2	†	111.5	†	118.4	*	111.6	*	111.0	*
C-11	66.2	149												
C-12	118.5	156												
C-13	141.5	*												
C-14	77.7	144												
C-15	36.5	132												
C-16	29.4	127												
C-17	72.9	*												
C-18	26.4	126												
C-19	23.3	126												
C-20	18.8	132												
-OC(1) ₃	56.1	149	56.3	149	55.6	149	56.3	146						

*Broadened signal; spin-spin coupling constant not determined.

†Signal at the level of the background noise.

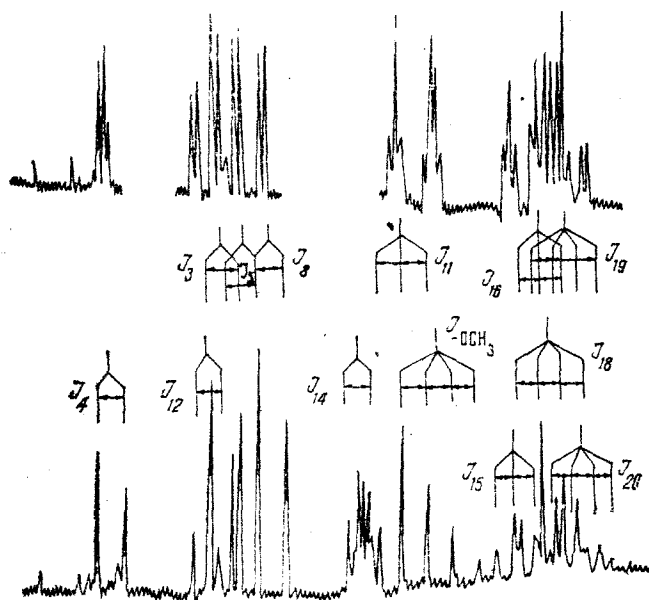


Fig. 2. ^{13}C NMR spectrum of bungeidiol (I) taken in the pulsed scanning regime. Above the spectrum are shown fragments of the spectrum of (I) taken in the off-resonance regime in order to confirm the multiplicities of the signals.

$\text{JC}_5\text{-H}$ [4]. The slight differences between the contribution of the substituents in (IV) can be explained by the use of different solvents for (IV) and (V), and by the appearance of an "ortho" steric interaction of the two substituents (hydroxy and methoxy groups) in (IV).

Thus, a comparison of the results obtained permits a positive conclusion to be drawn concerning the possibility of the application of the principle of additivity when a methoxy group is present in the coumarin nucleus. The assignment of the signals in the ^{13}C NMR spectra of (IV) was made on the basis of the results presented above.

To assign the signals in the ^{13}C NMR spectra of the quaternary carbon atoms of (I)-(III), using the principle of additivity it is necessary to know the contribution to the change in the chemical shift from a substituent, particularly a methoxy group, in position 6. In order to determine the contribution, from a preliminary assignment of the signals from (II) and (III) (see Table 1) made on the basis of a comparison of the experimentally determined chemical shifts and spin-spin coupling constants (Figs. 4 and 5) with literature information on analogous structures [1, 3, 5], we assigned the contributions of the $-\text{OH}$ and $-\text{OCH}_3$ groups found in umbelliferone (VI) and herniarin (IX).^{*} In this way we found the contribution to the change in the ^{13}C NMR chemical shift of a coumarin nucleus caused by an $-\text{OCH}_3$ group in position 6. It can be seen from Table 3 that for all the carbon atoms of the coumarin nuclei of compounds (II) and (III), a good agreement for the contribution of the methoxy group in position 6 is observed. Hence, having obtained similar results for two compounds (II and III), we have confirmed the assignments described above of the signals in the ^{13}C NMR spectra of compounds (II) and (III). Furthermore, using the calculated change in the ^{13}C chemical shifts for all the carbon atoms of the coumarin nucleus introduced by a methoxy group in position 6 and the calculated contribution to the change in the chemical shift due to the aliphatic substituent in marmin (X) [3], it is possible to find empirically the position of the ^{13}C carbon signals of the coumarin nucleus of bungeidiol (I). The calculated and experimental results are presented in Table 4. The good agreement of the experimental positions of the ^{13}C signals in the spectrum of (I) and those calculated empirically permits the conclusion that in this case, as well, the principle of the additivity of the contributions from various substituents (methoxy group and aliphatic side chain) to the change in the chemical shifts of the signals of the coumarin nucleus of (I) is obeyed. Thus, all the facts given above from the ^{13}C NMR spectra of (II)-(IV) and some model compounds (V)-(X) confirm the

^{*}Information on the contribution of the $-\text{OCH}_3$ group to ^{13}C NMR spectrum of (IX) was taken from the literature [1].

TABLE 2. Contributions to the Change in the Chemical Shifts of the Introduced Substituents (hydroxy and methoxy groups) in the ^{13}C NMR Spectrum of Compounds (IV), (VIII), and (IX)

Carbon atom	(VII),* 6-hydroxy- coumarin	(IX),* 7-methoxy- coumarin	IV	
			calc.	observed
C-2	0,5	0,5	1,0	0,4
C-3	0,2	-3,6	-3,4	-3,7
C-4	0,1	0,1	0,2	1,1
C-5	-15,7	1,0	-14,7	-15,7
C-6	29,6	-12,1	17,5	19,3
C-7	-11,8	30,9	19,1	20,2
C-8	1,0	-15,4	-14,4	-16,3
C-9	-7,7	1,9	-5,8	-5,3
C-10	0,6	-6,5	-5,9	-6,9

*Information on the contribution of the substituents to the ^{13}C NMR spectra of (VIII) and (IX) was taken from the literature [1].

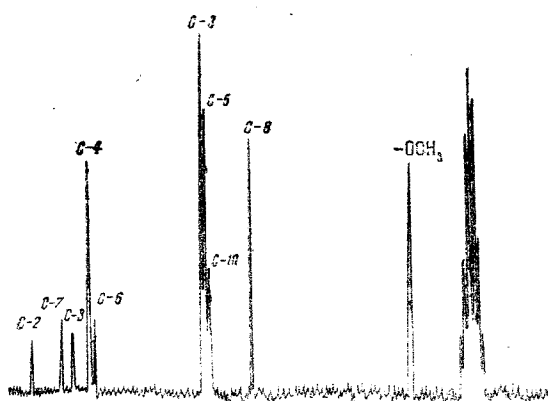


Fig. 3. ^{13}C NMR spectrum of 6-hydroxy-7-methoxy coumarin taken under the conditions of the complete suppression of spin-spin coupling with protons.

structure of bungeidiol as 7-(4',7'-dihydroxy-3',7'-dimethyloct-2'-enyloxy)-6-methoxycoumarin (I).

EXPERIMENTAL

We isolated substances (I), (II), and (IV) from *Haplophyllum bungei* and (III) was obtained by the methylation of (IV) with methyl iodide. Compounds (V-VII) were synthesized by methods given in the literature [9-11]. The purity of the compounds (I-VII) studied was established by thin-layer chromatography on Silufol plates in the benzene-acetone (10:1) and (10:3) systems, and their structures were confirmed by their IR and PMR spectra and chemical reactions.

The ^{13}C NMR spectra of compounds (I-VII) were obtained on a standard Bruker HX-90 spectrometer in the pulsed regime of accumulation with Fourier transformation. To record the spectra we used saturated solutions: of (I) and (V) in CDCl_3 , and of (II-IV), (VI), and (VII) in DMSO. Chemical shifts were measured with an accuracy of 0.1 ppm relative to the signal of the solvent with subsequent recalculation to the TMS scale from the formulas $\delta = \delta_{\text{DMSO}} + 39.6$ and $\delta = \delta_{\text{CDCl}_3} + 76.9$. Spin-spin coupling constants were determined with an accuracy of 3.0 Hz.

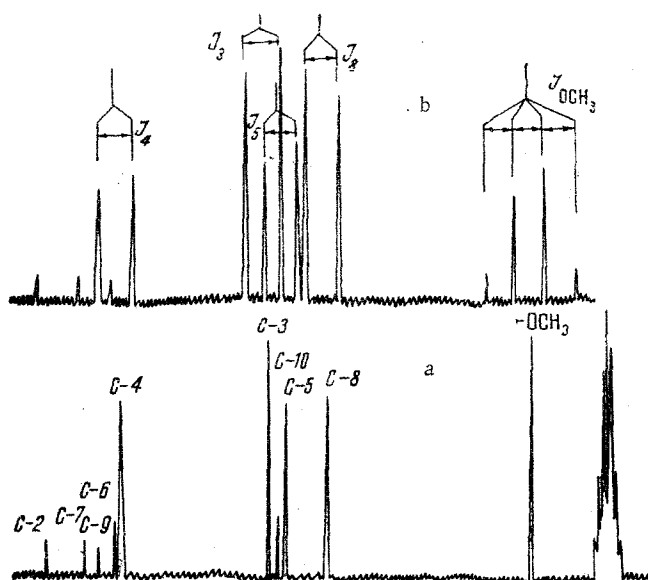


Fig. 4. ^{13}C NMR spectrum of scoparone: a) taken under the conditions of complete suppression of spin-spin coupling with protons; b) taken in the pulsed scanning regime.

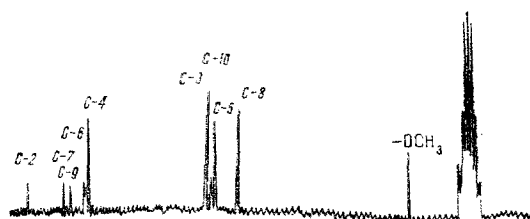


Fig. 5. ^{13}C NMR spectrum of scopoletin taken under the conditions of complete suppression of spin-spin coupling with protons.

TABLE 3. Contributions from Various Substituents (ppm) to the Magnitude of the Chemical Shifts of the Carbon Atoms of the Coumarin Nucleus in the ^{13}C NMR Spectra of Some Coumarins

Carbon atom	(VI), 7-hydroxy-coumarin	(II), 7-hydroxy-6-methoxycoumarin	(VIII), * 6-methoxycoumarin	(IX), † 7-methoxycoumarin	(III), 6,7-dimethoxycoumarin	(VIII), ‡ 6-methoxycoumarin	(VIII), ** 6-methoxycoumarin
C-2	0.7	0.4	-0.3	0.5	0.3	-0.2	-0.3
C-3	-4.6	-4.6	0	-3.6	-3.7	-0.1	0
C-4	1.3	1.3	0	0.1	1.2	1.1	0.6
C-5	2.5	-17.9	-20.4	1.0	-18.5	-19.5	-20.0
C-6	-10.6	21.6	32.2	-12.1	21.0	33.1	32.7
C-7	30.3	19.4	-10.9	30.9	21.0	-9.9	-10.4
C-8	-13.4	-13.5	-0.1	-15.4	-16.3	9.9	0.4
C-9	2.4	-4.2	-6.6	1.9	-4.4	-6.3	-0.4
C-10	-6.8	-7.9	-1.1	-6.5	-7.2	-0.7	-0.9

*Results obtained from an experiment using (VI) and (II).

†Results on the contribution of the substituents in ^{13}C NMR spectrum of (IX) taken from the literature [1]

‡Results obtained by using (IX) and (III).

**Mean value of the contribution of 6-methoxy substituents according to results * and **.

TABLE 4. Assignment of the ^{13}C NMR Signals in the Coumarin Nucleus of Bungeidiol Using the Contributions from Various Substituents to ^{13}C NMR Spectra

Carbon atom	(VIII), 6-methoxycoumarin	(X), [*] marmin	(I), bungeidiol	Chemical shifts of (I) in the ^{13}C NMR spectrum	
				calc. empirically	found experimentally
C-2					
C-3	-0.3	0.5	0.2	160.3	161.0
C-4	0	-3.7	-3.7	112.5	112.9
C-5	0.6	0.3	-0.9	145.3	143.1
C-6	-20.0	1.1	-18.9	108.6	107.8
C-7	32.7	-11.4	21.3	145.3	146.2
C-8	-10.4	30.0	19.6	151.0	151.6
C-9	0.4	-14.6	-14.2	102.0	100.9
C-10	-6.4	0.8	-5.6	147.9	149.3
	-0.9	-6.3	-7.2	111.2	111.1

*The figure for the contribution of the substituent in the ^{13}C NMR spectra of (X) was taken from the literature [3].

SUMMARY

The structure of a new terpenoid coumarin — bungeidiol — has been confirmed as 7-(4',7'-dihydroxy-3',7'-dimethyloct-2'-enyloxy)-6-methoxycoumarin with the aid of information obtained from ^{13}C NMR spectra and by the use of the additive contributions depending on natures and positions of various substituents (hydroxy and methoxy groups) in the aromatic ring of the coumarin nucleus.

A complete assignment of the signals of the carbon atoms in the ^{13}C NMR spectra of bungeidiol (I), scopoletin (II), scoparone (III), and isoscopoletin (IV) has been made.

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