A STUDY OF THE STRUCTURE AND CONFIGURATION OF THE TERPENOID COUMARINS KAMOLOL AND KAMOLONE BY PMR SPECTROSCOPY WITH THE ADDITION OF $Eu(DPM)_3$

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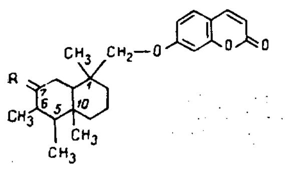
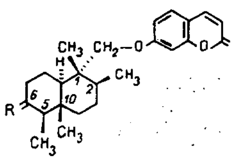
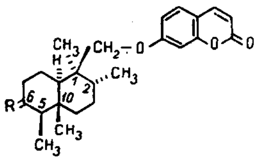
Structures (Ia) and (Ib), respectively, have previously been proposed for kamalol and kamolone – terpenoid coumarins from Ferula penninervis [1].



Ia R=H, –OH; Ib R=O



IIa R=α-H, β-OH; IIb R=O



IIIa R=β-H, α-OH; IIIb R=O

The following experimental facts form the basis of this structural formula for the sesquiterpene residue in (Ia) and (Ib). The selenium dehydrogenation of (Ia) and (Ib) gave 1,2,5-trimethylnaphthalene; it follows from the NMR spectra of kamolol and kamolone derivatives that the residue contains two tertiary and two secondary methyl groups with a $-C-CH_2-O$ grouping; and the hydroxyl in (Ia) (and, correspondingly, the carbonyl in (Ib)) is in the α position to one of the secondary methyls.

By analogy with other terpenoid coumarins isolated from plants of the genus Ferula an iresane skeleton was adopted as the most probable for the sesquiterpene moiety of kamolol and of kamolene.

On the basis of the theory of the biogenesis of terpenes, formulas (2a) and (2b), respectively, are proposed for kamolol and kamolone; they agree completely with the experimental facts published previously [1].

TABLE 1. Chemical Shifts of Some Groups in the PMR Spectra of Kamolol at Various Ratios of Reagent to Substance (M_r/M_s, $CDCl_3$, 0 – TMS, 20°C)

Group	δ (ppm), at the following M_r/M_s ratios					ΔEu, ppm
	0,23	0,33	0,41	0,47	0.60	
$CH-CH_3$	1,29	1,38	1,50	1,55	1,75	1,36
$C-CH_3$	1,41	1,50	1,62	1,68	1,88	1,41
$C-CH_3$	1,63	1,83	2,11	2,22	2,64	2,92
$CH-CH_3$	2,81	3,36	4,04	4,28	5,28	6,94
$-CH_2-O$	4,05	4,14	4,28	4,33	4,55	1,47

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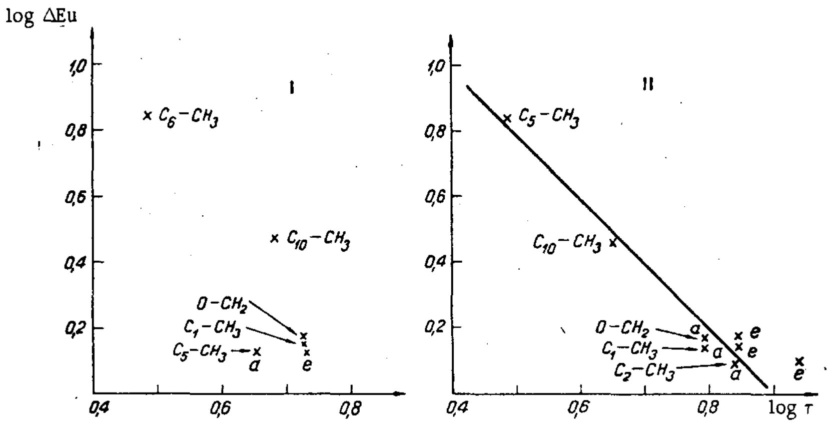

Fig. 1. Dependence of log ΔEu on log r for a number of the protons of kamolol: I) carbon skeleton of formula (1a); II) carbon skeleton of formula (2a). *a* and e are points corresponding to the axial and equatorial orientations of the groups given in the figure. In the structure of (Ia), the axial and equatorial groups at C_1 are located at the same distance from the hydroxyl, and therefore a single point is given for each of them.

For a definitive answer to the question of the structure and stereochemistry of the sesquiterpene residue in these compounds, we studied the PMR spectra of kamolol with additions of europium tris(dipivaloylmethanate) as paramagnetic shift reagent [3-5]. The same method of investigation was used as in preceding work [6]: the spectra of kamolol was taken in $CDCl_3$ with the successive addition of $Eu(DPM)_3$; the reduced shifts (ΔEu) for the signals of the methyl and C_1 methylene groups were measured at the tangents of the angles of slope of the straight lines drawn through the experimental points in plots of molar ratio of reagent to substance versus chemical shift in ppm (Table 1).

The distance from the oxygen atom of the hydroxy group to the groupings shown (r, Å) was measured on Dreiding models. The hydroxy group in kamolol is equatorial: on the spectrum of acetylkamolol the proton geminal to the acetoxy group gives a sextet at 4.68 ppm with two splitting constants of 10.5 Hz each and one constant of 5.0 Hz. It also follows from this that there are two axial protons and one equatorial proton in the α position to hydroxy group, i.e., the secondary methyl group adjacent to the hydroxyl is equatorial.

Figure 1 shows the logarithmic dependence of the reduced shift (ΔEu) on the distance of the protons of the groups under consideration to the oxygen atom of the hydroxyl for two variants of the carbon skeleton of the sesquiterpene residue (I) and (II). It can be seen from Fig. 2 that for variant (I) the points do not lie on a straight line. If, nevertheless, an attempt is made to draw such a straight line by treating the experimental results by the method of least squares, the tangent of the angle of its slope proves to be -2.82, which far exceeds the published value of -2.2 [4]. For the variant of carbon skeleton (II), on the other hand, there is a fairly good linear dependence of log ΔEu on log r. The tangent of the angle of slope of the straight line obtained by treating the results by the method of least squares is -1.98, which agrees well with the values given previously.

The axial orientation of the C_1-CH_2 and C_2-CH_3 groups and the equatorial orientation of the C_1-CH_3 group also follow from Fig. 1. The results of a consideration of the variant of the structure of kamolol with the hydroxy group in position 3 of formula (II) (which also corresponds to the experimental values obtained previously) shows that they likewise do not correspond to reality.

Thus, kamolol and kamolone correspond to structural formulas (IIIa) and (IIIb) or their mirror images.

The relative configurations of kamolol and kamolone postulated by Paknikar and Kirtany in [2] were not confirmed by the investigation performed.

SUMMARY

The relative configurations of kamolol and kamolone have been established by the PMR method using paramagnetic shift reagents.

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SOME REACTIONS OF COUMESTANS

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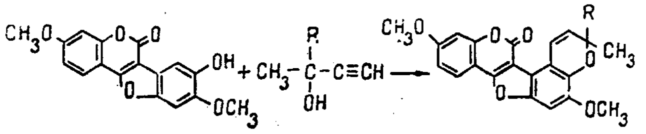
Continuing an investigation of coumestans, we have performed their condensation with acetylenic alcohols and their reduction with lithium tetrahydroaluminate.

The reaction of acetylenic alcohols with hydroxycoumarins and hydroxyacetophenones leads to ring closure with the acetylene residue to form dialkylchromenes [1]. The application of this reaction to hydroxycoumestans opens up the possibility of obtaining analogs of the natural coumestan sojagol isolated from soys beans [2]. We have studied the reaction of 11-hydroxy-7,12-dimethoxycoumestan (I) with 3-methylpent-1-yn-3-ol (II) and with 2-methylbut-3-yn-2-ol (III). Condensation took place only with the addition of small amount of zinc chloride to a mixture of equimolar amounts of a carbinol (II) or (III) with the coumestan (I).



I

II. $R = C_2H_5$

III. $R = CH_3$

IV. $R = C_2H_5$

V. $R = CH_3$

The structure of the products of the reaction of (I) with the alcohols (II) and (III) as the 7,12-dimethoxy-10,11-(2,2-dialkylchromeno)coumestans (IV) and (V) was confirmed mass spectrometrically. In the mass spectrum of (IV) there is a peak with m/e 392 (12%), which corresponds to the molecular weight of the coumestan (IV), and peaks with m/e 377 ($M^+ - CH_3$) and 363 ($M^+ - C_2H_5$). If the residue of the acetylenic alcohol was bound to the coumestan only by a simple ether bond, it would undergo cleavage with the formation of an ion with m/e 311 ($M^+ - 81$) corresponding to the ejection of an isopentyl residue ($C_5H_6 - CH_3$). However, there is no such peak in the mass spectrum of compound (IV). At the same time, the spectrum does contain the peaks of the doubly charged ions ($M^+ - C_2H_5$)/2 and ($M^+ - CH_3$)/2, which shows the stability of the ($M^+ - 29$) and ($M^+ - 15$) fragments formed. The appearance of such ions is possible in a number of cases, including those in which there is a closed conjugated system. In our case, this system can be produced only by the formation of the 10,12-(2-ethyl-2-methylchromeno)coumestan (IV). Peaks of a doubly charged ion are present in the mass spectrum of the coumestan sojagol [2]. No similar peaks were observed in the mass spectra of esters and ethers of coumestan that we prepared.

Grisebach, studying the biogenesis of coumestrol, put forward a hypothesis of a possible route of its formation in plants via pterocarpans [3]. A number of workers have shown the possibility of the synthetic passage from pterocarpan to coumestans and conversely [4, 5]. The reaction of coumestans with lithium tetrahydroaluminate is the first step of the transition from coumestans to pterocarpans, which confirms a possible biogenetic link between these compounds. The reduction of 7,11-12-tribenzyloxycoumestan (VII) with

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