STRUCTURE OF THE COUMARINS COLLADIN AND COLLADONIN. II

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We have previously reported [1] the isolation from **Colladonia triquetra** (family **Umbelliferae**) of two new coumarins, C_1 and C_2. This paper gives the results of a study of the structures of these compounds which we have called "**colladin**" (C_1) and "**colladonin**" (C_2). The investigation of these substances shows that colladin (I) has the composition $C_{26}H_{32}O_5$, mp 153–154° C, $[\alpha]_D^{22}$ – 65° (c 0.45; chloroform), and colladonin (II) $C_{24}H_{30}O_4$, mp 158.5–160° C, $[\alpha]_D^{22}$ – 50° (c 0.60; chloroform).

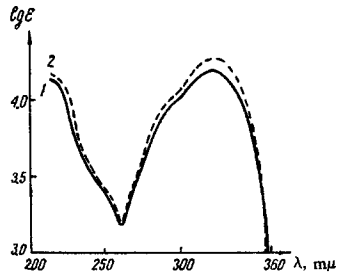


Fig. 1. UV spectra of colladin (1) and colladonin (2).

The UV and IR spectra (Figs. 1 and 2) confirm that these substances belong to the coumarin group [2, 3]. In addition to this, the IR spectrum shows the presence of a hydroxyl group in the molecule of II (3535 cm^{-1}).

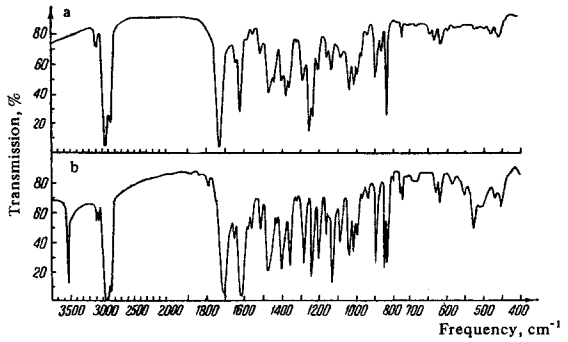


Fig. 2. IR spectra of colladin (a) and colladonin (b).

The NMR spectra of I and II (Fig. 3, Table 1) show that both compounds are 7-monosubstituted coumarins with a number of common structural elements.* The difference in the spectra of these compounds is connected with the presence in I of an O-acetyl grouping in place of the hydroxyl in II. In accordance with this, when colladin was saponified with caustic potash in methanol, colladonin was obtained, and the acetylation of colladonin with acetic anhydride in pyridine gave colladin. Thus, the two compounds are in a close structural relationship: colladin is the acetyl derivative of colladonin, and the study of their structures reduces to a consideration of the structure of one of them, colladonin.

The oxidation of II with Beckmann's mixture gave compound III, $C_{24}H_{28}O_4$, the IR spectrum of which lacked the hydroxyl band, while there were two bands in the carbonyl region, at 1741 cm^{-1} (C=O of an α-pyrone ring), and 1719 cm^{-1} (C=O of a saturated ketone). The compound obtained is therefore a ketone which shows that the hydroxyl group in II is attached to a secondary carbon atom (this corresponds to the features of the NMR spectrum). Compound III

*The assignments of the signals in the spectra were made on the basis of results of our previous works [4, 5].

Table 1. Features of the NMR Spectra of Colladin and Colladonin

Chemical shift, δ, ppm	Multiplicity, J, Hz	Intensity	Assignment
	Colladin		
0.85 0.88	Three superposed singlets	9H	$3CH_3-\overset{|}{\underset{|}{C}}-$
2.04	Singlet	3H	$CH_3-\overset{O}{\overset{\|\|}{C}}-O$
4.20	Doublet 6.0	2H	$>CH-CH_2-OAr$
4.53	Singlet	1H	$CH_2=C<$
4.90	Singlet	1H	
4.55	Multiplet	1H	$>CH-O-\overset{|}{C}=O$
6.20	Doublet, 10.0	1H	H_3
6.79	Doublet, 1.5	1H	H_8
6.79	Quartet, 1.5; 8.5	1H	H_6
7.35	Doublet, 8.5	1H	H_5
7.61	Doublet, 10.0	1H	H_4
	Colladonin		
0.80	Singlet	3H	
0.83	Singlet	3H	$3CH_3-\overset{|}{\underset{|}{C}}-$
1.00	Singlet,	3H	
3.25	Multiplet	1H	$>\underline{CH}-OH$
4.18	Doublet 6.0	2H	$>CH-\underline{CH_2}-OAr$
4.53	Singlet	1H	$CH_2=C<$
4.90	Singlet,	1H	
6.21	Doublet, 10.0	1H	H_3
6.79	Doublet, 1.5	1H	H_8
6.81	Quartet 1.5; 8.5	1H	H_6
7.35	Doublet, 8.5	1H	H_5
7.61	Doublet, 10.0	1H	H_4

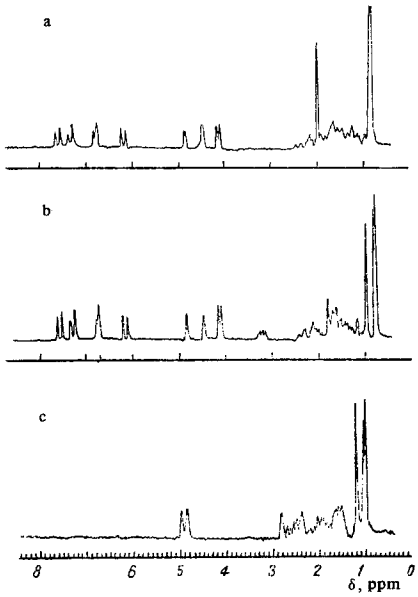
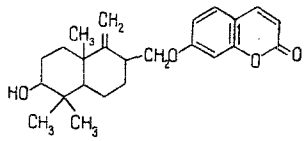


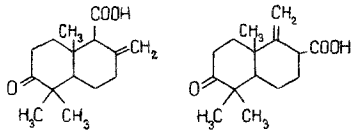
Fig. 3. NMR spectra of colladin (a), colladonin (b), and the keto acid IV (c).

proved to be identical with badrakemone*, a ketone obtained by N. P. Kir'yalov by the oxidation of the terpenoid coumarin badrakemin, for which the following structural formula has been proposed [6]:



The reduction of II with sodium borohydride gave colladonin, which shows the equatorial position of the hydroxyl group in it. From its physicochemical constants, II is identical with isobadrakemin, which is formed in the reduction of badrakemone [6]. As was to be expected, the dehydrogenation of II with selenium led to the formation of 1, 2, 5, 6-tetramethylnaphthalene and umbelliferone.

The position of the exocyclic methylene group of $C_{(9)}$ given by Kir'yalov [6] was put forward on the basis of indirect considerations. For a definitive solution of this question, we oxidized II with chromic anhydride to a keto acid which, in accordance with the results of dehydrogenation, should have structure IV or IV'.



IV IV'

The choice between these formulas was made on the basis of the NMR spectrum of the keto acid. For structure IV the signal of a proton on a carbon atom should appear in the form of a feebly resolved signal, and for structure IV' in the form of a triplet or a multiplet. In the spectrum of the keto acid (see Fig. 3), there is a somewhat broadened singlet signal with an intensity of one proton unit at 2.85 ppm, which permits the clear choice of structure IV.

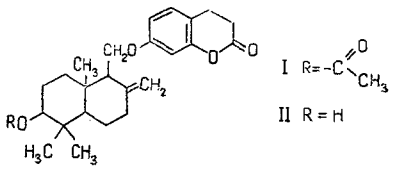
Thus, the structure of colladonin is similar to the structure of farnesiferol A [7]. Table 2 compares the constants of a series of derivatives of colladonin that we have obtained (see Scheme) and those of farnesiferol A [7].

Table 2. Some Constants of Colladonin, Farnesiferol A, and Their Derivatives

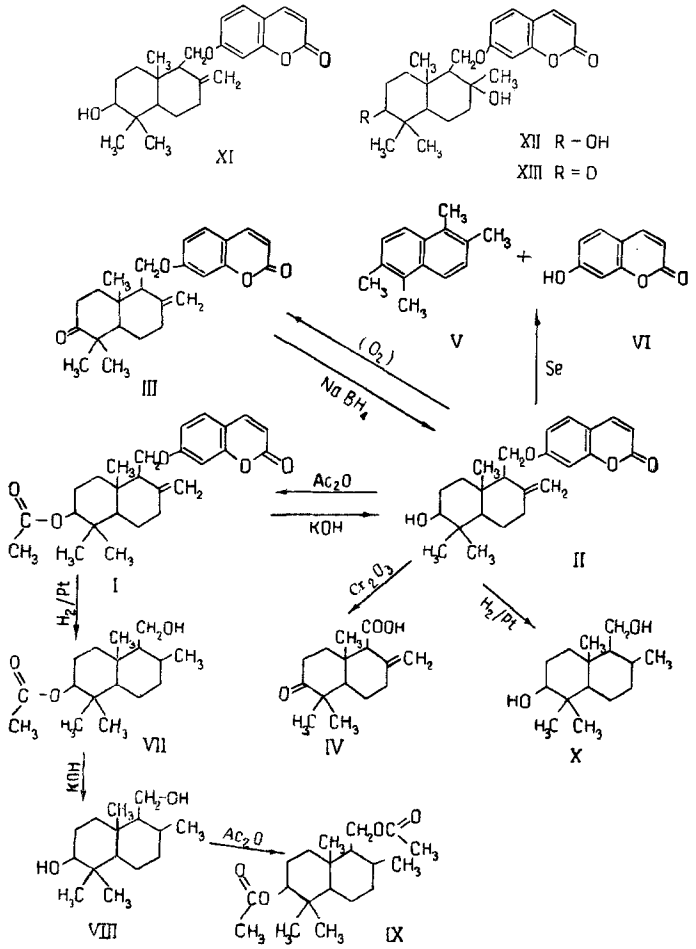
Compound	Composition	Mp, °C	$[\alpha]_D$, deg
Colladonin	$C_{24}H_{30}O_4$	158,5—160	—50
Farnesiferol A	$C_{24}H_{30}O_4$	155 —155,5	—55
Colladonin acetate (I)	$C_{26}H_{32}O_5$	154 —155	—65
Farnesiferol A acetate	$C_{26}H_{32}O_5$	142 —144	—55
The ketone III	$C_{24}H_{28}O_4$	184 —185	—40
The ketone from farnesiferol A	$C_{24}H_{28}O_4$	134 —135	—43
The keto acid IV	$C_{15}H_{22}O_3$	179 —180	+56
The keto acid from farnesiferol A	$C_{15}H_{22}O_3$	179 —180	—60
The diol VIII	$C_{15}H_{28}O_2$	177 —178	+26
The diol X	$C_{15}H_{28}O_2$	177 —178	—28
The diol from farnesiferol A	$C_{15}H_{28}O_2$	183 —185	+29
Monoacetate of the diol VII	$C_{17}H_{30}O_3$	107 —108	—35
Monoacetate of the diol from farnesiferol A	—	—	—
Diacetate of the diol IX	$C_{19}H_{32}O_4$	137 —138	—
Diacetate of the diol from farnesiferol A.	$C_{19}H_{32}O_4$	117 —119	+11.6

It can be seen from Table 2 that colladonin, and farnesiferol A differ in the constants of a number of derivatives and are therefore isomeric compounds. On the basis of what has been said above, the following formulas may be proposed for colladin (I) and colladonin (II):

*The sample of badrakemone was kindly given to us by N. P. Kir'yalov (BIN AN SSSR [Komarov Botanical Institute, AS USSR]).



According to the results presented, badrakemin [6], samarcandin, and samarcandone [8] must have structures XI, XII, and XIII.



Scheme of the transformations of colladin and colladonin

EXPERIMENTAL

The IR spectra were taken on a UR-10 spectrometer (mulls in paraffin oil), the UV spectra on an SF-4A spectrophotometer, and the NMR spectra on a JNM-4H-100 instrument (deuterochloroform). The chemical shifts are given relative to tetramethylsilane, the signal of which is taken as 0.

The optical rotations of the substances studied were measured in chloroform solution. The samples for microanalysis were dried at 60° C in vacuum for 6–8 hr. The melting points of the compounds are not corrected. The analytical results for all the compounds corresponded to the calculated figures.

O-Acetylcolladonin (I). A solution of 100 mg of colladonin (II) in 2 ml of a mixture of pyridine and acetic anhydride (1:1) was heated in the water bath for 1 hr. After the elimination of the solvent, substance I, $C_{26}H_{32}O_5$, was obtained with mp 154–155° C (ethanol), $[\alpha]_D^{22}$ – 65° (c 0.50). From the IR and NMR spectra and the absence of a depression of the melting point of a mixture, the compound obtained was shown to be identical with colladin.

Oxidation of II to III. In drops, 2 ml of Beckmann's chromic acid mixture was added to a solution of 100 mg of colladin in 15 ml of acetone, and the resulting mixture was left at room temperature for 10 min. Then it was diluted with 50 ml of water and extracted with diethyl ether (4 × 20 ml). The extract was washed with water, and dried with sodium sulfate, and the solvent was distilled off. This led to the deposition of crystals of III, $C_{24}H_{28}O_4$, mp 184–185° C from ether, $[\alpha]_D^{22}$ – 40° (c 1.02; chloroform). IR spectrum, cm^{-1}: 1738 (C=O of an α-pyrone), 1715 (C=O of a saturated ketone), 1631 (C=C bonds of aromatic rings).

Reduction of III with sodium borohydride. A solution of 50 mg of the ketone in 15 ml of 95% methanol was treated with 50 mg of sodium borohydride for 15 hr. The mixture was diluted with water, acidified with 20% H_2SO_4, and extracted with ether. The extract was washed with water and dried with sodium sulfate, and the solvent was distilled off. The residue consisted of a substance with the composition $C_{24}H_{30}O_4$, mp 155–156° C (from aqueous methanol), $[\alpha]_D^{22}$ – 50° (c 0.40). The IR spectrum of this compound was identical with that of colladonin. A mixture gave no depression of the melting point.

Dehydrogenation of II [6]. A mixture of 250 mg of the substance and 200 mg of selenium was ground to a fine powder and heated at 280–290° C for 30 min. The reaction product was treated with petroleum ether (bp 40–60° C). This gave 60 mg of an oil, which was chromatographed on alumina (10 g, activity grade II). The petroleum ether eluate gave 30 mg of an oil which crystallized from ethanol, mp 111–112° C. The 1,3,5-trinitrobenzoate of the hydrocarbon had mp 177–178° C (from ethanol).

Umbelliferone (VI). After the dehydrogenation product had been freed from hydrocarbons, the residue was treated with ether (8 × 25 ml) and the extract was shaken with 2% caustic potash solution (5 × 20 ml). The alkaline solution was acidified with 20% H_2SO_4 and extracted with ether, the extract was washed with water and dried with sodium sulfate, and the solvent was distilled off. The residue (40 mg) yielded crystals in the form of needles with mp 224° C (from water). The IR spectrum of the substance was identical with that of umbelliferone. The sample for analysis was sublimed in vacuum at 200° C.

The unsaturated keto acid IV. In 6 ml of glacial acetic acid, 500 mg of II was dissolved. Then the solution was oxidized with 50% chromic anhydride solution at room temperature for 5 hr. The reaction mixture was poured into cold water and extracted with ether (6 × 25 ml). The extract was shaken with 2% potassium bicarbonate solution (8 × × 25 ml), acidified with 20% H_2SO_4, and extracted with ether. The organic layer was washed with water to neutrality, dried with sodium sulfate, and evaporated. The residue (110 mg) was chromatographed on a column of silica gel (10 g), and was eluted with ether.

On standing, a mixture of the ethereal eluate and petroleum ether deposited crystals (60 mg) with mp 179–180° C, $[\alpha]_D^{21}$ + 56° (c 0.49). IR spectrum, cm^{-1}: 3220 (OH of a carboxyl), 1740 (C=O of a ketone), 1685 (C=O of a carboxyl), 1648 (C=CH_2). NMR spectrum (signals in ppm, s = singlet): 1.05 (s, 3H), 1.09 (s, 3H), 1.24 (s, 2H) (three tertiary methyls), 2.85 (s, 1H) (>CH–COOH) 4.84 (s, 1H); 4.96 (s, 1H) (>C=CH_2), 8.93 (1H) (COOH).

Found, %: C 72.10, 72.05; H 8.95, 9.07. Mol wt 250 (mass spectrometry). Calculated for $C_{15}H_{22}O_3$, %: C 71.97; H 8.86.

Hydrogenation of II. 400 mg of the substance was dissolved in 15 ml of glacial acetic acid and hydrogenated in the presence of 90 mg of Adams platinum catalyst.

The consumption of hydrogen was about 150 ml after 4 hr, and after this absorption ceased. The catalyst was filtered off, and the filtrate was diluted with water and extracted with chloroform. The extract was washed with water and dried with sodium sulfate. The solvent was distilled off, and the residue was saponified with 30 ml of 3% caustic potash solution in methanol in the water bath for 30 min.

The mixture was diluted and extracted with diethyl ether (4 × 20 ml). The ethereal solution was dried with sodium sulfate and evaporated. This gave 90 mg of crystals with mp 177–178° C, $[\alpha]_D^{26}$ – 28° (c 0.42).

Found, %: C 74.74, 75.21; H 11.72, 11.90. Calculated for $C_{15}H_{28}O_2$, %: 74.95; H 11.74.

Hydrolysis of I. 200 mg of the substance was saponified with 20 ml of 3% caustic potash solution for 30 min. The alkaline solution was diluted with water and acidified with 20% H_2SO_4. Colladonin (II) precipitated, and it was recrystallized from ethanol.

The oxidation of the hydrolysis product with Beckmann's chromic acid mixture gave the ketone III.

Hydrogenolysis of colladin (I). In solution in 15 ml of glacial acetic acid, 500 mg of the substance was hydrogenated over a platinum catalyst (100 mg) for 5 hr. After this time, 150 ml of hydrogen had been absorbed. The usual working up gave 510 mg of a residue which was chromatographed on a column of alumina (40 g, activity grade IV). Evaporation of the benzene eluate gave 120 mg of fine crystals of the **mono-O-acetyldiol** VII, with mp 107–108° C, $[\alpha]_D^{24}$ – 35° (c 0.50). IR spectrum, cm^{-1}: 3290 (OH) and 1730 (C=O of an acetyl group).

Found, %: C 72.15, 72.40; H 10.59, 10.86. Calculated for $C_{17}H_{30}O_3$, %: C 72.30; H 10.71.

Preparation of the diol VIII. 95 mg of the mono-O-acetyldiol VII was saponified in 20 ml of 3% caustic potash solution in methanol in the water bath for 30 min. The alkaline solution was diluted with ice water and extracted with ether (5 × 20 ml). The extract was washed with water, dried with anhydrous sodium sulfate, and distilled. This gave 80 mg of a residue crystallizing in the form of needles with mp 177–178° C [from a mixture of ether and petroleum ether (bp 40–60° C)], $[\alpha]_D^{22}$ + 26° (c 0.62). IR spectrum, cm^{-1}: 3230 (OH).

Found, %: C 74.86, 74.75; H 11.72; 11.88. Calculated for $C_{15}H_{28}O_2$, %: C 74.95; H 11.74.

The di-O-acetyldiol IX. 55 mg of the diol VIII was acetylated with 2 ml of a solution of acetic anhydride in pyridine (1 : 1). The usual working up led to the formation of crystals in the form of needles with mp 137–138° C (from ethanol). IR spectrum, cm^{-1}: 1732 (C=O of acetyl groups).

CONCLUSIONS

1. The structures of two new terpenoid coumarins have been established: colladin, $C_{26}H_{32}O_5$, with mp 153–154° C (from ethanol), $[\alpha]_D^{22}$ – 65 (c 0.45; chloroform) and colladonin, $C_{24}H_{30}O_4$, mp 158.5–160° C (from ethanol), $[\alpha]_D^{22}$ – – 50° (c 0.60; chloroform).
2. The structures of the coumarins badrakemin, samarcandin, and samarcandone have been corrected.

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