# A NEW TERPENOID COUMARIN FROM *Ferula kopetdaghensis*

A. A. Nabiev, T. Kh. Khasanov, and V. M. Malikov

UDC 547.9:582.89

From the roots of *Ferula kopetdaghensis* Eug. Kor. have been isolated nevskin and isosamarcandin and a new terpenoid coumarin kopeolone, $C_{24}H_{30}O_5$, $M^+$ 398, mp 125-126°C, $[\alpha]_D^{18}$ +70° (c 0.1, ethanol). On the basis of UV, IR, PMR, and mass spectrometry, and also of transformation into farnesiferols B and C, the configurations of kopeolone, kopeolin, kopeoside, fekrol, kopetdaghin, and fekolin have been established. The configuration of farnesiferol C suggested previously has been confirmed.

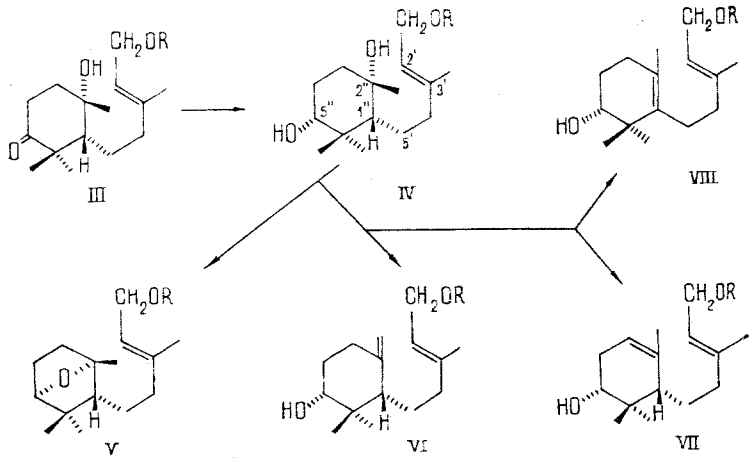
Continuing a study of *Ferula kopetdaghensis* Eug. Kor. [1, 2], we have isolated another three terpenoid coumarins.

By a comparison of physicochemical constants and spectral characteristics, substance (I) was identified as nevskin [3, 4] and (II) as isosamarcandin [5, 6]. The first compound proved to be new, and we have called it kopeolone.

Kopeolone (III) has the composition $C_{24}H_{30}O_5$, $M^+$ 398, mp 125-126°C, $[\alpha]_D^{18}$ +170° (c 1.0; ethanol). According to its UV spectrum, (III) is a 7-hydroxycoumarin derivative. The IR spectra contains absorption bands at ($cm^{-1}$) 1620, 1561, and 1515 (aromatic nucleus), 1712 and 1742 (C=O of an α-pyrone and of a ketone), and 3480 (hydroxy group).

The presence in the PMR spectrum of the signals of protons at (ppm) 6.15 (d, 1 H, $J_{3,4}$ = 9.5 Hz, $H_3$), 7.54 (d, 1 H, $J_{4,3}$ = 9.5 Hz, $H_4$), 6.70 (m, 2 H, $H_6$ and $H_8$), and 7.26 (d, 1 H, $J_{5,6}$ = 9.0 Hz, $H_5$) confirmed the assignment of (III) to the 7-monosubstituted coumarins. The spectrum also contained signals from the protons of two tertiary methyl groups at 1.01 and 1.12 ppm (singlets, 3 H each), of a hemihydroxylic methyl group — 1.33 ppm (s, 3H), and of a vinylmethyl group — 1.74 ppm (s, 3 H). In addition, signals due to the protons of an aryloxymethylene group at 4.49 ppm (d, 2 H, J = 7 Hz) and to an olefinic proton at 5.40 ppm (t, 1 H, J = 7 Hz) were observed.

From its composition and the characteristics of the PMR spectrum, the terpenoid part of kopeolone is monocyclic and it is possible to ascribe the structure (III) (R — coumarin) to it. The correctness of this structure was confirmed by the formation of kopeolin (XII) [7] when (III) was reduced with sodium tetrahydroborate.




Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, Vol. 1, pp. 48-51, January-February, 1982. Original article submitted June 2, 1981.

 0009-3130/82/1801-0044$07.50 

It must be mentioned that in the determination of the structure of kopeolin [7], the equatorial orientation of the $C_5''$—OH group had been shown. The configurations of the asymmetric centers at $C_1''$ and $C_2''$ remained undetermined. We have solved this problem in the following way. When kopeolin was dehydrated with sulfuric acid in anhydrous acetone, a mixture of substances consisting of four components was obtained. Subsequent separation on a column gave an anhydro product with the composition $C_{24}H_{30}O_4$, $M^+$ 382, mp 82-84°C, $[\alpha]_D^{20}$ −33° (c 1.0; chloroform), which, by a comparison of PMR spectra, was identified as farnesiferol C (V) [8-11]). On further elution, crystals with mp 105-106°C were isolated. PMR spectroscopy and TLC showed that they consisted of farnesiferol B (VI) [8, 9], kopetdaghin (farnesiferol D) (VII), [12, 13], and an isomer of kopetdaghin at the double bond (VIII) [12] with the latter predominating.

The formation of these compounds is explained in the following way. Farnesiferol C (V) is formed only when $C_2''$—OH and $C_5''$—OH are present in the same plane as the cyclohexane ring. As has been shown above, $C_2''$—OH has the equatorial orientation, and therefore the isolation of farnesiferol C unambiguously shows the axial orientation of the $C_2''$—OH group. In this position, it is spatially close to the $C_5''$—OH group.

Kopetdaghin (VII) is formed as the results of trans-diaxial elimination with the participation of $C_2''$—OH and $C_3''$—H, and the isomer of kopetaghin (VIII) is formed with the participation of $C_2''$—OH and $C_1''$—H.

One of the $C_2''$—$CH_3$ protons takes part in the formation of farnesiferol B (VI).

Thus, kopeolin has the configuration (IV) in which the $C_2''$—OH and $C_1''$—H are oriented axially. The analogous configuration exists in the new coumarin kopeolone (III) and in coumarins known previously: fekolin [1], kopetdaghin (VII), kopeoside [7], and fekrol [14].

The formation of farnesiferols B and C from one and the same coumarin kopeolin confirms the configuration of farnesiferol C suggested previously [8, 9], since it was adopted provisionally by the authors by analogy with the configurations of farnesiferols B and A [8, 9].

In conclusion, we note that on the basis of the results obtained, kopeolin is, in all probability, a biogenetic precursor of farnesiferol B, farnesiferol C, and kopetdaghin.

## EXPERIMENTAL

The conditions for recording the spectra have been described previously [2]. The $R_f$ values of the substances were determined by TLC on Silufol UV-254 in the chloroform—ethyl acetate (2:1) system.

Isolation of the Coumarins. The neutral fraction of an extract of the roots of *Ferula kopetdaghensis* (135 g) was chromatographed on a column (5.5 × 150 cm) of silica gel (KSK 60-120 μ, 1250 g) with elution by mixtures of hexane and ethyl acetate with increasing concentrations of the latter: fractions 1-28 (3:1), 29-43 (2:1), 44-51 (1:1). Fractions with a volume of 400 ml each were collected.

Nevskin (I). The concentrated eluate of fractions 28-31 deposited 0.51 g (0.019% of the weight of the dry plant) of colorless acicular crystals with the composition $C_{24}H_{32}O_5$, $M^+$ 400, mp 193-194°C (hexane—ethyl acetate), $[\alpha]_D^{20}$ −20° (c 1.0; ethanol), $R_f$ 0.15.

Kopeolone (III). Fractions 33-34 yielded 0.35 g (0.014%) of kopeolone with mp 125-126°C, $R_f$ 0.12. UV spectrum: $\lambda_{max}$ 221, 254, 295, 325 nm (log ε 4.14, 3.54, 3.79, 4.01).

Isosamarcandin (II). After the solvent had been distilled off from fractions 36-38, 0.5 g (0.019%) was obtained of a substance with the composition $C_{24}H_{32}O_5$, $M^+$ 400, mp 221°C (hexane—ethyl acetate), $[\alpha]_D^{20}$ +27° (c 0.4; ethanol). $R_f$ 0.11.

Reduction of Kopeolone. A solution of 0.3 g of (III) in 35 ml of 85% aqueous methanol was treated with 0.45 g of sodium tetrahydroborate. After 45 min, the mixture was diluted with water, acidified with 5% sulfuric acid solution, and extracted with ether. The etheral solution was washed with water, dried with anhydrous sodium sulfate, and evaporated. The residue was recrystallized from a mixture of diethyl ether and hexane to give kopeolin with mp 146-147°C, $[\alpha]_D^{25}$ −16° (c 0.98; ethanol), $R_f$ 0.05.

Dehydration of Kopeolin. A solution of 0.25 g of the substance in 25 ml of anhydrous acetone containing 1 ml of concentrated sulfuric acid was heated for 30 min, and it was then diluted with water and treated with ether. The etheral extract was washed with water, dried

with sodium sulfate and evaporated, and the 0.2 g of oily residue was chromatographed on a column (1 × 180 cm) of silica gel with elution by chloroform–hexane (1:1). Fractions 8-15 deposited 0.08 g (40%) of farnesiferol C (V), $C_{24}H_{30}O_4$, $M^+$ 382, mp 82-84°C, $R_f$ 0.55. From the subsequent fractions 24-35 was isolated 0.122 g (60%) of a crystalline mixture with mp 105-106°C, $R_f$ 0.37. According to PMR spectroscopy, it was a mixture of farnesiferol B (VI) (PMR spectrum: singlet signals from tertiary methyl groups at 0.68 and 0.96 ppm and a singlet signal from one proton of an exocyclic methyl group at 4.68 ppm), kopetdaghin (VII) (singlet signals from two tertiary methyl groups at 0.79 and 0.93 ppm and a multiplet signal from an olefinic proton at $C_3$", 5.17 ppm, $W_{1/2}$ = 15 Hz), and a double-bond isomer of kopetdaghin (VIII) (singlet signals from two tertiary methyl groups at 0.96 and 1.12 ppm, and a singlet signal of a methyl group at a double bond ($C_2$" in the 1.55 ppm region). The ratio of the anhydro products in the mixture was 1:1:2, respectively (from the integral intensities of the signals).

## CONCLUSION

From the roots of *Ferula kopetdaghensis* Eug. Kor. have been isolated nevskin, isosamarcandin, and the new terpenoid coumarin kopeolone (III), which is the ether of 7-hydroxycoumarin and 5'(e)-[2"(a)-hydroxy-5"-oxo-2",6",6"-trimethylcyclohexyl]-3'-methylpent-2'-en-1'-ol

By performing the passage to farnesiferols C and B, the configurations of kopeolin, kopeoside, fekrol, kopetdaghin, and fekolin have been established. The configuration of farnesiferol C proposed previously has been confirmed.

## LITERATURE CITED


1. A. A. Nabiev, T. Kh. Khasanov, and V. M. Malikov, Khim. Prir. Soedin., 516 (1978).
2. A. A. Nabiev, T. Kh. Khasanov, and V. M. Malikov, Khim. Prir. Soedin., 17 (1979).
3. V. Yu. Bagirov and N. P. Kir'yalov, Khim. Prir. Soedin., 387 (1972).
4. V. Yu. Bagirov, V. I. Sheichenko, and A. I. Ban'kovskii, Khim. Prir. Soedin., 450 (1976).
5. N. P. Kir'yalov and G. V. Bukreeva, Khim. Prir. Soedin., 643 (1972).
6. V. N. Borisov, A. I. Ban'kovskii, V. I. Sheichenko, and V. S. Kabanov, Khim. Prir. Soedin., 786 (1974).
7. Kh. M. Kamilov and G. K. Nikonov, Khim. Prir. Soedin., 308 (1973).
8. L. Caglioti, H. Naef, D. Arigoni, and O. Jeger, Helv. Chim. Acta, 41, 2278 (1958).
9. L. Caglioti, H. Naef, D. Arigoni, and O. Teger, Helv. Chim. Acta, 42, 2557 (1959).
10. V. Yu. Bagirov, R. Yu. Gasanova, O. I. Burma, and A. I. Ban'kovskii, Khim. Prir. Soedin., 279 (1977).
11. D. G. Turabelidze and É. P. Kemertelidze, Khim. Prir. Soedin., 657 (1976).
12. E. E. Tamelen and R. M. Coates, Chem. Commun., 13, 413 (1966).
13. Kh. M. Kamilov and G. K. Nikonov, Khim. Prir. Soedin., 422 (1974).
14. N. V. Veselovskaya, Yu. E. Sklyar, D. A. Fesenko, and M. G. Pimenov, Khim. Prir. Soedin., 851 (1979).