UDC 577.15/17: 582.89

ISOLATION OF THE COUMARIN BADRAKEMIN FROM THE ROOTS OF FERULA BADRAKEMA

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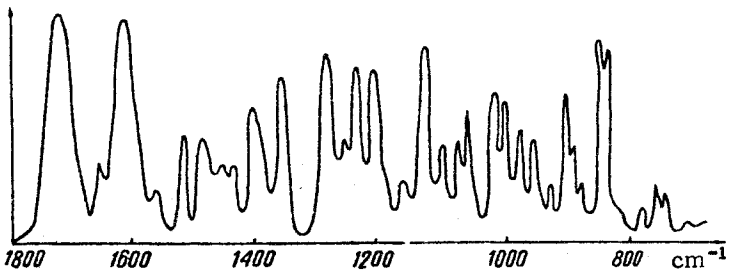
Khimiya Prirodnykh Soedinenii, Vol. 3, No. 6, pp. 363-367, 1967

A substance with the composition $C_{24}H_{30}O_4$, which the UV and IR spectra indicate to be a coumarin, has been isolated from the roots of Ferula badrakema (K. Pol.); it has been called badrakemin. The action of mineral acids on badrakemin decomposes it with the liberation of umbelliferone, and dehydrogenation with selenium gives 1, 2, 5, 6-tetramethyl-naphthalene. From the features of its IR spectrum (figure) and PMR spectrum, badrakemin contains a double bond of the $CH_2=$ type, a gem-dimethyl group, and one hydroxyl. The presence of the latter is confirmed by the formation of the acetate $C_{26}H_{32}O_5$.

The hydroxy group is secondary because on oxidation with chromic anhydride badrakemin forms a keto compound, badrakemone $C_{24}H_{28}O_4$, the IR spectrum of which exhibits a band at 1703 cm^{-1} which is characteristic for the CO group of a nonconjugated ketone with a six-membered ring. The hydroxy group of badrakemin is apparently axial since on reduction with sodium borohydride badrakemone is converted into isobadrakemin $C_{24}H_{30}O_4$. Like badrakemin, on acetylation isobadrakemin forms an acetate $C_{26}H_{32}O_5$, but with mp 151-152° C. The position of the gem-dimethyl group and the hydroxyl in badrakemin are possibly the same as in farnesiferol A [1] or in gummosin [2], which explains the ease of the removal of the hydroxyl and the migration of one methyl group in the dehydrogenation of the substances.

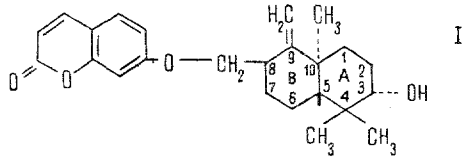
These results show that badrakemin has a structure similar to that of gummosin. However, on exhaustive hydrogenation did not give the saturated diol $C_{15}H_{28}O_2$ with mp 140-141° C which is characteristic for the hydrogenated decomposition product of gummosin [2]. Instead of this diol, on hydrogenation badrakemin formed a diol $C_{15}H_{28}O_2$ with mp 158-159° C and tetrahydrobadrakemin $C_{24}H_{34}O_4$ with mp 200-202° C. The diol $C_{15}H_{28}O_2$ with mp 173.5-175° C arising through the cleavage of an ether linkage and the reduction of a CO group to hydroxyl in the exhaustive hydrogenation of badrakemone is also not identical with the diol from farnesiferol A. The melting point of this diol is 183-185° C [1]. The impossibility of obtaining identical diols from badrakemin and gummosin or farnesiferol A indicates that badrakemin differs from gummosin and farnesiferol A in the arrangement of the ether linkage connecting the molecule of umbelliferone with the sesquiterpene diol. The position of the oxygen bridge in badrakemin is most probably at C-8, since its PMR spectrum does not contain the doublet of a secondary methyl group.

Another difference between badrakemin and gummosin or farnesiferol A is the position of the methylenic double bond in these substances. As compared with gummosin or farnesiferol A, the primary-tertiary double bond in badrakemin may be located not at C-8 but at C-9, i.e., adjacent to the angular methyl group. This is confirmed by the results of a study of the PRM spectra of badrakemin and gummosin. Although these PMR spectra are similar, the intensities of their maxima are different. Thus, the maximum at τ 9.2 in badrakemin is considerably more intense than that in gummosin. And, conversely, the signal with τ 9.07 is more intense in gummosin than in badrakemin. This difference is due, in our opinion, to a difference in the closeness of the double bond to the angular methyl group (the influence of a double bond on the chemical shift of the angular methyl group) since after the hydrogenation of badrakemin (for example, to tetrahydrobadrakemin) the difference in the intensities of the maxima in the region of the CH_3 group is obliterated.



IR spectrum of badrakemin (in paraffin oil).

At the present time, we may propose for badrakemin one of two possible formulas, I or II, differing only in the nature of the linkage of rings A and B. In I the configuration at C-5 and C-10 is similar to that of farnesiferol A and gummosin, and in II the possibility of a linkage of rings A and B in badrakemin of the type characteristic for triterpene substances is considered. From giogenetic considerations, I is preferable.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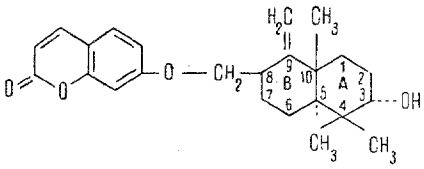
II

The material for the investigation was collected by B. Berdyev and V. V. Nikitin in the Kyzyl-Dzhar region (Badkhyz, TurkmSSR).

Experimental

Production of badrakemin. The dry comminuted roots were twice steeped in acetone (for 5 days each time). The yield of resin was 15–17%. The viscous yellowish liquid, smelling strongly of terpenes, was dissolved in ether and shaken with a solution of Na_2CO_3 and then with KOH. Acidification of the alkaline solution yielded 5–7% of amorphous substances which did not crystallize from a mixture of diethyl ether and petroleum ether.

On standing, the neutral ethereal layer deposited acicular crystals of badrakemin. Yield 2–3% (of the weight of the dry roots), mp 198–199° C (from ethanol), $[\alpha]_D$ −64° C (c 5; chloroform). The crystals gave one spot (R_f 0.2) on a plate of alumina (activity grade II) with chloroform as solvent. IR spectrum: 3600, 1725, 1650, 1615, 1557, 1508, 1477, 1448, 1432, 1400, 1388, 1354, 1280, 1270, 1234, 1205, 1183, 1157, 1150, 1126, 1070, 1056, 1043, 1015, 1000, 975, 952, 927, 902, 894, 850, 843, 820, 782, 760, 753, 715 cm^{-1}. UV spectrum: λ_{max} 322, 252 mμ (log ε 4.08, 3.35).

Found, %: C 75.25, 75.35, H 8.08, 8.07. Calculated for $C_{24}H_{30}O_4$, %: C 75.39, H 7.85.

Cleavage of badrakemin. To a solution of 0.2 of the substance in 3 ml of acetic acid 2 ml of sulfuric acid was gradually added. After 10 min, 50 ml of water was added to the mixture and it was heated to boiling and filtered. The crystals that deposited from the filtrate were recrystallized from water, mp 231–232° C. In admixture with umbelliferone the substance gave no depression of the melting point.

Dehydrogenation of badrakemin. A mixture of 0.25 g of the substance and 0.2 g of selenium was heated to 260–280° C for 30 min. After cooling it was treated with petroleum ether (2 × 15 ml). The extract was filtered through a 10-cm layer of alumina(activity grade II, 15 g). Then it was washed with 20 ml of petroleum ether. This gave 55 mg of 1, 2, 5, 6-tetramethylnaphthalene with mp 113–115° C (from aqueous ethanol).

Acetylation of badrakemin. A mixture of 0.5 g of the substance and 6 ml of acetic anhydride and pyridine (3:3) was heated for 1 hr. The solvent was evaporated off, and badrakemin acetate, which is sparingly soluble in ether, was isolated from the residue, with mp 175.5–177° C (from ethanol); $[\alpha]_D$ −16° (c 6.25; chloroform). On a plate of alumina (activity grade II) with chloroform the substance gave a single spot with R_f 0.7. IR spectrum: 1723, 1641, 1616, 1551, 1502, 1460, 1432, 1414, 1398, 1375, 1357, 1290, 1255, 1236, 1206, 1128, 1072, 1048, 1038, 1022, 986, 970, 930, 890, 844, 818 cm^{-1}. There were no bands in the OH region. UV spectrum: λ_{max} 323 mμ (log ε 4.35), shoulders at 296, 250, and 240 mμ.

Found, %: C 73.9, 73.55; H 7.7, 7.55. Calculated for $C_{26}H_{32}O_5$, %: C 73.58, H 7.54.

Oxidation of badrakemin. 1 g of the substance was dissolved in 100 ml of hot acetone, the solution was cooled to +15° C, and a solution of chromic anhydride (1.7 g) in 1 ml of water and 20 ml of acetone was added. After 10 min, 20 ml of water was added together with ether to give separate layers. The ethereal layer was evaporated and the residue was dissolved in hot ethanol. On cooling snow-white crystals of badrakemone deposited with mp 185–186° C, $[\alpha]_D$ −42° (c 5; chloroform). The substance gave a single spot with R_f 0.48 on a plate of alumina (activity grade II) with chloroform. Yield 0.85 g. IR spectrum: 1727, 1703, 1648, 1618, 1505, 1460, 1425, 1392, 1365, 1346, 1326, 1275, 1230, 1210, 1150, 1125, 1097, 1005, 985, 917, 893, 833 cm^{-1}. There were no bands in the OH region UV spectrum: λ_{max} 322, 288 and 253 mμ (log ε 4.1, 3.8, 3.35). Badrakemone is readily soluble in chloroform and sparingly soluble in ether and ethanol.

Found, %: C 75.45; H 7.41. Calculated for $C_{24}H_{28}O_4$, %: C 75.78, H 7.36.

Reduction of badrakemone. With heating, 0.7 g of the substance was dissolved in 50 ml of 96% ethanol and then 0.5 ml of water and 0.5 g of $NaBH_4$ were added. On standing for 1.5 hr, the solution became yellow and the crystals

disappeared. The solution was treated with 20 ml of cold 2% sulfuric acid and extracted with ether. An isomer of badrakemin with mp 156–157° C (from aqueous ethanol), $[\alpha]_D$ −50° (c 9; chloroform) passed into the ether. The substance gave one spot with R_f 0.2 (conditions for chromatography as in the case of badrakemin). IR spectrum: 3580, 1707, 1653, 1609, 1510, 1484, 1445, 1430, 1404, 1356, 1283, 1240, 1200, 1160, 1129, 1082, 1034, 1014, 996, 968, 935, 892, 848, 833, 765, 755 cm^{-1}. UV spectrum: λ_{max} 324 (log ε 4.1) and shoulders at 304 and 252 mμ.

Found, %: C 75.57, 75.83, H 8.05, 8.20. Calculated for $C_{24}H_{30}O_4$, %: C 75.39, H 7.85.

Acetylation of isobadrakemin. A mixture of 0.25 g of the substance, 3 ml of acetic anhydride, and 3 ml of pyridine was heated in a water bath for 1 hr. The solvent was evaporated in vacuum. The residue was recrystallized from ethanol, mp 151–152° C, $[\alpha]_D$ −64.28° (c 5.6; chloroform). It gave a single spot near the finish (Al_2O_3, activity grade II, ether or chloroform). IR spectrum: 1726, 1642, 1616, 1577, 1541, 1510, 1456, 1435, 1402, 1372, 1355, 1284, 1248, 1234, 1204, 1154, 1132, 1036, 1005, 990, 974, 898, 842, 831 cm^{-1}. λ_{max} 324–326, 252 mμ (log ε 4.18, 3.37), shoulders at 296 and 238 mμ.

Found, %: C 73.85, 74.00, H 7.79, 7.83. Calculated for $C_{26}H_{32}O_5$, %: C 73.58. H 7.54.

Hydrogenation of badrakemin. A solution of 2.85 g of the substance in 50 ml of acetic acid was treated with 0.3 g of platinum oxide. Hydrogenation was carried out at 40–50° C. The amount of hydrogen consumed was 702 ml (for 3–4 double bonds). The solution was separated from the catalyst, diluted with water, and extracted with ether. The ethereal layer was washed with water and sodium carbonate solution, and was evaporated to small bulk. Crystals (0.7 g) deposited with mp 200–202° C (from ethanol), $[\alpha]_D$ −28.5° (c 3.5; chloroform). On elution with chloroform, the substance gave a single spot (chromatography on Al_2O_3, activity grade II). IR spectrum: 3620, 1765, 1630, 1590, 1515, 1480, 1460, 1430, 1390, 1370, 1330, 1270, 1245, 1210, 1160, 1140, 1105, 1075, 1060, 1020, 990, 970, 945, 900, 850, 820, 785 cm^{-1}. UV spectrum: λ_{max} 318–322, 284, 276 mμ (log ε 1.73, 3.58, 3.61).

Found, %: C 74.46, 74.36, H 9.18, 9.08. Calculated for $C_{24}H_{34}O_4$, %: C 74.6, H 8.80.

The mother liquor was evaporated to dryness and the residue was dissolved in 30 ml of ethanol and saponified with 5 ml of 50% KOH for 1 hr. Extraction with ether gave a substance with mp 158–159° C (from a mixture of diethyl and petroleum ethers), $[\alpha]_D$ −8° (c 2.5; ethanol). On elution with chloroform on a plate of alumina (activity grade II) the substance gave a single spot with R_f 0.05. IR spectrum: 3370, 1467, 1450, 1410, 1390, 1369, 1350, 1314, 1250, 1200, 1166, 1120, 1095, 1069, 1060, 1026, 984, 966, 936, 916, 864, 844, 810, 790 cm^{-1}. The substance was transparent in the UV region (400 to 220 mμ).

Found, %: C 75.41, 75.32, H 11.81, 11.85. 20H (Zerewitinoff). Calculated for $C_{15}H_{28}O_2$, %: C 75.00, H 11.66.

Hydrogenation of badrakemone. A solution of 0.3 g of the substance in 10 ml of acetic acid was hydrogenated in the presence of 0.1 g of platinum oxide (252 ml of H_2 was consumed). Just as in the hydrogenation of badrakemin, a product was obtained which was saponified with 10 ml of 5% ethanolic caustic potash for 1 hr. Ether extracted a substance with mp 173.5–175° C (ether–petroleum ether). The substance gave a single spot with a R_f value identical with that of the diol $C_{15}H_{28}O_2$ with mp 158–159° C (on elution with chloroform or diethyl ether.) IR spectrum: 3365, 1459, 1451, 1416, 1387, 1368, 1352, 1332, 1302, 1250, 1200, 1177, 1140, 1114, 1091, 1075, 1065, 1031, 1025, 1000, 993, 980, 972, 963, 950, 915, 870, 845, 812 cm^{-1}. The substance was transparent in the UV region (from 400 to 220 mμ).

Found, %: C 74.95, 74.88, H 11.82, 11.75. Calculated for $C_{15}H_{28}O_2$, %: C 75.0, H 11.66.

The IR spectra of the substances (in paraffin oil) were recorded by T. V. Bukreva on a UR-10 spectrophotometer, and the PMR spectra by T. N. Timofeeva on a 40-MHz spectrograph. The microanalyses were carried out by E. A. Solokova.

Summary

The roots of Ferula badrakema (K. Pol.) have yielded a coumarin badrakemin with the composition $C_{24}H_{30}O_4$, mp 198–199° C, $[\alpha]_D$ −64° (chloroform). The results of a chemical study and of UV, IR, and PMR spectroscopy have enabled us to propose structure I for badrakemin.

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17 December 1966

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