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The Structure of Adenostylone and Isoadenostylone - Two Furoeremophilanes from Adenostyles alliariae (Gouan) Kern.

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As a continuation of our studies of constituents isolated from plants of the Petasites family[1], we investigated sesquiterpenic substances from a plant of a related family Adenostyles Cass. From the light petroleum extract of the rhizomes of Adenostyles alliariae (Gouan) Kern, two crystalline sesquiterpenic compounds were isolated: adenostylone (main component) and isoadenostylone (minor component), both of molecular formula $C_{19}H_{24}O_4$ (m.w. = 316, mass spectrometry).

Adenostylone (m.p. 75-78°C, $[\alpha]_D^{24} = -69°$, $\lambda_{max}^{EtOH} = 302$ nm, log ε = 4.17, $\lambda_{max}^{EtOH} = 243$ nm, log ε = 3.68) exhibited the following bands in the infra-red spectrum: $\nu_{max}^{CCl_4} = 1535$ cm^{-1} (furan ring), 1680 and 1631 cm^{-1} ($\alpha,\beta,\alpha',\beta'$-unsaturated ketone), 1739 and 1150 cm^{-1} (saturated ester). The above data, the properties of adenostylone and our chemotaxonomical considerations[2,3] led us to postulate that the compound in question are of the furanoeremophilane type (I). The PMR spectrum (100 MHz, $CDCl_3$) contained signals characteristic for a secondary methyl group (doublet 3H; 9.04 τ, J = 6.5 Hz), tertiary methyl group (singlet 3H; 8.87 τ) methyl group on $C_{(11)}$ (3H; 8.09 τ, $J_{13,12}$ = 1.2 Hz) and α-furan proton on $C_{(12)}$ (1H; 2.62 τ, $J_{12,13}$ = 1.2 Hz), all in accordance with the proposed structure.

According to elemental analysis, the molecule contains a C_4-carboxylic acid attached in the form of an ester to hydroxyl group on ring B or A. The analysis further reveals the presence of a double bond which can be located only in ring A. According to the PMR spectrum, the ester moiety of adenostylone was isobutyric acid (doublets, 6H; 8.73τ , J = 7.0 Hz corresponding CH at 7.32τ) bound to hydroxy group in position $C_{(6)}$ (proton $H_{(6)}$ as singlet at 3.66); for chemical evidence see below.

Hydrogenation in ethyl acetate in the presence of 5% $Pd/SrCO_3$, adenostylone afforded a dihydro derivative $C_{19}H_{26}O_4$ (m.p. 84-86°C, $[\alpha]_D^{24} = -70.5^o$, $\lambda_{max}^{EtOH} = 278$ nm, log $\varepsilon = 4.10$, $\lambda_{max}^{EtOH} = 244$ nm, log $\varepsilon = 3.60$, $\nu_{max}^{CCl_4} = 1537$, 1693 and 1738 cm^{-1}). From the ultra-violet spectrum it follows that the carbonyl group conjugated with the furan ring is situated on $C_{(9)}$; the position of the ultra-violet maximum at 278 nm is characteristic for this type of compound[4].

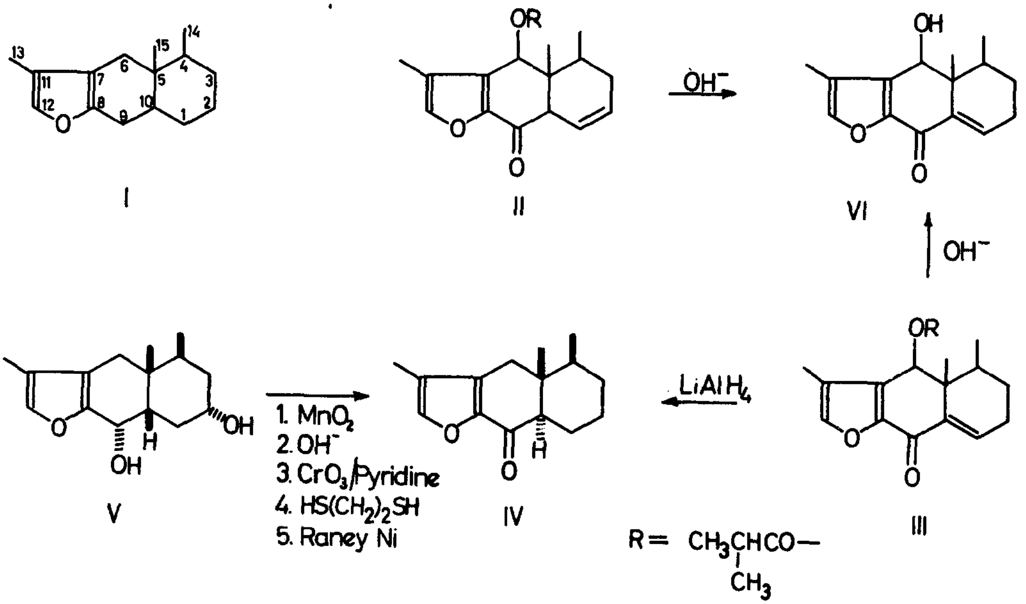
The shift of ultra-violet maximum from 302 nm at adenostylone to 278 nm at dihydroadenostylone shows that the double bond in adenostylone is conjugated with the carbonyl group. This agrees with the PMR spectrum according to which the double bond is trisubstituted (only a signal of one proton is present as a triplet at 3.05τ). On the basis of these facts, we suggest structure III for adenostylone.

Isoadenostylone (m.p. 92-94°C, $[\alpha]_D^{24} = \pm 0^o$, $\lambda_{max}^{EtOH} = 284$ nm, log $\varepsilon = 4.16$, $\lambda_{max}^{EtOH} = 243$ nm, log $\varepsilon = 3.61$) has the following infrared bands: $\nu_{max}^{CCl_4} = 1535$ cm^{-1} (furan ring), 1685 and 1631 cm^{-1} (α,β-unsaturated ketone), 1738 and 1150 cm^{-1} (saturated ester).

The PMR spectrum of this compound (100 MHz, $CDCl_3$) contains signals of all characteristic groups of the PMR spectrum of adenostylone III, except for the signals corresponding to protons of a double bond; here the double bond was disubstituted (2H; broad singlet at 4.2 τ). Frequency-swept-decoupling experiments and a spectrum measured in C_6D_6 solution proved that the double bond had to be in position 1.2. Thus isoadenostylone differs from adenostylone in the position of the double bond only and we suggest for it structure II.

On hydrogenation in ethyl acetate in the presence of 5% $Pd/SrCO_3$, isoadenostylone yielded a dihydro derivative $C_{19}H_{26}O_4$ (m.p. 56-58°C, $[\alpha]_D^{24} = -113.4^o$, $\lambda_{max}^{EtOH} = 282$ nm, log $\varepsilon = 4.08$, $\lambda_{max}^{EtOH} = 242$ nm, log $\varepsilon = 3.54$; $\nu_{max}^{CCl_4} = 1536$, 1685, 1738 cm^{-1}) stereoisomeric with dihydroadenostylone.

Lithium aluminium hydride reduction of adenostylone III gave a product $C_{15}H_{20}O_2$ (m.p. 148-150°C, $[\alpha]_D = -22.6^\circ$, $\lambda_{max}^{EtOH} = 278$ nm, log $\varepsilon = 4.10$, $\nu_{max}^{CCl_4} = 1538$, 1610 and 1686 cm^{-1}) identical with furoeremophilone (IV) isolated from Petasites hybridus rhizomes[5].



9-Oxo-furoeremophilane (IV) was correlated with a product prepared from furanopetasine, the structure which is known[4]. This product was prepared by manganese dioxide oxidation of the allylic hydroxyl group of furanopetasol (V), subsequent alkaline isomerisation, oxidation of the other hydroxyl group by chromium trioxide-pyridine complex, and conversion of the carbonyl group into a thioketal and its desulfuration by Raney-nickel.

Alkaline hydrolysis of adenostylone and isoadenostylone yielded the same product - 9-oxo-6-hydroxy-$\Delta^{10,1}$-furoeremophilane $C_{15}H_{18}O_3$ (VI) (m.p. 171-173°C, $[\alpha]_D^{23} = +108.8^\circ$, $\lambda_{max}^{EtOH} = 302$ nm, log $\varepsilon = 4.22$, $\nu_{max}^{CHCl_3} = 1539$, 1667 and 3575 cm^{-1}. The double bond of isoadenostylone shifted in the alkaline medium into conjugation with the keto group (VI) and this corroborated the isomeric relationship between the two compounds. The acidic material after hydrolysis contained isobutyric acid; the latter was characterized as a methyl ester by direct comparison with an authentic sample on gas chromatography.

The study of absolute configuration of both compounds is in progress. These results will be published in detail in Collection Czech.Chem.Commun.

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