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SYNTHESES OF PREREMIROL, ISOEVODIONOL, ACRONYLIN AND EVODIONOL

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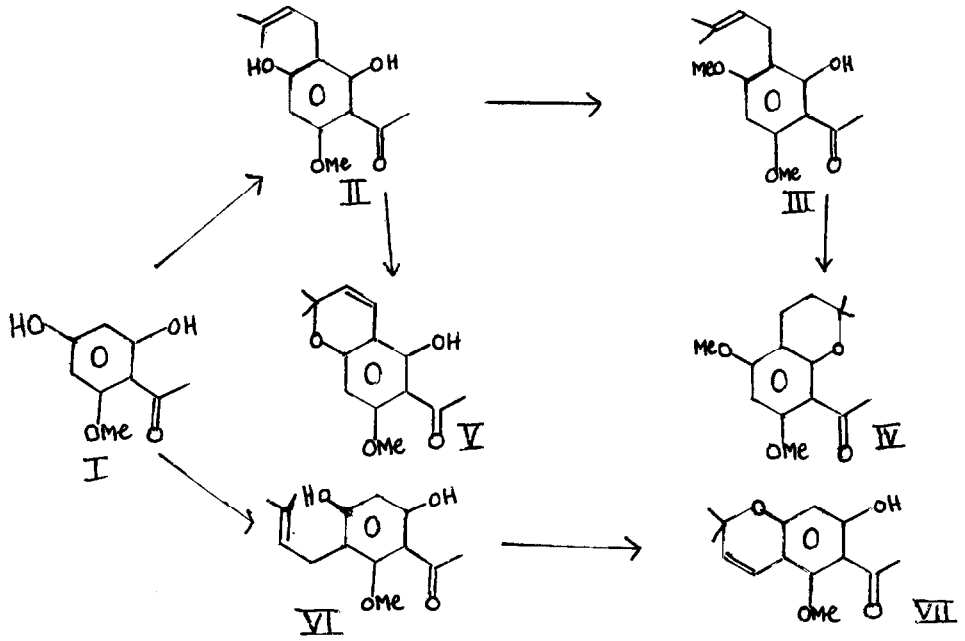
From the rhizomes of the tropical sea-shore plant Remirea maritima Aubl. (Cyperaceae), four phenolic ketones and three quinones all having isoprenoid units were isolated recently.[1-3] Two of these phenolic ketones viz. preremirol (II) and isoevodionol (V) are related to each other, the latter being the oxidatively cyclised product of the former. The structure of preremirol as 2-O-methyl 5-C-prenyl phloroacetophenone (II) was deduced mainly on the basis of 100 MHz n.m.r. and mass spectral data.[3] The possibility of the alternative 3-C-prenyl isomeric structure was ruled out because it gave on acid cyclisation two 2,2-dimethyl chroman derivatives, one showing ferric reaction and the other not. Similarly isoevodionol was assigned the structure as 2,2-dimethyl-6-aceto-7-methoxy-5-hydroxychromene (V) first on the basis of u.v. , n.m.r. and mass spectral data and then by the identity of its methyl ether with evodionol methyl ether and non-identity of isoevodionol with evodionol.[2]

Now both preremirol (II) and isoevodionol (V) have been synthesized, thus establishing their structures unequivocally. 2-O-Methyl phloroacetophenone (I) was prepared by partial demethylation of 2,4-di-O-methyl phloroacetophenone with anhydrous aluminium chloride in chlorobenzene medium according to the procedure of Manaktala and Seshadri[4] and subsequent column chromatography; the product has the same m.p. as reported by these workers and also earlier by Gulati and Venkataraman.[5] The ketone (I) was prenylated with excess prenyl bromide in the presence of methanolic potash as in the case of β-resacetophenone.[6] The major product separated by column chromato-

graphy was proved to be 5-C-prenyl-2-O-methyl phloroacetophenone (II), m.p. 171-172°; λ_{max} in ethanol: 227-230, 290,340(sh) nm (log ϵ 3.90, 4.13, 3.19 respectively) which shifted in alkali to 228(sh),243,323 nm (log ϵ 3.63, 3.56, 4.30 respectively); 60 MHz n.m.r. signals in $CDCl_3$ at δ 1.73, 1.78 (2d,J=5Hz, 6H, $\underline{Me}_2C=$), 2.58(1s, 3H,-CO-C$\underline{H}_3$), 3.32 (1d, J=7Hz, 2H, Ar-C$\underline{H}_2$-),3.82(1s,3H, -O$\underline{Me}$), 5.16(1m, 1H, -C$\underline{H}$=C$<$), 5.88 ppm (1s, aromatic H). That prenylation occurred in 5 position is in analogy with β-resacetophenone experiment under similar conditions[6] and also confirmed by partial methylation to (III, m.p. 113-114°, green ferric reaction) and subsequent acid cyclisation when 2,2-dimethyl chroman (IV, m.p. 76-77°)was obtained having no ferric reaction. The synthetic ketone (II) agrees completely in m.p. (173-174°) and u.v. data with preremirol.[3] Oxidative cyclisation of (II) with DDQ afforded only isoevodionol(V) as yellow needles, m.p. 127-128°; λ_{max} in ethanol; 270,292,304 (sh), 350 nm (log ϵ 4.48, 3.98, 3.90, 2.90 respectively) with no shift in alkali; 60 MHz n.m.r. signals in $CDCl_3$ at δ 1.42(1s,6H, $\underline{Me}_2C<$), 2.56(1s, 3H,-COC$\underline{H}_3$), 3.81 (1s, 3H, OC$\underline{H}_3$), 5.41, 6.63(2d, J=10Hz, 2H,-C$\underline{H}$=C$\underline{H}$-),5.83(1s,1 aromatic H). It also agrees in all properties as described in the case of natural isoevodionol.[2]

Acronylin has recently been isolated by Biswas and Chatterjee[7] from the light petroleum extract of the bark of Acronychia laurifolia BL (Family:Rutaceae) Its molecular formula $C_{14}H_{18}O_4$, u.v. and i.r. spectra suggested it to be a resacetophenone derivative and n.m.r. spectra of this itself and its diacetate pointed out the presence of a C-prenyl unit and a methoxyl group. In agreement with these, acronylin gave diacetate, dihydro-and demethyl-derivatives. The orientation of groups was determined by acid degradation of dihydroacronylin to isoamyl phloroglucinol and n.m.r. spectra of demethyl acronylin and isoacronylin and thus acronylin was given the structure of 3-C prenyl 2-O-methyl phloroacetophenone (VI). Now we confirm the structure of acronylin by its synthesis. It consists in prenylation of 2-O-methyl phloroacetophenone (I) with 2-methyl but-3-en-2-ol in the presence of boron trifluoride etherate according to the general procedure of Bohlmann and Kleine.[8] The product is a mixture of two mono C-prenyl derivatives and 3,5-di-CC-prenyl derivative. Separation was achieved

by column chromatography on silica gel. This result is similar to nuclear prenylation of β-resacetophenone under identical conditions.[9] 5-C-prenyl derivative was identified by comparison with preremirol as described above and therefore the other mono-C-prenyl isomer must be 3-C-isomer(VI) which was obtained as colourless crystals, m.p. 127-128°; λmax in ethanol: 235,282,315nm (log ε 4.19, 4.26, 3.81 respectively) shifting in alkali to 250,332 nm (log ε 3.95, 4.46 respectively); 60 MHz n.m.r. signals at δ 1.75, 1.77 (2d, J=7Hz,6H, $\underline{Me}_2C{=}CH$), 2.67 (1s, 3H,-CO-$C\underline{H}_3$), 3.32 (1d,J=7Hz, 2H, Ar $C\underline{H}_2$-), 3.71 (1s,3H,$O\underline{CH}_3$) 5.24 (1m, 1H,-$C\underline{H}{=}C$<), 6.19 ppm (1s, 1H, aromatic). It agreed with acronylin (VI) in all its properties.[7] Acronylin (VI) has further been oxidatively cyclised with DDQ to give 2,2-dimethyl-6-aceto-5-methoxy-7-hydroxy chromene as yellow prisms (VII); m.p. 85-86°; λmax in ethanol: 254-60,288(s), 340nm having no shift in alkali; 60 MHz nmr signals at δ 1.42 (1s, 6H, $\underline{Me}_2C$<),2.65 (1s, 3H,-CO-$C\underline{H}_3$), 3.78(1s, 3H,$O\underline{CH}_3$), 5.57, 6.49 (2d,J=10 Hz, 2H,-$C\underline{H}{=}C\underline{H}$-),6.16 ppm (1s, 1H, aromatic). It agrees with evodionol wich occurs in the Queensland plant Evodia littoralis[10] and the bark of the Newzealand plant Melicope simplex.[11] This constitutes the first synthesis of evodionol (VII).



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