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HEDYCHENONE: A FURANOID DITERPENE FROM *HEDYCHIUM SPICATUM**

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Key Word Index—*Hedychium spicatum*; Zingiberaceae hedychenone; diterpene.

Abstract—The structure of hedychenone, a furanoid diterpene, isolated from the rhizomes of *Hedychium spicatum* has been deduced on the basis of spectroscopic and chemical evidence.

INTRODUCTION

Hedychium spicatum Hem. is a perenial rhyzomatous herb growing at an altitude of 3500–7500 ft. Its rhizomes, which have a bitter camphor-like taste and a strong aromatic odour, have been used as an insect repellant and as a tobacco perfume [1]. Medicinally, the rhizomes have found use in stomach ailments and for treatment of pain and inflammation [2]. The present studies were undertaken since a 50% EtOH extract of the rhizomes, collected from Pithoragarh (Northern Uttar Pradesh) in April, showed anti-inflammatory activity [3]. Column chromatography on Si gel of the biologically active benzene soluble fraction yielded a new diterpene designated hedychenone, found to have structure **1**.

RESULTS AND DISCUSSION

Hedychenone, mp 135–36°, $[\alpha]_D$ +142° ($CHCl_3$), analyzed for $C_{20}H_{26}O_2$, M^+ 298. It gave a violet ring in the Liebermann–Burchard colour test and a yellow–green–black sequence of colours with impure thionyl chloride. A positive Ehrlich test and an orange colour with AcOH and a drop of H_2SO_4 [4], suggested that the hedychenone was a furanoid diterpene. The UV spectrum of hedychenone had a strong broad maxima at 239 nm (ε, 35600) with a shoulder at 215 nm and suggested that the molecule had two or more conjugated systems. Its IR spectrum (ν_{max}1664 and 1639 cm^{-1}) indicated that the molecule was an α,β-unsaturated ketone. The IR spectrum also indicated the presence of gem dimethyl (1381, 1372, 1225 and 1164 cm^{-1}) and furan (1502, 872 and 785 cm^{-1}) [5] moieties in the molecule.

The NMR spectrum of hedychenone integrated for 26 protons. One $\underline{H}$ multiplets at 2·52, 2·58 and 3·41τ confirmed the presence of a furan ring attached through a β-carbon atom [6]. Other features of this spectrum were three tertiary $C\underline{H}_3$ singlets at 9·04, 8·85 and 8·82τ, a triplet for a $C\underline{H}_3$ on a double bond at 8·2 (*J* 1·3 Hz), a methine $\underline{H}$ singlet at 7·9τ, a one $\underline{H}$ doublet (*J* 10 Hz) of quartets (*J* 1·3 Hz) centred at 7·07τ, doublets of 2 olefinic $\underline{H}$ at 3·54τ (*d*, *J* 16 Hz), 4·2τ (*d*, *J* 10 and 16 Hz) and a quartet attributed to the α-vinylic $\underline{H}$ of the α,β-enone at 4·1τ (*J* 2 Hz). The remaining methylenes resonated between 8·44–8·65τ.

The mass spectrum of hedychenone is similar to that of other bicyclic diterpenes [7]. The more abundant ions in its mass spectrum are the M^+ ion *m/e* 298 and ions *m/e* 175, 174, 123, 109, 93, 81 and 67. The base peak ion *m/e* 174 is likely to be formed as a result of a retro-Diels–Alder type cleavage. Its formation identifies the enone as a 7-en-6-one. This being the only position with which the right fragment (in the structure as depicted) would be *m/e* 174 and the left fragment less 15 mass units, *m/e* 109. The formation of the *m/e* 109 and 123 ions preclude the possibility of a substituent in ring A. The *m/e* 124 ion is less abundant. The abundance

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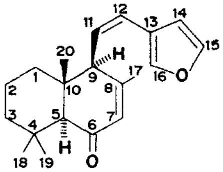
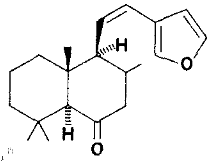
of the *m/e* 123 peak supports the location of a 6-keto function as this would enable ready transfer of a hydrogen atom in a peri position. The corresponding retro-Diels–Alder peak for the right fragment would then be at *m/e* 175, an abundant peak in the mass spectrum of hedychenone.

The mass of the ion from the right fragment (174) also indicates that this fragment contains in addition to the furan ring, the unplaced double bond. This double bond can be placed at Δ^{11}-conjugated to the furan ring on the basis of the UV spectrum and receives support from the formation of the ion *m/e* 93, which most probably arises from fission of the C9-C11 bond. The corresponding ions in the spectrum of 11,12-dihydrohedychenone are at *m/e* 176 and 95 respectively. The ions *m/e* 67 and 81 are likely to originate respectively from the furan ring and from the furan ring and an adjoining carbon atom after double bond rearrangement and transfer of one hydrogen atom.

The location of the side chain double bond at Δ^{11} received support from the spectral properties of 11,12-dihydrohedychenone formed on hydrogenation with Pd/C. This compound had $\lambda_{\max}$ 220 nm (ϵ, 9500) and 240 nm (ϵ, 11900) assignable largely to the furan and enone chromophores respectively. Ozonolysis of hedychenone also yielded β-furaldehyde, which was identified as a 2,4-dinitrophenylhydrazone.



(**1**)



(**2**)

The inert behaviour of the keto function is in support of its placement at position 6 [8, 9]. LAH reduction of hedychenone and 11,12-dihydrohedychenone (**2**) reduced the conjugated double bond (Δ^7) but not the keto function. The NMR spectrum of dihydrohedychenone indicates that this compound has a methyl on a double bond. The fact that the spectra of both LAH reduction products had signals for the new C–$C\underline{H}_3$ at 8·82τ, places this methyl as in other bicyclic diterpene at C-8.

The *cis* relationship of the C-20 $C\underline{H}_3$ and C-9(11) bond is suggested by a consideration of the chemical shifts of the C-20 $C\underline{H}_3$ in hedychenone and its derivatives. The respective chemical shifts of this $C\underline{H}_3$ in the NMR spectra of hedychenone, 11,12-dihydrohedychenone, hedychanone (**2**) and 11,12-dihydrohedychanone are 9·04, 9·15, 8·9 and 9·23. The Δ^{11} double bond, therefore, exerts a significant deshielding effect on the chemical shift of the C-20 $C\underline{H}_3$. This is only likely if the C-9(11) bond is *cis* to the C-20 $C\underline{H}_3$.

Tentative stereochemical assignments at C-9 and C-10 can be made from a consideration of optical rotations. There is good correlation between structure and optical rotation in bicyclic diterpenes [10]. The ring systems of almost all compounds having β-C-20 Me and C-9 (11) bonds are dextrorotatory. On the other hand the furanoid diterpenes daniellic acid [11] and polyalthic acid [12], which have α-stereochemistry are laevorotatory. The optical rotations of 11,12-dihydrohedychenone and 11,12-dihydrohedychanone are dextrorotatory and of the same order as those reported for the related 6-oxocativic acid and 6-oxolabdan-15-oic acid [8]. Hedychenone should, therefore, have β-stereochemistry at C-9 and C-10 as in (**1**). The related furanoid diterpene soladagenone [9] has been converted to a compound having a structure like 11,12-dihydrohedychenone but with uncertain stereochemistry at C-9. The optical rotation of this compound is not reported but its reported mp and that of dihydrohedychenone are the same. The high dextrorotation observed for hedychenone suggests that the material isolated is possibly contaminated with the $\Delta^{8(9)}$ and $\Delta^{8(17)}$ isomers which would be expected to be strongly dextrorotatory [10]. The material, however, behaves as a single compound on GLC and on TLC and its NMR spectrum integrates correctly for the assigned structure.

EXPERIMENTAL

Uncorrected capillary mp and photoelectrically measured $[\alpha]_D$ in $CHCl_3$ are reported. IR, UV and 60 Mcs NMR spectra were determined in KBr, EtOH and $CDCl_3$ with TMS as internal standard unless indicated otherwise. TLC was done on Si gel plates.

Isolation of hedychenone (**1**). Dried, chopped and milled rhizomes of *H. spicatum* (13 kg) were extracted with 50% EtOH by cold percolation and the extract concd under red. pres. to 1/10 vol. This concentrate was diluted with an equal vol. H_2O and extracted with C_6H_{14}, C_6H_6, EtOAc and H_2O (2 l. each). As almost all biological activity was extracted out into the C_6H_6 fraction (125 g), 50 g of this fraction were chromatographed on neutral alumina (1 kg). Elution with C_6H_{14}, C_6H_{14}–C_6H_6, C_6H_6 and EtOAc yielded hedychenone (570 mg) from the C_6H_6 eluate. It crystallized as needles from C_6H_{14} mp 135–36°, $[\alpha]_D$ $+142°$. (Found: C, 80·85; H, 8·61. $C_{20}H_{26}O_2$ requires: C, 80·53; H, 8·73%).

Dihydrohedychenone. **1** (500 mg) was hydrogenated in the presence of Pd/C (10%) in EtOH for 1 hr. Filtration, removal of solvent and recrystallization from light petrol (40–60°) yielded the product mp 56–58°; M^+ 300; $[\alpha]_D$ $+33°$; IR, ν_{max} 2865, 1669 (α,β-unsat. ketone), 1506 (furan), 1462, 1441, 1381 + 1362 (gem dimethyl), 1292, 1241, 1161, 1131, 1068, 1027, 996, 975, 878 and 785 cm^{-1}. UV, λ_{max} 220 nm (ϵ, 9500), 240 nm (ϵ, 11900). NMR (τ), 9·15, 8·89, 8·84 (3 *s* C-20, 19 and 18 $C\underline{H}_3$ resp.), 8·05 (*t*, *J* 1·3 Hz C-8 $C\underline{H}_3$), 7·57 (*m*, C-9 H, *J* 1 Hz), 7·25 (C-5 $\underline{H}$), 4·23 (*q*, *J* 1·3 Hz C-7 $\underline{H}$), 3·73 (*m* C-14 $\underline{H}$). MS (*m/e*): 300 (M^+), 285, 219, 176, 148, 135, 123, 109, 95 (base peak), 91, 82, 81, 68, 67, 66, 55, 53, 43. (Found: C, 79·88; H, 9·17. $C_{20}H_{28}O_2$ requires C, 80·00; H, 9·33%).

Hedychanone (**2**). $LiAlH_4$ was added to a stirred soln of (**1**) in THF at 0°. After stirring for a further 4 hr, excess $LiAlH_4$ was decomposed with EtOAc, the reaction mixture treated with dil. H_2SO_4 and the product extracted with Et_2O. The major product was isolated by preparative TLC but did not crystallize. M^+ 300; $[\alpha]_D$ $+62°$. UV λ_{max} 216 nm (ϵ, 18200) and 232 nm (ϵ, 20260). IR, ν_{max} ($CHCl_3$) 2907, 1712, 1431, 1362, 1236, 1214, 1160, 1094, 1071, 1027, 977, 918, 874 cm^{-1}. NMR (τ): 8·96, 8·9, 8·7, 8·4 (3*s* 12H), 7·9 (*s* 1H), 7·67, 7·60 (2*m* 2H), 7·5 (*bs*, 1H), 4·47 (*d J* 10 Hz) and 4·23 (*d J* 10 Hz, 1H), 3·98 (*s* 1H), 3·62 (1H), 2·7 (2H). (Found: C, 79·70; H, 9·1. $C_{20}H_{28}O_2$ requires: C, 80·00; H, 9·3%).

Dihydrohedychanone. $LiAlH_4$ was added to a stirred soln of 11,12-dihydrohedychenone in THF at 0°. After 4 hr stirring, the reaction mixture was worked up as above. The product purified by preparative TLC did not crystallize. M^+ 302; $[\alpha]_D$ $+26°$. UV, λ_{max} 216 nm (ϵ, 4900). IR, ν_{max} ($CHCl_3$) 2907, 1712, 1502, 1462, 1391, 1362, 1157, 1066, 1026 and 878 cm^{-1}. NMR (τ): 9·23, 9·08 (2*s* 6H), 8·82 (*s* 6H), 8·78–7·48 (14H), 7·0 (*m* 1H), 3·84 (*m* 1H), 2·88, 2·35 (2*m* 2H). (Found: C, 79·10; H, 9·50. $C_{20}H_{30}O_2$ requires: C, 79·47; H, 9·93%).

Ozonolysis of hedychenone. O_3 was passed through a soln of (**1**) (100 mg) in CH_2Cl_2 (25 ml) at $-10°$ for 4 hr. The reaction soln was then allowed to warm to room temp, stirred with Zn dust (400 mg) and AcOH (4 ml) for 1 hr, filtered and steam distilled: β-furaldehyde was identified in the distillate by extraction with Et_2O and conversion to a 2,4-dinitrophenylhydrazone mp 147°. (Found: N, 19·86. $C_{11}H_8O_5N_4$ requires N, 20·39%).

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