CHEMISTRY LETTERS, pp. 1687 - 1690, 1984.

TWO NEW SESQUITERPENOIDS (ALPINOLIDE AND HANAMYOL) FROM ALPINIA JAPONICA (THUNB.) MIQ.

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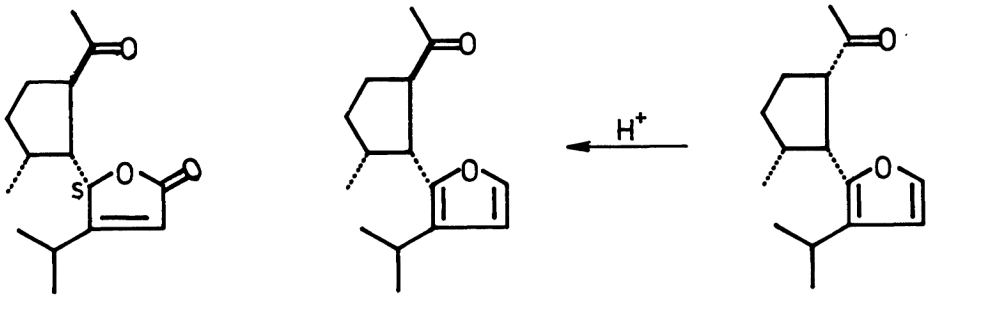
Two new sesquiterpenoids (alpinolide and hanamyol) were isolated from Alpinia japonica (THUNB.) MIQ. and the structures were determined by the spectral, the chemical evidence and X-ray analysis. The chemical transformation of hanalpinol into alpinolide may suggest the biogenesis of furopelargone A and B.

In our previous paper,[1,2] we have reported the isolation of 4α-hydroxydihydroagarofuran, 3α,4α-oxidoagarofuran, α-agarofuran, β-eudesmol, hanalpinol,[3] alpiniol, and pogostol from Alpinia japonica (THUNB.) MIQ. Biogenetically, furopelargone A and B are considered to be derived from hanalpinol or its analog through a cleavage of C9-C10 bond of its guaiane skeleton.[3] This paper concerns with the structure determination of alpinolide and the chemical transformation of hanalpinol into alpinolide, which may suggest the biogenetical pathway from hanalpinol to furopelargone A and B, and hanamyol containing a cyclic ether linkage.

Fresh rhizome of Alpinia japonica were extracted by the same manner as previously reported.[1] The chloroform-soluble fraction was further separated by silica gel column chromatography, and the eluates were finally purified by HPLC on silica gel and silver nitrate-coated silica gel to afford compounds 1, 2, 3, and 4.[4]

Compound 1 was isolated as colorless needles, $[\alpha]_D^{20}$ -19.7°(c 0.5, $CHCl_3$), mp 41-43 °C. The molecular formula $C_{15}H_{22}O_3$ was established by high resolu-



alpinolide (1) furopelargone A (2) furopelargone B (3)

tion mass spectrometry (250.1560). The IR (CCl_4), UV (EtOH), and ^{1}H-NMR ($CDCl_3$) spectra indicated the presence of an α,β-unsaturated butenolide (1760 and 1635 cm^{-1}; 217 nm, ε7100) and a methyl ketone group (1710 cm^{-1}; δ2.22, 3H, s). The ^{1}H-NMR spectrum of compound 1 furthermore exhibited signals for an isopropyl group (δ1.21, 3H, d, J=7 Hz; 1.27, 3H, d, J=7 Hz), a methyl proton on C4 (δ0.78, 3H, d, J=8 Hz), a vinylic proton (δ5.76, 1H, dd, J=2 Hz) due to the α-proton on an α,β-unsaturated butenolide, a lactonic methine proton (δ5.02, 1H dd, J=2, 3.5 Hz) and a methine proton adjacent to carbonyl group (δ3.35, 1H, dd d, J=6, 11 and 11 Hz). Decoupling experiments in C_6D_6 showed that the α-proton on an α,β-unsaturated butenolide at δ5.45 exhibited clear long-range couplings to the lactonic methine proton at δ4.82 and the isopropyl methine proton at δ2.07 in the values of J=2 Hz respectively, the C1 methine proton was coupled to α-H2, β-H2 and H5 in the values of J=6 or 11, 11 or 6, and 11 Hz respectively.

Based on the spectral properties as mentioned above, structural formula 1 was deduced for alpinolide which was a new sesquiterpenoid with an α,β-unsaturated butenolide. This was further corroborated by its ^{13}C-NMR spectrum ($CDCl_3$): δ16.2(q), 20.2(q), 22.1(q), 26.7(t), 28.1(d), 29.9(q), 34.1(t), 35.1 (d), 43.4(d), 51.2(d), 83.3(d), 114.6(d), 173.3(s), 178.8(s), 210.2(s).

The absolute configuration of alpinolide was determined by the chemical evidence as follows. Oxidation of hanalpinol[3] with pyridinium chlorochromate in methylene chloride afforded hanalpinol-9-one, which on reaction with BF_3-Et_2O afforded a sesquiterpenoid containing the α,β-unsaturated butenolide. It was completly identical with alpinolide by comparison of the spectral and optical properties. The reaction pathway is shown in Chart 1.

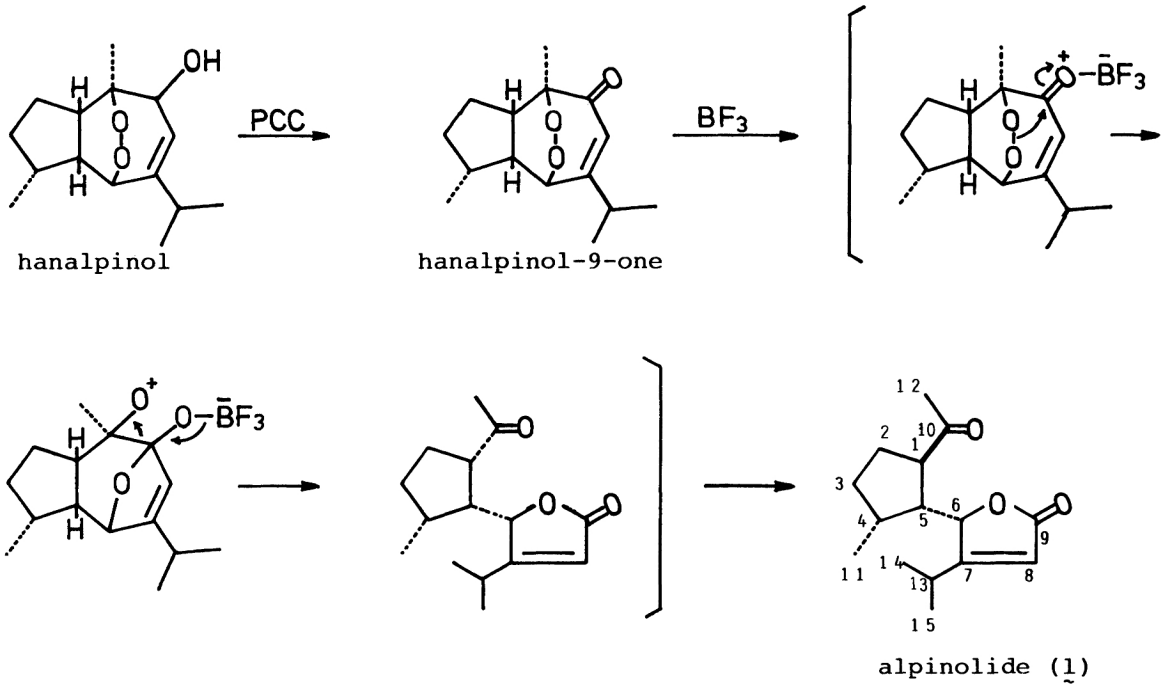


Chart 1.

The configuration of the acetyl group was determined by comparison of ^{1}H- and ^{13}C-NMR chemical shifts with those of furopelargone A and B, confirmed by X-ray analysis.

Compounds 2 and 3 were isolated as colorless oil, identified as furopelargone A and B, respectively by comparison of the spectral data with those of authentic samples reported in the literature.[5] Furopelargone B was isomerized to furopelargone A on addition of p-toluenesulfonic acid.

Compound 4 was isolated as colorless needles, $[\alpha]_D^{15}$ -18.0°(c 0.1, $CHCl_3$), mp 90-93 °C. The molecular formula $C_{15}H_{26}O_2$ was established by high resolution mass spectrometry (238.1950). In ^{1}H-NMR spectrum, signals of four methyl groups (δ0.95, 3H, d, J=7 Hz; 1.12, 3H, s; 1.20, 3H, s; 1.30, 3H, s) were observed. The IR (3650 cm^{-1}), a carbamate resonance signal (δ8.12, 1H, s) in ^{1}H-NMR spectrum on addition of trichloroacetylisocyanate(TAI)[6], and ^{13}C-NMR spectrum (δ90.64, 75.70, 73.57) suggested the presence of a tertiary hydroxyl group and a cyclic ether linkage in the molecule. The above data suggest a few possible structures for hanamyol, of which the structure shown below was proved by X-ray analysis.

Crystalographical data: $C_{15}H_{26}O_2$, monoclinic, space group C2, Z=16, a=25.897, b=10.229, c=22.311 Å, β=103.28°, recrystallized from n-hexane. A total of 5018 reflections were recorded on a Philips fourcircle diffractometer with graphite-monochromated Cu-Kα radiation. The structure was solved by direct methods and the refined final R value was 0.07. The asymmetric unit contains four independent molecules.

Hanamyol is considered to be derived from guaian-1,10-epoxide by the same biogenetical pathway reported in the literature.[2]

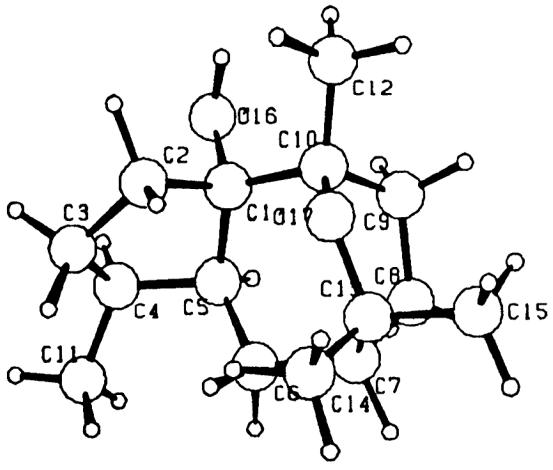
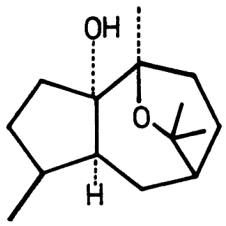


Fig.1. Molecular structure of hanamyol.



hanamyol (4)

References

1) H. Itokawa, K. Watanabe, S. Mihashi, and Y. Iitaka, Chem. Pharm. Bull., 28, 681 (1980).
2) H. Itokawa, H. Morita, K. Watanabe, and Y. Iitaka, Chem. Lett., 1984, 451.
3) H. Itokawa, K. Watanabe, S. Mihashi, and Y. Iitaka, 23rd Symposium on the Chemistry of Natural Products, Nagoya, 1980, Symposium Papers, pp. 428-435; H. Itokawa, K. Watanabe, H. Morita, S. Mihashi, and Y. Iitaka, Chem. Pharm. Bull., submitted.
4) Alpinolide $[\alpha]_D^{20}$-19.7°(c 0.5, $CHCl_3$). IR(CCl_4): 2975, 2880, 1760, 1710, 1635, 1470, 1355, 1310, 1260, 1166, 970.
Furopelargone A $[\alpha]_D^{22}$-128.6°(c 0.07, $CHCl_3$). IR(CCl_4): 2970, 2880, 1712, 1515, 1470, 1460, 1365, 1170, 1145, 1065, 705. ^{1}H-NMR(CCl_4): δ 0.68(3H, d, J=6 Hz), 1.13(6H, d, J=7 Hz), 1.98(3H, s), 2.80(1H, sept., J=7 Hz), 6.14(1H, d, J=2 Hz), 7.14(1H, d, J=2 Hz). ^{13}C-NMR($CDCl_3$): δ16.3 (q), 23.9(q), 24.1(q), 24.3(d), 28.0(t), 29.2(q), 34.2(t), 39.3(d), 42.1(d), 55.5(d), 108.6(d), 127.1(s), 140.2(d), 149.4(s), 209.8(s).
Furopelargone B $[\alpha]_D^{22}$+56.8°(c 0.4, $CHCl_3$). IR(CCl_4): 2985, 2905, 1720, 1520, 1475, 1360, 1150, 1075, 715. ^{1}H-NMR(CCl_4): δ0.70(3H, d, J=6 Hz), 1.13(6H, d, J=7 Hz), 1.73(3H, s), 3.52(1H, t, J=6 Hz), 6.13(1H, d, J=2 Hz), 7.14(1H, d, J=2 Hz). ^{13}C-NMR($CDCl_3$): δ16.1(q), 23.6(q), 24.4(q), 24.5(d) 24.7(t), 28.6(q), 31.9(t), 40.3(d), 43.8(d), 57.8(d), 108.0(d), 128.4(s), 140.9(d), 147.3(s), 208.1(s).
Hanamyol $[\alpha]_D^{15}$-18.0°(c 0.1, $CHCl_3$). IR(CCl_4): 3650, 2960, 2880, 1470, 1460, 1380, 1370, 1230, 1180, 1160, 1100, 1030, 1010, 905. ^{13}C-NMR ($CDCl_3$): δ90.6(s), 75.7(s), 73.6(s), 47.9(d), 36.4(d), 35.3(d), 32.3(t), 29.5(t), 29.3(q), 29.1(q), 26.7(q), 26.2(t), 24.4(t), 19.2(t), 15.0(q).
5) G. Lukas, J. C. N. Ma, J. A. Mccloskey, and R. E. Wolff, Tetrahedron., 20, 1789 (1964).
6) V. W. Goodlett, Anal. Chem., 37, 431 (1965).

(Received July 7, 1984)