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Novel Spiro-Compound, Hyperolactone from Hypericum chinense L.

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A novel metabolite spiro-compound, hyperolactone was isolated from stems and leaves of Hypericum chinense L. The structure was deduced by 2D-NMR experiment, chemical transformation and finaly by X-ray crystallography.

The plants belonging to Guttiferae family are well known folk medicines for the external wound in Japan. Previously, we reported two new antimicrobial compounds, chinesin I and II from flowers of Hypericum chinense L.[1] In this paper we describe a structure of novel constituent, which was named hyperolactone, from leaves and stems of H. chinense L.

Hyperolactone (1), (1098 mg), white crystalls, mp 57 °C, $[\alpha]_D$ -228.93 (MeOH, c 0.13), were isolated from methanol extract of leaves and stems (1.1 kg) of H. chinense L. by silica gel column chromatography. Molecular formula ($C_{14}H_{18}O_4$) was presumed from high mass (Found: 250.1195; Calcd: 250.1205) and ^{13}C-NMR ($CDCl_3$) spectrum. The IR (3100, 1796, 1701, 1647, 1615, 1596, 1585, 1010, 981 cm^{-1}) and UV [λ_{max}^{EtOH} 209 nm (ε 3500), 267 nm (ε 9400)] spectra showed absorption bands of carbonyl, conjugated carbonyl, enol ether and vinyl groups. Partial structures (Fig. 1) were obtained by the 2D-NMR ($CDCl_3$) experiments [^{1}H-^{1}H COSY, ^{1}H-^{13}C COSY,[2] and INEPT[3]]. The connection of these partial structures and quarternary carbons or disubstituted sp^2 carbons was deduced from the ^{1}H-^{13}C COSY for long range coupling (J_{C-H}=10 and 15 Hz) and INADEQUATE[4] experiments to show hyperolactone is formulated by (1) or its stereoisomers.

Chemical transformation of hyperolactone was then examined to complete the structure deduction.

Hydrogenation of hyperolactone (Pd/C) gave dihydro compound (2). Hydrolysis of hyperolactone with NaOH in MeOH caused decarboxylation to form two diastereomeric compounds (3). This suggests that hyperolactone has a β-keto ester or β-keto lactone system. Reduction of hyperolactone with $LiAlH_4$ produced an alcohol (4) which was acetylated to give diacetate (5). The structure of compounds 2, 3, 4, and 5 was deduced from the similar 2D-NMR experiments, IR, and mass spectra.[5] The stereochemistry was presumed by NOESY[6] experiment of diacetate 5. NOE peaks were observed between H-12 and H-14, which showed the stereochemistry at C-3 and C-4 of 5. These result led the conclusion that the structure of hyperolactone is displayed as (1) or its enantiomeric structure.

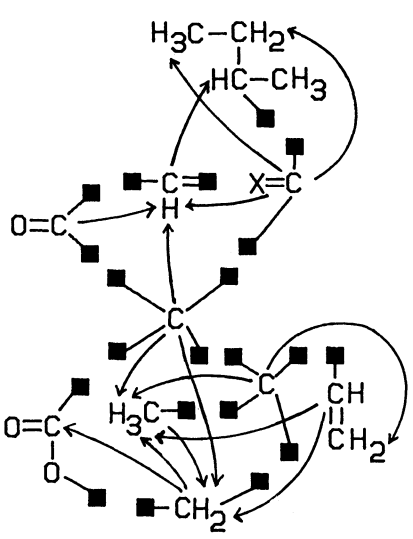

Fig. 1. Connection of partial structures by ^{1}H-^{13}C COSY (long range coupling, arrows: from carbon to hydrogen).

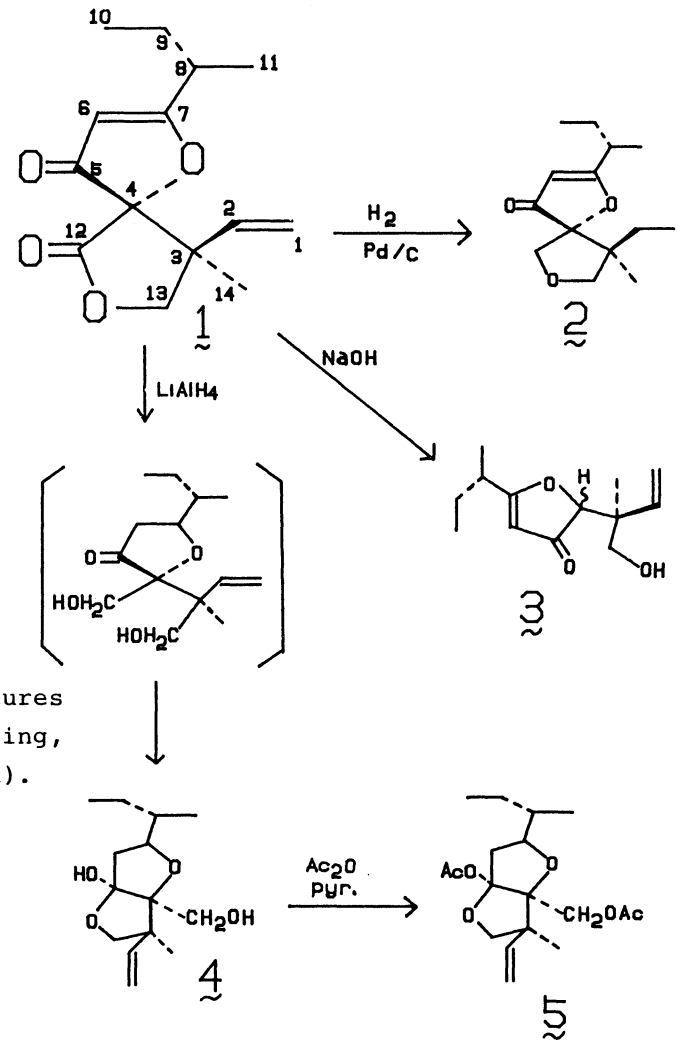

Fig. 2. Chemical transformation of hyperolactone.

The enol ether carbon of 1 , however, is observed at abnormally low chemical shift (δ 200.14). X-ray crystallography was finally examined.

Crystal data: $C_{14}H_{18}O_4$, MW 250.29, $P2_12_12_1$, a=13.568(1), b=13.750(1), c=7.484(3) A, V=1396 A^3, Z=4, Dx=1.191 (g cm^{-3}). A total of 1679, reflections were obtained, of which independent 1614 reflections were used for the structure determination. The structure was solved by the direct method and refined by full-matrix least-squares method. The residual values were R=0.0564, wR=0.0685. The result of X-ray crystallography proved that the structure of hyperolactone is the previously deduced structure 1 or its enantiomer. Refined structure of hyperolactone by X-ray crystallography showed very strained five membered rings. The biosynthetic route of hyperolactone is under consideration.

Table 1. NMR data of hyperolactone (1)

C	^{13}C-NMR (DEPT)	^{1}H-NMR (J/Hz)
1	118.76(CH)	5.25 d (17)
		5.28 d (11)
2	134.22(CH_2)	5.93 dd (17, 11)
3	48.32	
4	92.36	
5	197.24	
6	102.00(CH)	5.38 s
7	200.14	
8	37.01(CH)	2.69 tq (7, 7)
9	26.99(CH_2)	1.73 ddq (7, 7, 14)
		1.63 ddq (7, 7, 14)
10	10.94(CH_3)	0.97 t (7)
11	16.86(CH_3)	1.25 d (7)
12	167.90	
13	73.88(CH_2)	4.05 d (8)
		4.88 d (8)
14	19.21(CH_3)	1.41 s

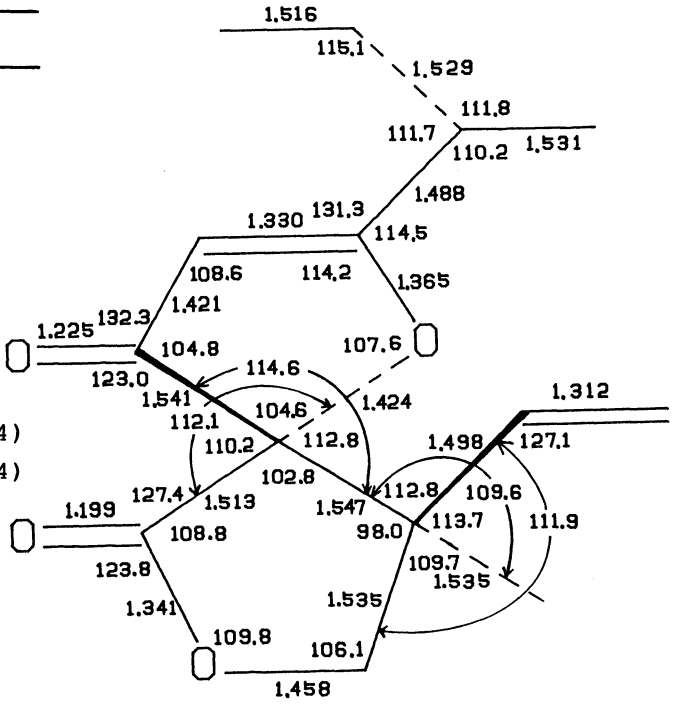

Fig. 3. Molecular structure of hyperolactone.

References

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5) The enantiometric structure of the derivatives 2, 3, 4, and 5 satisfy these experimental data.
6) J. Jeener, B. H. Meier, P. Bachmann, and R. R. Ernst, J. Chem. Phys., 71, 4546 (1979); S. Macura, Y. Huang, D. Suter, and R. R. Ernst, J. Magn. Reson., 43, 259 (1981).

Spectral data,

(2): IR, 3110, 1783, 1693, 1598, 1342, 1101, 1001 cm^{-1}, ^{1}H-NMR($CDCl_3$) δ 5.45(1H, d, J=0.4 Hz), 4.62(1H, dd, J=8, 0.8 Hz) 4.02(1H, d, J=8 Hz), 2.69(1H, tq J=6.5, 6.5 Hz), 1.78(1H, ddq, J=7, 14, 7 Hz), 1.58(1H, ddq, J=7, 14, 7 Hz), 1.62(2H, m), 1.29(3H, d, J=0.8 Hz), 1.27(3H, d, J=7 Hz), 1.00(3H, t, J=7 Hz), 0.83(3H, t, J=8 Hz), ^{13}C-NMR($CDCl_3$) δ 199.42(s), 197.76(s), 168.71(s), 102.60(d), 93.10(s), 75.75(t), 46.52(s), 37.33(t), 27.05(t), 25.02(t), 19.40(q), 17.02(q), 11.39(q), 8.16(q).

(3): a mixture of two diastereomers MS, M^+ m/z found 224.1394, calcd for $C_{13}H_{20}O_3$ 224.1411, IR, 3400, 3080, 1684, 1585, 1044 cm^{-1}, ^{1}H-NMR ($CDCl_3$)δ 5.86(1H, dd, J=11, 17 Hz), 5.78(1H, dd, J=11, 17 Hz), 5.45(1H, s), 5.44(12H, s), 4.57)1H, s), 4.50(1H, s), 3.82 (1H, d, J=11 Hz), 3.63(1H, d, J=11 Hz), 3.76(1H, d, J=12 Hz), 3.66(1H, d, J=12 Hz), 2.55(1H, m), 1.23(3H, s), 1.06(3H, s), ^{13}C-NMR($CDCl_3$)δ 204.63(s), 198.78(s), 139.43(d), 136.55(d), 116.75(t), 115.33(t), 103.88(d), 103.71(d), 89.11(d), 88.36(d), 67.64(t), 46.02(s), 45.48(s), 37.22(d), 26.98(t), 26.90(t), 18.62(q), 14.71(q), 17.23(q), 16.93(q), 11.45(q), 11.36(q).

(4): MS, M^+ m/z found 238.1579, calcd for $C_{14}H_{22}O_3$ 238.1569, IR, 3350, 3082, 1634, 1457, 1114, 1007 cm^{-1}, ^{1}H-NMR ($CDCl_3$)δ 6.14(1H, dd, J=11, 18 Hz), 5.14(1H, dd, J=1, 11 Hz), 5.10(1H, dd, 1, 18 Hz), 3.98(1H, ddd, J=8, 8, 8 Hz), 3.91(1H, d, J=8 Hz), 3.59(1H, d, J=8 Hz), 3.86(1H, d, J=12 Hz), 3.71(1H, d, J=12 Hz), 2.32(1H, dd, 8, 13 Hz), 2.18(1H, dd, 7, 13 Hz), 1.70(1H, m), 1.48(1H, m), 1.29(3H, s), 1.13(1H, m), 0.98(3H, d, J=7 Hz), 0.91(1H, t, J=7 Hz), ^{13}C-NMR($CDCl_3$)δ 139.36(d), 114.76(t), 114.60(s), 92.48(s), 81.69(d), 76.76(t), 60.74(t), 49.39(s), 44.09(t), 39.63(d), 25.46(t), 18.60(q), 15.02(q), 11.36(q).

(5): IR, 3086, 1747, 1654, 1637, 1224, 1039 cm^{-1}, ^{1}H-NMR($CDCl_3$)δ 5.94(1H, dd, J=11, 18 Hz), 5.25(1H, dd, J=1, 11 Hz), 5.17(1H, dd, J=1, 18 Hz), 4.34(1H, D, J=11 Hz), 4.23(1H, d, J=11 Hz), 4.12(1H, d J=11 Hz), 4.06(1H, d, J=11 Hz), 4.12(1H, dd, J=6, 11 Hz), 2.53(1H, dd, J=6, 18 Hz), 2.33(1H, dd, J=11, 18 Hz), 2.02(3H, s), 2.01(3H, s), 1.62(1H, m), 1.45(1H, m), 1.20(3H, s), 1.14(1H, m), 1.06(3H, d, J=6.6 Hz), 0.94(3H, t, J=7 Hz), ^{13}C-NMR($CDCl_3$)δ 214.84(s), 170.39(s), 170.12(s), 137.97(d), 116.91(t), 84.56(s), 84.56(d), 79.76(t), 67.74(t), 46.74(s), 42.41(t), 40.89(d), 25.44(t), 20.92(q), 20.80(q), 15.74(q), 14.95(q), 11.25(q).

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