STRUCTURES OF CUDRAFLAVANONE A AND EUCHRESTAFLAVANONE C[1]

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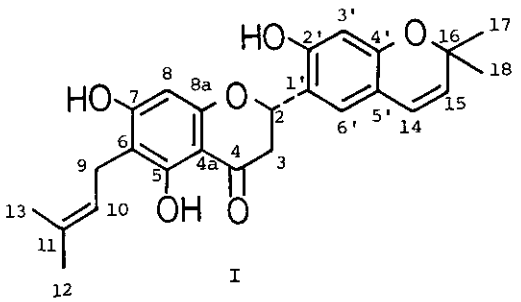
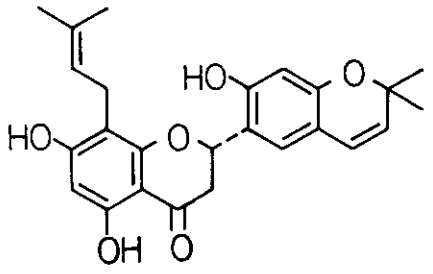
Abstract ——— From the benzene extract of the root bark of Cudrania tricuspidata (Carr.) Bur. (Japanese name "Hariguwa", Moraceae), an isoprene substituted flavanone derivative, named cudraflavanone A, was isolated, for which structure (I) was determined on the basis of the spectral and chemical evidences. From this result, the structure of euchrestaflavanone C which had been isolated from Euchresta japonica Hook. f. ex Regel, was reversed from the structure (I) to (II).

In the previous papers[2,3] we reported the structure determination of four isoprenylated xanthone and two flavone derivatives isolated from the root bark of Cudrania tricuspidata (Carr.) Bur. which belongs to family Moraceae. In the course of our studies, a new flavanone, named cudraflavanone A (I), was isolated from the benzene extract of the root bark. In this paper, we report the structure determination of this new compound, and the revision of the structure of euchrestaflavanone C for which the structure (I) had been proposed.[4]

The dried root bark (250 g) of Cudrania tricuspidata was extracted with n-hexane and then with benzene. The benzene extract was fractionated sequentially by the silica-gel column chromatography and by preparative thin layer chromatography. This procedure yielded a new flavanone, cudraflavanone A (I, 70 mg). Cudraflavanone A (I) was obtained as yellow prisms, mp 194°C, $[\alpha]_D^{18}$ -109.8°(c= 0.0984, EtOH), $C_{25}H_{26}O_6$ (high-resolution mass spectrum, m/z 422.1700), and was positive to methanolic ferric chloride (a dark violet color), magnesium-hydrochloric acid, and sodium borohydride tests.[5] The compound (I) showed the following spectra; IR ν_{max}^{KBr} cm^{-1}: 3430(br), 1635, 1500, 1450; UV λ_{max}^{EtOH} nm(log ε): 294(4.45), 314(sh 4.15), 332(sh 3.69); $\lambda_{max}^{EtOH+AlCl_3}$: 295(4.41), 314(sh 4.23), 334(sh 3.61). These findings suggest that I is a flavanone derivative.[6] This assumption was substantiated by the ^1H nmr spectrum (acetone-d_6) of I, in which the signals were



I



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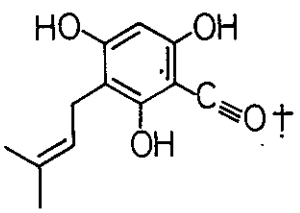

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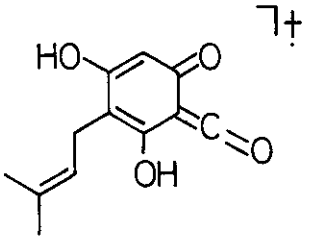

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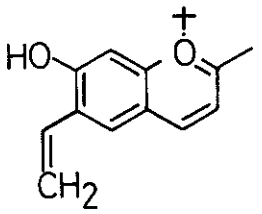
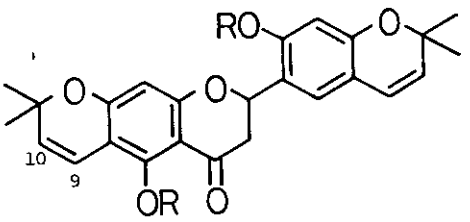


V



VI :R=H

VIa:R=$COCH_3$

Table 1 ^{13}C nmr chemical shifts (ppm)

compd.	I		I
C-2	73.6	C-9	20.1
C-3	41.4	C-10	122.8
C-4	196.7	C-11	130.2
C-4a	101.6	C-12	25.4
C-5	161.6	C-13	17.6
C-6	107.6	C-14	121.6
C-7	164.3	C-15	125.2
C-8	94.5	C-16	76.2
C-8a	160.7	C-17	27.8
C-1'	117.3	C-18	27.8
C-2'	153.4		
C-3'	103.1		
C-4'	155.5		
C-5'	113.0		
C-6'	127.8		

solvent;DMSO-d_6

Table 2 Chemical shift for C-9-H and C-10-H in VI and VIa (ppm)

	C-9-H	C-10-H
VI	6.52	5.56
VIa	6.40	5.73 or 5.71
Δ	+0.12	-0.17 or 0.15

measured in acetone-d_6

Table 3 Uv spectral data [λmax] (nm)

solvent/reagent	EtOH	$AlCl_3$
cudraflavanone A	294	295
	314(sh)	314(sh)
	332(sh)	334(sh)
euchrestaflavanone C	293	312
	342(sh)	

observed at δ 2.72(1H, dd, J=3.5 and 17, C-3-H), 3.13(1H, dd, J=13 and 17, C-3-H), and 5.65(1H, dd, J=3.5 and 13, C-2-H). The ^{1}H nmr spectrum showed the characteristic signals for a 3,3-dimethylallyl group, a 2,2-dimethylchromene ring, and a hydrogen bonded hydroxyl group as follows: δ 1.64, 1.75(each 3H, s), 3.25(2H, d, J=7.5), 5.23(1H, t, J=7.5); 1.38(6H, s), 5.53(1H, d, J=10), 6.33(1H, d, J=10); 12.44 (1H, s). The mass spectrum of I showed the significant peaks at m/z 407(M^+-CH_3), 221($C_{12}H_{13}O_4$, III), 220($C_{12}H_{12}O_4$, IV), 213($C_{13}H_9O_3$), 187($C_{12}H_{11}O_2$, V). These results indicate that A ring contains a 3,3-dimethylallyl group and B ring contains a 2,2-dimethylchromene ring. Arrangement of substituents in the B ring was deduced from the ^{1}H nmr spectrum of I: two singlet signals at δ 6.35(1H, s, C-3'-H) and δ 7.14(1H, s, C-6'-H) suggesting that the B ring of I was substituted in the 2'-, 4'- and 5'-positions. The biogenetic analogy to other prenylflavonoids isolated from Morus species suggests that B ring has the 2',4'-dioxygenated function.[8] The ^{1}H nmr spectrum of I showed the signal at δ 6.04(1H, s) attributed to the A ring proton. These results indicate that the structure of cudraflavanone A is possibly represented by I or II. The two possible structures for cudraflavanone A were substantiated by examination of the ^{13}C nmr with some model compounds (Table 1).[4,8a]

To discriminate the two structures (I and II), the following experiments were carried out. In the uv spectrum of I in the presence of aluminum chloride, no bathochromic shift was observed. Taking the report on the aluminum chloride-induced shift into account, the 3,3-dimethylallyl group is suggested to be located ortho to a chelated hydroxyl group.[9] Treatment of I with 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) in dry benzene yielded the compound (VI) which showed the following spectra: MS (m/z): 420(M^+), 203, 187; UV λ_{max}^{EtOH} nm(log ε): 267(infl. 4.61), 273(4.66), 295(4.25), 305(sh 4.19), 332(sh 3.47); $\lambda_{max}^{EtOH+AlCl_3}$: 267(infl. 4.53), 273(4.61), 282 (infl. 4.40), 307(4.18), 343(sh 3.32). On treatment with acetic anhydride in pyridine, VI formed a diacetate (VIa) to show the following spectra: MS (m/z): 504 (M^+); ^{1}H nmr (acetone-d_6): 2.23, 2.32(each 3H, s, $COCH_3$). The change in chemical shift for the proton at C-9 position when VI was acetylated (Table 2) indicates that the relation of the proton at C-9 to the hydroxyl group at C-5 position is peri in VI.[10] On the basis of the specific optical rotation (-) and the CD spectrum [[θ]$_{340}$ +11605, [θ]$_{310}$ -20573, [θ]$_{288}$ -47475, [θ]$_{254}$ +6330 (c=0.002 %, EtOH)], I has the (s)-configuration at C-2.[11]

On the other hand, Shirataki, et al. proposed the same structure (I) for euchrestaflavanone C obtained from Euchresta japonica.[4] Direct comparison of cudraflavanone A

with euchrestaflavanone C was carried out. Cudraflavanone A was proved to be not identical with euchrestaflavanone C by thin layer chromatography, and by uv spectrum. In the uv spectrum of euchrestaflavanone C, the absorption at 293 nm showed a bathochromic shift after the addition of aluminum chrolide (Table 3). From these evidences, the structure of euchrestaflavanone C seems to be reversed to the structure (II). To confirm the structures of these flavanones, the following synthesis was carried out.[12]

(±)-Cudraflavanone A (I') and (±)-euchrestaflavanone C (II') were synthesized from phloroacetophenone (VII) via the routes as shown in Chart 1 and 2, respectively. Treatment of VII with methoxymethyl chloride gave the compound (VIII)[12], which was prenylated with prenyl bromide to give 2-hydroxy-4,6-dimethoxymethoxy-5-C-prenylacetophenone (IX, liquid, 9% yield from VIII) and 2-hydroxy-4,6-dimethoxymethoxy-3-C-prenylacetophenone (X, amorphous powder, 1% yield)[12]. The compound (IX) showed the following spectra: MS (m/z): 324(M^+),279, 247, 205; ^{1}H nmr ($CDCl_3$): 1.72, 1.80 (each 3H, s), 2.74 (3H, s), 3.35(2H, br d, J=7.5), 3.50, 3.57(each 3H, s), 5.01, 5.27(each 2H, s), 5.20(1H, t, J=7.5), 6.52(1H, s), 13.17(1H, s, OH); UV λ_{max}^{EtOH} nm (log ε): 280(4.05), 328(3.56); $\lambda_{max}^{EtOH+AlCl_3}$: 285(3.94), 302(3.93), 332(sh 3.43), 364 (sh 3.19). The compound (X) showed the following spectra: MS (m/z): 324(M^+), 279, 247, 205; ^{1}H nmr ($CDCl_3$): 1.66, 1.78(each 3H, s), 2.67(3H, s), 3.32(2H, br d, J=7), 3.49, 3.53(each 3H, s), 5.26, 5.27(each 2H, s), 5.12-5.32(1H, m), 6.42(1H, s), 14.17 (1H, s, OH); UV λ_{max}^{EtOH} nm(log ε): 285(4.09), 318(sh 3.39); $\lambda_{max}^{EtOH+AlCl_3}$: 285(4.05), 318(sh 3.37). The discrimination of IX from X was proved by comparative examination of the above uv spectra after addition of aluminum chloride.[9] The compound (X) was also obtained from VII via the route shown in Chart 2. Treatment of 2,4-dihydroxybenzaldehyde (XII) with 1,1-dimethyl-2-propen-1-ol gave XIII[13], mp 141°C, which showed the following spectra: MS (m/z): 206(M^+); ^{1}H nmr ($CDCl_3$): 1.74, 1.77(each 3H, s), 3.26(2H, d, J=7.5), 5.23(1H, t, J=7.5), 6.31(1H, s), 7.16(1H, s), 9.65(1H, s), 11.28(1H, s, OH). The compound (XIII) was cyclized with DDQ to give the chromene (XIV)[13], mp 78°C, which showed the following spectra: MS (m/z): 204(M^+); ^{1}H nmr (acetone-d_6): 1.43(6H, s), 5.67(1H, d, J=10), 6.19(1H, s), 6.36(1H, d, J=10), 7.33 (1H, s), 9.76(1H, s), 11.41(1H, s, OH). The compound (XIV) was converted to XV, mp 80°C, with methoxymethyl chloride. The condensation of IX with XV in alkaline solution gave the chalcone (XVI, amorphous powder) in 66% yield, which showed the following spectra: MS (m/z): 554(M^+), 509, 263, 213; ^{1}H nmr ($CDCl_3$): 1.45(6H, s), 1.70, 1.80 (each 3H, s), 3.38(2H, br d, J=7.5), 3.48, 3.51, 3.53(each 3H, s), 4.93, 5.24, 5.26

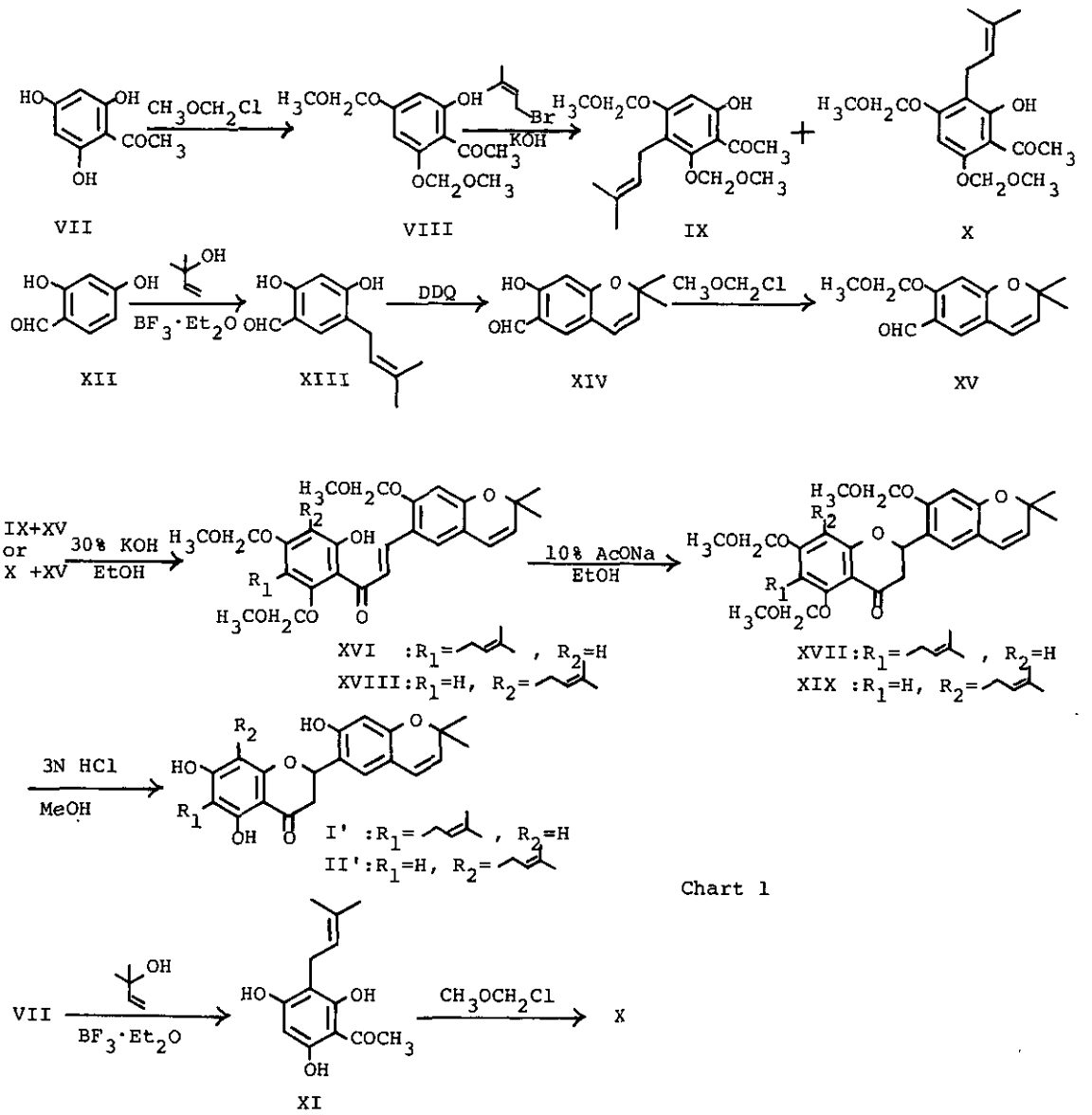


Chart 1

Chart 2

(each 2H, s), 5.08-5.34(1H, m), 5.58(1H, d, J=10), 6.35(1H, d, J=10), 6.53(1H, s), 6.66(1H, s), 7.35(1H, s), 7.77(1H, d, J=16), 8.21(1H, d, J=16), 13.65(1H, s, OH); UV λ_{max}^{EtOH} nm(log ε): 291(4.18), 316(sh 4.01), 325(sh 4.00), 396(4.31); $\lambda_{max}^{EtOH+AlCl_3}$: 298(4.07), 324(sh 3.95), 440(4.24). The chalcone (XVI) was cyclized to the flavanone (XVII) with sodium acetate in ethanol in 20% yield, and XVII was converted into I' in acidic solution. The compound (I') thus obtained was identical with cudraflavanone A by the thin layer chromatography, the uv and the ir spectroscopy.

The condensation of X with XIV gave the chalcone (XVIII, mp 118-119°C) in 60% yield, which showed the following spectra: MS (m/z): 554(M^+), 509, 263, 213; ^{1}H nmr ($CDCl_3$): 1.43(6H, s), 1.67, 1.78(each 3H, s), 3.31(2H, br d, J=6.5), 3.46(6H, s), 3.48(3H, s), 4.99-5.33(1H, m), 5.19(2H, s), 5.21(4H, s), 5.52(1H, d, J=10), 6.25(1H, d, J=10), 6.36(1H, s), 6.70(1H, s), 7.24(1H, s), 7.83(1H, d, J=16), 8.11(1H, d, J=16), 13.80 (1H, s, OH); UV λ_{max}^{EtOH} nm(log ε): 234(infl. 4.51), 293(4.28), 330(sh 4.25), 335(4.26), 394(4.53); $\lambda_{max}^{EtOH+AlCl_3}$: 234(infl. 4.51), 293(4.26), 330(sh 4.23), 335(4.25), 394 (4.52). The chalcone (XVIII) was cyclized to the flavanone (XIX) in 46% yield, which was converted into II'. The compound (II') thus obtained was identical with euchrestaflavanone C by the thin layer chromatography, the uv and the ir spectroscopy.[14]

From these results, cudraflavanone A is represented by the formula (I), and the formula (I) for euchrestaflavanone C should be reversed to the formula (II).

ACKNOWLEDGEMENT We are grateful to Prof. M. Komatsu and Dr. I. Yokoe, Faculty of Pharmaceutical Sciences, Josai University, for their kind donation of the data of euchrestaflavanone C, for useful discussion for determination of the two flavanones, and for CD spectrum measurement.

REFERENCES AND FOOTNOTES

1 A part of this work was presented at the 103rd Annual Meeting of the Pharmaceutical Society of Japan, Tokyo, April, 1983. At the Meeting, our group proposed orally the formula (I) for a structure of cudraflavanone A.

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14 Dr. I. Yokoe, Faculty of Pharmaceutical Sciences, Josai University, informed us

that his group reversed the structure (I) for euchrestaflavanone C to (II) by the long-range selective proton decoupling (LSPD) technique [November 25th, 1983]. Our group will report the revision for the structure of euchrestaflavanone C in collaboration with Josai group at the 104th Annual Meeting of the Pharmaceutical Society of Japan, Sendai, March, 1984.

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Received, 19th December, 1983