THREE NEW ISOPRENYLATED XANTHONES, CUDRAXANTHONE A, B AND C, FROM THE ROOT BARKS OF CUDRANIA TRICUSPIDATA (CARR.) BUR.

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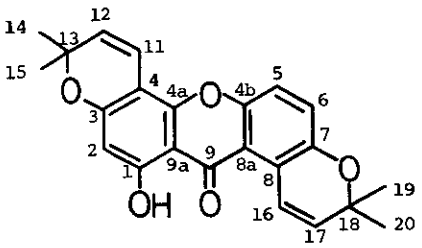
Abstract ——— From the hexane extract of the root barks of Cudrania tricuspidata(Carr.) Bur.(Japanese name "Hariguwa", Moraceae), these new isoprenylated xanthones were isolated and named cudraxanthone A, B and C. The structures of cudraxanthone A, B and C were shown to be I ~ III, respectively, on the basis of spectral data.

In the previous papers[1], our group reported the isolation and structure determination of a series of natural Diels-Alder adducts as well as of an isoprenylated flavonoid derivative obtained from the Chinese crude drug "Sāng-Bái-Pí"(Japanese name "Sōhakuhi") imported from the People's Republic of China. Some of the Diels-Alder adducts showed a significant hypotensive effect. It was reported that the Chinese crude drug "Sāng-Bái-Pí" obtained from market had been found to be adulterated with the root barks of Cudrania tricuspidata(Carr.) Bur. and Broussonetia papyrifera(L.) Vent., both of which belong to the family Moraceae[2].

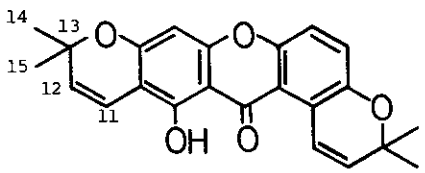
In the course of our studies on the constituents of the Morus root barks, we studied the phenolic constituents of the root barks of Cudrania tricuspidata(Carr.) Bur., and three new isoprenylated xanthone derivatives, cudraxanthone A ~ C, were isolated from the extract. In this paper, we report the structure determination of these new compounds.

The dried root barks(250 g) of Cudrania tricuspidata(Carr.) bur. was extracted with n-hexane. The n-hexane extract was dissolved in methanol, and fractionated sequentially by the column and the preparative thin-layer chromatography over silica gel to give cudraxanthone A(3 mg), B(10 mg) and C(15 mg).

Cudraxanthone A (I) was obtained as yellow needles, mp 212-216 °C, M^+ 376.1304 (Calcd. for $C_{23}H_{20}O_5$: 376.1309), $C_{23}H_{20}O_5$, exhibiting positive ferric chloride test



I



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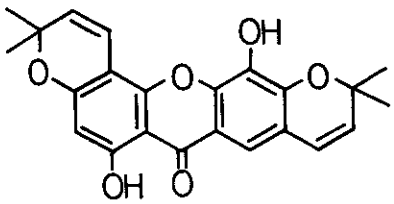
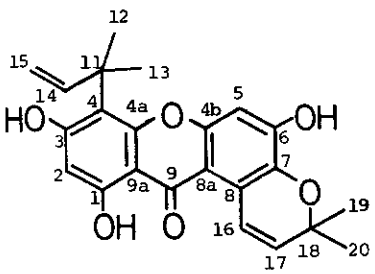


V



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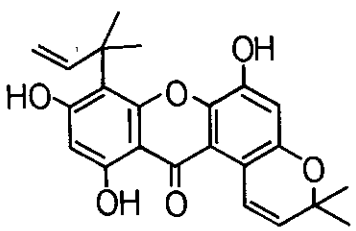
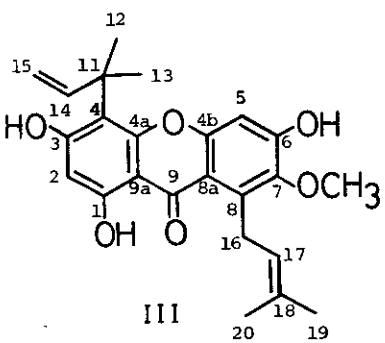


II'



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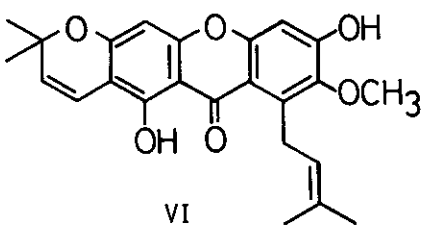

VI

Table 1 ^{13}C nmr chemical shifts

compd.	I*	IV*	V**	II*	III*	VI*
C-1	160.6	160.3	166.5	161.8	161.9	157.8
C-2	99.1	104.2	98.1	100.2	100.2	104.4
C-3	163.4	157.7	162.1	162.0	161.9	159.8
C-4	100.4	94.0	100.6	108.2	108.9	94.0
C-4a	154.6	156.5	159.5	155.2	155.2	156.1
C-4b	149.4	149.1	145.8	151.0	155.0	155.6
C-5	120.8	120.7	133.0	101.9	101.2	101.6
C-6	124.2	124.0	150.9	152.6	154.7	154.5
C-7	151.8	151.4	118.2	136.9	142.8	142.7
C-8	115.6	115.3	120.9	119.6	137.0	136.9
C-8a	119.0	119.8	113.4	109.0	111.8	112.1
C-9	181.5	183.1	179.5	182.8	182.3	181.8
C-9a	104.4	104.2	102.2	104.6	104.5	103.6
C-11	115.1	115.5	111.8	40.9	40.9	115.6
C-12	126.8	127.0	131.0	28.0	28.1	126.9
C-13	78.1	77.9	77.3	28.0	28.1	77.8
C-14	28.3	28.3	27.7	149.3	149.3	28.3
C-15	28.3	28.3	27.7	113.3	113.2	28.3
C-16	117.6	117.3	114.8	120.9	26.5	26.5
C-17	132.8	132.6	126.5	132.4	123.0	123.1
C-18	75.6	75.3	77.6	[75.8]	132.2	131.8
C-19	27.4	27.3	27.7	27.3	25.8	25.6
C-20	27.4	27.3	27.7	27.3	18.2	18.1
				C-7-$\underline{C}H_3$	62.1	61.8

solvent; *: $CDCl_3$, **: [$^2H_6$]DMSO-$CDCl_3$(1:1), [ ]: acetone-d_6

and negative Gibbs test. The ir spectrum disclosed absorption bands for conjugated carbonyl and aromatic ring as follows: ν_{max}^{Nujol} 1645, 1630(sh), 1565 cm^{-1}. The UV spectra [λ_{max}^{EtOH} nm(log ε): 267(sh 4.56), 275(4.63), 283(4.62), 336(sh 3.85), 354(sh 4.02), 360(4.04), 405(3.61); $\lambda_{max}^{EtOH+AlCl_3}$: 271(sh 4.42), 290(4.65), 297(4.66), 345(4.02), 385(3.99), 465(3.53)] resembled those of xanthone derivatives[3] suggesting that I possesses a xanthone skeleton. The ^1H nmr spectrum of I ($CDCl_3$) showed a low field signal at 13.29 indicating the presence of a chelated hydroxyl group. The presence of two 2,2-dimethylchromene rings was suggested by the ^1H nmr spectrum as follows: δ 1.46, 1.47(each 6H, s, C_{13}- or C_{18}-CH_3x2), 5.58(1H, d, J=10, C_{12}-H), 5.82(1H, d, J=10, C_{17}-H), 6.79(1H, d, J=10, C_{11}-H) and 8.01(1H, d, J=10,

C_{16}-H). The evidence is also available from the mass spectral fragments[4,5] at m/z 361(M^+-CH_3), 173. The chemical shift value of the low field doublet at δ 8.01 indicated that one of the 2,2-dimethylchromene rings is an angular fused structure.[4] The three aromatic protons appeared as a singlet at δ 6.22(1H, C_2-H) and two doublets at δ 7.16 and δ 7.24(each 1H, J=9, C_5- and C_6-H). From these spectral data and the result of Gibbs test, the structure (I) is possible for cudraxanthone A. In order to corroborate the structure of I, the ^{13}C nmr spectrum was analysed as shown in Table 1. Assignments of the carbon atoms in I were performed by comparison of the ^{13}C nmr spectra of model compounds, thwaitesixanthone (IV)[6] and rheediaxanthone A (V)[7] (Table 1). From the above results, we propose the formula (I) for a structure of cudraxanthone A.

Cudraxanthone B (II) was obtained as yellow prisms, mp 163-167 °C, M^+ 394.1416(Calcd. for $C_{23}H_{22}O_6$: 394.1415), $C_{23}H_{22}O_6$, exhibiting positive ferric chloride test and negative Gibbs test. The compound (II) showed the following spectra: ir ν_{max}^{Nujol}: 3520, 3300(br), 1630, 1590(sh), 1570, 1490 cm^{-1} ; UV λ_{max}^{EtOH} nm(log ε): 247(4.13), 268(4.17), 288(sh 3.53), 328(sh 4.06), 334(4.07), 383(3.51), 392(sh 3.49); $\lambda_{max}^{EtOH+AlCl_3}$: 223(4.13), 248(4.07), 276(4.11), 290(sh 3.79), 352(sh 4.11), 356(4.13), 428(3.53). The UV spectra suggested that II possesses a xanthone skeleton.[3] The mass spectrum of II showed the following fragments at m/z 379(M^+-CH_3), 326($C_{18}H_{14}O_6$), 311($C_{17}H_{11}O_6$). The ^1H nmr spectrum ($CDCl_3$) revealed the presence of a 1,1-dimethylallyl group[8] and a 2,2-dimethylchromene ring as follows: 1.69(6H, s, C_{11}-CH_3x2), 5.38(1H, d, J=11.5, C_{15}-H), 5.48(1H, d, J=18, C_{15}-H), 6.49(1H, dd, J=11.5 and 18, C_{14}-H); 1.50(6H, s, C_{18}-CH_3 x2), 5.83(1H, d, J=10, C_{17}-H), 8.00(1H, d, J=10, C_{16}-H). The two aromatic proton signals and a low field signal appeared as three singlets at δ6.24(1H, C_2-H), 6.85 (1H, C_5-H) and 12.37(1H, C_1-OH). From these spectral data and the result of Gibbs test, two possible structures (II and II') were suggested. The structure (II) is suggested to be more likely than II' by the biogenetic analogy to other xanthone derivatives isolated from Moraceae,[8-10] as well as by the biogenetic pathway of macluraxanthone(1,3,5,6-tetraoxygenated xanthone derivative).[8] Moreover, the chemical shift value of the singlet at δ 6.85 was similar to those of the C_5-protons of the 6,7-dioxygenated xanthone derivatives.[11,12] In order to corroborate the structure (II), the ^{13}C nmr spectrum was analysed (Table 1). Assignments of the carbon atoms in II were performed by comparison of the ^{13}C nmr spectra of the

model compounds[1d,6,7,13] and by using the model compound, cudraxanthone A (I), taking into account the substituent effect of a hydroxyl group on a benzene nucleus in the B ring.[6,14,15] The chemical shift values of the C-2 and C-4 signals of II were in good agreement with those of the C-4 isoprenylated xanthones[6,7] and C-8 isoprenylated flavone derivatives.[1d,13] From these results, we propose the formula (II) for the structure of cudraxanthone B.

Cudraxanthone C (III) was obtained as yellow powder,[16] M^+ 410.1731(Calcd. for $C_{24}H_{26}O_6$: 410.1727), $C_{24}H_{26}O_6$, exhibiting positive ferric chloride test and negative Gibbs test. The compound (III) showed the following spectra: ir ν_{max}^{Nujol} : 3400(br), 1645(br), 1595(br), 1575 cm^{-1}; UV λ_{max}^{EtOH} nm(log ε): 246(4.35), 258 (4.27), 317(4.17), 354(3.75); $\lambda_{max}^{EtOH+AlCl_3}$: 237(4.30), 270(4.23), 278(sh 4.17), 343(4.23), 401(3.64). The UV spectra suggested that III possesses a xanthone skeleton. The mass spectrum of III showed the following fragments at m/z 395 (M^+-CH_3), 367($M^+-C_3H_7$, base peak), 341($M^+-C_5H_9$), 299($M^+-C_3H_7-C_5H_8$). The ^1H nmr spectrum ($CDCl_3$) revealed the presence of an α,α-dimethylallyl group and a γ,γ-dimethylallyl group as follows: 1.70(9H, s, $C_{11}-CH_3$x2 and $C_{18}-CH_3$), 5.38 (1H, d, J=10, $C_{15}-H$), 5.47(1H, d, J=18, $C_{15}-H$), 6.49(1H, dd, J=10 and 18, $C_{14}-H$); 1.84(3H, s, $C_{18}-CH_3$), 4.09(2H, br d, J=5, $C_{16}-H$x2), 5.24(1H, m, $C_{17}-H$). The other proton signals appeared as follows: δ 3.83(3H, s, OCH_3), 6.25(1H, s, C_2-H), 6.87 (1H, s, C_5-H) and 12.43(1H, s, C_1-OH). ^{13}C nmr spectrum of III was analysed (Table 1). Chemical shifts of the carbon atoms of the α,α-dimethylallyl group and those of the carbon atoms in A ring were similar to those of the relevant carbon atoms of II (Table 1). Chemical shifts of the carbon atoms of the γ,γ-dimethylallyl group and those of the carbon atoms in B ring were similar to those of the relevant carbon atoms of the compound (VI)[15] (Table 1). The mass spectrum of III showed the significant fragmentation at m/z 367, suggesting that the γ,γ-dimethylallyl group is adjacent to a methoxyl group.[17] From these results, we propose the formula (III) as the structure of cudraxanthone C.

On the other hand, any xanthone derivative could not be isolated from the mulberry root barks[13] and the Chinese crude drug "Sāng-Bái-Pí"[1]. These results suggested that the Chinese crude drug[1] which our group examined had not been adulterated with the root barks of Cudrania tricuspidata(Carr.) Bur.

ACKNOWLEDGEMENT We are grateful to Mr. Kobayashi, the Medical Plants Garden, Tokyo Metropolitan Government, for his kind donation of the root of Cudrania

tricuspidata cultivated at the Medical Plants Garden. We are also grateful to Prof. S. Sakai, Faculty of Pharmaceutical Sciences, Chiba University, for mass spectrum measurement, and grateful to Dr. M. Takase, Research Laboratory of Zen-Yaku Kogyo Co., Ltd, for ^{1}H nmr and ^{13}C nmr spectrum measurement.

REFERENCE AND FOOTNOTE

1a) T. Nomura, T. Fukai, Y. Hano, Y. Sugaya and T. Hosoya, Heterocycles, 1980, 14, 1785; b) T. Nomura, T. Fukai and Y. Hano, Planta medica, in press; c) T. Nomura, T. Fukai, Y. Hano and S. Urano, Planta medica, in press; d) T. Nomura, T. Fukai, Y. Hano and J. Uzawa, Heterocycles, 1981, 16, 2141; e) T. Nomura, T. Fukai, Y. Hano and J. Uzawa, Heterocycles, 1982, 17, 381.

2 Y. Zhen-ying, Chinese J. Pharmaceutical Analysis, 1981, 1, 94.

3 J.C. Roberts, Chem. Rev., 1961, 61, 591.

4 M. Dahanayake, I. Kitagawa, R. Somanathan and M.U.S. Sultanbawa, J. Chem. Soc. Perkin I, 1974, 2510.

5 J.R. Lewis and J.B. Reary, J. Chem. Soc. (C), 1970, 1662.

6 P.W. Westerman, S.P. Gunasekera, M. Uvais, S. Sultanbawa and R. Kazlauskas, Org. Mag. Resonance, 1977, 9, 631.

7 F.D. Monache, B. Botta, M. Nicoletti, J.S. de Barros Coêlho and F.D. de Andrade Lyra, J. Chem. Soc. Perkin I, 1981, 484.

8 M.L. Wolfrom, F. Komitsky, Jr.G. Fraenkel, J.H. Looker, E.E. Dickey, P. McWain, T. Thompson, P.M. Mundell and O.M. Windrath, J. Org. Chem., 1964, 29, 692.

9 M.L. Wolfrom, F. Komitsky, Jr. and P.M. Mundell, J. Org. Chem., 1965, 30, 1088.

10 P.J. Cotterill and F. Scheinmann, J. Chem. Soc. Chem. Comm., 1975, 664.

11 V.H. Deshpande, A.V. Rama Rao, M. Varadan and K. Venkataraman, Indian J. Chem., 1973, 11, 518.

12 A.K. Sen, K.K. Sarkar, P.C. Majumder and N. Banerji, Indian J. Chem., 1980, 19B, 1008.

13 T. Nomura and T. Fukai, Heterocycles, 1981, 15, 1531.

14 J.B. Stothers, "Carbon-13 NMR Spectroscopy", Academic press, New York and London, 1972, p. 191.

15 A.K. Sen, K.K. Sarkar, P.C. Mazumder, N. Banerji, R. Unsvuori and T.A. Hase, Phytochemistry, 1980, 19, 2223.

16 Although only one spot was detected on tlc, this compound could not be isolated as crystalline form.

17a) G.H. Stout, M.M. Krahn, P. Yates and H.B. Baht, J. Chem. Soc. Chem. Comm., 1968, 211; b) N.S. Kumar, G. Pavanasasivam, M.U.S. Sultanbawa and R. Mageswaran, J. Chem. Soc. Perkin I, 1977, 1243.

Received, 12th October, 1982