Phytochemistry, Vol. 28, No. 2, pp. 595–598, 1989.
Printed in Great Britain.

0031-9422/89 $3.00+0.00

FOUR PRENYLATED XANTHONES FROM *CUDRANIA COCHINCHINENSIS*

CHENG-HSIUNG CHANG, CHUN-CHING LIN, *MASAO HATTORI† and TSUNEO NAMBA†

Department of Pharmacy, Chia-Nan Junior College of Pharmacy, Tainan Hsien, Taiwan, Republic of China; *School of Pharmacy, Kaohsiung Medical College, Kaohsiung, Taiwan, Republic of China; †Research Institute for Wakan-Yaku, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama 930-01, Japan

(*Received* 3 *June* 1988)

Key Word Index—*Cudrania cochinchinensis*; Moraceae; prenylated xanthones; structure elucidation; ^{13}C NMR; gerontoxanthone.

Abstract—From the root bark of *Cudrania cochinchinensis* four new prenylated xanthones, named gerontoxanthones A, B, C and D, were isolated together with the known xanthones, cudraxanthone A and osajaxanthone.

INTRODUCTION

As part of our studies on Taiwan folk medicines, we have reported that the botanical source of the Taiwan folk remedy 'Hwang-jin-guey' is the root and stem of *Cudrania cochinchinensis* (Lour.) Kudo & Masamune var. *gerontogea* (S. & Z.) Kudo & Masamune [1]. Two known chemical constituents of this folk medicine are morin [2] and cudranone [3]. In our search for active constituents of *C. cochinchinensis* var. *gerontogea*, the fresh root bark of this plant was examined for triterpenes, flavonoids and xanthones.

In this paper, we report the isolation and structure elucidation of four new prenylated xanthones along with two known xanthones.

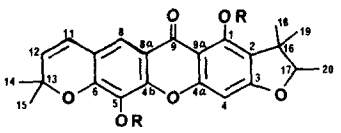
RESULTS AND DISCUSSION

The benzene-soluble portion of the methanol extract of the fresh root bark of *C. cochinchinensis* yielded four new prenylated xanthones, gerontoxanthones A (**1**), B (**2**), C (**3**) and D (**4**), in addition to the known xanthones, cudraxanthone A (**5**) and osajaxanthone (**6**). The latter two compounds were identified by comparison of the spectral data with those reported [4–7].

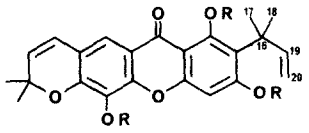
Gerontoxanthone A (**1**) was assigned the molecular formula $C_{23}H_{22}O_6$ (*m/z* 394). Its UV spectrum was indicative of a 1,3,5,6-tetraoxygenated xanthone chromophore [8–10] conjugated with a 2H-pyran ring system (characteristic shoulder at 360 nm) [8]. In the ^{1}H NMR spectrum, the signals at δ1.50 (6H, 2 × Me), 6.58 (1H, *d*, *J* = 10 Hz) and 5.89 (1H, *d*, *J* = 10 Hz) established the presence of a 2,2-dimethyl-2H-pyran ring system. The signals at δ1.40 (3H, *d*, *J* = 6.6 Hz), 1.25, 1.50 (each 3H, 2 × Me) and 4.55 (1H, *q*, *J* = 6.6 Hz) showed the presence of a 2,3-dihydro-2,3,3-trimethylfuran ring system in the molecule [8, 10]. Furthermore, the singlet proton signals at δ6.37 and 7.43 were assignable to H-4 or H-2 and H-8, respectively, and the low field signals at δ13.45 and 8.46 were assignable to 1-OH (chelated) and 5-OH. On acetylation, **1** gave a diacetate (**1a**), supporting the presence of the two free hydroxyl groups. From these findings, two structures were possible, i.e. **1** and **7**. However, the latter was excluded by direct comparison with an authentic sample of **7**. In addition, in the ^{1}H NMR spectrum in pyridine-d_6, the solvent-induced shifts of +0.31 for H-8, +0.08 for H-4, −0.08 for H-11 and −0.19 for H-12 indicated that the pyran ring and the furan ring were co-linear [8, 10, 11]. On the basis of the above evidence the structure of **1** was concluded to be 4″,5″-dihydro-1,5-dihydroxy-6′,6′-dimethylpyrano(2′,3′:6,7)-4″,4″,5″-trimethylfurano (2″,3″:3, 2) xanthone.

Gerontoxanthone B (**2**) was assigned the molecular formula $C_{23}H_{22}O_6$ (*m/z* 394). It also contained a 1,3,5,6-tetra-oxygenated xanthone chromophore conjugated with a 2H-pyran ring similar to that of **1**. On acetylation, **2** gave a triacetate (**2a**), indicating the presence of three free-hydroxyl groups. These groups were shown to be located at C-1, C-3 and C-5 by means of the UV and ^{1}H NMR spectral data. The ^{1}H NMR spectrum showed in addition to the signals of a 2,2-dimethyl-2H-pyran ring, characteristic signals at δ1.64 (2 × Me), 4.86 (1H, *dd*, *J* = 10.5, 1.5 Hz), 4.96 (1H, *dd*, *J* = 17.5, 1.5 Hz) and 6.39 (1H, *dd*, *J* = 17.5, 10.5 Hz) due to the presence of a 1,1-dimethylprop-2-enyl group. Since **2** showed a delayed shift of the UV maximum with $AlCl_3$, in contrast with the immediate shift shown by **8** which possesses an isoprenyl chain at C-4 [8], the isoprenyl chain of **2** could be located at C-2. The two singlet aromatic proton signals at δ6.47 and 7.43 were therefore assigned to H-4 and H-8. Upon measurement of the pyridine-d_6-induced solvent effects on the ^{1}H NMR signals, H-4 underwent an apparent paramagnetic shift (+0.20) in accordance with the presence of a free hydroxyl group at C-3 (shift with NaOAc) [8, 12], and the 1,1-dimethylprop-2-enyl group was consequently located at C-2. The above evidence led us to conclude the structure of **2** to be 1,3,5-trihydroxy-6′,6′-dimethylpyrano(2′3′:6,7)-2-(1,1-dimethylprop-2-enyl)xanthone.

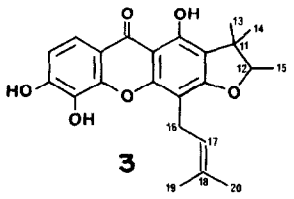
Gerontoxanthone C (**3**) was assigned the molecular formula, $C_{23}H_{24}O_6$ (*m/z* 396). Its UV spectra showed a characteristic 1,3,5,6-tetraoxygenated xanthone chromophore with three free-hydroxy groups, in which one was located at C-1 and the others *ortho* to each other at C-5 and C-6 [8–10]. The ^{1}H NMR spectrum showed the presence of a 2,3-dihydro-2,3,3-trimethylfuran ring, a 3-



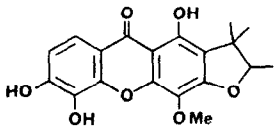
1 R=H
1a R=Ac



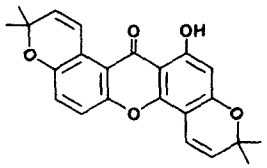
2 R=H
2a R=Ac



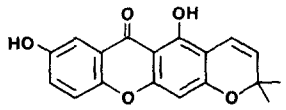
3



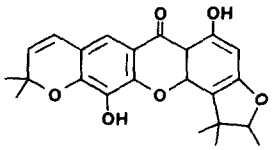
4



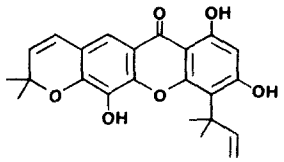
5



6



7



8

methylbut-2-enyl chain, a chelated hydroxy group (1-OH) and two *ortho* coupled aromatic protons (δ6.98, *d*, J = 9 Hz; δ7.65, *d*, J = 9 Hz) assignable to H-7 and H-8. No delayed shift was observed on the UV maximum with $AlCl_3$, suggesting that the 3-methylbut-2-enyl chain is attached to C-4 rather than C-2. The structure of **3** was finally characterized as 4′,5′-dihydro-1,5,6-trihydroxy-4′,4′,5′-trimethylfurano(2′,3′: 3,2)-4-(3-methyl-but-2-enyl)-xanthone.

Gerontoxanthone D (**4**), $C_{19}H_{18}O_7$ (*m/z* 358), showed the typical feature of xanthones from the IR and UV spectral observation. The bathochromic shift of the UV maxima in the presence of shift reagents (AlC_3, NaOAc, NaOAc + H_3BO_4) and the presence of the D_2O exchangeable proton signals at δ13.24 (1H) and 9.0 (2H) in the ^{1}H NMR spectrum indicated that **4** had three free-hydroxy groups at C-1 (chelated OH), C-5 and C-6 (*ortho* di-OH). Furthermore, the ^{1}H NMR spectrum showed characteristic signals for a 2,3-dihydro-2,3,3-trimethylfuran ring (δ1.53, *s*, Me; 1.29, *s*, Me; δ1.46, *d*, J = 7 Hz, Me; δ4.63, 1H, *q*, J = 7 Hz), two *ortho* coupled aromatic proton signals at δ7.08 (1H, *d*, J = 9 Hz) and 7.69 (1H, *d*, J = 9 Hz) for H-7 and H-8, respectively, and a singlet signal at δ3.98 for a methoxyl group (δ61.5 in ^{13}C NMR) at C-4 [13]. The above evidence and the MS and ^{13}C NMR spectral data led us to conclude the structure of **4** to be 4′,5′-dihydro-1,5,6-trihydroxyl-4-methoxyl-4′,4′,5′-trimethylfurano (2′,3′:3,2) xanthone.

EXPERIMENTAL

Mps: uncorr; ^{1}H NMR and ^{13}C NMR: 100 and 400 MHz respectively; MS: 70 eV.

Plant material. Fresh root bark of *Cudrania cochinchinensis* var. *gerontogea* was collected at Chai-I, Taiwan in Sept. 1984. The plant was identified by Muh-Tsuen Kao (National Taiwan University).

Extraction and separation. The fresh root bark of *C. cochinchinensis* var. *gerontogea* (1.5 kg) was chopped and extracted several times with hot MeOH. The MeOH extract was evapd under reduced pressure and the resultant aqueous suspension partitioned with C_6H_6, $CHCl_3$, EtOAc and *n*-BuOH. The C_6H_6 extract was fractionated sequentially on a silica gel column by using C_6H_6, EtOAc and $CHCl_3$. The fractions were collected and separated into several groups (monitored by TLC). Each group was further subjected to repeated silica gel CC, eluting successively with C_6H_6 and C_6H_6–EtOAc (8:1, 6:1, 4:1 and 1:1), followed by prep. TLC. These procedures led to the isolation of cudraxanthone A (42 mg, **5**) from the C_6H_6 eluate, gerontoxathone A (29 mg, **1**), osajaxanthone (8 mg, **6**) and gerontoxanthone B (16 mg, **2**) from the C_6H_6–EtOAc (6:1) eluate, gerontoxanthone C (15 mg, **3**) and D (21 mg, **4**) from the C_6H_6–EtOAc (1:1).

Table 1. ^{13}C NMR data of compounds **1–6**

C	1	2	3	4	5	6
1	165.6[a]	163.1[a]	161.6[a]	158.6[a]	160.5[a]	161.6[a]
2	113.4	113.5	113.1	113.7	99.0	104.9
3	158.8[a]	161.8[a]	164.8[a]	154.7[a]	163.2[a]	158.2[a]
4	89.7	95.7	106.9	125.7	100.3	95.5
4a	157.6	155.8	151.9[b]	152.4	151.5[b]	155.2
4b	144.5	144.7[b]	147.1	147.0	149.4	151.7
5	131.9	131.7	133.6	133.3	120.7[c]	119.8
6	144.5	144.9[b]	152.2[b]	150.2	124.2	125.3
7	117.7	117.6	113.1	117.3	151.3[b]	147.0
8	121.4	121.4	117.4	118.1	115.0	109.1
8a	116.9	113.6	114.9	114.6	119.9[c]	121.7
9	180.5	180.5	181.2	181.7	183.3	181.7
9a	103.8	103.2	103.4	104.0	104.2	103.8
11	113.4	114.5	44.8	44.5	114.9	115.6
12	130.9	130.8	91.3	92.3	126.8	129.1
13	78.8	78.6	25.8	25.4	75.5	78.5
14	28.5	28.4	21.4	20.9	28.3	28.5
15	28.5	28.4	14.6	14.3	28.3	28.5
16	43.3	40.9	22.2		117.6	
17	90.9	26.9	122.8		132.7	
18	25.1	26.9	131.9		78.1	
19	20.6	149.6	25.8		27.3	
20	14.3	113.7	17.8		27.3	
−OMe				61.5		

[a–c] Assignments are interchangeable.

Gerontoxanthone A (**1**). Yellow needles (EtOAc), $C_{23}H_{22}O_6$, mp 236–238°, R_f 0.49 on TLC (C_6H_6–EtOAc 8:1, solvent A), $[\alpha]_D$ −22.12 ($CHCl_3$, *c* 0.6). Orange yellow in UV, positive reaction with Flavone T. (red) and $FeCl_3$ (greenish brown). UV λ_{max}^{MeOH} nm (log ε): 256 (sh) (4.40), 276 (4.63), 333 (4.26), 360 (sh) (4.01); +$AlCl_3$: 243, 252, 283, 365, 394 (sh), +NaOMe: 279, 323, 345 (sh); +NaOAc:277, 324, 341, 358 (sh). IR ν_{max}^{KBr} cm^{-1}: 3350 (OH), 1665, 1610, 1579, 1475. EIMS *m/z* (rel. int.): 394 $[M]^+$ (33), 380 (29), 379 $[M-Me]^+$ (100), 182 $[M-2Me/2]^+$ (13); ^{1}H NMR (acetone-d_6): δ 13.45 (1H, *s*, ex. D_2O, 1-OH), 8.46 (1H, *s*, ex. D_2O, 5-OH), 7.43 (1H, *s*, H-8), 6.58 (1H, *d*, *J* = 10 Hz, H-11), 6.37 (1H, *s*, H-4), 5.89 (1H, *d*, *J* = 10 Hz, H-12), 4.55 (1H, *q*, *J* = 6.6 Hz, H-17), 1.50 (6H, *s*, 2Me-13), 1.40 (3H, *d*, *J* = 6.6 Hz, Me-17), 1.25, 1.50 (each 3H, *s*, 2Me-16). Δδ = δ(pyridine-d_5) − δ (acetone-d_6): H-8 (+0.31), H-4 (+0.08), H-11 (−0.08), H-12 (−0.19); ^{13}C NMR (acetone-d_6): Table 1.

Gerontoxanthone A diacetate (**1a**). Colourless needles (MeOH), mp 203–205°, ^{1}H NMR ($CDCl_3$): δ 7.72 (1H, *s*, H-8), 6.66 (1H, *s*, H-4), 6.40 (1H, *d*, *J* = 10 Hz, H-11), 5.69 (1H, *d*, *J* = 10 Hz, H-12), 4.55 (1H, *q*, *J* = 6.6 Hz, H-17), 2.49 (3H, *s*, OAc-1), 2.34 (3H, *s*, OAc-5), 1.56 (6H, *s*, 2Me-13), 1.46, 1.20 (each 3H, *s*, 2Me-16), 1.39 (3H, *d*, *J* = 6.6 Hz, Me-17).

Gerontoxanthone B (**2**). Yellow needles (EtOAc), $C_{23}H_{22}O_6$, mp 216–218°, R_f 0.2 (solvent A), orange yellow colour in UV, red with Flavone T. and greenish brown with $FeCl_3$. UV λ_{max}^{MeOH} nm (log ε): 258 (sh) (4.38), 276 (4.59), 325 (sh) (4.06), 333 (4.15), 360 (sh) (3.92); +$AlCl_3$: 243, 250 (sh), 286, 363, 396 (sh); +NaOAc: 264 (sh), 278, 334, 364; +NaOMe: 269 (sh), 287, 297 (sh), 337, 379. IR ν_{max}^{KBr} cm^{-1}: 3350, 1645, 1570. EIMS *m/z* (rel. int.): 394 $[M]^+$ (53), 379 $[M-Me]^+$ (100), 365 (29), 353 (53), 352 (20), 339 (30), 182 $[M-2Me/2]^+$ (12), 162 (27), 154 $[M-2Me-CO/2]^+$ (9). ^{1}H NMR (acetone-d_6): δ 14.20 (1H, *s*, ex. D_2O, 1-OH), 9.40 (1H, *br s*, ex. D_2O, OH), 8.44 (1H, *s*, ex. D_2O, OH), 7.43 (1H, *s*, H-8), 6.47 (1H, *s*, H-4), 6.58 (1H, *d*, *J* = 10 Hz, H-11), 6.39 (1H, *dd*, *J* = 17.5, 10.5 Hz, X part of ABX, H-19), 5.88 (1H, *d*, *J* = 10 Hz, H-12), 4.96 (1H, *dd*, *J* = 17.5, 1.5 Hz, A part of ABX, Ha-20), 4.86 (1H, *dd*, *J* = 10.5, 1.5 Hz, B part of ABX, Hb-20), 1.49 (6H, *s*, 2Me-13), 1.64 (6H, *s*, 2Me-16). Δδ = δ (pyridine-d_5) − δ(acetone-d_6): H-8 (+0.34), H-4 (+0.20), H-11 (−0.08), H-12 (−0.02).

Gerontoxanthone B triacetate (**2a**). Colourless needles (MeOH), mp 176–179°, ^{1}H NMR (acetone-d_6): δ 7.74 (1H, *s*, H-8), 7.26 (1H, *s*, H-4), 6.63 (1H, *d*, *J* = 10 Hz, H-11), 6.18 (1H, *dd*, *J* = 18, 10 Hz, X part of ABX, H-19), 5.94 (1H, *d*, *J* = 10 Hz, H-12), 4.94 (1H, *dd*, *J* = 18, 1 Hz, A part of ABX, Ha-20), 4.90 (1H, *dd*, *J* = 10, 1 Hz, B part of ABX, Hb-20), 2.41 (3H, *s*, OAc-1), 2.36 (3H, *s*, OAc), 2.31 (3H, *s*, OAc), 1.54 (6H, *s*, 2Me-16), 1.48 (6H, *s*, 2Me-13).

Gerontoxanthone C (**3**). Pale yellow needles (MeOH), $C_{23}H_{24}O_6$, mp 204–206°, R_f 0.15 (solvent A), orange yellow in UV, red with Flavone T. and greenish brown with $FeCl_3$. UV λ_{max}^{MeOH} nm (log ε):241 (sh) (4.52), 251 (4.68), 288 (4.13), 329 (4.40); +$AlCl_3$: 240, 274, 296, 332 (sh), 392; +NaOAc: 240, 256, 294, 366; +NaOAc+H_3BO_3: 261, 292, 348, 382 (sh). IR ν_{max}^{KBr} cm^{-1}: 1650; EIMS *m/z* (rel. int.): 396 $[M]^+$ (48), 381 $[M-Me]^+$ (46), 353 (28), 341 (100), 342 (20), 325 (18); ^{1}H NMR (acetone-d_6): δ 13.7 (1H, *s*, 1-OH), 8.77 (2H, *br s*, 5, 6-OH), 7.56 (1H, *d*, *J* = 9 Hz, H-8), 6.98 (1H, *d*, *J* = 9 Hz, H-7), 5.28 (1H, *m*, H-17), 4.58 (1H, *q*, *J* = 7 Hz, H-12), 3.28 (2H, *d*, *J* = 7 Hz, H-16), 1.64 (6H, *s*, 2Me-18), 1.77, 1.34 (each 3H, *s*, 2Me-11), 1.42 (3H, *d*, *J* = 7 Hz, Me-12).

Gerontoxanthone D (**4**). Yellow needles (MeOH), $C_{19}H_{18}O_6$, mp 300°, R_f 0.06 (solvent A), reddish brown in UV, red with Flavone T. and greenish brown with $FeCl_3$. UV λ_{max}^{MeOH} nm (log ε): 241 (sh) (4.47), 253 (4.67), 285 (4.13), 326 (4.39). +$AlCl_3$: 239, 273, 293 (sh), 363, 385; +NaOMe: 240, 257, 291, 365, +NaOAc: 256, 288, 364; +NaOAc+H_3BO_3: 256, 261, 290, 347. IR ν_{max}^{KBr} cm^{-1}: 1640; EIMS *m/z* (rel. int.): 358 $[M^+]$ (56), 343 $[M-Me]^+$ (100), 328 $[M-2Me]^+$ (16), 313 (16); ^{1}H NMR (acetone-d_6): δ 13.24 (1H, *s*, 1-OH), 9.0 (2H, *br s*, 5,6-OH), 7.69 (1H, *d*, *J* = 9 Hz, H-8), 7.08 (1H, *d*, *J* = 9 Hz, H-7), 4.63 (1H, *q*, *J* = 7 Hz, H-12), 3.93 (3H, *s*, OMe-4), 1.53, 1.29 (each 3H, *s*, 2Me-11), 1.46 (3H, *d*, *J* = 7 Hz, Me-12).

Cudraxanthone A (**5**). Orange yellow needles (EtOAc), $C_{23}H_{20}O_5$, mp 213–216°, R_f 0.68 (solvent A). The compound was identified as cudraxanthone A by comparison of the spectral data with those reported [4].

Osajaxanthone (**6**). Yellow needles (EtOAc), $C_{18}H_{14}O_5$, mp 245–248°, R_f 0.42 (solvent A). The compound was identified by comparison of the spectral data with those reported [7, 14].

Acknowledgement—The authors are deeply indebted to Dr T.-H. Wang (President of Chia-Nan Junior College of Pharmacy) and Dr C.-N. Lin (Kaohsiung Medical College) for their encouragement. We are grateful to The National Science Council for financial support. We thank Mr Muh-Tsuen Kao (National Taiwan University) for identification of plant specimens, Dr Giuliano Delle Monache (Universita Cattolica del S. Cuore, Italy) for his kind gifts of authentic compounds (**7**, **8**) and Dr Taro Nomura (Toho University, Japan) for the spectral data of cudraxanthone A. We also thank Mrs B.-G. Liu and L.-H. Ten (National Tsiung Hua University) for mass and ^{13}C NMR spectral measurements and Miss B.-J. Luh (National Cheng Kung University) for ^{1}H NMR spectral measurements, respectively.

REFERENCES

1. Chang C.-H., Lin C.-C. and Namba T. (1988) *Shoyakugaku Zasshi* (in press).

2. Sasaki, S., Chiang, H. H., Habaguchi, K., Yamada, T., Nakanishi, N., Matsueda, S., Hsii, H. Y. and Wn, W. N. (1966) *Yakugaku Zasshi* **14**, 803.
3. Hassain, M., Niazi, S., Arambulo, A. and Long, D. M. (1977) *J. Pharm. Sci.* **66**, 908.
4. Nomura, T., Halo, Y. and Fujimoto, T. (1983) *Heterocycles* **20**, 213.
5. Fujimoto, T., Hano, Y. and Nomura, T. (1984) *Planta Med.* 2184.
6. Jackson, B., Locksly, H. D. and Scheinmann, F. (1967) *J. Chem. Soc. C*, 2500.
7. Wolfrom, M. L., Komitsky, F. Jr. and Looker, J. H. (1965) *J. Org. Chem.* **30**, 144.
8. Dell Monache G., Botta, B., de Mello, J. F. and de Barros Coelho. (1984) *J. Nat. Prod.* **47**, 620.
9. Wolfrom, M. L., Komisky, F. Jr. Fraenkel, G., Looker, J. H., Dickey, E. E., McWain, P., Thompson, A., Mundell, P. M. and Windrath, O. M. (1964) *J. Org. Chem.* **29**, 672.
10. Dell Monache G., Dell Monache, F., Marini Bettolo G. B. and Alves de Lima R. (1983) *J. Nat. Prod.* **46**, 655.
11. Delle Monache, F., Ferrari, F. and Pomponi, M. (1984) *Phytochemistry* **23**, 1489.
12. Lins Mesguita, A. A., de Oliveira, W. G. and Taveira Neiva, R. M. (1975) *Phytochemistry* **14**, 803.
13. Delle Monache, F., Nicoletti, M., de Barros Coelho, J. S. and de Andrade Lyra, F. D. (1981) *J. Chem. Soc. Perkin 1*, 484.
14. Jackson, B., Locksley, H. D. and Scheinmann (1967) *J. Chem. Soc.* (C) 2500.