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ON THE STRUCTURES OF MULBERRIN, MULBERROCHROMENE, CYCLOMULBERRIN, AND CYCLOMULBERROCHROMENE

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Direct comparison of mulberrin with kuwanon C, and mulberrochromene with morusin were carried out. Mulberrin and mulberrochromene were proved to be identical with kuwanon C and morusin, respectively. The linear structures of mulberrin and mulberrochromene as well as cyclomulberrin and cyclomulberrochromene should be reversed to the angular structures, I, II, III, and IV, respectively.

A series of prenylflavonoids have been isolated from the root bark of Morus alba L., a plant of Moraceae family.[1-8] In this paper, we report the identification of mulberrin with kuwanon C, that of mulberrochromene with morusin, and the revision of structures of four mutually interrelated prenylflavones, mulberrin (I'), mulberrochromene (II'), cyclomulberrin (III'), and cyclomulberrochromene (IV'), isolated from the Morus alba root bark by Deshpande et al.[1a]

The initial work on the flavones of the Morus alba stem and root bark led to the structure postulates I'-IV' for mulberrin, mulberrochromene, cyclomulberrin, and cyclomulberrochromene, respectively. The relation of these flavones to each other and to artocarpin (V) was demonstrated by carring out the conversions outlined in Chart 1.[1a]

In subsequent work on the same plant source, our group reported[3,4] the isolation and the structure determination of five prenylflavones, kuwanon C, morusin, cyclomorusin, compound A, and oxydihydromorusin (morusinol[5]), and the structures were shown to be I, II, IV, VI, and VII, respectively. These five prenylflavones were correlated to each other as shown in Chart 2. Furthermore, the synthesis of tetrahydrokuwanon C tetramethyl ether (VIII) was achieved by Baker-Venkataraman method from 2-hydroxy-3-isopentyl-4,6-dimethoxyisoheptophenone (IX)

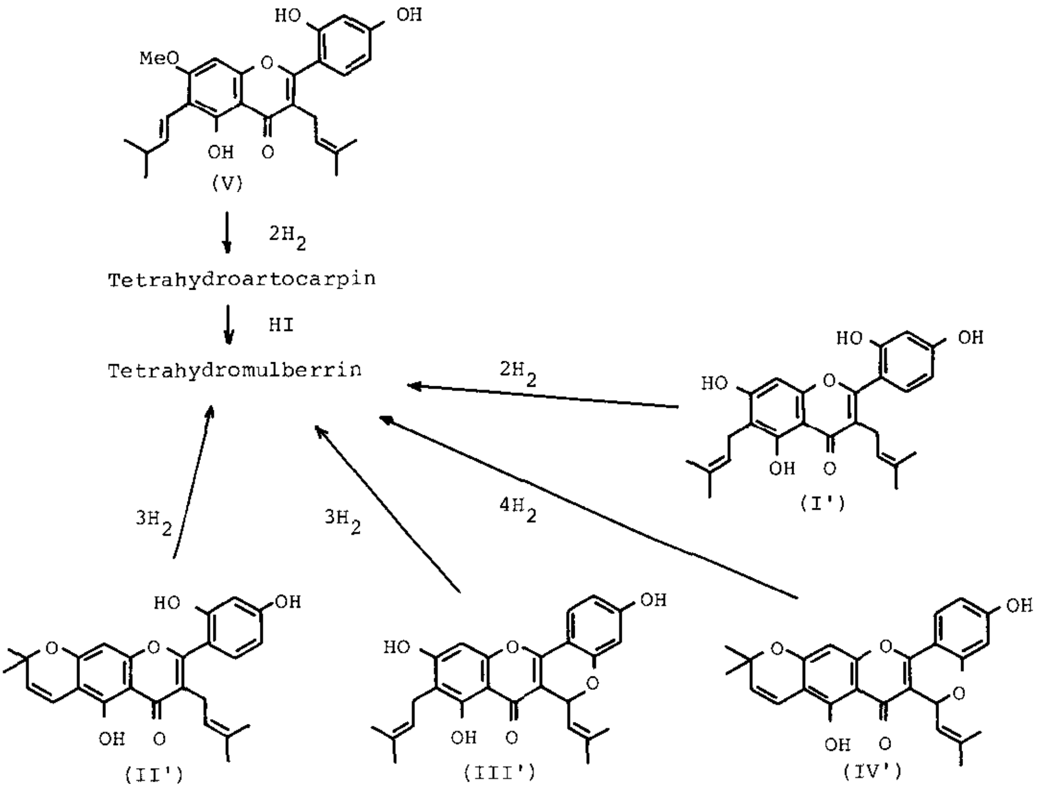

Chart 1

derived from phloroglucinol and 2,4-dimethoxybenzoyl chloride.[9] From this result, the structures of five prenylflavones were confirmed.

Recently, Chari _et al_ reported[10] that reappraisal of the ^{13}C nmr data on mulberrin (I') and mulberrochromene (II') which had been presented by Wenkert and Gottlieb,[11] indicate a revision of structure for these two compounds as well as for cyclomulberrin (III') and cyclomulberrochromene (IV'). The signals at 98.0 ppm and 98.9 ppm in the respective ^{13}C nmr spectra have been assigned to C-8 of mulberrin (I') and mulberrochromene (II') by Wenkert and Gottlieb.[11] But, Chari _et al_ insist[10] that these chemical shift values are _ca_ 4.0 ppm downfield of the C-8 signal in 5,7-dihydroxyflavonoids and that they are in the range expected for the corresponding unsubstituted C-6 by comparing with the C-8 signal of the ^{13}C nmr spectra of the linear chromeno-flavone and the C-4 signal of the chromeno-xanthone derivatives. From these results, Chari _et al_ reported[10] that the four mutually interrelated prenylated Morus flavones, isolated by Deshpande _et al_, have the 8-C rather than the 6-C-substitution as

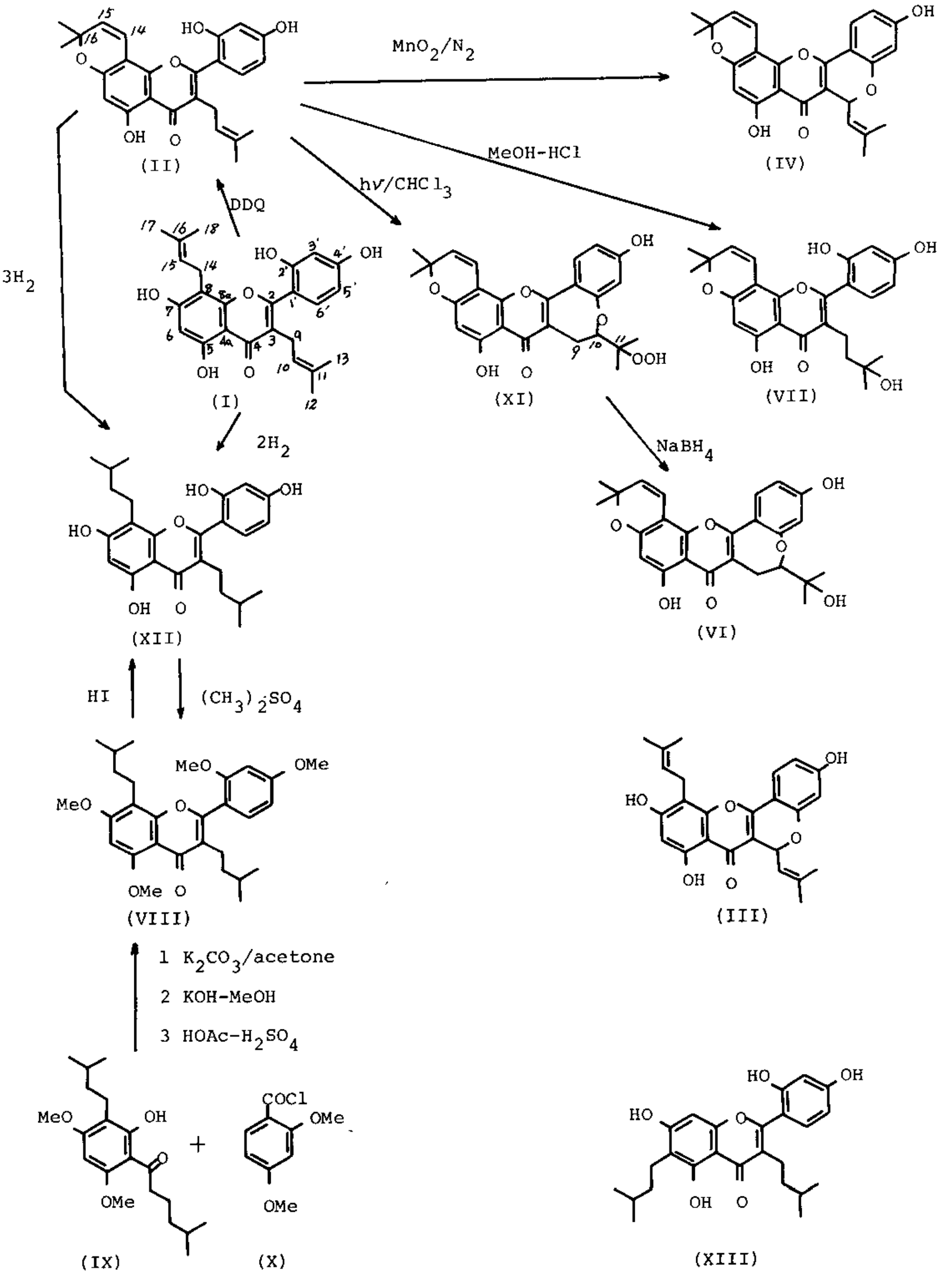
(II)
MnO_2/N_2
(IV)
MeOH-HCl
hν/$CHCl_3$
DDQ
(I)
$3H_2$
$2H_2$
(XI)
(VII)
$NaBH_4$
(VI)
(XII)
HI
$(CH_3)_2SO_4$
(VIII)
(III)
1 K_2CO_3/acetone
2 KOH-MeOH
3 HOAc-H_2SO_4
(IX)
(X)
(XIII)

Chart 2

initially proposed and they described[10] that mulberrin (I') is identical with kuwanon C (I), mulberrochromene (II') with morusin (II), and cyclomulberrochromene (IV') with cyclomorusin (IV).

In order to clear these points, we studied the ^{13}C nmr spectra of the derivatives of morusin (II) and related prenylflavones. The ^{13}C nmr spectra of kuwanon C (I), tertahydrokuwanon C (XII), morusin (II), 2',4'-diacetylmorusin (IIa),

Table 1. Carbon-13 NMR spectra data

Carbon	I$^{1)}$	I$^{2)}$	VIII$^{1)}$	II$^{1)}$	II$^{2)}$	IIa$^{1)}$	VI$^{1)}$	XI$^{1)}$
2	158.5	158.9	158.2	159.5	158.6	159.8	159.7	159.8
3	120.9	119.4	121.8	121.5	120.2	121.7	117.2	117.1
4	183.3	181.8	183.6	183.1	181.8	182.3	181.7	181.7
4a	105.1	103.4	104.1	101.3	100.5	101.2	101.4	101.3
5	151.2	155.0	156.8	152.9	151.9	152.4	152.2	152.1
6	98.9	97.9	98.5	99.6	98.9	100.2	99.9	99.9
7	162.9	161.7	162.6^{*1}	162.7	162.0	162.3	163.6	163.6
8	106.9	105.5	107.9^{*2}	105.6	104.4	105.3	104.5	104.4
8a	162.9	160.3	162.0^{*1}	162.7	160.7	162.3	161.4	161.6
9	24.9	23.5	23.6	24.8	23.7	24.3	25.5	22.7
10	123.2	121.7	38.1^{*4}	122.7	121.6	121.7	90.9	86.0
11	131.7	131.2	28.3	132.0	131.3	131.7	71.9	82.9
12	25.8	25.4	22.6^{*3}	25.8	25.4	25.7	25.2	25.9
13	17.9	17.3		17.8	17.3	17.8	27.6	20.3
14	22.3	21.1	20.8	115.4	114.3	114.8	115.4	115.4
15	123.2	122.1	38.9^{*4}	127.1	127.6	127.7*	127.6	127.6
16	131.2	130.7	28.3	78.2	78.0	78.3	78.3	78.3
17	25.8	25.4	22.8^{*3}	28.1	27.7	28.0	28.1	28.1
18	17.9	17.3						
1'	113.2	111.3	113.1	112.7	110.9	120.0	114.2	114.0
2'	161.0	156.5	153.9	158.5	156.7	151.2	151.1	158.2
3'	104.4	102.7	104.1	104.5	103.0	114.8	112.3	112.4
4'	162.4	161.2	160.3^{*1}	162.7	161.1	153.4	162.4	162.4
5'	108.0	106.7	108.1^{*2}	108.1	107.0	118.2	109.0	108.8
6'	132.3	131.2	132.1	132.3	131.3	132.6*	130.7	130.8
$CO\underline{C}H_3$						20.5		
						20.8		
$\underline{C}OCH_3$						168.7		
						168.9		

1) δ : ppm from TMS (internal) in pyridine-d_5

2) δ : ppm from TMS (internal) in DMSO-d_6

* Assignments may be reversed.

compound A (VI), and morusinhydroperoxide (XI) were analyzed as shown in Table 1. Assignments of the carbon atoms in these compounds were carried out on the basis of existing literatures[5,11,12] and off-resonance decoupling. In these spectra, the C-6 signal appeared in the range of 97.9-100.2 ppm. These results are good agreement with the literatures.[10,13]

Direct comparison of mulberrin (I') with kuwanon C (I), and mulberrochromene (II') with morusin (II) were carried out as follows. Mulberrin (I') which was send from Dr. Deshpande was proved to be identical with kuwanon C (I) by mixed melting point[14] and comparison of ir and pmr spectra and mulberrochromene (II') was identical with morusin (II) by mixed melting point.[15] Furthermore, we attempted the photooxidative cyclization of mulberrochromene (II') which occurred in the case of morusin (II).[16] A solution of mulberrochromene (0.3 mg) in chloroform was externally irradiated in the glass vessel with a 100 W high-pressure mercury lamp for 6 hr. The precipitate was filtered off and recrystallized from methanol to give yellow needles, mp 204-206° This product was negative to Gibbs test and was identified with authentic specimen of morusinhydroperoxide (XI)[16] by mixed melting point.[17] These results indicate that the linear structures of the four prenylated morus flavones, mulberrin (I'), mulberrochromene (II'), cyclomulberrin (III'), and cyclomulberrochromene (IV'), should be reversed to the angular structures, I, II, III, and IV, respectively. Chari <u>et al</u> insist[10] that, in the conversion of artocarpin to tetrahydromulberrin (Chart 1), an isomerization must have taken place and the only conceivable possibility is that of a Wessely-Moser rearrangement in the demethylation. In order to examine the possibility of the isomerization, the demethylation of tetrahydrokuwanon C tetramethyl ether (VIII) by hydriodic acid was carried out. A mixture of VIII (110 mg), hydriodic acid (1 ml, 57 % HI), and glacial acetic acid (1 ml) was heated in a sealed tube at 170° for 90 min. The products were purified by preparative TLC to give demethylated product (XII) in 55 % yield. The product (XII) was identified with authentic specimen of tetrahydrokuwanon C (XII)[9] by mixed melting point and ir spectroscopy. But isomeric product (XIII), 3,6-diisopentyl-5,7,2',4'-tetrahydroxyflavone, could not be obtained. On the ring isomeric change of 2'-hydroxyflavone derivatives, it was reported[18] that there was no isomeric change under ordinary conditions of demethylation with hydriodic acid. If the Wessely-Moser rearangement was occurred in the demethylation of tetrahydroartocarpin, as Chari *et al* insisted on,[10] it seems to be interesting example, so we are now in progress to elucidate the possibility of isomerization of the prenylflavones obtained from the Morus root bark.

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REFERENCES AND FOOTNOTES

1a V.H. Deshpande, P.C. Parthasarathy, and K. Venkataraman, *Tetrahedron Letters*, 1968, 1715; b V.H. Deshpande, P.V. Wakharkar, and A.V. Rama Rao, *Indian J. Chem.*, 1976, **14B**, 647.

2 K. Venkataraman, *Phytochemistry*, 1972, **11**, 1571.

3 T. Nomura, T. Fukai, S. Yamada, and M. Katayanagi, *Chem. Pharm. Bull.(Tokyo)*, 1978, **26**, 1394.

4 T. Nomura, T. Fukai, and M. Katayanagi, *Chem. Pharm. Bull.(Tokyo)*, 1978, **26**, 1453.

5 C. Konno, Y. Oshima, and H. Hikino, *Planta medica*, 1977, **32**, 118.

6 T. Nomura, T. Fukai, and M. Katayanagi, *Heterocycles*, 1978, **9**, 745.

7 T. Nomura and T. Fukai, *Heterocycles*, 1978, **9**, 1295.

8 T. Nomura and T. Fukai, *Heterocycles*, 1979, **12**, 943.

9 T. Nomura, Y. Sawaura, T. Fukai, S. Yamada, and S. Tamura, *Heterocycles*, 1978, **9**, 1355.

10 V.M. Chari, S. Ahmad, and B-G. Österdahl, *Z. Naturforsch*, 1978, **33b**, 1547.

11 E. Wenkert and H.E. Gottlieb, *Phytochemistry*, 1977, **16**, 1811.

12a J.B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York,1972; b G.C. Levy and G.L. Nelson, "Carbob-13 Nuclear Magnetic Resonance for Organic Chemists", Wiley-Interscience, New York, 1972.

13a H. Wagner, V.M. Chari, and J. Sonnenbichler, *Tetrahedron Letters*, 1976, 1799; b V.M. Chari, M. Ilyas, H. Wagner, A. Neszmélyi, F. Chen, L. Chen, Y. Lin, and Y. Lin, *Phytochemistry*, 1977, **16**, 1273.

14 As a trace amount of impurity was detected in the specimen which was sent from Dr. Deshpande by TLC, ir, and pmr spectra, it was purified by preparative TLC (benzene:acetone=4:1) and crystallization from benzene afforded prisms, mp 154-161°. The mixed melting point with kuwanon C (I, mp of I, 153-160°), 154-160°, was undepressed.

15 Although the melting point of mulberrochromene (II') was reported to be 232-235°,[1a] the specimen which was sent from Dr. Deshpande showed mp 202-207°. The mixed melting point with morusin (II, mp of II, 202-210°), 200-210°, was undepressed.

16 T. Nomura, T. Fukai, S. Yamada, and M. Katayanagi, Chem. Pharm. Bull.(Tokyo), 1978, **26**, 1431.

17 The mixed melting point with morusinhydroperoxide (XI, mp of XI, 204-206°), 204-206°, was undepressed.

18 T.R. Seshadri, "The Chemistry of Flavonoid Compounds", ed. by T.A. Geissman, Pergamon Press, Oxford, 1962, p 188.

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