[Chem. Pharm. Bull.
24(11)2898—2900(1976)]

UDC 547.814.5.02 : 581.142

Phenolic Constituents of the Cultivated Mulberry Tree (*Morus alba* L.)

The structures of three new flavone derivatives, morusin, cyclomorusin, and compound A, which had been isolated from the root bark of the cultivated mulberry tree (a variety of *Morus alba* L.), were shown to be I, II, and III, respectively.

The root bark of the mulberry tree (*Morus alba* L. and other plants of the genus *Morus*) has been used as an antiphlogistic, diuretic, and expectorant in the Chinese herb medicine. The constituents of this root bark have been studied by many investigators and some phenolic compounds, triterpenoids, and a glyceride have been isolated.¹⁻³ In recent years a series of flavones have been isolated from the heart wood of *Artocarpus* (Moraceae) and the root bark of *Morus* species by Venkataraman and his co-workers.^{4,5} In the course of our studies on the constituents of the root bark, three new flavone derivatives, morusin (I), cyclomorusin (II), and compound A (III), have been isolated from the benzene extract of the root bark of the cultivated mulberry tree (a variety of *Morus alba* L.). In this communication, we wish to describe the structure determination of these new flavone derivatives. These compounds, I, II, and III, gave characteristic color reactions for flavones and exhibited an intense green color with methanolic-FeCl₃.

Morusin⁶ (I), C₂₅H₂₄O₆, mp 214—216° (pale yellow prisms from hexane-ether), positive to the Gibbs test, ultraviolet (UV) absorption $\lambda_{\text{max}}^{\text{EtOH}}$ nm (log ϵ): 206 (4.49), 220 (sh 4.43), 270 (4.60), 300 (sh 4.00), 320 (sh 3.90), 350 (3.81); infrared (IR) absorption $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3250, 1660, 1600; proton magnetic resonance (PMR), δ in (CD₃)₂SO, 1.42 (9H, s, C₁₄-CH₃ × 2 and C₁₁-CH₃), 1.57 (3H, s, C₁₁-CH₃), 3.02 (2H, d-like, $J=8$ Hz, C₉-H × 2), 5.03 (1H, t-like, $J=8$ Hz, C₁₀-H), 5.67 (1H, d, $J=10$ Hz, C₁₃-H), 6.21 (1H, s, C₆-H), 6.37 (1H, dd, $J=2.5$ and 7.5 Hz, C₅-H), 6.45 (1H, d, $J=2.5$ Hz, C₃-H), 6.53 (1H, d, $J=10$ Hz, C₁₂-H), 7.14 (1H, d, $J=7.5$ Hz, C₆-H), 9.78, 9.85, 13.17 (each 1H, s, 3 × OH, disappeared on addition of D₂O); Mass Spectrum m/e : 420 (M⁺), 405 (M⁺ - CH₃), 203 (VI, formed from the ion at 405 by a reverse Diels-Alder reaction). I forms a dimethyl ether⁷ (Ia), C₂₇H₂₈O₆ (M⁺ 448), mp 140—146°, on treatment with ethereal CH₂N₂, and Ia shows a green coloration with methanolic-FeCl₃ indicating the presence of a bonded hydroxyl group. On prolonged treatment with (CH₃)₂SO₄ and K₂CO₃ in boiling acetone, a trimethyl ether (Ib), C₂₈H₃₀O₆ (M⁺ 462) was obtained as an amorphous solid. Treatment of I with Ac₂O in pyridine at room temperature yielded a diacetate⁷ (Ic), C₂₉H₂₈O₈ (M⁺ 504), mp 137—138°, which showed a green color with FeCl₃ and was negative to the Gibbs test. When treated with the same reagents on a water bath, I gave a triacetate (Id), C₃₁H₃₀O₉ (M⁺ 546), mp 70—75°, which was negative to FeCl₃ test. Hydrogenation of I in the presence of Adams catalyst yielded a tetrahydro derivative⁷ (Ie), C₂₅H₂₈O₆ (M⁺ 424), mp 248—252°, showing the presence of two ethylenic bonds. From these data, I can be regarded as a mulberrochromene-type flavone having the 2,2-dimethylchromene and γ,γ -dimethylallyl group attached to the 3-position of the chromone ring.⁴ The angular structure (I) for morusin is supported by the consideration of the changes in the chemical shift of chromene olefinic protons in its diacetate (Ic) compared with the triacetate (Id) (Table I). These changes are of the same sign and the same order of magnitude as those

1) T. Uno, *Sanshi Shikenjo Hokoku* (Tokyo), **24**, 437 (1970).

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4) V.H. Deshpande, P.C. Parthasarathy, and K. Venkataraman, *Tetrahedron Letters*, **1968**, 1715.

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6) Elemental analysis and high resolution mass spectra of the compound gave a satisfactory result.

7) Elemental analysis of the compound gave a satisfactory result.

Chart 1

Chart 2

TABLE I. Chemical Shift (ppm) for C_{12} -H and C_{13} -H in Ic and Id^{a)}

Compound	C_{12} -H	C_{13} -H
Ic	6.52	5.49
Id	6.60	5.59
Δ	-0.08	-0.10

^{a)} measured in $CDCl_3$

observed by many investigators for similar compounds.⁸⁾ From these results, morusin is represented by the formula I.

Cyclomorusin (II), $C_{25}H_{22}O_6$ (M^+ 418), mp 246–248° (pale yellow prisms from MeOH), $[\alpha]_{D}^{20} +20^\circ$ ($c=0.15$ in MeOH, from ORD measurement); UV λ_{max}^{EtOH} nm (log ϵ): 223 (4.45), 225 (4.38), 283 (4.43), 383 (4.19), $\lambda_{max}^{MeOH-AlCl_3}$ nm (log ϵ): 229 (4.51), 265 (4.35), 285 (4.41), 379 (4.24), 429 (3.83), $\lambda_{max}^{MeOH-MeONa}$ nm (log ϵ): 270 (4.42), 409 (4.41); IR ν_{max}^{KBr} cm^{-1} : 3500, 1660, 1620, 1590; PMR, δ in $(CD_3)_2CO$: 1.60 (6H, s, $C_{14}-CH_3 \times 2$), 1.72, 1.98 (each 3H, s, $C_{11}-CH_3 \times 2$), 5.49 (1H, d, $J=10$ Hz, $C_{10}-H$), 5.79 (1H, d, $J=10$ Hz, $C_{13}-H$), 6.19 (1H, s, C_6-H), 6.24 (1H, d, $J=10$ Hz, C_9-H), 6.46 (1H, d, $J=2$ Hz, $C_{3'}-H$), 6.67 (1H, dd, $J=2$ and 9 Hz, $C_{5'}-H$), 6.95 (1H, d, $J=10$ Hz, $C_{12}-H$), 7.82 (1H, d, $J=9$ Hz, $C_6'-H$). These spectral data suggest that the structure of cyclomorusin closely resembles that of cyclomulberrochromene rather than mulberro-

8) B. Jackson, P.J. Owen, and F. Sheinmann, *J. Chem. Soc. (C)*, 1968, 1899.

chromene.⁴⁾ The structure (II) for cyclomorusin is supported by its mass spectral fragmentation (Chart 2)⁹⁾ and negative Gibbs test. From the consideration of these data, we propose the formula (II) as a tentative structure of cyclomorusin.

Compound A⁶⁾ (III), C₂₅H₂₄O₇, mp 258—260° (yellow prisms from MeOH); UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 218 (4.49), 234 (4.49), 278 (4.51), 334 (4.24), $[\alpha]_{\text{D}}^{25}$ 0° ($c=0.15$ in MeOH, from ORD measurement); IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3500 (sh), 3400, 3200, 1660, 1630, 1600; PMR, δ in pyridine-*d*₅, 1.48 (6H, s, C₁₄-CH₃ × 2), 1.55, 1.58 (each 3H, s, C₁₁-CH₃ × 2), 2.96 (1H, dd, $J=10$ and 16 Hz, C₉-H), 3.93 (1H, dd, $J=2$ and 16 Hz, C₉-H), 4.28 (1H, dd, $J=2$ and 10 Hz, C₁₀-H), 5.76 (1H, d, $J=11$ Hz, C₁₃-H), 6.51 (1H, s, C₆-H), 6.95 (1H, d, $J=11$ Hz, C₁₂-H), 7.02 (1H, dd, $J=2$ and 10 Hz, C₅'-H), 7.05 (1H, d, $J=2$ Hz, C₃'-H), 8.13 (1H, d, $J=10$ Hz, C₆'-H), 12.70 (1H, s, OH); Mass Spectrum m/e : 436 (M⁺), 421 (M⁺-CH₃), 403 (M⁺-CH₃-H₂O), 203 (VI); negative to the Gibbs test. Treatment of III with Ac₂O in pyridine at room temperature yielded a diacetate⁷⁾ (IIIa), mp 249—250°, C₂₉H₂₈O₉ (M⁺ 520); IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3510, 1775, 1760, negative to FeCl₃ test. When treated with the same reagents on a water bath (60°) for 20 hr, III gave a triacetate (IIIb), mp 218—222°, C₃₁H₃₀O₁₀ (M⁺ 562); IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 1772, 1740. III forms a monomethyl ether (IIIc),⁷⁾ C₂₆H₂₆O₇ (M⁺ 450), mp 227—229°, on treatment with ethereal CH₂N₂, which showed a green color with FeCl₃. These experimental results suggest the presence of two phenolic hydroxyls and a tertiary alcoholic hydroxyl group. Treatment of III with SOCl₂ in pyridine gave a dehydrated product (IV),⁶⁾ mp 266—272°, C₂₅H₂₂O₆, UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm (log ϵ): 219 (4.45), 235 (4.45), 278 (4.47), 334 (4.16); IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3200, 1665, 1640, 1615; PMR, δ in CDCl₃ and pyridine-*d*₅, 1.49 (6H, s, C₁₄-CH₃ × 2), 1.88 (3H, s, C₁₁-CH₃), 2.80—3.15 (2H, m, C₉-H × 2), 4.83 (1H, m, C₁₀-H), 4.93, 5.06 (each 1H, s, C₁₁=CH₂), 5.56 (1H, d, $J=10$ Hz, C₁₃-H), 6.62 (1H, s, C₆-H), 6.63—6.88 (3H, m, C₁₂-H, C₃'-H, and C₅'-H), 7.79 (1H, d, $J=8$ Hz, C₆'-H), Mass Spectrum m/e : 418 (M⁺), 403 (M⁺-CH₃), 337 (M⁺-C₃H₅), 363 (M⁺-C₄H₇), 203 (VI). IV afforded a monoacetate⁷⁾ (IVa), mp 227—232°, C₂₇H₂₄O₇ (M⁺ 460), on treatment with Ac₂O in pyridine, and when treated with the same reagents on a water bath, gave a diacetate (IVb), mp 195—197°, C₂₉H₂₆O₈ (M⁺ 502), which showed no IR absorption in the hydroxyl region. Further evidence supporting the structure of IV was obtained by comparing the IR and PMR spectral data, and mixed melting point with those of compound (IV) obtained by the action of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) on I. In the light of the DDQ reactions discussed in the earlier papers by Venkataraman and his co-workers,^{5,10)} it is most likely that the action of DDQ on I does not lead to II but to IV. From these considerations, we propose the formula (III) for compound A.

Acknowledgement We are grateful to Prof. H. Mitsuhashi, Faculty of Pharmaceutical Sciences, Hokkaido University, for his valuable advices and encouragement. We also thank Miss Y. Sakamoto for PMR spectral measurement and Miss Y. Taniguchi for mass spectral measurement.

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Received August 4, 1976

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