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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-$FeCl_3$.

Morusin[6] (I), $C_{25}H_{24}O_6$, mp 214—216° (pale yellow prisms from hexane–ether), positive to the Gibbs test, ultraviolet (UV) absorption λ_{max}^{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 ν_{max}^{Nujol} cm^{-1}: 3250, 1660, 1600; proton magnetic resonance (PMR), δ in $(CD_3)_2SO$, 1.42 (9H, s, C_{14}–$CH_3 \times 2$ and C_{11}–CH_3), 1.57 (3H, s, C_{11}–CH_3), 3.02 (2H, d-like, $J=8$ Hz, C_9–$H \times 2$), 5.03 (1H, t-like, $J=8$ Hz, C_{10}–H), 5.67 (1H, d, $J=10$ Hz, C_{13}–H), 6.21 (1H, s, C_6–H), 6.37 (1H, dd, $J=2.5$ and 7.5 Hz, $C_{5'}$–H), 6.45 (1H, d, $J=2.5$ Hz, $C_{3'}$–H), 6.53 (1H, d, $J=10$ Hz, C_{12}–H), 7.14 (1H, d, $J=7.5$ Hz, $C_{6'}$–H), 9.78, 9.85, 13.17 (each 1H, s, $3\times$OH, disappeared on addition of D_2O); Mass Spectrum m/e: 420 M^+), 405 (M^+-CH_3), 203 (VI, formed from the ion at 405 by a reverse Diels–Alder reaction). I forms a dimethyl ether[7] (Ia), $C_{27}H_{28}O_6$ (M^+ 448), mp 140—146°, on treatment with ethereal CH_2N_2, and Ia shows a green coloration with methanolic-$FeCl_3$ indicating the presence of a bonded hydroxyl group. On prolonged treatment with $(CH_3)_2SO_4$ and K_2CO_3 in boiling acetone, a trimethyl ether (Ib), $C_{28}H_{30}O_6$ (M^+ 462) was obtained as an amorphous solid. Treatment of I with Ac_2O in pyridine at room temperature yielded a diacetate[7] (Ic), $C_{29}H_{28}O_8$ (M^+ 504), mp 137—138°, which showed a green color with $FeCl_3$ and was negative to the Gibbs test. When treated with the same reagents on a water bath, I gave a triacetate (Id), $C_{31}H_{30}O_9$ (M^+ 546), mp 70—75°, which was negative to $FeCl_3$ test. Hydrogenation of I in the presence of Adams catalyst yielded a tetrahydro derivative[7] (Ie), $C_{25}H_{28}O_6$ (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

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[1] T. Uno, *Sanshi Shikenjo Hokoku* (Tokyo), 24, 437 (1970).
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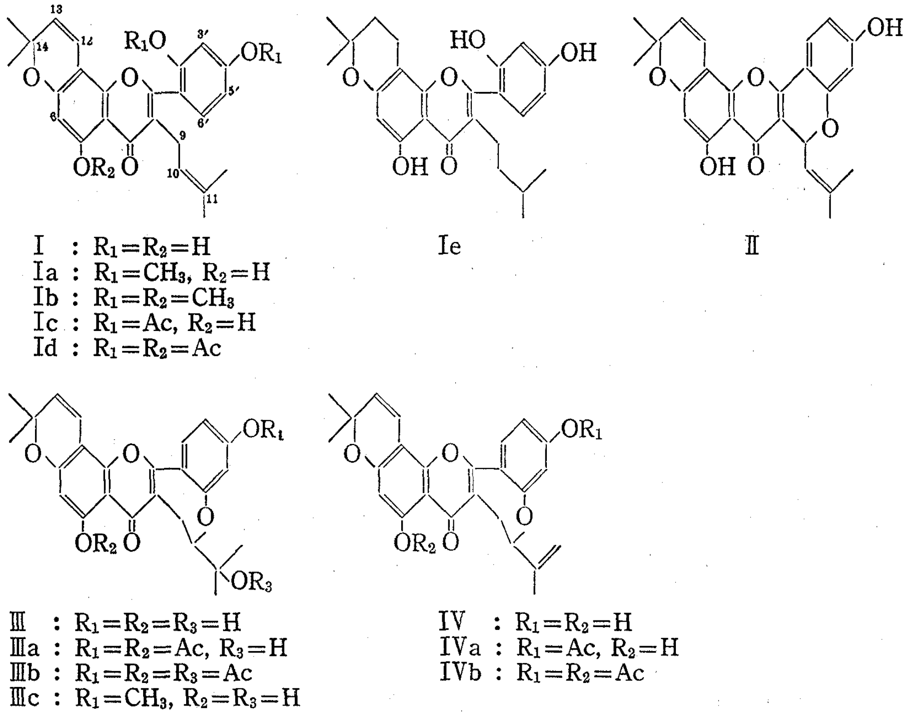
[5] K. Venkataraman, *Phytochemistry*, **1972**, 1571.
[6] Elemental analysis and high resolution mass spectra of the compound gave a satisfactory result.
[7] Elemental analysis of the compound gave a satisfactory result.



I : $R_1=R_2=H$
Ia : $R_1=CH_3$, $R_2=H$
Ib : $R_1=R_2=CH_3$
Ic : $R_1=Ac$, $R_2=H$
Id : $R_1=R_2=Ac$

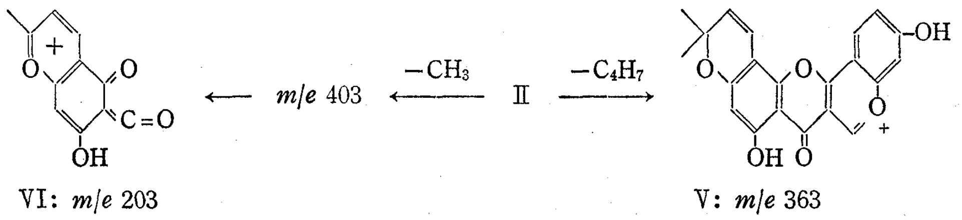
Ie

II

III : $R_1=R_2=R_3=H$
IIIa : $R_1=R_2=Ac$, $R_3=H$
IIIb : $R_1=R_2=R_3=Ac$
IIIc : $R_1=CH_3$, $R_2=R_3=H$

IV : $R_1=R_2=H$
IVa : $R_1=Ac$, $R_2=H$
IVb : $R_1=R_2=Ac$

Chart 1



VI: m/e 203

V: m/e 363

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), $[\alpha]_{589}^{20}$ $+20°$ ($c=0.15$ in MeOH, from ORD measurement); UV $\lambda_{\max}^{\text{EtOH}}$ nm ($\log \varepsilon$): 223 (4.45), 225 (4.38), 283 (4.43), 383 (4.19), $\lambda_{\max}^{\text{MeOH-AlCl}_3}$ nm ($\log \varepsilon$): 229 (4.51), 265 (4.35), 285 (4.41), 379 (4.24), 429 (3.83), $\lambda_{\max}^{\text{MeOH-MeONa}}$ nm ($\log \varepsilon$): 270 (4.42), 409 (4.41); IR $\nu_{\max}^{\text{KBr}}$ 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-

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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 A[6] (III), $C_{25}H_{24}O_7$, mp 258—260° (yellow prisms from MeOH); UV λ_{max}^{MeOH} nm (log ε): 218 (4.49), 234 (4.49), 278 (4.51), 334 (4.24), $[\alpha]_{589}^{20}$ 0° (c=0.15 in MeOH, from ORD measurement); IR ν_{max}^{Nujol} cm^{-1}; 3500 (sh), 3400, 3200, 1660, 1630, 1600; PMR, δ in pyridine-d_5, 1.48 (6H, s, C_{14}-$CH_3 \times 2$), 1.55, 1.58 (each 3H, s, C_{11}-$CH_3 \times 2$), 2.96 (1H, dd, J=10 and 16 Hz, C_9-H), 3.93 (1H, dd, J=2 and 16 Hz, C_9-H), 4.28 (1H, dd, J=2 and 10 Hz, C_{10}-H), 5.76 (1H, d, J=11 Hz, C_{13}-H), 6.51 (1H, s, C_6-H), 6.95 (1H, d, J=11 Hz, C_{12}-H), 7.02 (1H, dd, J=2 and 10 Hz, $C_{5'}$-H), 7.05 (1H, d, J=2 Hz, $C_{3'}$-H), 8.13 (1H, d, J=10 Hz, $C_{6'}$-H), 12.70 (1H, s, OH); Mass Spectrum m/e: 436 (M^+), 421 (M^+-CH_3), 403 ($M^+-CH_3-H_2O$), 203 (VI); negative to the Gibbs test. Treatment of III with Ac_2O in pyridine at room temperature yielded a diacetate[7] (IIIa), mp 249—250°, $C_{29}H_{28}O_9$ (M^+ 520); IR ν_{max}^{Nujol} cm^{-1}: 3510, 1775, 1760, negative to $FeCl_3$ test. When treated with the same reagents on a water bath (60°) for 20 hr, III gave a triacetate (IIIb), mp 218—222°, $C_{31}H_{30}O_{10}$ (M^+ 562); IR ν_{max}^{Nujol} cm^{-1}: 1772, 1740. III forms a monomethyl ether (IIIc),[7] $C_{26}H_{26}O_7$ (M^+ 450), mp 227—229°, on treatment with ethereal CH_2N_2, which showed a green color with $FeCl_3$. These experimental results suggest the presence of two phenolic hydroxyls and a tertiary alcoholic hydroxyl group. Treatment of III with $SOCl_2$ in pyridine gave a dehydrated product (IV),[6] mp 266—272°, $C_{25}H_{22}O_6$, UV λ_{max}^{EtOH} nm (log ε): 219 (4.45), 235 (4.45), 278 (4.47), 334 (4.16); IR ν_{max}^{Nujol} cm^{-1}: 3200, 1665, 1640, 1615; PMR, δ in $CDCl_3$ and pyridine-d_5, 1.49 (6H, s, C_{14}-$CH_3 \times 2$), 1.88 (3H, s, C_{11}-CH_3), 2.80—3.15 (2H, m, C_9-$H \times 2$), 4.83 (1H, m, C_{10}-H), 4.93, 5.06 (each 1H, s, C_{11}=CH_2), 5.56 (1H, d, J=10 Hz, C_{13}-H), 6.62 (1H, s, C_6-H), 6.63—6.88 (3H, m, C_{12}-H, C_3'-H, and $C_{5'}$-H), 7.79 (1H, d, J=8 Hz, $C_{6'}$-H), Mass Spectrum m/e: 418 (M^+), 403 (M^+-CH_3), 337 ($M^+-C_3H_5$), 363 ($M^+-C_4H_7$), 203 (VI). IV afforded a monoacetate[7] (IVa), mp 227—232°, $C_{27}H_{24}O_7$ (M^+ 460), on treatment with Ac_2O in pyridine, and when treated with the same reagents on a water bath, gave a diacetate (IVb), mp 195—197°, $C_{29}H_{26}O_8$ (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.

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