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NEW PHENYL PROPANOIDS HAVING WEAK PISCICIDAL ACTION AND THE RELATED COMPOUND: WUTAIENSOL, WUTAIENSAL, WUTAIALDEHYDE, AND METHYL DEMETHOXYWUTAIENSATE

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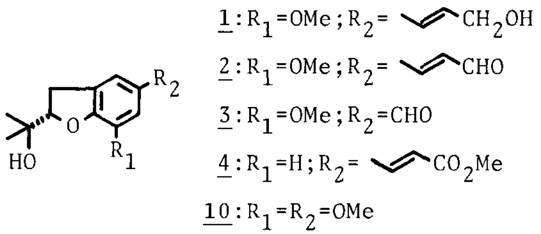
Summary: *The structures of three new prenylphenyl propanoids, wutaiensol (1), wutaiensal (2), and methyl demethoxywutaiensate (4) were established by correlating with S-rutaretin methyl ether (19) or S-marmesin (24) by chemical means. The structure of wutaialdehyde (3), a related compound, was also established by total synthesis of the racemate and by correlating with 1. Preliminary piscicidal test on these compounds disclosed that 2 and 4 are weakly but distinctly positive.*

In the course of studies[1)] on the chemical constituents of Rutaceous plants, we isolated three optically active phenyl propanoids and a related compound classified into a new category from the root wood of *Xanthoxylum wutaiense* Chen,[2)] which was known as a piscicidal plant in Formosa. In this communication, we describe their structural establishment involving absolute configurations.

Wutaiensol (1)-- Yellow oil[3)]; MS m/z: 264 (M^+, $C_{15}H_{20}O_4$); IR ($CHCl_3$) cm^{-1}: 3600; UV λ_{max}^{MeOH} nm (log ε): 213 (4.05), 277 (3.81); CD[4)] (MeOH) [θ] (nm): + 3223 (273); PMR ($CDCl_3$) δ: 1.21* and 1.35* (each 3H, s, CH_3), 1.65 and 2.10 (each 1H, br. s, OH), 3.15* (2H, d, J=10.0 Hz, $CH\underline{H_2}$), 3.86 (3H, s, OMe), 4.27 (2H, d, J=6.0 Hz, $C{=}CH\underline{H_2}O-$), 4.65* (1H, t, J=10.0 Hz, $C\underline{H}CH_2$), 6.14 (1H, dt, J=16.0 and 6.0 Hz, $CH{=}C\underline{H}CH_2$), 6.31 (1H, d, J=16.0 Hz, $C\underline{H}{=}CH$), 6.75 and 6.81 (each 1H, s, ArH).



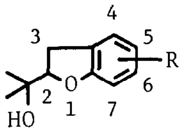
Wutaiensal (2)-- Yellow oil; MS m/z: 262 (M^+, $C_{15}H_{18}O_4$); IR ($CHCl_3$) cm^{-1}: 3595, 1670; UV λ_{max}^{MeOH} nm (log ε): 229 (4.02), 247 (4.01), 342 (4.17); CD[4)] (MeOH) [θ] (nm): + 4130 (350); PMR ($CDCl_3$) δ: 1.24* and 1.38* (each 3H, s, CH_3), 2.00 (1H, br. s, OH), 3.21* (2H, d, J=10.0 Hz, $CH\underline{H_2}$), 3.90 (3H, s, OMe), 4.72* (1H, t, J=10.0 Hz, $C\underline{H}CH_2$), 6.54 (1H, dd, J=16.0 and 8.0 Hz, $CH{=}C\underline{H}CHO$), 6.91 and 7.02 (each 1H, s, ArH), 7.34 (1H, d, J=16.0 Hz, $C\underline{H}{=}CHCO$), 9.56 (1H, d, J=8.0 Hz, $CHC\underline{H}O$). p-Nitrophenylhydrazone (5): red prisms; mp 164-167° (MeOH), $C_{21}H_{23}N_3O_5$.[5)]

Wutaialdehyde (3)-- Yellow oil; MS m/z: 236 (M^+, $C_{13}H_{16}O_4$); IR ($CHCl_3$) cm^{-1}: 3595, 1690;

UV λ_{max}^{EtOH} nm (log ε): 238.5 (4.35), 316 (4.36); CD[4] (MeOH) [Θ] (nm): + 4432 (300); PMR ($CDCl_3$) δ: 1.24* and 1.38* (each 3H, s, CH_3), 1.96 (1H, br. s, OH), 3.25* (2H, d, J=10.0 Hz, $CHC\underline{H}_2$), 3.93 (3H, s, OMe), 4.77* (1H, t, J=10.0 Hz, $C\underline{H}CH_2$), 7.30 (2H, dif. s, ArH), 9.76 (1H, s, CHO). p-Nitrophenylhydrazone (6): yellow fine needles; mp 189-191° (MeOH), $C_{19}H_{21}N_3O_5$.[5]

Methyl Demethoxywutaiensate (4)-- Colorless prisms; mp 113-115°; $C_{15}H_{18}O_4$,[5] MS m/z: 262 (M^+); IR ($CHCl_3$) cm^{-1}: 3595, 1715; UV λ_{max}^{MeOH} nm (log ε): 215 (4.10), 230 (4.06), 298sh (4.08), 320.5 (4.20); CD[4] (MeOH) [Θ] (nm): + 5649 (320); PMR ($CDCl_3$) δ: 1.21* and 1.33* (each 3H, s, CH_3), 1.99 (1H, br. s, OH), 3.14* (2H, d, J=10.0 Hz, $CHC\underline{H}_2$), 3.75 (3H, s, OMe), 4.62* (1H, t, J=10.0 Hz, $C\underline{H}CH_2$), 6.20 (1H, d, J=16.0 Hz, $CH{=}C\underline{H}CO$), 6.71 and 7.25 (each 1H, d, J=8.5 Hz, ArH), 7.30 (1H, s, ArH), 7.58 (1H, d, J=16.0 Hz, $C\underline{H}{=}CHCO$).

The existence of the common moiety, $Me_2C(-O-)CH(-O-)CH_2Ar$, (7) in these four compounds was demonstrated by the appearance of the astered signals in the PMR spectrum of each compound. Taking into consideration that these compounds have commonly a benzene ring, the above spectral deduction allowed us to extend the common structure to either 2,3-dihydrobenzofuran derivative (8) or 3,4-dihydrobenzopyran (9). During our studies[6] on structures of 2,3-dihydrofurano- and 3,4-dihydropyranocoumarins in detail, we occasionally found that the former shows two strong peaks at m/z (M^+-58) and at m/z (M^+-59) in the mass spectrum, while the latter at m/z (M^+-70) and at m/z (M^+-71). Since all of our new phenyl propanoids show two strong peaks at m/z (M^+-58) and at m/z (M^+-59) but not at m/z (M^+-70) and at m/z (M^+-71), the 2,3-dihydrobenzofuran moiety (8) was preferred to the other (9) as a tentative formula.



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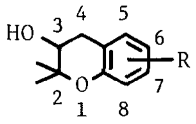

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On the other hand, the first three compounds (1, 2, and 3) could be correlated by the chemical experiments that treatment of 1 with MnO_2 in $CHCl_3$ gave 2, while 3 was obtained by oxidation of 1 with OsO_4 followed by $NaIO_4$. These correlation works demonstrate that 2 is an oxidative product in which the $-CH{=}CHCH_2OH$ group of 1 was transformed into a $-CH{=}CHCHO$ and that an aldehyde group situates at the corresponding position in 3. Thus, in order to establish the substituent pattern of the aromatic ring, 3 was converted into the dimethoxy-product (10) [oil; MS m/z: 238 (M^+, $C_{13}H_{18}O_4$), PMR ($CDCl_3$) δ: 1.22 and 1.36 (each 3H, s, CH_3), 2.13 (1H, br. s, OH), 3.14 (2H, dif. d, J=9.0 Hz, $ArC\underline{H}_2CH$), 3.75 and 3.86 (each 3H, s, OMe), 4.62 (1H, t, J=9.0 Hz, $CH_2C\underline{H}O-$), 6.34 (2H, s, ArH). p-Nitrobenzoate (11): yellow prisms; mp 90-92° (Et_2O-hexane), $C_{20}H_{21}NO_7$[5]] by Baeyer-Villiger oxidation followed by methylation. The comparative inspection[7] of the signal pattern and the chemical shift of a 2H singlet due to two aromatic protons of 10 with those of other reported trimethoxybenzene derivatives[8] led us to assume that 10 would have their two methoxy groups at the C_5- and the C_7-positions. Therefore, a racemic 5,7-dimethoxy product (10) was prepared according to the synthetic sequence shown in Chart 1. Identity of the synthetic material with the dimethoxy derivative (10) derived from 3 remained the two possibilities that the aldehyde group of 3 located at either C_5- or C_7-position. However, the spectral fact that, in the PMR spectrum, the aromatic protons of 3 appear as a diffused singlet having a

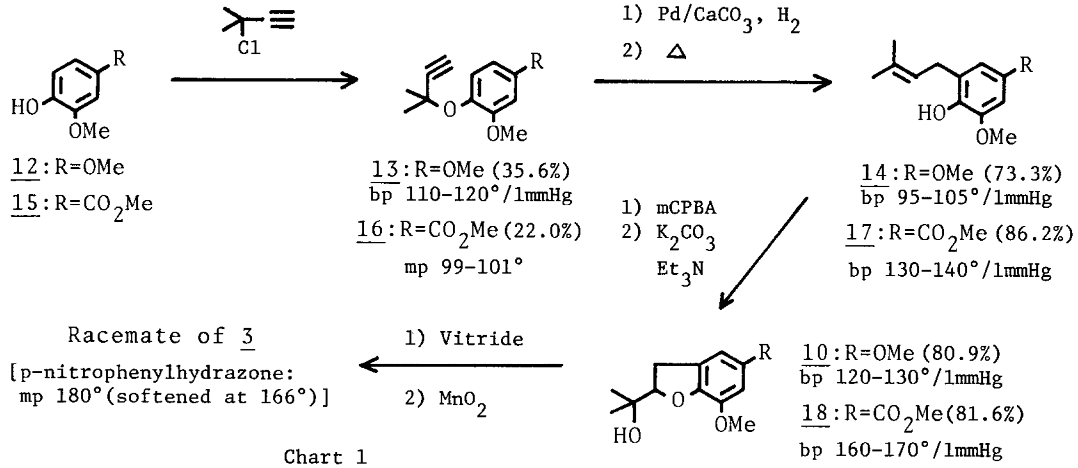


Chart 1

relatively small half band width, denies the latter possibility. The formula (3) is also supported by the biogenetical concept that coniferyl alcohol is the most general precursor for naturally occurring phenyl propanoids. Therefore, synthesis of the racemate of 3 from 15 was also achieved according to the synthetic pathway shown in Chart 1. Since the synthetic material itself and its p-nitrophenylhydrazone were identical with samples of the naturally occurring product (3) and its p-nitrophenylhydrazone (6) except optical activity, respectively, the structure of the natural product was established as the formula (3).

In the course of establishment[9] of the absolute configuration of S-rutaretin methyl ether (19), hexahydrorutaretin methyl ether (20) had been prepared. Acetylation of 20 with Ac_2O at room temperature gave the monoacetate (21) which was converted to the deoxy-product (22) [oil, MS m/z: 266 (M^+, $C_{15}H_{22}O_4$); CD[4] (MeOH) [θ] (nm): - 355 (289). 3,5-Dinitrobenzoate (23), yellow prisms, mp 95.5-97° (Et_2O-hexane), $C_{22}H_{24}N_2O_9$[5]] by treatment[10] with diethyl phosphoryl chloride in $CHCl_3$ containing NEt_3 followed by Birch reduction. On the other hand, catalytic hydrogenation of 1 over PtO_2 in EtOH yielded the dihydro derivative (22) which was identical with a sample derived from S-rutaretin methyl ether (19) even on the negative Cotton effect in the CD spectrum. These evidences described above are enough to establish the structures of these three new phenyl propanoids as formulae [(1), (2), and (3)] having an S configuration, respectively.

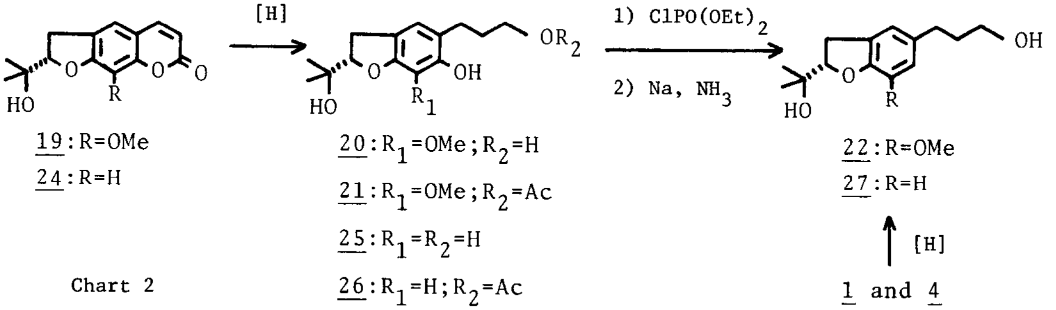
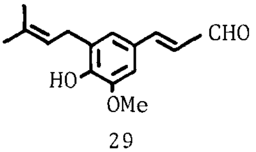


Chart 2

From these results, the structure of the fourth phenyl propanoid was arbitrarily speculated as the formula (4). Confirmation of the validity of our speculation was achieved by chemical means. Hexahydromarmesin[9] (25) was also converted to the deoxy-derivative (27) [oil, MS m/z: 236 (M^+, $C_{14}H_{20}O_3$); CD[4] (MeOH) [θ] (nm): - 1711 (290). 3,5-Dinitrobenzoate (28), yellow needles, mp 98-100° (Et_2O-hexane), $C_{21}H_{22}N_2O_8$[5]] through the same reaction sequence as hexahydrorutaretin methyl ether (20). 4 was also transformed into the deoxy-derivative (27) by catalytic hydrogenation over PtO_2 followed by treatment with Vitride [a 70 % benzene solution of $NaAlH_2(OCH_2CH_2OCH_3)_2$]. The both deoxy-derivatives (27) were also completely identical even on the negative Cotton effect, indicating that the chiral center of 4 is also S.

In 1967, Taylor *et al*[11] reported the natural occurrence of a biogenetically possible precursor for 2 , parvifloral (29), in *X. parviflorum* Benth. This is a sole compound classified in our prenylphenyl propanoids among reported ones as far as we know. Furthermore, in the previous papers, we reported the natural occurrence of several prenyloxyphenyl propanoids, cuspidiol[12,13] (30), boninenal[13,14] (31), and methyl boninenalate (32) from several *Xanthoxylum* species. It is of importance that our results suggest the natural occurrence of many varieties of phenyl propanoid other than coumarins distributed widely in *Xanthoxylum* plants.



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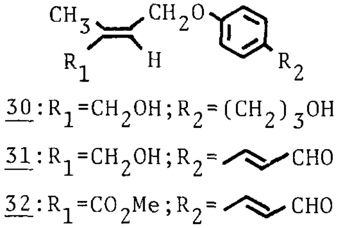

It should be added here that 2 and 4 show a weak but distinct piscicidal activity on preliminary test. The precise examinations on this problem are in progress in our laboratory.

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References and Notes

1) This communication forms part XLVII of the series "Ishii, Studies on the Chemical Constituents of Rutaceous Plants." Part XLVI, H. Ishii, K. Koyama, I.-S. Chen, S.-T. Lu, and T. Ishikawa, Chem. Pharm. Bull., 30, 1992 (1982).
2) This plant was newly discovered and designated by Chen, one of our group. [I.-S. Chen, Formosan Science, 26, 56 (1972)].
3) All trials to find a crystalline derivative for characterization failed.
4) The maximum of the first Cotton effect.
5) The compound gave satisfactory elemental analysis for the formula given.
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7) Precise discussion on this matter will be written in the full paper.
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