# 6-OXO-6a, 12a-DEHYDRO-α-TOXICAROL, A 6-OXO-DEHYDROROTENONE FROM THE ROOTS OF *DERRIS OBLONGA* BENTH

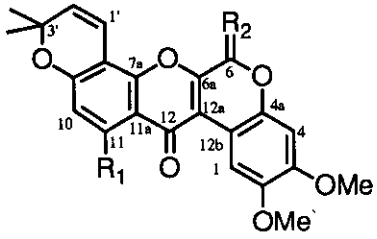
Yun-Lian Lin[a] and Yueh-Hsiung Kuo[b*]

National Research Institute of Chinese Medicine,[a] Taipei Hsien, Taiwan, ROC

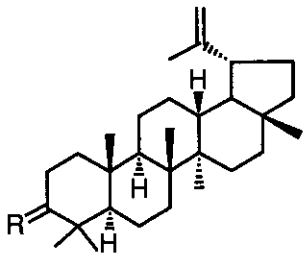
Department of Chemistry, National Taiwan University,[b] Taipei, Taiwan, ROC

**Absract** --------- A 6-oxodehydrorotenone, 6-oxo-6a,12a-dehydro-α-toxicarol, together with nineteen known compounds containing sugar, triterpenes, isoflavones, anthraquinones, rotenone, dehydrorotenones, 12a-hydroxyrotenones, coumestans, coumaronochromones and pterocarpen, were isolated from the roots of *Derris oblonga*, and characterized on the basis of spectral and chemical evidence.

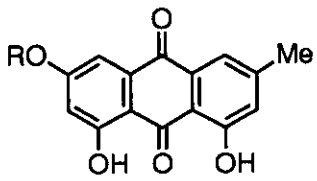
*Derris laxiflora, D. oblonga*, and *D. trifoliata* are the only three species of *Derris* indigenous to Taiwan. Two flavone glycosides were isolated from the roots of *D. trifoliata*.[1] Flavones, flavonols, chalcones, dihydrochalcones, isoflavans, rotenones, stilbenes, coumarins, aurones, pterocarpans, coumestans, triterpene, glycosides, and other interesting components have been observed from other species of *Derris*.[2-8] In connection with our interest in flavonoids and in view of the biological activity of the root,[3] chemical studies on *D. laxiflora* were undertaken in our laboratory.[9,10]
In the previous reports,[11-13] we described the isolation of five new compounds, oblongin **(1)**, oblonginol **(2)**, 6a,12a-dehydro-β-toxicarol **(3)**, derricarpin **(4)**, and 12-deoxo-12a-acetoxyelliptone **(5)** together with a known compound, 6a,12a-dehydro-α-toxicarol **(6)** from the ethanol extract of the root of *D. oblonga*. In this paper, we wish to describe the detailed isolation of ethanol extract of the roots of this plant, from which nineteen known compounds, lupenone **(7)**,[14] β-amyrin **(8)**,[9] lupenol **(9)**,[9] physcion **(10)**,[15] 6a,12a-dehydrodeguelin **(11)**,[16] 6a,12a-dehydrorotenone **(12)**,[17] villosol **(13)**,[18] sumatrol **(14)**,[17] maackiain **(15)**,[19] toxicarol isoflavone **(16)**,[20] 6-hydroxy-6a,12a-dehydro-α-toxicarol **(17)**,[21] tephrosin **(18)**,[22] 12a-hydroxyrotenone **(19)**,[5] 11-hydroxytephrosin **(20)**,[23] daidzein



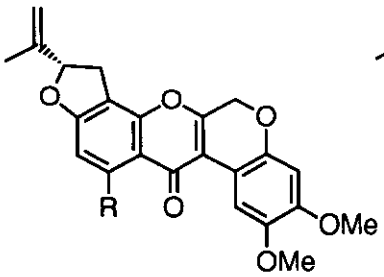
**6** $R_1$ = OH, $R_2$ = $H_2$
**11** $R_1$ = H, $R_2$ = $H_2$
**17** $R_1$ = OH, $R_2$ = H, OH
**26** $R_1$ = OH, $R_2$ = O
**27** $R_1$ = OAc, $R_2$ = O



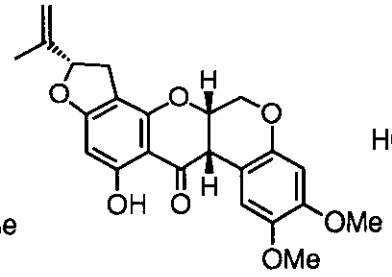
**7** R = O
**9** R = β-OH,H



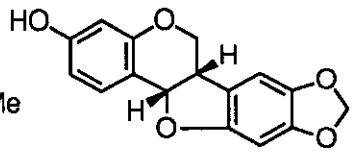
**10** R = Me
**23** R = H



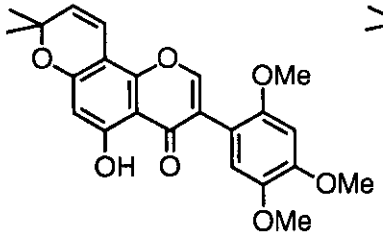
**12** R =H
**13** R =OH



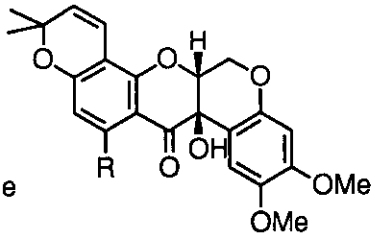
**14**



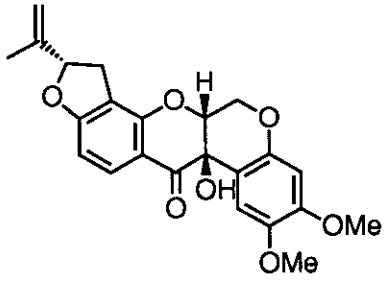
**15**



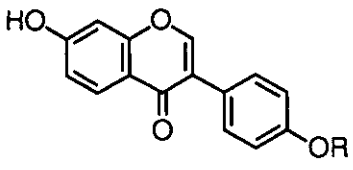
**16**



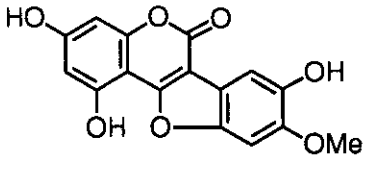
**18** R = H
**20** R = OH



**19**



**21** R = H
**22** R = Me



**24**

Table I $^{1}H$- and $^{13}C$-nmr data (δ- value) of **26** and **6** (300 MHz, 75 MHz, $CDCl_3$)

| H | 26 | 6 | C | 26 | 6 |
|---|---|---|---|---|---|
| 1 | 8.77 s | 8.23 s | 6a | 162.2 | 156.8 |
| 4 | 6.84 s | 6.51 s | 7a | 160.8 | 159.2 |
| 6 | | 4.95 s | 8 | 100.8 | 100.5 |
| 10 | 6.30 s | 6.25 s | 9 | 162.2 | 162.3 |
| 1' | 6.86 d (10.0) | 6.62 d (10.0) | 10 | 94.1 | 94.6 |
| 2' | 5.63 d (10.0) | 5.57 d (10.0) | 11 | 150.6 | 150.8 |
| 4' | 1.48 s | 1.46 s | 11a | 100.8 | 100.6 |
| 5' | 1.48 s | 1.46 s | 12 | 180.9 [a)] | 179.2 |
| OMe | 3.92 s | 3.84 s | 12a | 106.2 | 105.9 |
| OMe | 3.97 s | 3.91 s | 12b | 109.9 | 109.9 |
| OH | 12.46 s | 12.96 s | 1' | 114.3 | 114.3 |
| **C** | | | 2' | 127.9 | 127.7 |
| 1 | 107.6 | 110.7 | 3' | 79.0 | 79.8 |
| 2 | 145.2 | 144.1 | 4' | 28.2 | 28.2 |
| 3 | 151.2 | 149.2 | 5' | 28.4 | 28.2 |
| 4 | 99.6 | 101.0 | OMe | 56.1 | 55.9 |
| 4a | 146.8 | 146.2 | OMe | 56.2 | 56.3 |
| 6 | 180.1 [a)] | 64.7 | | | |

a : Assignment may be interchanged.

**(21)**,[24] formononetin **(22)**,[25] emodin **(23)**,[15] 8-methoxycoumestrol **(24)**,[26] and sucrose **(25)**, together with a new rotenone derivative, 6-oxo-6a,12a-dehydro-α-toxicarol **(26)** were observed. The components of this plant are very interesting. They involve extensive different skeleton's structures including terpenens **(7, 8, 9)**, anthraquinones **(10, 23)**, isoflavones **(16, 21, 22)**, coumestans **(4, 24)**, coumaronochromones **(1, 2)**, pterocarpen **(15)**, rotenone **(14)**, dehydrorotenones **(3, 6, 11, 12, 13, 17, 26)**, 12a-hydroxyrotenones **(18, 19, 20)**, deoxorotenone **(5)**, and sugar **(25)**. The structural elucidation of new compound 6-oxo-6a,12a-dehydro-α-toxicarol **(26)** based on the following evidence.

6-Oxo-6a,12a-dehydro-α-toxicarol **(26)** was obtained as orange red needles, mp 289-291 °C. Elemental analysis gave its molecular formula as $C_{23}H_{18}O_8$, and mass spectral fragmentation

provided peaks at 422 ($M^+$, 16%), 407 ($M^+$-$CH_3$, 100%), 391 (19%), and 203 (20%). The ultraviolet spectrum exhibited absorption bands at $\lambda_{max}^{MeOH}$ (log ε) : 272 (4.22), 304 (4.07), and 328 (3.94) nm. Compound **(26)** shows the ir spectrum absorptions at 3400, 1740, 1650, 1580, and 1520 $cm^{-1}$ attributable to hydroxy, lactone, ketone, and aromatic functionalities, respectively. The $^1$H-Nmr spectrum (Table I) of **26** shows singnal at δ 3.92 and 3.97 (each 3H, s) for two phenolic methyl ethers, δ 6.30, 6.84 and 8.77 (each 1H, s) for three aromatic protons, and δ 12.46 (1H, s) for a chelated phenolic proton. The signal at δ 8.77 is a characteristic signal of H-1 in dehydrorotenone which suffers deshielding effect by the C-12 carbonyl group.[27-29] The doublets at δ 5.63 and 6.86 (each 1H, d, $J$ = 10.0 Hz), and the singlet at δ 1.48 (6H, s) are characteristic of the *cis* double bond and gem-dimethyl group of a 2,2-dimethylchromene moiety.[9,30] The $^1$H-Nmr spectrum of **26** is similar to that of 6a,12a-dehydro-α-toxicarol **(6)** (Table I) except for the presence of a carbonyl group in **26** in place of methylene group. The 2,2-dimethylchromene group was assigned as been fused onto a neighboring ring at the C-8 and C-9 positions based on the following evidence. Compound **(26)** was converted to its monoacetate **(27)** [$\nu_{max}^{KBr}$ 1770, 1740, and 1640 $cm^{-1}$; δ 2.47 (3H, s) and 6.96 (1H, d, $J$ = 10.0 Hz, H-1')]. The downfield (0.10 ppm)[9,31-33] shift of H-1' in **27** compared with H-1' in **26**, the presence of 2.8% nuclear Overhauser effect between H-10 and AcO-11 in **27**, and $^{13}$C-Nmr spectrum (Table I) of **26** are all the evidence for supporting the assigned structure. The chemical correlation between **26** and **6** was achieved as follows. Compound **(26)** was produced from **6** by the oxidation with fresh manganese dioxide.[18] The proposed structure was also supported by the ms spectral fragmentation.[34,35]

## EXPERIMENTAL

Melting point were determined on a Yanagimoto micromelting point apparatus and are uncorrected. Ir spectra were recorded on a Perkin-Elmer 781 spectrophotometer. $^1$H- and $^{13}$C-Nmr spectra were run on a Brucker AM 300 at 300 MHz in $CDCl_3$ solution with tetramethylsilane(TMS) as an internal standard. Chemical shifts are given in δ-value and coupling constants ($J$) are given in hertz (Hz). EI-ms and uv spectra were taken on a JEOL JMS-100 spectrometer and Hitachi U-3200 spectrophotometer, respectively.

## Extraction and Isolation

The roots of *Derris oblonga* were crushed into small pieces and dried at 50 °C to give 6.1 kg of raw material, which was extracted with 95% ethanol (80 l) three times (8 h each time) at 60 °C. The combined extracts were evaporated *in vacuo* to give residue (293 g), which was subsequently subjected to partition with ether and $H_2O$ (each 1 l). The upper layer provided a black viscous mass (270 g). The aqueous layer was partitioned with butanol (1 l) to yield butanol soluble layer which was purified on a Diaion HP-20 and Sephadex LH-20 chromatography to give sucrose **(25)** (2.6 g) only. The ether soluble fraction (100 g) was subjected to column chromatography on silica gel with hexane-$CHCl_3$, $CHCl_3$ and $CHCl_3$-MeOH gradient solvent systems. After repeatedly chromatographed on silica gel, $AgNO_3$-coated silica gel, and Sephadex LH-20, the hexane-$CHCl_3$(6 : 4) eluent gave lupenone **(7)** (18 mg), the $CHCl_3$ eluent gave β-amyrin **(8)** (34 mg), lupenol **(9)** (162 mg), 6-oxo-6a,12a-dehydro-α-toxicarol **(26)** (16 mg), physcion **(10)** (26 mg), 6a,12a-dehydrodeguelin **(11)** (16 mg), 6a,12a-dehydrorotenone **(12)** (14 mg), 6a,12a-dehydro-α-toxicarol **(6)** (253 mg), 12-deoxo-12α-acetoxyelliptone **(5)** (18 mg), villosol **(13)** (12 mg), sumatrol **(14)** (23 mg), 6a,12a-dehydro-β-toxicarol **(3)** (12 mg), derricarpin **(4)** (18 mg), maackiain **(15)** (38 mg), toxicarol isoflavone **(16)** (26 mg), 6-hydroxy-6a,12a-dehydro-α-toxicarol **(17)** (15 mg), tephrosin **(18)** (50 mg), 12a-hydroxyrotenone **(19)** (30 mg), and 11-hydroxytephrosin **(20)** (5.76 g). The 5% MeOH/$CHCl_3$ eluent yielded daidzein **(21)** (11 mg), formononetin **(22)** (182 mg), emodin **(23)** (21 mg), oblongin **(1)** (18 mg), oblonginol **(2)** (35 mg), and 8-methoxycoumestrol **(24)** (16 mg).

**6-Oxo-6a,12a-dehydro-α-toxicarol (26)** : mp 289-291 °C. Ir (KBr)(ν $cm^{-1}$) : 3400, 1650, 1570, 1510, 1255, 1040, 870, 820, 775. $^1H$- and $^{13}C$-Nmr ($CDCl_3$) : Table I. *Anal.* Calcd for $C_{23}H_{18}O_8$ : C, 65.40; H, 4.30. Found : C, 65.58; H, 4.22.

## Acetylation of 26 with Acetic Anhydride

Compound **(26)** (5 mg) was allowed to react with $Ac_2O$ (1.0 ml) in pyridine (1.0 ml) at 60 °C overnight. Usual work-up gave monoacetate **(27)** (4 mg) [mp 263-266 °C. Ir (KBr)(ν $cm^{-1}$) : 1770, 1740, 1640, 1610, 1500, 1280, 1180. $^1H$-Nmr ($CDCl_3$) δ 1.51 (6 H, s), 2.47, 3.94, 3.99 (each 3H, s), 5.72, 6.96 (each 1H, d, $J$ = 10.0 Hz, H-1', H-2'), 6.54, 6.87, 8.88 (each 1H, s, H-4, H-10, H-1).

### Oxidation of 6 With Manganese Dioxide

Compound **(6)** (5 mg) and excess $MnO_2$ (50 mg) in 20 ml of $CH_2Cl_2$ was heated under reflux for 3 days. The reaction mixture was purified on silica gel preparative thin layer chromatography (hexane:$CHCl_3$=1:4) to yield **26** (3 mg).

### ACKNOWLEDGEMENT

This research was supported by the National Science Council of the ROC.

### REFERENCES

1. A. G. R. Nair, T. R. Seetharaman, S. Sankarasubramanian, and G. R. Rao, *J. Nat. Prod.*, 1986, **49**, 710.
2. Y. H. Obara, H. Matsubara, and K. Munakata, *Agr. Biol. Chem.*, 1976, **40**, 1245.
3. T. Komada, T. Yamakawa, and Y. Minoda, *Agr. Biol. Chem.*, 1980, **44**, 2387.
4. M. C. D. Nascimento and W. B. Mors, *Phytochemistry*, 1981, **20**, 147.
5. S. S. Chibber and R. P. Sharma, *Phytochemistry*, 1979, **18**, 1802.
6. M. Garcia, M. H. C. Kano, D. M. Vieir, and M. C. D. Nascimento, *Phytochemistry*, 1986, **25**, 2425.
7. C. P. Falshaw, R. A. Harmer, W. D. Ollis, R. F. Wheeler, V. B. Lalitha, and N. V. Subba, *J. Chem. Soc.* (C), 1969, 374.
8. M. Marlier, G. Darsenne, and J. Casimir, *Phytochemistry*, 1976, **15**, 183.
9. Y. L. Lin, Y. L. Chen, and Y. H. Kuo, *Chem. Pharm. Bull.*, 1991, **39**, 3132.
10. Y. L. Lin, Y. L. Chen, and Y. H. Kuo, *Chem. Pharm. Bull.*, 1992, **40**, 2295.
11. Y. L. Lin and Y. H. Kuo, *Heterocycles*, 1993, **36**, 1501.
12. Y. L. Lin, Y. L. Chen, and Y. H. Kuo, *J. Nat. Prod.* 1993, **56**, 1187.
13. Y. L. Lin, Y. L. Chen, and Y. H. Kuo, *Chem. Pharm. Bull.*, 1993, **41**, 1456.
14. J. H. Lin, *The Annual Reports of the National Research Institute of Chinese Medicine*, **1983**, 131
15. S. Takahashi, M. Takido, U. Sankawa, and S. Shibata, *Phytochemistry*, 1976, **15**, 1295.
16. L. Crombie and J. W. Lown, *J. Chem. Soc.* (C), 1962, 775.
17. S. Kadota, N. Lami, Y. Tezuka, and T. Kikuchi, *Chem. Pharm. Bull.*, 1988, **36** 834.

18. G. L. D. Krupadanan, P. N. Sarma, G. Srimannarayana, and N. V. S. Rao, *Tetrahedron Lett.*, 1977, 2125.

19. H. D. Vanetten, P. S. Mattews, and E. H. Mercer, *Phytochemistry*, 1983, **22**, 2291.

20. M. Tsukayama, Y. Iguchi, T. Horie, M. Masumura, and M. Nakayama, *Heterocycles*, 1984, **24**, 709.

21. T. Somleva and I. Ognyanov, *Planta Medica*, 1985, 219.

22. R. B. Filho, O. R. Gottlieb, A. P. Mourao, A. I. da Rotha, and F. S. Oliveira, *Phytochemistry*, 1975, **14**, 1454.

23. L. A. Mitscher, A. A. Shama, T. Haas, P. B. Hundson, and Y. H. Park, *Heterocycles*, 1979, **12**, 1033.

24. K. Kyogoku, K. Hatayama, K. Suzuki, S. Yokomori, K. Majima, and M. Komatsu, *Chem. Pharm. Bull.*, 1973, **21**, 1436.

25. T. Saitoh, H. Noguchi, and S. Shibata, *Chem. Pharm. Bull.*, 1978, **26**, 144.

26. R. R. Spencer, E. M. Bickoff, R. E. Lundin, and B. E. Knuckles, *J. Agr. Food Chem.*, 1966, **14**, 162.

27. D. G. Carlson, D. Weisleder, and W. H. Tallent, *Tetrahedron*, 1973, **29**, 2731.

28. J. Reisch, M. Gombos, K. Szendrei, and I. Novak, *Phytochemistry*, 1976, **15**, 234.

29. L. Crombie, P. J. Godin, D. A. Whiting, and K. S. Siddalingaiah, *J. Chem. Soc.* (C), **1961**, 2871.

30. J. S. P. Schwarz, A. I. Cohen, W. D. Ollis, E. A. Kaczka, and L. M. Jackman, *Tetrahedron*, 1964, **20**, 1317.

31. T. M. Smalberger, R. Vleggear, and J. C. Webber, *Tetrahedron*, 1974, **30**, 3927.

32. M. Shabbir, A. Zaman, L. Crombie, B. Tuck, and D. A. Whiting, *J. Chem. Soc.* (C), **1968**,1899.

33. A. K. Singhal, R. P. Sharma, G. Thyagrajan, W. Herz, and S. V. Govinelon, *Phytochemistry*, 1980, **19**, 929.

34. H. Audier, *Bull. Chem. Soc.* France, **1966**, 2892.

35. R. I. Reed and J. M. Wilson, *J. Chem. Soc.*, **1963**, 5949.

Received, 13th February, 1995