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NEW β-ORCINOL DEPSIDONES FROM *XANTHOPARMELIA QUINTARIA* AND A *THELOTREMA* SPECIES

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Abstract—A new depsidone isolated from a new species of *Thelotrema* was identified as hyopstictic acid. *Xanthoparmelia quintaria* contains hypostictic and hyposalazinic acids.

INTRODUCTION

The large crustose lichen family Thelotremataceae, comprising the genera *Leptotrema*, *Ocellularia*, *Phaeotrema* and *Thelotrema*, is widely distributed in tropical and subtropical zones. Although the chemistry of the family has been little studied, it appears to be dominated by the β-orcinol depsidones with the exclusion of the depsides and orcinol compounds [1]. An interesting feature is the joint occurrence of the rare compounds, hypoprotocetraric (**1**) and 2-*O*-demethylnotatic acids, in many of the species examined [2]. As has been previously proposed by Culberson and Hale [2], these compounds are probably derived from the corresponding depsides, 4-*O*-demethylbarbatic acid and obtusatic acid respectively, which are found in many lichen genera. It is noteworthy, however, that while the aldehydic β-orcinol depsidones (taxonomist's P + compounds) are among the most common of the lichen acids, their corresponding depside precursors are unknown thus suggesting a different mode of formation for these compounds. It seems more likely that the β-orcinol depsidones all arise from a common precursor, hypoprotocetraric acid, by successive oxidations and, in the case of psoromic acid, concurrent decarboxylation (Scheme 1). In this paper we report the isolation of hypostictic acid (**4**), a probable intermediate in this pathway, from a new species of *Thelotrema*. Its occurrence along with hyposalazinic acid (**3**) in *Xanthoparmelia quintaria* (Hale) Hale is also reported. The isolation of other intermediates in this biosynthetic pathway will be reported in subsequent papers.

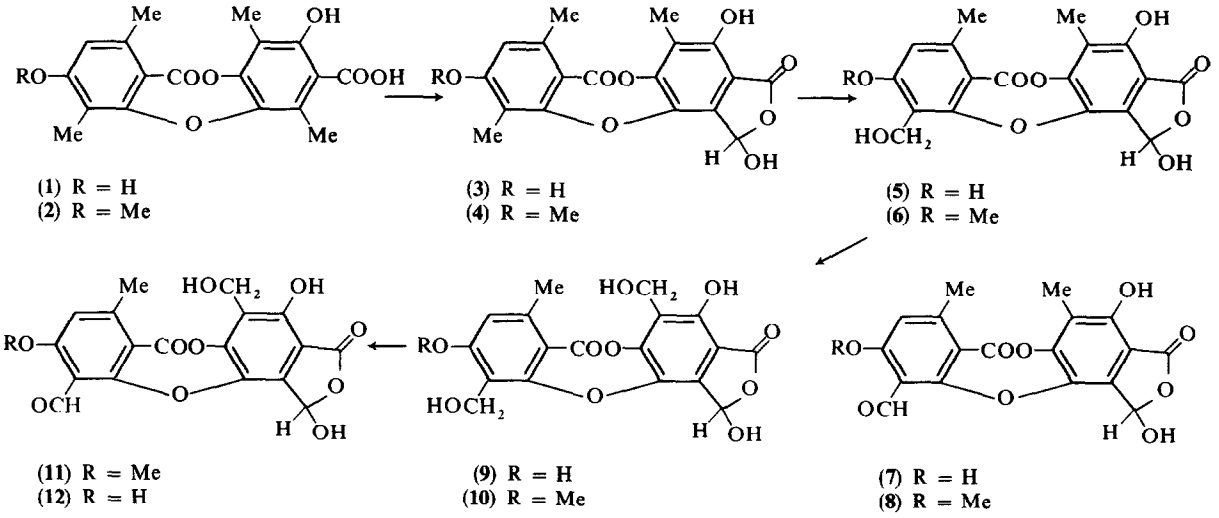
RESULTS AND DISCUSSION

TLC analysis of a micro extract of the lichen, *Thelotrema* sp., showed the presence of two components. Continuous extraction of the lichen with petrol removed some triterpenoid material present in the adhering bark while subsequent extraction with Me_2CO afforded a mixture of two compounds. Compound (**4**) was readily isolated by fractional crystallization of the mixture from Me_2CO but an insufficient quantity of the minor compound was obtained to permit detailed study.

Compound (**4**) whose elemental analysis suggested a molecular formula of $C_{19}H_{16}O_8$ forms a diacetate on treatment with Py/Ac_2O. The IR spectrum shows a sharp peak at 3410 cm^{-1} (OH) and strong absorptions at 1750 (lactone), 1710 (depsidone), 1600 and 1560 (aromatic). The NMR spectrum (DMSO-d_6) shows two one-proton signals at δ 6.70 and δ 6.85. The latter signal is considerably sharpened on the addition of D_2O suggesting that the proton is geminal to an OH. This was further confirmed by the large paramagnetic shift produced both on acetylation ($\Delta \sim 0.6$, the signal is also considerably sharpened) and on changing the solvent to Py-d_5 ($\Delta \sim 0.6$). These observations and the high-field position of the signal are characteristic of the proton on the hydroxy lactone ring of the depsidones stictic (**8**), norstictic (**7**), salazinic (**12**), and constictic acids (**11**) and indicated the presence of this moiety in (**4**). The solubility of the compound in $KHCO_3$, although there is no evidence of a carboxylic group in the molecule, supports this hypothesis. Acidification of the basic solution leads to the recovery of (**4**) unchanged.

Reduction of (**4**) with Pd/C gives (**2**), lacking the lactone ring as shown by IR and the replacement of the signal at δ 6.85 by an ArMe signal at δ 2.59. A methoxy (δ 3.87), two relatively low-field Ar-Me resonances (δ 2.20 and δ 2.27), and one at higher field (δ 2.43, typical of a Me ortho to a C=O) complete the spectrum of (**4**). Double resonance established an ortho relationship between the high-field ArMe and the proton at δ 6.70, while the large aromatic solvent induced shift of the OMe in the spectrum of the diacetate showed this proton also to have an ortho disposition to the OMe. A similar ASIS has been reported [3] in the spectra of stictic tetraacetate and constictic pentaacetate. The substitution pattern on the 'A' ring must therefore be Me, H, OMe, Me as occurs in 4-*O*-methylprotocetraric acid. A second possibility (Me, H, OMe, OH) was considered unlikely on biosynthetic grounds. These data were compatible with the proposed structure (**4**), hypostictic acid.

Hypostictic acid has not been previously reported as a natural product but was first prepared by Asahina [4] by reduction of naturally occurring stictic acid with Pd/C prepared *in situ* as catalyst. Repeating this procedure we obtained hypostictic acid in high yield, which was identical (IR, NMR, TLC) with the natural product and thus confirmed the structure of (**4**). We found, however, that commercially available Pd/C catalyst was too active and that its use led to considerable hydrogenolysis of the hydroxylactone ring affording mixtures of (**4**) and (**2**). Similarly, (**2**) was found to be identical with 4-*O*-Me-hypoprotocetraric acid formed on reduction of stictic acid under more vigorous conditions. The possibility that the minor component of the lichen might be hyposalazinic acid (**3**), the 4-*O*-demethylated derivative of (**4**), was also considered. However, cochromatography of the



(1) R = H
(2) R = Me

(3) R = H
(4) R = Me

(5) R = H
(6) R = Me

(11) R = Me
(12) R = H

(9) R = H
(10) R = Me

(7) R = H
(8) R = Me

extract with authentic (3) prepared by reduction of (12), showed the two compounds to be distinct.

Four unidentified compounds have been previously detected in *Xanthoparmelia quintaria* [5] and have been named PQ1, PQ2, PQ3 and PQ4 by Culberson [6]. Hale also reported the presence of these compounds in *Pseudoparmelia neoquintaria* Hale, in *Relicina abstrusa* (Vanio) Hale, which also produces usnic and norstictic acids, and in some of the brown Parmeliae [7]. On TLC plates these compounds give a red colour, distinct from that of any of the known depsidones, after spraying with H_2SO_4 reagent. Hale, who identified our *Thelotrema* sp., suggested that PQ1 was identical with our hypostictic acid. Cochromatography, in the three standard solvent systems [6], of an acetone extract of *X. quintaria* with hypostictic acid supported this hypothesis. Likewise PQ2 was found to be identical with hyposalazinic prepared by reduction of salazinic acid (12) with Pd/C. Further confirmation was obtained by cochromatography of the acetylation product of the micro extract with the acetate of (4) and hyposalazinic triacetate.

EXPERIMENTAL

Plant material. The *Thelotrema* sp. which was shown to be a new species, was collected in the cloud forest (alt 2300 m) San Eusebio, State of Mérida. A specimen is deposited in the herbarium of this faculty (MFK 20001). A fragment of *Xanthoparmelia quintaria*, a South African endemic, was kindly provided by Dr. M. E. Hale.

Diacetate of (4). Hypostictic acid (200 mg) was dissolved in in a mixture of Py and Ac_2O, and after standing at room temp. for *ca* 18 hr was worked up in the usual manner to give the diacetate (190 mg) mp 244°. IR (KBr) bands at 1785, 1768, 1735, 1360, 1180 and 988 cm^{-1}. PMR ($CDCl_3$, δ); 2.15; 2.21, 2.30, 2.41 and 2.50 (3H each, all *s*, 5 × Me), 3.90 (3H, *s*, OMe), 6.61 (1H, *s*, ArH), 7.43 (1H, *s*, lactone H). (Found; C, 60.48; H, 4.34. $C_{23}H_{20}O_{10}$ requires; C, 60.56; H, 4.38%).

Synthesis of (4). A soln of $PdCl_2$ (0.5%, 8 ml) mixed with activated C (200 mg) and HOAc (8 ml) was reduced at room temp. and press. with H_2. Stictic acid (100 mg) was then added to the mixture and shaken under H_2 for 12 hr. The reaction mixture was filtered and the C extracted with boiling Me_2CO to afford hypostictic acid identical (mp, IR, PMR) with the natural product, mp 260° d (Me_2CO/H_2O, lit. [4] 264° d).

Hyposalazinic acid (3). Salazinic acid (200 mg) was reduced as in the case of stictic to afford hyposalazinic acid mp 280° d (Me_2CO/H_2O). IR bands at 1700 (*br*), 1612, 1582, 1264, 1129 and 840 cm^{-1}. PMR (DMSO-d_6, δ); 2.20, 2.27 and 2.33 (3H each, all *s*, ArMe), 6.63 (1H, *s*, ArH), 6.66 (1H, *s*, lactone H).

Triacetate of (4). The acid (100 mg) was suspended in HOAc (4 ml), cooled to 0° and treated with 1 drop of conc H_2SO_4. After standing *ca* 18 hr the resulting clear soln was worked up in the normal manner to afford the triacetate of (4) mp 203–205° (Me_2CO/H_2O). IR bands at 1780–1730, 1360, 1190, 1110 and 990 cm^{-1}. PMR ($CDCl_3$, δ); 2.13, 2.20, 2.30, 2.32, 2.40 and 2.47 (3H each, all *s*, 6 × Me), 6.87 (1H, *s*, ArH), 7.42 (1H, *s*, lactone H). (Found; C, 59.25; H, 4.05, $C_{24}H_{20}O_{11}$ requires; C, 59.50, H, 4.13%).

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