Dysoxylentin A, the first 21-nortriterpenoid bearing a 2-(propan-2-ylidenyl)furan-3(2H)-one, from Dysoxylum lenticellatum

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Introduction

The genus Dysoxylum (Meliaceae) comprises about 200 species, which are mainly distributed in India, Southeast Asia, and Polynesia. Among these species, fourteen are distributed in China and ten have been found to grow in Yunnan Province. Many species have been traditionally used as medicines by the indigenous people in Fiji, Papua New Guinea, and New Zealand to relieve fever, convulsions, hemorrhage, rigid limbs, and facial distortion in children. Phytochemical investigations of more than twenty species in this genus have led to the isolation of a number of structurally diverse and biologically active compounds including cytotoxic alkaloids, anti-feeding limonoids, cytotoxic diterpenoids, anti-leukemic triterpenoid glucosides, antibacterial and cytotoxic triterpenoids, sesquiterpenoids, oxyneolignans, bioflavonoids, and a sulfur-containing compound. Dysoxylum lenticellatum is a plant endemic to southwest Yunnan province. Previous investigations of the twigs and leaves of D. lenticellatum have revealed the presence of triterpenoids, diterpenoids, and ceramids in this plant. As part of our ongoing project aiming at structurally diverse natural products, the stems of D. lenticellatum have been chemically investigated. As a result, dysoxylentin A, a new 21-nortriterpenoid with a 2-(propan-2-ylidenyl)furan-3(2H)-one unit, was isolated. In this Letter, we report the isolation, structural elucidation, and biological activity of the new compound. A plausible biosynthetic pathway was also postulated.

Dysoxylentin A (1) was isolated as a white amorphous powder. Its molecular formula was determined to be C_{29}H_{42}O_{3} by the HREIMS ion at m/z 438.3138 (calcd 438.3134) showing 9 degrees of unsaturation. The UV spectrum of dysoxylentin A (1) showed absorption maxima at 204, 260, and 307 nm, suggesting the presence of a conjugated system. The IR spectrum indicated the presence of hydroxyl (3440 cm\(^{-1}\)), conjugated carbonyl (1707 cm\(^{-1}\)) and double bond (1641, 1591 cm\(^{-1}\)) groups. In the \(^1\)H spectrum (Table 1), signals for seven quaternary methyls [\(\delta_H 0.79\) (s, 6H), 0.91, 0.93, 1.06, 1.98, 2.26], two olefinic protons [\(\delta_H 5.30\) (t-like) and \(\delta_H 5.63\) (s)], one oxygenated methine proton [\(\delta_H 3.47\) (br s)], and one methine...
H 2.91 (t, J = 9.0 Hz) adjacent to a methylene were easily identified. The $^{13}$C NMR (Table 1) and DEPT spectra exhibited 29 carbon resonances, which corresponded to seven methyls, seven methylenes, six methines (one oxygenated and two olefinic), and nine quaternary carbons (one ketone and four olefinic). The above functionalities accounted for 41.76 of unsaturation, the remaining 58.24 of unsaturation suggested the presence of a pentacyclic system in dysoxylentin A. The aforementioned data were very different from those of the compounds isolated from the same plant, suggesting that dysoxylentin A (1) possibly possessed a new structural skeleton. Extensive 2D NMR experiments ($^{1}H$–$^{1}H$ COSY, HSQC, HMBC, and ROESY) were thus performed and the structure of 1 was established. All proton signals were unambiguously assigned to their respective carbon atoms by using HSQC experiment. Four spin

 systems drawn with bold bonds were established on the basis of $^{1}H$–$^{1}H$ COSY spectrum (Fig. 1). The further HMBC correlation analysis (Fig. 1) led to the assembly of the four subunits with the quaternary carbons and other functionalities. In particular, HMBC correlations of H$_{17}$-19 to C-1, C-5, C-9, and C-10, of H$_{18}$-17 to C-5, C-13, C-14, and C-17, of H$_{17}$ to C-3, C-13, C-14, and C-15, and of H-7 to C-14 indicated that dysoxylentin A (1) possessed a carbon skeleton with an ABCD-ring system as that of a 3-hydroxy tirucallane-type triterpenoid. The tetracyclic feature of the above structure required the presence of an additional ring in the rest part of dysoxylentin A. The remaining $^{1}H$- and $^{13}$C-NMR data for one ketone (dC 187.2), one trisubstituted double bond (dH 5.63, dC 107.3, 144.9, 184.0), and two olefinic methyls (dH 1.98, 2.26, dC 17.0, 19.9) suggested the presence of a 2-(propan-2-ylidene)furan-3(2H)-yl group in dysoxylentin A. HMBC correlations from H-22 to C-17, C-20, C-23, and C-24, and from H$_{3}$-26/27 to C-23, C-24, and C-25 further confirmed this conclusion, while correlations from H-17 to C-20 and C-22 indicated that the group was located at C-17. Thus, the planar structure of dysoxylentin A was established as shown in Figure 1.

The relative configuration of dysoxylentin A (1) was determined by the coupling patterns and ROESY correlations. The broad singlet of H-3 suggested the $\beta$-orientation of H-3, which was further confirmed by the ROESY correlation of H-3 with H$_{3}$-28. The $\alpha$-orientations of H-5 and H-9 were deduced from...
the correlations of H-5/H3-29, H-9/H3-18. The β-orientation of H-17 was determined by the correlations of H-17/H3-23. Consequently, the relative stereochemistry of dysoxylentin A was determined as depicted (Fig. 2).

To the best of our knowledge, this is the first 21-nortirucallane triterpenoid that bears a 2-(propan-2-ylidenyl)furan-3(2H)-one-5-yl group, which has never been reported to be present in nature. Although two endophytic fungi \(^1^5\) and one plant \(^1^6\) were reported to produce natural products with such a structural unit, this unit was only present as a part of benzofuranone \(^1^5\) or as a simple aglycone. \(^1^6\) The biogenetic origin of dysoxylentin A (1) could be traced back to 24,25-epoxytirucall-7-ene-3,23-dione (3),3a a tirucallane triterpenoid that bears a 2-(propan-2-ylidenyl)furan-3(2H)-one-5-yl group, which has never been reported to be present in nature.

**References and notes**
13. Dysoxylentin A (1): white amorphous powder; \(\delta^1^H 5.44, 5.45, 4.55, 1.94 \mu M\) against HL-60. Dysoxylentin A showed selective activity (IC\(_{50}\) 34.61 \mu M) against the HL-60 cell line but did not show any obvious cytotoxicity (IC\(_{50}\) >100 \mu M) against the other cell lines.

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**Supplementary data**
Supplementary data (experimental details, NMR spectrum, MS data) associated with this article can be found in the online version, at doi:10.1016/j.tetlet.2011.12.109.