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LETTERS

A Triterpenoid with a Novel *abeo*-Dammarane Skeleton from *Dysoxylum cauliflorum*.

Rong Huang, Leslie J. Harrison* and Keng-Yeow Sim

Department of Chemistry, National University of Singapore, 10, Kent Ridge Crescent, Singapore 119260.

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Abstract: A hexane extract of the fruits of *Dysoxylum cauliflorum* Hiern. (Meliaceae) has afforded a triterpenoid with a novel *abeo*-dammarane carbon skeleton. Extensive NMR studies (^{1}H, ^{13}C, HMQC, HMBC, difference NOE) enabled its identification as 23(24→25)*abeo*-20*R*,24-dihydroxydammaran-3-one. © 1999 Elsevier Science Ltd. All rights reserved.

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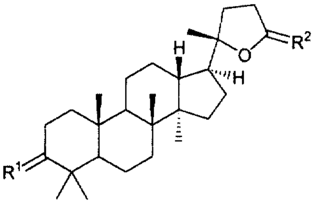
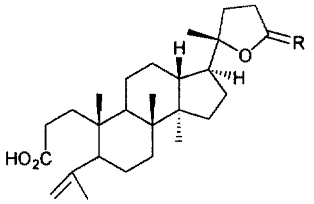
The Meliaceae family is a well-known source of structurally complex, degraded triterpenoids belonging to the limonoid class.[1] Members of the genus *Dysoxylum*, however, characteristically produce non-degraded compounds, *e.g.* dammarane,[2] glabretal[3],[4] and apotirucallane[5] triterpenoids, although some limonoids have been reported.[6] The hexane-soluble material of a methanol extract of the fresh fruits of *Dysoxylum cauliflorum* Hiern. collected in Singapore gave five known dammarane triterpenoids, ocotillone (**1**),[7] ocotillol-II (**2**),[8] cabralealactone (**3**),[9] shoreic acid (**4**),[10] and eichlerialactone (**5**).[11]



(**1**) R^1=O, R^2=α-C(Me$_2$)OH,β-H
(**2**) R^1=α-H,β-OH, R^2=α-C(Me$_2$)OH,β-H
(**3**) R^1=R^2=O



(**4**) R=α-C(Me$_2$)OH,β-H
(**5**) R=O

In addition, a minor metabolite (**6**) was obtained as white fluffy needles, mp. 177-179°C, $[\alpha]_D$ +4.9, $C_{30}H_{52}O_3$, *m/z* 442.3806 $[M-H_2O]^+$, ν_{max} 3446 (OH) and 1700 cm^{-1} (ketone C=O). The ^{1}H and ^{13}C NMR spectra[12] showed signals for a ketone [δ_C 218.3 (s, C-3)], a hydroxymethyl group [δ_H 3.33 and 3.31 (ABq, J_{AB} = 10.9 Hz, H$_2$-24); δ_C 71.1 (t, C-24)], a tertiary oxygenated carbon [δ_C 75.9 (s, C-20)], a methylene group α to a carbonyl [δ_H 2.49 (ddd, *J* 7.6, 9.6, 14.6 Hz, H-2β); 2.44 (ddd, *J* 4.5, 6.8, 14.6 Hz, H-2α); δ_C 34.1 (t, C-2)] and eight tertiary methyl groups [δ_H 1.13, 1.08, 1.04, 1.01, 0.95, 0.89, 0.87 and 0.86 (each 3H, s, H$_3$-21, H$_3$-28, H$_3$-29, H$_3$-30, H$_3$-19, H$_3$-18, H$_3$-26 and H$_3$-27), δ_C 26.7, 24.3, 24.1, 23.5, 21.0, 16.3, 16.0 and 15.3 (each q, C-28, C-26, C-27, C-21, C-29, C-18, C-19 and C-30)] in addition to ten methylenes, four methines and five fully substituted carbons. The compound was therefore a tetracarbocyclic triterpenoid ketone with a tertiary alcohol

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*Author to whom correspondence should be addressed. E-mail: chmhl@leonis.nus.edu.sg

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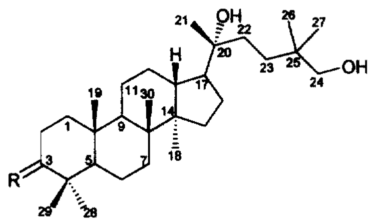
and a primary alcohol group. The presence of nine methyl equivalents immediately ruled out structures belonging to the common tetracyclic triterpenoid classes such as the dammaranes since these all possess eight methyl groups or their equivalents.



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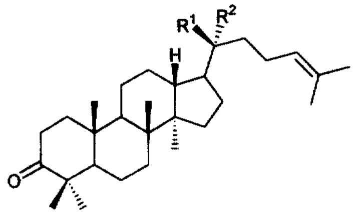


(7) $R^1=CH_3$, $R^2=OH$
(8) $R^1=OH$, $R^2=CH_3$

The structure and the ^1H and ^{13}C NMR assignments of **6** were established using HMQC and, especially, HMBC spectra. The HMBC correlations (Fig. 1) of the methyl groups attached to C-4, C-8, C-10 and C-14 established the connectivity of these carbons and C-3, C-4, C-5, C-7, C-8, C-9, C-10, C-13, C-14 and C-15. Rings A, B, C and D were completed following consideration of the correlations of the methylene protons attached to C-1, C-2, C-7, C-11, C-12, C-15 and C-16 as well as those of the C-17 methine proton.

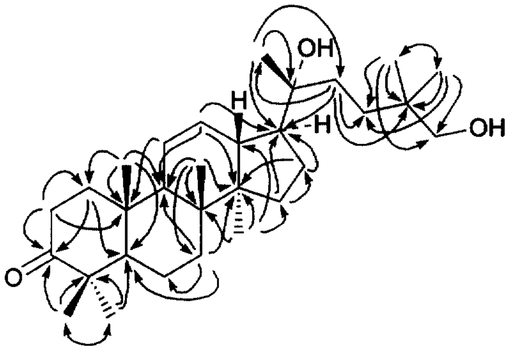


Fig. 1. Selected HMBC Correlations for **6**

All four of the rings were now accounted for and C-17 therefore carried an acyclic side chain. The protons of the most deshielded methyl group (H_3-21) showed correlations to only three carbons, one methine (C-17), one methylene (C-22) and one fully-substituted oxygenated carbon (C-20). The five still unassigned carbon atoms were those of the final two tertiary methyl groups (C-26 and C-27), the hydroxymethyl group (C-24), a fully substituted carbon atom (C-25) and a methylene group (C-23). No couplings were observed between any of the sets of protons, revealing that the protonated groups were all attached to C-25. This was confirmed by the fact that the hydrogen-bearing groups correlated with each other and with the fully substituted carbon atom. All of the atoms in the molecule were now accounted for and the final bond must be placed between C-22 and C-23.

Comparison of the ^{13}C NMR shifts of **6** with those of the ocotillone[7] (**1**) and cabralealactone[9] (**3**) supported the proposed structure and established the 3-oxodammarane stereochemistry at C-5, C-8, C-9, C-10, C-13, C-14 and C-17. This was confirmed using difference NOE spectroscopy (see Fig. 2). The presence of an NOE between the methyl group at C-20 and H-16β suggested the 20*R* stereochemistry but, in view of the possibility of rotation around the C-17 - C-20 bond, support for this hypothesis was sought elsewhere. It has been found for 20-hydroxydammaranes that the ^{13}C chemical shift of the carbons around C-20 can be used to

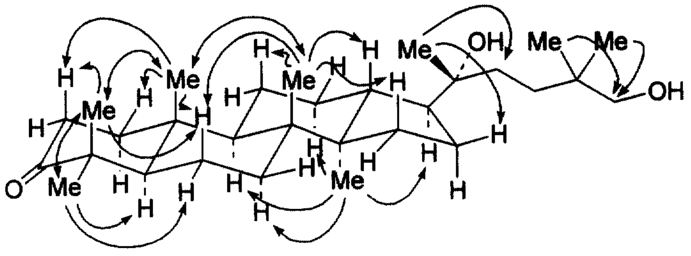


Fig. 2. NOE enhancements for **6**

determine the C-20 configuration.[13] The method is most secure for 12β-hydroxyl derivatives in which large differences are observed between the chemical shifts for C-17, C-21 and C-22 of C-20 epimers. In cases where the compound lacks the 12-OH function, *e.g.* (20*R*)-20-hydroxydammar-24-en-3-one (**7**) and (20*S*)-20-hydroxydammar-24-en-3-one (**8**), C-21 in the 20*S*-series is more deshielded than in the case of the corresponding compound of the 20*R*-series (δ_C 24.7 and 23.5, respectively). It was expected that the changes in the side chain of **6** would have a significant effect on the ^{13}C shift of C-22 but were too far removed from C-21 to influence it. Thus, the fact that the C-21 resonance was observed at δ_C 23.5 supported the *R* configuration for C-20. The compound was therefore (20*R*)-23(24→25)*abeo*-20,24-dihydroxydammaran-3-one which is a novel natural product and the first example of a 23(24→25)*abeo*-dammarane.

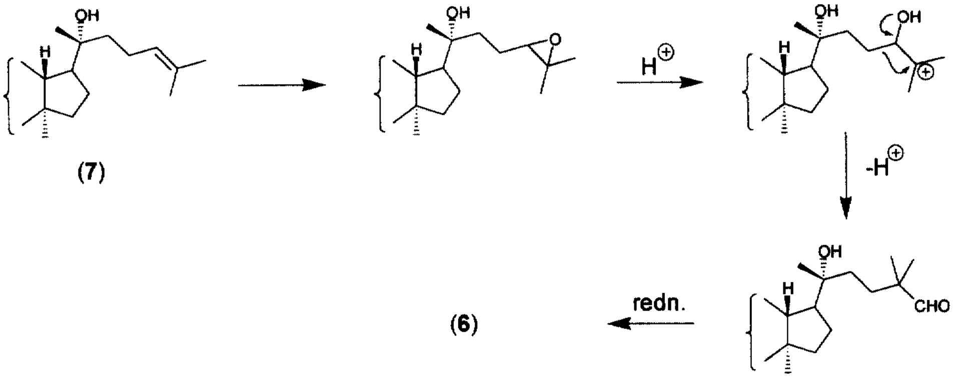
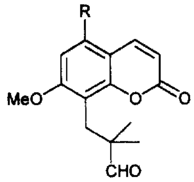


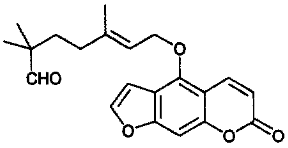
Fig. 3. Proposed biogenesis of (**6**)

6 is obviously a dammarane which has undergone a side-chain rearrangement and the 24,25-epoxide of (20*R*)-20-hydroxydammar-24-en-3-one (**7**) is the likely starting point for such a process. Opening of the epoxide (see Fig. 3) under acidic conditions gives a cation which is identical to that involved in a pinacol rearrangement. Migration of the 23(24) bond to C-25 with concomitant carbonyl formation leads to the required carbon skeleton. Finally, reduction of the aldehyde to a primary alcohol affords **6**. This type of rearrangement has also been observed in the case of three prenylated coumarins. Seselinal (**9**) has been isolated from ***Seseli sibiricum*** (Umbelliferae)[14] whilst 7-methoxy-8-(2-formyl-2-methyl-propyl)-coumarin (**10**) and 5-[(3,6-dimethyl-6-formyl-

2-heptenyl)-oxy]psoralen (**11**) were isolated from the peel oil of *Citrus decumana* (Rutaceae).[15] The proposed rearrangement has been mimicked in the synthesis of **9** which was formed (amongst other products) upon treatment of the epoxide of osthol (**12**) with boron trifluoride.[16]



(9) R=H
(10) R=OMe



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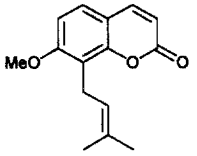

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