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A REVISION OF THE STRUCTURES OF THREE LIMONOIDS

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Key Word Index—Limonoids; ^{13}C NMR spectra; IR spectra.

Abstract—Three limonoids, two from *Aphanamixis polystacha* and one from *Trichilia prieuriana*, have been found to have ^{13}C NMR spectra at variance with the assigned structures. Alteration of the position of certain lactone rings gives structures which agree with the spectra.

The group of limonoids related to prieurianin is rapidly growing and more than 20 are now known. In the course of compiling a collection of the ^{13}C NMR spectra of these compounds, we have discovered a discrepancy. The structure of prieurianin acetate (**1**) is securely based on an X-ray crystal structure determination [1]. In this compound there are only two tertiary oxygen functions, and it is easy to assign the singlet resonance at δ 84.6 to C-4. In *Aphanamixis rohituka* 2 acetate [2], which was believed only to differ from **1** by having an acetoxy group at C-15 in place of the ketone, C-4 resonates at δ 88.4. While this discrepancy was not noted originally when few comparison substances were known, it now appears quite striking. Other compounds with a similarly low field resonance for C-4 are the closely related rohituka substance 1 [2], differing only in the substituent at C-12, *Trichilia prieuriana* substance D_5 [3], to which the structure **2** was assigned, the hydrolysis products with a γ-lactone ring similar to PM_2 (**3**) [3], in which C-4 resonates at δ 87.3, and dregeanin, now believed to have the structure **4** [4], in which it is at δ 88.6.

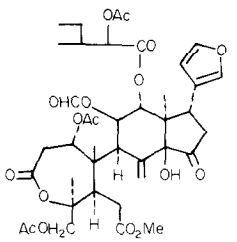
The deduction is clear, that the low field position of the C-4 resonance depends on it being in a γ-lactone ring. This requires that the structures of rohituka substances 1 and 2 are revised to **5** and **6** respectively, while that of prieuriana substance D_5 is revised to **7**. It should be possible to detect signals for the γ-lactone ring in the IR spectrum. In the hydrolysis products similar to PM_2 the lactone vibration frequency is 1790 cm^{-1}, while in D_5 it is 1775 cm^{-1}. Although of a lower frequency, this is well in the range accepted for a γ-lactone.

This new formulation explains four observations that were previously difficult to accommodate. The first is the very existence and relative stability of these compounds, which survived extraction with refluxing hexane and isolation by chromatography, whereas a hydroxy ester such as **2** would be expected to lactonize very readily in solution.

The second is the fact that borohydride reduction of prieurianin does not give rohituka compound 2. Only one reduction product has been obtained [MacLachlan, L. K. and Taylor D. A. H., unpublished results], and although this could of course be the 15-epimer of the natural compound, there seems to be more difference between the two compounds than can be accounted for in this way. In particular while rohituka compound 2 has the C-4 resonance at δ 88.4, as already mentioned, in the acetate of prieurianin reduction product it is in the normally expected position of δ 84.9.

The third is the strange hydrolysis result of dregeanin and related compounds [3]. It was shown that dregeanin (**4**) and D_5 (**7**) gave the same complex set of hydrolysis products, while two other compounds, the related 7,29 lactone which is *Guarea thompsonii* substance B [3], and its 1,2 anhydro derivative D_4 [3], give only one of these products.

It is known that dregeanin methanolyses very readily [Okorie, D. A. and Taylor, D. A. H., unpublished results], probably due to the presence of the eight-membered lactone ring [5]. Thus the first stage



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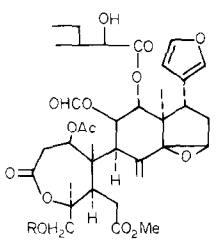
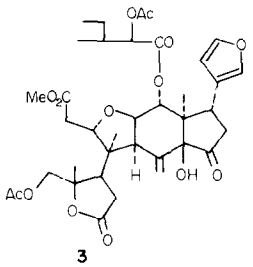


2 R = H
8 R = Ac



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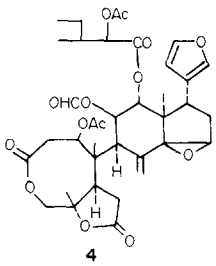

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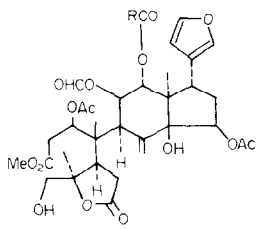
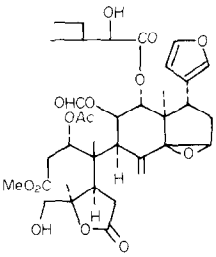


5 R = Me_2CHCH_2 –
6 R = EtMeCHCHOH –



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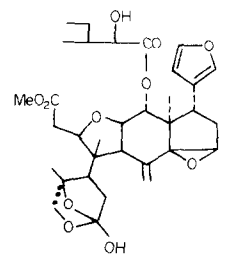

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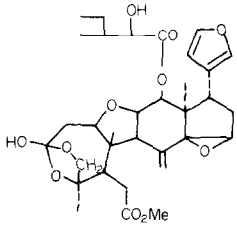

10

in the hydrolysis is likely to be the production of D_5 (7), which shows why these two compounds give the same hydrolysis products. One of these is a hemi-*ortho* ester DM_1 [3], which may have either the structure **9** or **10**, the latter being analogous to nymanin and hispidin [6, 7]. While the hemi-*ortho* ester of **9** can be formed directly from D_5 and hence also from dregeanin by addition of the free hydroxyl to the existing lactone carbonyl, formation of **10** needs opening of this lactone and re-formation of the original seven-membered lactone. The spectra of the three hemi-*ortho* esters show that nymanin and hispidin have the C-4 resonance at δ 82.6, while in DM_1, it is at δ 86.6. Hence we conclude that the structures are not analogous, and that DM_1 is most probably correctly represented as **9**. The shift noted for the resonance of C-4 is not associated with the oxide ring in **9**, since other compounds with this oxide have the resonance in the normal position.

The fourth observation explained by these new structures is that a compound which has the structure **8** has recently been isolated from *Guarea guidona* [8]. Although it is not possible to obtain the monoacetate from D_5 for direct comparison, both D_5 and the new *Guarea* compound readily give diacetates. The spectra of these two compounds are different in many details, especially in the chemical shifts of the methyl groups (D_5 acetate, 1.71, 1.62, 1.05; *Guarea* acetate, 1.55, 1.51, 0.97). Therefore, D_5 does not have the structure **2** originally assigned to it.

It must be considered whether these compounds are true natural products. Since dregeanin methanolyses very readily, as mentioned above, it may be that D_5 and the rohituka substances 1 and 2, and possibly other compounds as well, are artefacts of isolation, formed from dregeanin or a similar substance. There is at present no evidence to resolve this problem.

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