# Absolute Stereochemistry of Tanabalin, an Insect Antifeedant Clerodane from *Tanacetum balsamita*

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The absolute structure of tanabalin (=12*S*-acetoxyhautriwaic acid), an insect antifeedant isolated from *Tanacetum balsamita*, was determined by X-ray crystallography together with modified Mosher's method, in which an anomalous Δδ value of a proton was verified with an L-adrenaline derivative as a model compound.

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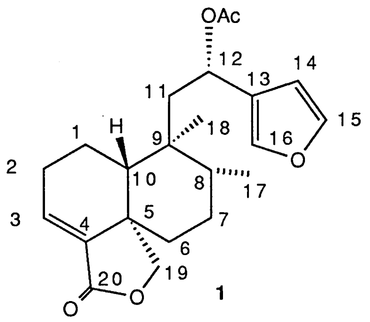
In our continuing search for alternative insect control agents from plant sources,[1] an antifeedant against the pink bollworm *Pectinophora gossypiella* has been isolated from the dried flower of a Brazilian medicinal plant *Tanacetum balsamita* (Compositae),[2] in a leaf disk assay.[3] This bitter tasting flower locally known as "catinga-de-mulata" and the antifeedant isolated is undoubtedly principally responsible for this bitter taste.[4] This antifeedant, tanabalin, m.p. 147 °C, $[\alpha]_D$ -132.0° (c 0.10, EtOH), was a white needle whose molecular formula, $C_{22}H_{28}O_5$, was established by EI mass spectrometry in conjunction with NMR data.

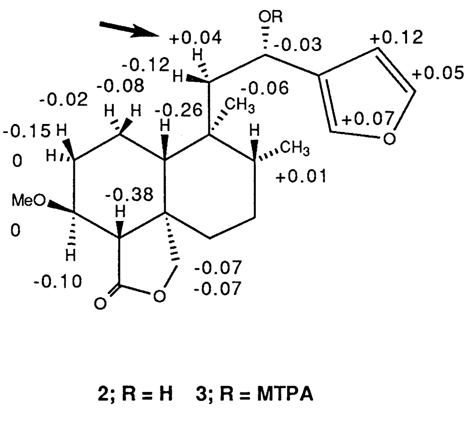
The extensive NMR analysis[5] together with other spectroscopic properties of the antifeedant led to the clerodane structure **1** (plain). This structure, 12-acetoxyhautriwaic acid,[6] including the relative stereochemistry was unambiguously established by X-ray crystallography[7] performed on the single crystal of **1** (Figure 1).

To determine the absolute configuration of **1**, modified Mosher's method[8] was applied for **2**,[9] which was obtained by treatment of **1** with sodium methoxide in methanol. The Δδ values [$\delta_S$ - $\delta_R$] for **3** are shown in **3a**. The *S*-configuration at C-12 was deduced by the distribution of positive and negative Δδ values of the protons, although the anomalous value (+0.04) of one of the methylene protons on C-11 was observed. Inspection of molecular models suggests that the proton in question is located close to the furan moiety. The chemical shift, therefore, may be affected greatly by the anisotropy of the heteroaromatic ring. In both diastereomers [(*R*) and (*S*)-MTPA esters] the conformation of the furan rings may be slightly different. This different orientation of the furan ring may cause the exceptional Δδ value of the proton. To verify this assumption, another evidence was sought for.

The model compound **4** was prepared by selective acetylation of L-adrenaline. Δδ Values obtained for **5** are shown in the structure. The *S*-configuration at C-2 suggested by these values



**1**



**2**; R = H **3**; R = MTPA

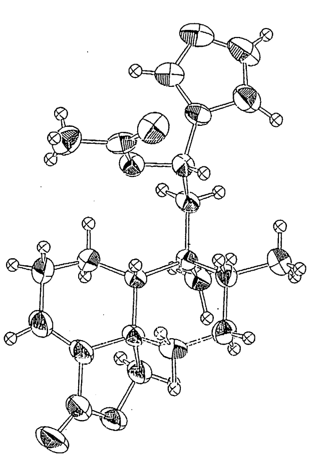
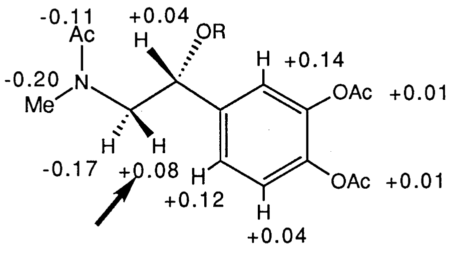
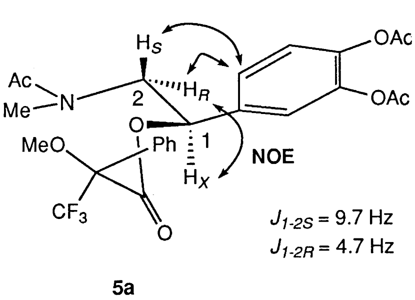


**Figure 1.** X-ray structure of **1**.



**4**; R = H **5**; R = MTPA



**5a**

is identical with the known one of L-adrenaline. Again the anomalous Δδ value (+0.08) is obtained for one of the methylene protons. The coupling patterns of the ABX proton system ($H_1$-$H_{2R}$-$H_{2S}$) together with the NOEs obtained by NOESY spectrum indicates the conformation **5a**, in which *pro R* proton possesses the abnormal positive value. These findings strongly suggest that the slight orientational difference of the diacetoxyphenyl rings of the (*R*) and (*S*)-MTPA esters is the major cause of the anomaly.

It should be emphasized, however, that the modified Mosher's method is valid to determine the absolute configurations of the 'benzylic' secondary alcohols even in the case that anomaly is observed for the proton located opposite to the phenyl or furan rings.

Very recently the similar abnormal phenomena in aromatic compounds have been observed by Isobe's group.[10]

The authors are indebted to Dr. J. M. Pine for identification of the plant and Mr. J. M. Takeda for assistance in obtaining it.

## Reference and Notes

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2 The dried flowers of *T. balsamita* were purchased at market places in Juazeiro do Norte, Brazil. The flowers possess distinct odors by which it is named as "catinga" ("distinct odor" in English). The voucher specimen was deposited at Museu Goeldi, Belem, Brazil. The dried flowers (500 g) were extracted with hexane to yield crude extract (10.9 g). This was followed by extraction with methanol to give an additional extract. Subsequent bioassays found the hexane extract to be active but not the methanol extract. The active antifeedant (**1**) was separated by repeated chromatographic methods. It showed antifeedant activity against the pink bollworm at $PC_{50}$ 100 μg/cm$^2$.[3] In addition, from the same hexane extract, a known furano diterpenoid, centipedaoic acid,[11] was isolated in fairly large quantities, but did not show any antifeedant activity up to 2 mg/cm$^2$.

3 I. Kubo, in "*Methods in Plant Biochemistry*," (K. Hostettmann and P. J. Lea, eds.), Academic Press, London (1993), Vol. 6, pp 179-193.

4 I. Kubo, *Physiol. Behavior*, **56**, 1203 (1994).

5 *$^{13}C$* and $^1H$-NMR (400 MHz, $CDCl_3$) data for **1** (position number): δ *20.22*; δ 1.11 (dq, *J* 3.9, 12.3), 2.05 (m) (1), δ *34.29*; δ 2.17 (m), 2.40 (dm, *J* 18.0) (2), δ *135.51*; δ 6.74 (dd, *J* 7.4, 2.1) (3), δ *138.63* (4), δ *45.70* (5), δ *27.82*; δ 1.20 (dt, *J* 3.7, 13.1), 1.90 (td, *J* 3.0, 13.1 ) (6), δ *27.54*; δ 1.45 (m), 1.60 (m) (7), δ *37.18*; δ 1.62 (m) (8), δ *39.47* (9), δ *49.10*; δ 1.84 (m) (10), δ *42.04*; δ 1.83 (dd, *J* 4.5, 15.8), 2.16 (dd, *J* 7.7, 15.8) (11), δ *64.93*; δ 5.94 (dd, *J* 7.7, 4.5) (12), δ *126.25* (13), δ *108.63*; δ 6.40 (dd, *J* 1.7, 0.7) (14), δ *143.39*; δ 7.36 (t, *J* 1.7) (15), δ *140.08*; δ 7.42 (bs) (16), δ *15.66*; δ 0.75 (d, *J* 6.5) (17), δ *17.47*; δ 0.59 (s) (18), δ *71.66*; δ 3.90 (dd, *J* 8.0, 2.0), 4.27 (d, *J* 8.0) (19), δ *169.98* (s) (20), δ *169.12* , *21.46*; δ 2.01 (s) (Ac).

6 This clerodane can be named as 12*S*-acetoxyhautriwaic acid based on hautriwaic acid.[12,13] However, this naming is not appropriate since this clerodane does not possess any carboxylic group.

7 Crystal date for **1**: $C_{22}H_{28}O_5$, F.W.=372.46, orthorhombic, space group $P2_12_12_1$, a=11.969(7), b=16.966(3), c=9.551(2) Å, Z=4, Dc=1.275 g/cm$^3$. Data were collected on a Rigaku AFC5R diffractometer with graphite monochromated $MoK_\alpha$ radiation. The structure was solved by a direct method. The final cycle of full matrix least square refinement based on 2548 reflections ($I>3.00\sigma(I)$) gave R=0.040 and $R_W$=0.045 for isotropic hydrogen atoms. C. K. Johnson, "ORTEP-II, Oak Ridge National Laboratory Report, ORNL-TM-5138", Oak Ridge, TN, USA (1976).

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9 $^1H$-NMR (500 MHz, $CDCl_3$) data for **2** (position number): δ 1.39 (1H, m) (2), 2.20 (1H, m) (2), 3.37 (1H, td, *J* 10.2, 4.3) (3), 3.39 (3H, s) (OMe), 2.05 (1H, d, *J* 10.2) (4), 1.40 (2H, m) (7), 1.72 (1H, m) (8), 2.02 (1H, dd, *J* 11.8, 3.3) (10), 1.61 (1H, dd, *J* 16.3, 2.5) (11), 1.98 (1H, dd, *J* 16.3, 9.0) (11), 4.85 (1H, dd, *J* 9.0, 2.5) (12), 6.39 (1H, bs) (14), 7.38 (1H, bs), 7.39 (1H, bs) (15 and 16), 0.77 (3H, d, *J* 5.0) (17), 0.57 (3H, s) (18), 4.19 (1H, dd, *J* 9.5, 1.0) (19), 4.16 (d, *J* 9.5) (19).

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