Phytochemistry, Vol. 26, No. 8, pp. 2406–2407, 1987.
Printed in Great Britain.

0031-9422/87 \$3.00 + 0.00

ABSOLUTE STEREOCHEMISTRY OF TAGITININ A

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(*Received* 5 *November* 1986)

Key Word Index—*Tithonia diversifolia*; Compositae; tagitinin A; zexbrevin; X-ray analysis; melampolide.

Abstract—Single crystal X-ray diffraction studies of the melampolide (**3a**) obtained from the reaction of tagitinin A (**1a**) with chlorotrimethylsilane and sodium iodide strongly suggest that C-4 methyl in tagitinin A is α-oriented.

INTRODUCTION

Of the four sesquiterpene lactones isolated from *Tithonia diversifolia* [1] only tagitinin A (**1a**) possesses insecticidal properties [2]. Earlier studies on chemical correlation of tagitinin A (**1a**) with tagitinin D (**1b**), a compound of authenticated stereochemistry, established its absolute stereochemistry as shown in formula **1a** [1]. However, in view of a recent report on the X-ray analysis of zexbrevin (**2**) [3] it became imperative to re-examine the C-4 methyl stereochemistry of tagitinin A. Since all attempts to obtain its single crystal were unsuccessful, it was decided to seek indirect evidence on this subject.

RESULTS AND DISCUSSION

In connection with some other studies, it has been described that the reaction of tagitinin A (**1a**) with chlorotrimethylsilane (CTMS) and sodium iodide furnishes one major product which was assigned structure (**3a**) on the basis of spectral data and chemical transformations [4]. Recently X-ray analysis of this substance was undertaken by us and crystal data are listed in the Experimental section. Figure 1 shows the stereoscopic drawing of the molecule and it therefore possesses the stereochemistry as shown in formula **3a**. The conformation of the 10-membered ring in the melampolide (**3a**) is closely related to that found in the crystal structure of other melampolides [5–8].

The reaction of tagitinin A with CTMS–NaI when critically examined was found to furnish, in fact, a mixture of two products, the ratio of their yields depends upon the reaction time and temperature. At low temperature (0–5°) and reaction time of 2 min, the less polar product is formed in 80% yield and 20% unreacted starting material is recovered. At room temperature and reaction time of 10 min, the product ratio is 9:1 (more polar:less polar) and no starting material is left. Reaction of the less polar product with CTMS–NaI for 20 min furnishes the more polar product in quantitative yield. Besides, the less polar product during purification on TLC (silica gel) is partially converted into the more polar product. These results indicate that the two reaction products are isomeric at C-4. Since the more polar product has been shown to possess the absolute stereochemistry as shown in formula **3a** on the basis of X-ray results, the less polar product could be assigned the stereostructure as in **3b**. The above observations clearly suggest that the C-4 methyl group in tagitinin A (**1a**) is α-oriented.

EXPERIMENTAL

Crystals of **3a** suitable for analysis were prepared by slow crystallization from $CHCl_3$–MeOH. They are orthorhombic, space group $P2_12_12_1$ with 4 molecules in a unit cell of dimensions $a = 13.022(4)$, $b = 18.266(4)$, $c = 8.026(3)$ Å. $V = 1909(2)$ Å^3. 3094 intensities ($1.1 < \theta < 30°$) were measured on a NONIUS CAD4 diffractometer using graphite monochromatized MoKα radiation. 2050 were below the $3\sigma(I)$ level and were treated as unobserved.

The structure was solved by means of the procedure GENTAN of the program system XTAL [9] using the RANDOM option based on the random phase approach in ref. [10]. Refinement proceeded by means of block-diagonal least-squares calculations, anisotropic for C and O, isotropic for H. The H atoms were located in a ΔF-synthesis. A weighing scheme $w = 1/(2 + F_0 + 0.04 F_0^2)$ was employed. The final R value was 0.063 ($R_w = 0.105$) for 1044 observed reflexions. The calculations were performed by means of XTAL. Final atomic co-ordinates of the non-hydrogen atoms and equivalent isotropic thermal para-

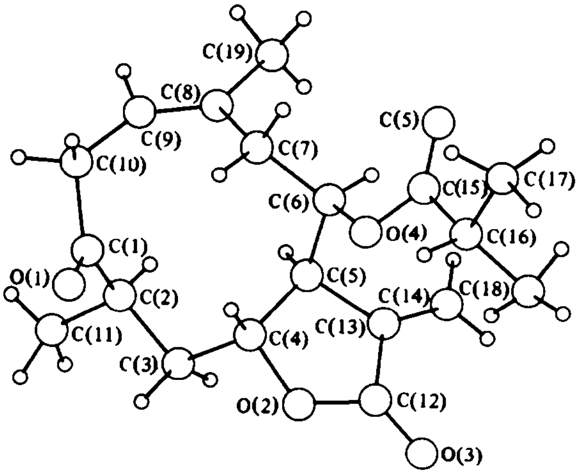
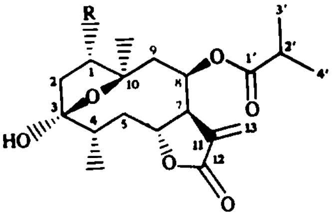
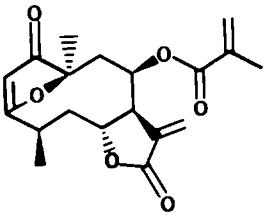


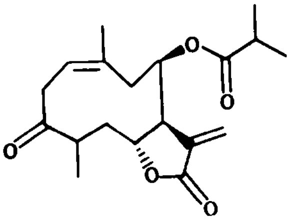
Fig. 1.



1a R = OH
1b R = H



2



3a C-4 Me β
3b C-4 Me α

meters, bond lengths and bond angles, anisotropic thermal parameters, fractional co-ordinates of the hydrogen atoms and isotropic thermal parameters, bond distance and bond angles of hydrogen atoms along with the Newman-projections have been deposited at the Cambridge Crystallographic data centre.

^{1}H NMR spectrum (60 MHz) of (**3b**) (a gum): δ6.22 (*d*, *J* = 1.75 Hz, H-13a), 5.65 (*d*, *J* = 1.75 Hz, H-13b), 5.60 (*m*, H-1), 4.5–5.0 (overlapping signals of two protons H-6 and H-8), 1.90 (*br*, H-14), 1.20 (*d*, *J* = 7 Hz, H-15, H-3′ and H-4′).

Acknowledgement—We (JCS and RPS) are grateful to our Director, Dr J. N. Barua for providing us the necessary facilities to carry out this work.

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