

Structure and Synthesis of Futronolide

By Tadahiro Kato, Toshiaki Iida, Takeshi Suzuki, Yoshio Kitahara*

(Department of Chemistry, Faculty of Science, Tohoku University,
Sendai 980, Japan)

and K. H. Overton

(Department of Chemistry, University of Glasgow,
Glasgow GR 8QQ, Scotland)

(Received in Japan 30 August 1972; received in UK for publication 12 September 1972)

As part of synthetic studies in the drimane series of sesquiterpenoids,¹ we have attempted to synthesize futronolide (I),² a plausible progenitor of bemadienolide (II)³ and cinnamosmolide (III).⁴ Because of its limited supply, the structure (I) for futronolide was tentatively assigned² by one of us mainly from a comparison of its NMR and UV spectra with those of related natural products.

This paper describes the syntheses of racemic (Ia, Ib) and its isomers (IVa, IVb) and establishment of the structure of futronolide as IVb.

Treatment of dl-cinnamolide (V) with NBS afforded the bromo lactone (VI),³ which in hot aqueous dioxan gave a 1:1 mixture of hydroxy lactones (Ia, and Ib), which were separated by repeated recrystallization from benzene-chloroform (10:1). The mass spectra of (Ia) and (Ib) were similar, but unlike that of natural futronolide.

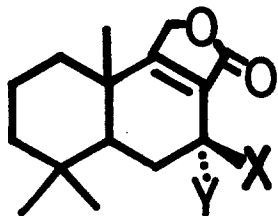
Ia, mp 209-211°; IR (CHCl₃) 3550, 1740, 1665 cm⁻¹; NMR (CDCl₃) 4.59 (C₇-H), 4.76 (C₁₁-H).

Ib, mp 229-231°; IR (CHCl₃) 3560, 1750 cm⁻¹; NMR (CDCl₃) 0.93, 1.00 and 1.14 (3H each), 4.63 (C₇-H), 4.83 (C₁₁-H).

The isomeric bromolactone (VII) was next obtained from the keto ester (VIII), derived from bicyclofarnesic acid methyl ester by photooxidation.^{1a} Direct NBS oxidation of (VIII) afforded the dienone (IX), mp. 142-143°, NMR 6.30 (C₆-H), 3.99 (d, J=10) and 4.27 (d, J=10), but the ketal lactone (X), when treated with NBS and then hot water, gave the keto lactone (XI) in 51% yield from (VIII).

XI, mp 111-112°, IR (KBr) 1750, 1678 cm⁻¹, NMR (CCl₄) 4.71 (C₁₂-H, bs).

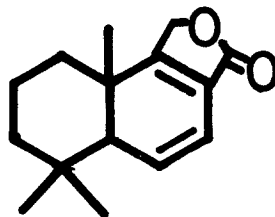
Reduction of (XI) with NaBH₄ afforded exclusively the hydroxy lactone (IVa), which was not



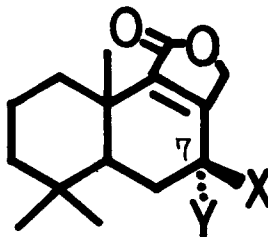
Ia: X=OH, Y=H

Ib: X=H, Y=OH

VI: X=H, Y=Br



II

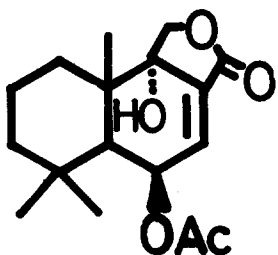


IVa: X=OH, Y=H

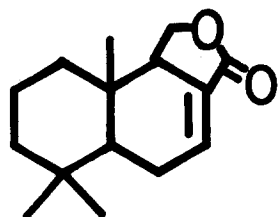
IVb: X=H, Y=OH

VII: X=H, Y=Br

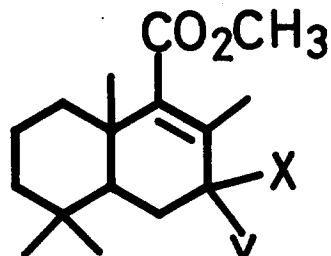
XI: X, Y = O



III

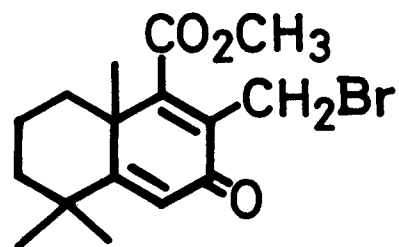


V



VIII: X, Y = O

X: X, Y = $\begin{bmatrix} \text{O} \\ | \\ \text{O} \end{bmatrix}$



IX

identical with futronolide. The bromo lactone (VII), mp. 126-128.5°, obtained from (IVa) by treatment with PBr_3 furnished with hot aqueous dioxan a 1:1 mixture of IVa and IVb. The NMR and mass spectra of (IVb), separated from (IVa) by repeated recrystallization, were identical with those of natural futronolide. The stereochemistry at C_7 in IVa and IVb was deduced from the coupling mode of the C_7 -hydrogen and exclusive formation of IVa from XI.

IVa, mp 203-204°, NMR ($CDCl_3$) 0.93 (6H, s), 1.23 (3H), 4.60 (C_7 -H, bd, $J=8$), 4.87 (C_{12} -H, d, $J=4$), and 4.90 (C_{12} -H, s).

IVb, mp 195-196°, NMR 0.92 (3H), 0.97 (3H), and 1.12 (3H), 4.54 (C_7 -H, bs), 4.77 (C_{12} -H, s), and 4.87 (C_{12} -H, s).

References

*To whom all correspondences should be addressed.

1. a) Y. Kitahara, T. Kato, T. Suzuki, S. Kanno, and M. Tanemura, *Chem. Commun.*, 342 (1969).
b) T. Suzuki, M. Tanemura, T. Kato, and Y. Kitahara, *Bull. Chem. Soc. Japan*, 43, 1268 (1970).
c) H. Yanagawa, T. Kato, and Y. Kitahara, *Synthesis*, 1970, 257.
d) T. Kato, T. Suzuki, M. Tanemura, A. Kumanireng, and Y. Kitahara, *Tetrahedron Letts.*, 1971, 1961.
2. H. H. Appel, R. P. M. Bond, and K. H. Overton, *Tetrahedron*, 19, 635 (1963).
3. L. Canonica, A. Corbella, P. Gariboldi, G. Jommi, and J. Krepinsky, *Tetrahedron*, 25, 3903 (1969).
4. L. Canonica, A. Corbella, G. Jommi, and J. Krepinsky, *Tetrahedron Letts.*, 2137 (1967).