Tetrahedron Vol. 35, pp. 2693 to 2695
Pergamon Press Ltd., 1979. Printed in Great Britain

A HYDROGENATION PRODUCT DERIVED FROM THE DITERPENOID BARBATUSIN:

A REVISED STRUCTURE

RAYMOND ZELNIK,[a] HUGO E. GOTTLIEB[b] and DAVID LAVIE[b]
[a]Department of Organic Chemistry, Instituto Butantan, São Paulo, Brasil. [b]Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot, Israel

(*Received in UK* 16 *May* 1979)

Abstract—The structure of the hydrogenation product of barbatusin, a diterpenoid from *Coleus barbatus* Bentham has been revised on the basis of NMR and X-ray data. A geminal coupling of unusually high magnitude has been observed and analysed.

In a previous publication[1] on the diterpenoid constituents of *Coleus barbatus* Bentham (Labiatae) we reported on the structure of barbatusin **1a** and on the hydrogenation of its acetate **1b** yielding two products: the first (compound **2**) (**4a** in the original publication[1]) is the result of a 1,2-addition of H_2 to the C(11) CO. The second, a strongly yellow product containing a quinone system, was given at the time structure **3** (**5** in the original publication[1]) primarily on the basis of NMR data.

Prof. C. H. Eugster and Dr. P. Rüedi from the University of Zurich called our attention to the fact that they believed that the acetoxy group left in ring B should preferably be located at C(6). On the basis of this remark we reinvestigated the structure of this compound.

An NMR spectrum carried out at 270 MHz (Table 1) including selective decoupling of each proton signal in turn, indicated that the 5α-H is adjacent to the proton geminal to the acetoxy group, which should be located therefore at C(6). Indeed when the 6α-H signal at δ 5.53, a double triplet, was irradiated, the 5α-H signal (δ 2.60 doublet) collapsed to a singlet. Irradiation on the latter signal produced a considerable narrowing of the dt at δ 5.53. Furthermore, the splitting of the H-12 signal, J = 1 Hz, was shown to be an allylic coupling to H-15. The structure of the yellow compound is therefore **4**.

In order to confirm unequivocally the structure of this product (**4**), an X-ray analysis was carried out† and the result is shown in Fig. 1. It can be seen that indeed the remaining acetoxy group of ring B is located at C(6) and is β-oriented. Furthermore it is interesting to note that the three rings of this molecule assume a screw-like structure whereby ring C is almost perpendicular towards ring A.

The formation of this product can be accounted for by a mechanism involving a 1,4-addition of hydrogen to intermediate **a** which is ideally suited for the β-elimination of the 12-OAc group leading to product **b**. The final step would be the hydrogenolysis of the allylic 7α-OAc group, producing the yellow compound **4**, see Scheme 1.

An interesting feature of the NMR spectrum of **4** is the geminal coupling between the two C(7) hydrogens, the absolute value of which was found to be 20.5 Hz. Such a value, although not unique, is rather unusually large, and since we had available from the X-ray data all the necessary angles, an analysis of this phenomenon is hereby presented.

Table 1. ^1H NMR data of 4

	δ	Multiplicity	J (Hz)
H-1	1.78	ddd	12.5;9;8
	1.5[a]		
H-2	2.81	ddd	13.5;8;5.5
	2.6[a]		
H-5α	2.60	d	1.5[b]
H-6α	5.53	dt	4.5;1.5[b]
H-7α	2.57	dd	20.5;4.5[b]
H-7β	2.89	dd	20.5;1.5[b]
H-12	6.43	d	1
H-15	3.02	septet d	7;1
C(4) Me	1.20	s	
C(4) Me	1.18	s	
C(15) Me	1.14	d	7
C(15) Me	1.12	d	7

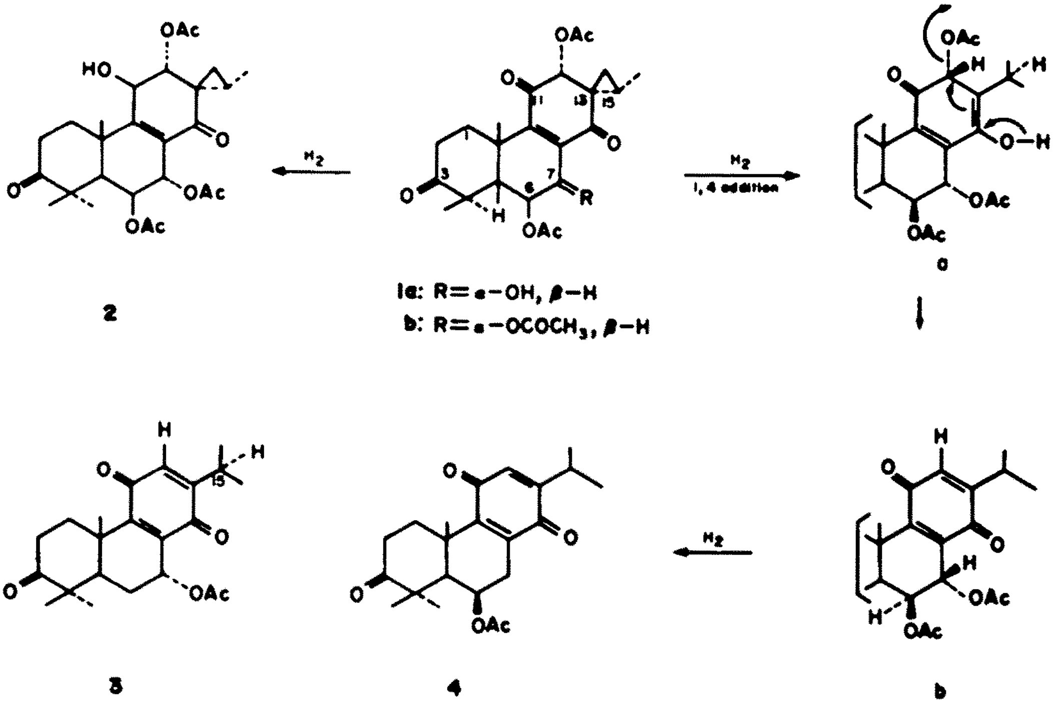
[a]Signal partially obscured.

[b]The values of the vicinal coupling constants together with the dihedral angles obtained from the X-ray diffraction data are in general agreement with the Karplus equation[2]. The angles are as follows: H(6)-C(6)-C(7)-H(5): -69°; H(6)-C(6)-C(7)-H(7)α: 43° and H(6)-C(6)-H(7)β: -75°.

The geminal coupling ($^2J_{HH}$) in cyclohexane is *ca.* −12.5 Hz, we have to account therefore for an additional −8 Hz. Three factors are known to influence directly the magnitude of the proton geminal coupling for a C–CH_2–C system.[3] The first involves the angle formed by the three carbons in question. In our case the C(6)–C(7)–C(8) angle is 110.4°, not significantly different than the cyclohexane value of 111.5°.[3] Therefore no major influence is expected from this factor.[4] The second influence could come from an electronegative group on

---

†The X-ray analysis was kindly performed by Dr. D. Rabinovich and F. Frolow of the Structural Chemistry Department, The Weizmann Institute of Science. Full details will be submitted for publication separately.



Scheme 1.

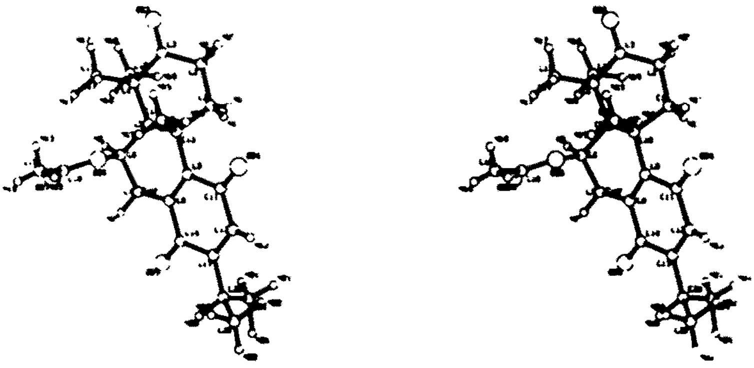


Fig. 1. Stereoscopic view of a single molecule of 4 (the numbering system is slightly different from the one used in the text).

an adjacent carbon such as the 6-OAc in our case. Such an influence is known[3] to be dependent on the angle formed between the C-heteroatom bond and the plane P that bisects the Hα-C-Hβ group. When this angle is 0° or 180° (the substituent is in the plane), the contribution is minimal, and when it is 90° (perpendicular to the plane), the effect is maximal (ca. −3 Hz). In compound 4 the 6-OAc forms a 104.5° angle with plane P, see Fig. 2, and therefore its influence should be high.

The third influence on the magnitude of $^2J_{HH}$ is a hyperconjugative interaction with an adjacent π system.[2] Again there is a strong angular dependence to this effect. When the angle between the p-orbitals of the adjacent carbon and plane P (as defined above) is 0°, the effect is minimal and when 90°, maximal. In compound 4 the second adjacent carbon C(8) is part of a quinone system. The angle formed between the p-orbitals of C(8) (assumed to be perpendicular to the C(8)–C(9)–C(14) plane) and plane P is 105.1° (see Fig. 3), close to a 90° orientation, and therefore an almost maximal contribution is expected. The maximum effect for an isolated double bond is ca. −4.5 Hz and for a more electron withdrawing group as a carbonyl, the value can be as high as −7.5 Hz.[2,6] A quinone system as in compound 4

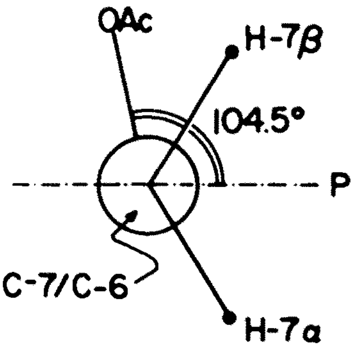


Fig. 2.

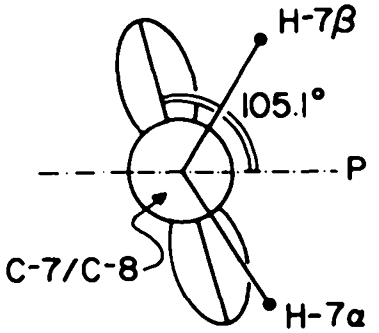


Fig. 3.

is surely a stronger electron withdrawing moiety than a simple double bond, and therefore a value in the −5 to −6 Hz range, as calculated in the present case, is reasonable. All these influences put together help to explain the geminal coupling constant of −20.5 Hz for the C(7) methylene.

EXPERIMENTAL

^{1}H NMR was recorded in $CDCl_3$ solution on a Bruker WH-270 instrument. X-ray single crystal analysis was made using three-dimensional intensity data (two quadrants) collected at room temp. on an Enraf-Nonius CAD-4 diffractometer with graphite monochromatised MoKα radiation. A set of 1769 independent reflexions were used for structure analysis. Structure was solved by MULTAN, and refined by least squares to the discrepancy factor R = 0.056.

REFERENCES

[1] R. Zelnik, D. Lavie, E. C. Levy, A. H.-J. Wang and I. C. Paul, *Tetrahedron* 33, 1457 (1977).
[2] R. Cahill, R. C. Cookson and T. A. Crabb, *Ibid* 25, 4711 (1969); S. Sternhell, *Quart. Rev.* 23, 236 (1969); L. M. Jackman and S. Sternhell, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*. Pergamon Press, Oxford (1969); F. A. Bovey, *Nuclear Magnetic Resonance Spectroscopy*. Academic Press, New York (1969).
[3] M. Davis and O. Hassel, *Acta Chem. Scand.* 17, 1181 (1963).
[4] R. C. Cookson, T. A. Crabb, J. J. Frankel and J. Hudec, *Tetrahedron Suppl.* 7, 355 (1966).
[5] A. Aksel and A. Bothner-By, *Advan. Magn. Reson.* 1, 195 (1965); T. N. Huckerby, *Annual Reports on NMR Spectroscopy* (Edited by E. F. Mooney) Vol. 5A. Academic Press, London (1972).
[6] T. Takahashi, *Tetrahedron Letters* 564 (1964).