Available online at www.sciencedirect.com
SCIENCE DIRECT
Journal of Molecular Structure 753 (2005) 27–34
Journal of MOLECULAR STRUCTURE
www.elsevier.com/locate/molstruc

On the structure and spectroscopic properties of two 13-hydroxylupanine epimers

Teresa Borowiak[a,*], Irena Wolska[a], Waleria Wysocka[b], Tadeusz Brukwicki[b]

[a]*Department of Crystallography, Faculty of Chemistry, Adam Mickiewicz University, Grunwaldzka 6, 60-780 Poznań, Poland*
[b]*Laboratory of Heterocyclic Compounds Chemistry, Faculty of Chemistry, Adam Mickiewicz University, Grunwaldzka 6, 60-780 Poznań, Poland*

Received 13 May 2005; accepted 23 May 2005
Available online 21 July 2005

Abstract

The crystal structures of 13α- and 13β-hydroxylupanines present a rare case of unexpected configuration and conformation of bis-quinolizidine alkaloid free bases. The configuration of A/B and C/D ring junctions is *trans–cis* and *quasi trans–cis* in α and β epimers, respectively. Ring C adopts a distorted chair form in both of them which is unusual for lupin alkaloids free bases. Such a drastic rearrangement of electronic configuration at N16 is caused by intermolecular hydrogen bonds formation between the OH and C=O groups. In spite of different orientations of the OH groups - an axial or an equatorial in α and β epimers, respectively, the hydrogen bond geometry is the same in both crystal structures. This causes different distortions in all four rings of bis-quinolizidine skeletons. The Duax-Norton approach has been used to analyze them.

In solution, both epimers occur in conformational equilibrium with considerable domination of the C-boat conformer (85–90%). This conformation is stabilized by the other type of intermolecular hydrogen bonds in comparison with that operating in the solid. Intermolecular deuterium bonds between 13α- and/or 13β-hydroxylupanine molecules and the solvent $CDCl_3$ molecules as well as the N16···H–O association have been found to play a crucial role.
© 2005 Elsevier B.V. All rights reserved.

Keywords: Bis-quinolizidine alkaloids; 13α-hydroxylupanine; 13β-hydroxylupanine; X-ray analysis; NMR; IR; The solid state conformation; Solution conformational equilibrium

1. Introduction

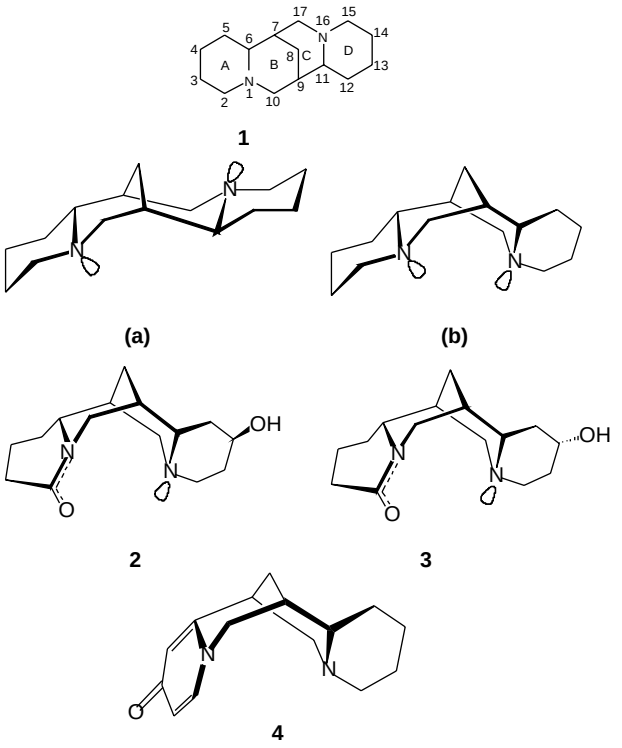
Sparteine (**1**) (Scheme 1), the prototype of the family of bis-quinolizidine alkaloids, is composed of two quinolizidine systems. One of them forms a double-chair *trans*-quinolizidine system A/B, which is relatively resistant to configurational-conformational changes and the other one, of rings C and D, which is much more susceptible to inversion at the N16 atom. In consequence, a rearrangement may occur between a *trans*-boat–chair C/D (**1a**) and *cis*-chair–chair C/D (**1b**) configurations and conformations (Scheme 1). Recent DFT results have conclusively established that **1** has a strong preference (3.4 kcal/mol) for conformation **1a** over **1b** [1]. There is a considerable amount of experimental evidence that in the solid state also other bis-quinolizidine free bases adopt the same configuration and conformation of the C/D part of the molecule. In particular, all sparteine derivatives with the A/B modified part of the molecule are good examples, e.g. lupanine (2-oxosparteine) [2], 2-phenylsparteine [3], 2-cyano-2-methylsparteine [4], 2-cyano-2-phenylsparteine [5] or multiflorine whose ring A contains a γ-oxo-α,β-enamine system [6].

Chemical modifications occurring in the more flexible C/D part of sparteine framework may cause configurational/conformational changes of this fragment. Its final configuration/conformation depends on a competition between forces which destabilize a chair or a boat form of ring C, in another words, these are the forces which lead to a boat or a chair form of ring C, respectively. Thus, a few different interactions may cause ring C to adopt a boat form:

1. repulsions between N1 and N16 free electron pairs,
2. steric hindrances between non-bonded hydrogen atoms: H8α···H12β, H12β···H17β, and H14β···H17β

* Corresponding author. Tel.: +48 618 291 286; fax: +48 618 658 008.
E-mail address: borowiak@amu.edu.pl (T. Borowiak).

0022-2860/$ - see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.molstruc.2005.05.027



Scheme 1. Sparteine (**1**), ring labeling and atom numbering; the lowest-energy conformers of sparteine (**1a** and **1b**); 13α-hydroxylupanine (**2**); 13β-hydroxylupanine (**3**); 5,6 didehydromultiflorine (**4**)

and on the other hand, interactions between the N16 free pair and H8α may cause ring C to adopt a chair form. It is worthy mentioning that the chair form in the molecules of lupin alkaloids free bases is rare. The first example has been found in 15-phenyl-14-dehydrosparteine molecule [7]. The forces which destabilize the C-chair conformation are weakened for two reasons: the free pair at N16 is involved in a mesomeric effect with the double bond C14=C15 and there are no interactions H14β···H17β.

However, there are far more examples which indicate that the repulsive interactions between the free pairs at N1 and N16 are decisive towards a boat form of ring C. It is the case of 13-oxolupanine in the solid state at least [8]. In solution the conformer with a chair form of ring C occurs in equilibrium with the conformer of C-boat form (45%:55%, respectively) [9,10]. Also, 17β-isopropyllupanine [11] and 17β-isopropyl-2-phenyl-2-dehydrosparteine [12] occur in the solid state with ring C in a boat form.

Another example of the surprising molecular conformation with ring C in a chair form has been found in the molecule of 13α-hydroxylupanine. Its crystal structure was determined by Kałuski et al. [13]. One could rather expect the same conformation as for 13-oxolupanine [8]. However, based on photographic X-ray data, the model obtained by Kałuski was not precise. We have redetermined the crystal structure of **2** (Scheme 1) for three reasons: (i) according to [13] the hydroxy-group in position 13 is involved in an intermolecular hydrogen bond to the oxo-group of ring A which turned out to be crucial to the inversion of electronic configuration at N16, so the hydrogen bond parameters should be precisely determined; (ii) we obtained also the β-epimer of 13-hydroxylupanine (**3**) (Scheme 1) with an equatorial orientation of the OH-group and a precise model for α-epimer has been necessary to compare both structures; and at last, (iii) the unexpected conformation of 13α-hydroxylupanine as determined in [13] has prompted the search for possible factors that can bring about conformational transitions, in particular by introducing substituents in the C/D part of the molecule.

2. Experimental

2.1. General techniques

Melting points were determined on a Boetius apparatus (PHMK 05 VEB Wägetechnik Rapido, Radebeul). IR spectra were recorded on a FT-IR Bruker IFS 113 v spectrometer (KBr pellets technique and in 0.4, 0.2 and 0.1 M $CDCl_3$ solutions dried with molecular sieves (type 3A), in 0.2 mm KBr absorption cells).

^{13}C NMR spectra were obtained on a Varian 300 Mercury spectrometer at 75.462 MHz (number of transients 10000, acquisition time 1.5 s, spectral width 13718 Hz, number of points 27372, digital resolution 0.50 Hz. ^1H NMR spectra: number of transients 64, acquisition time 3.0 s, the 90° pulse width 8 μs, the 45° pulse width 4 μs, spectral width 9000 Hz, number of points 54016, digital resolution 0.167 Hz per point). The ^1H and all 2D NMR (^1H–^1H COSY, ^1H–^1H NOESY, HSQC) spectra were recorded with a Bruker Avance 600 spectrometer equipped with a 5 mm TBI ^1H inverse probe head, operating at 600.31 MHz using standard Bruker programs. The concentrations were ca 0.15 M; twice and fivefold dilution changed the spectra in a minimal extent.

2.2. Substances

13α-Hydroxylupanine was extracted from seeds of *Lupinus angustifolius* according to the method described previously [14]. M.p. 173 °C. IR (cm^{-1}): KBr 3293 (OH···O), 2802 and 2762 (Bohlmann band), 1599 (NC=O); 0.2 M $CDCl_3$ solution: 3612 (free OH), 3397 (OH···O), 3154 (probably O–H···N16 association), 2824, 2778 and 2684 (Bohlmann band), 2253 (‘free’ C–D), ca 2240 (C–D···O=CN), 2187 (C–D···N), 1625 (C=O).

13β-Hydroxylupanine was obtained from 13-oxolupanine [15] by $NaBH_4$ reduction according to the method reported previously [16]. M.p. 176–177 °C. IR (KBr, cm^{-1}) 3331 (OH···O), 2825 (Bohlmann band), 1615 (NC=O). The Bohlmann band of lupanine (0.2 M in $CDCl_3$, cm^{-1}): 2816, 2767 and 2685.

Download English Version:

https://daneshyari.com/en/article/9769855

Download Persian Version:

https://daneshyari.com/article/9769855

Daneshyari.com