Molecular complex of isosteviol with aniline

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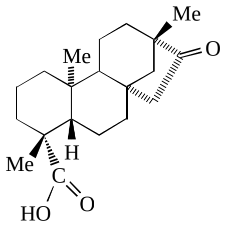
Isosteviol forms a crystalline molecular complex with aniline in the ratio 2:1, whose supramolecular structure looks like a double chiral helix cross-linked by aniline molecules.

Earlier, we have isolated the glycoside stevioside[1] and tetracyclic diterpenes of the kaurenic structure, steviol and isosteviol **1**, from an extract of the plant *Stevia rebaudiana Bertoni*.[2] We have examined the reactivity of these kaurenoids and the interaction of isosteviol **1** with aniline **2**. Regardless of the reaction conditions, the interaction results in formation of crystal compound **3** with mp 225–228 °C, which consists of **1** and **2** in the ratio 2:1, according to elemental analysis.



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According to X-ray single-crystal diffraction data,[†,3] isosteviol forms a molecular complex with aniline in the ratio 2:1.

An asymmetric part of the unit cell of **3** contains two independent molecules of isosteviol **1a** and **1b** and a molecule of aniline **2**. A proton of the amino group of aniline forms an intermolecular hydrogen bond with the carbonyl oxygen of the COOH group of **1a**, and another, with the hydroxyl oxygen of the COOH group of a symmetrically transformed (1 – *y*, *x*, –1/4 + *z*) molecule of **1b′**. In turn, each of the molecules of **1a** and **1b′** forms dimers with other isosteviol molecules by intermolecular H-bonding between protons of the COOH groups of **1a** and **1b′** and oxygen atoms of the keto groups of other molecules of **1b″** (1 + *x*, *y*, *z*) and **1a‴** (1 – *y*, *x* – 1, –1/4 + *z*), respectively. Thus, two isosteviol molecules form a pseudocage structure of the ‘head-to-tail’ type (Figure 1).

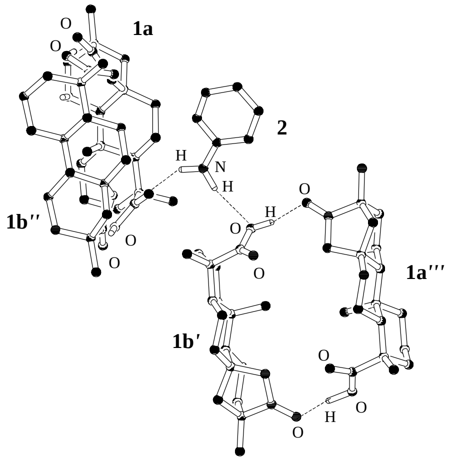

Figure 1 A motif of hydrogen bonds in the crystal structure of **3**.

It is interesting that the amino group of aniline is a proton donor, and the COOH group of isosteviol is a proton acceptor in this compound.

Note that a motif of hydrogen bonds results in the structure of a chiral double spiral of isosteviol molecules around the crystallographic axis 4_3 strands of which are cross-linked by amino groups of aniline molecules. Aniline molecules are located strictly at one side of the spiral (Figure 2). In turn, each chiral spiral interacts with others spirals by intermolecular H-bonding between isosteviol molecules (Figure 3). Because isosteviol is an enantiopure compound with the definite absolute configuration of all asymmetric centres (4*R*, 5*S*, 8*R*, 9*S*, 10*S*, 13*S*), all spirals in a crystal are only left-hand.

Thus, the supramolecular structure of complex **3** shown in Figures 2 and 3, namely, the shape of a double helix and the alternation of acidic and basic functional groups, is somewhat similar to the structure of nucleic acids.

Complex **3** is a host–guest compound like complexes of urea, cholic acid, *etc.*[4,5]

It is of interest that the calculated free volume, which is potentially accessible for a guest molecule in the unit cell of compound **3**, is equal to 180 Å^3, whereas it is only 39 Å^3 in individual crystals of isosteviol.[2] A molecule of aniline fits loosely into the cavity. Thus, large amplitudes of thermal vibrations of carbon atoms remote from the NH_2 group are observed for aniline.

Thus, isosteviol forms with aniline a crystal molecular complex in the ratio 2:1, which is characterised by (i) a supra-

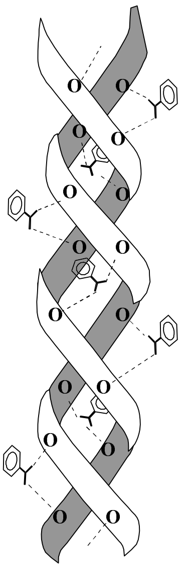

Figure 2 Double helix of isosteviol molecules cross-linked by amino groups of aniline.

[†] An Enraf-Nonius CAD4 diffractometer was used; crystals of **3** are tetragonal, at 20 °C a = 10.819(4), c = 35.169(3) Å, V = 4117(2) Å^3, d_{calc} = = 1.27 g cm^{-3}, Z = 8, space group $P4_3$, λCuKα radiation, $\omega/2\theta$ scan, $\theta \leq 74.3°$, 3577 reflections with $I \geq 3\sigma(I)$. The structure was solved by direct methods SIR,[6] hydrogen atoms were solved from difference Fourier syntheses. Absolute structures were established by the Hamilton test ratio[7] with a probability of 90%. R = 0.052 , wR = 0.065 for 3368 unique reflections. All calculations were carried out on a DEC Alpha Station 200 computer with the MolEN[8] system. H-bonds, free volume calculations and PLUTO diagrams were performed using the PLATON program.[9]

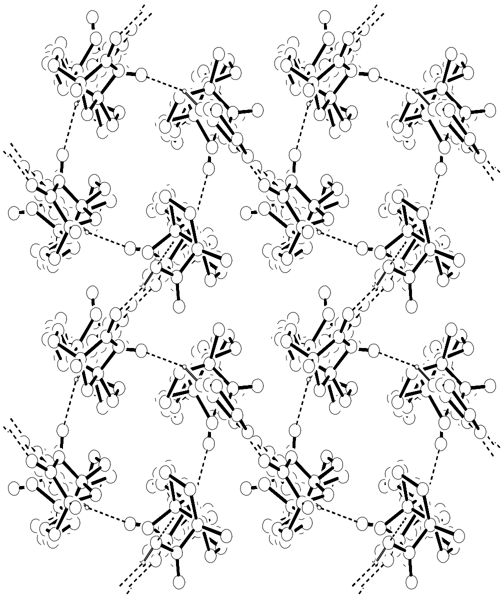

Figure 3 Intermolecular hydrogen bonds between isosteviol molecules in separate spirals (top view).

molecular structure of H-bonded chiral double spirals around the 4_3 axes, (ii) pseudocage structure of isosteviol dimers of the head-to-tail type and (iii) a system of hydrogen bonds, in which the NH_2 group of aniline is a donor, and the COOH group of isosteviol is an acceptor of protons.

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