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Journal of Molecular Structure 797 (2006) 92–98
Journal of MOLECULAR STRUCTURE
www.elsevier.com/locate/molstruc

^{1}H, ^{13}C and ^{15}N NMR, FT-IR as well as PM5 studies of a new Schiff base of gossypol with 3,6-dioxadecylamine in solution

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Received 10 February 2006; accepted 1 March 2006
Available online 24 April 2006

Abstract

The Schiff base of racemic gossypol with 3,6-dioxadecylamine (GSDN) has been synthesised and its structure has been studied by FT-IR, ^{1}H, ^{13}C and ^{15}N NMR spectroscopy as well as by the PM5 semiempirical method. All spectroscopic methods have provided respective evidences that GSDN in solution exists exclusively in the enamine–enamine tautomeric form. The structure of the enamine–enamine tautomer is visualized and the hydrogen bonds stabilising this structure are discussed.

Keywords: Gossypol; Schiff base; 3,6-Dioxadecylamine; ^{15}N NMR; ^{13}C NMR; ^{1}H NMR; COSY; HETCOR; FT-IR; PM5; Tautomers; Hydrogen bonds

1. Introduction

Gossypol 2,2′-bis(8-formyl-1,6,7-trihydroxy-5-isopropyl-3-methylnaphthalene) is a well-known disesquiterpene showing great biological activity together with a relatively high toxicity [1–11]. Much lower toxicity than that of gossypol has been noted for its derivatives such as Schiff bases. It is also well known that gossypol can occur in three symmetrical tautomeric forms shown in Scheme 1. The Schiff bases of gossypol can be present in only two symmetrical tautomeric forms: imine–imine and enamine–enamine forms which are analogous to the aldehyde–aldehyde and ketol–ketol tautomeric forms of gossypol, respectively. Up to now we have studied the structures of several Schiff bases of gossypol with L-amino acids [12–14], crown ether amines [14–16], oxaalkyl amines [14,17,18], *n*-butylamine [19], (*R*)-tetrahydrofurfuryl amine [20], allylamine [21,22]. As a continuation of these studies, in the present paper we report the synthesis and spectroscopic as well as semiempirical PM5 studies of a new Schiff base of gossypol with 3,6-dioxadecylamine. This synthesis was performed to endow gossypol with the ability to complex monovalent cations, which is very often directly connected with its antibacterial activity. Furthermore, the structure of this new Schiff base, especially its dominant tautomeric form, is discussed.

2. Experimental

Racemic gossypol was extracted from cotton seeds of *Gossypium herbaceum* following the procedure given in [23]. The 3,6-dioxadecylamine was synthesised following the procedure given in [24]. The purity of the gossypol extracted and the amine synthesised was controlled by ^{1}H NMR spectra.

2.1. Synthesis of new Schiff base of gossypol with 3,6-dioxadecylamine (GSDN)

GSDN was synthesised by addition of 869 mg of 3,6-dioxadecylamine (1.08×10^{-3} mol) in 30 cm^3 absolute ethanol to a solution of 280 mg of gossypol (5.40×10^{-4} mol) in 50 cm^3 absolute ethanol. The mixture was stirred under reflux for 3 h under argon atmosphere. After cooling of the mixture, the product crystallized as a brown powder. Schiff base of gossypol was filtered and dried under reduced

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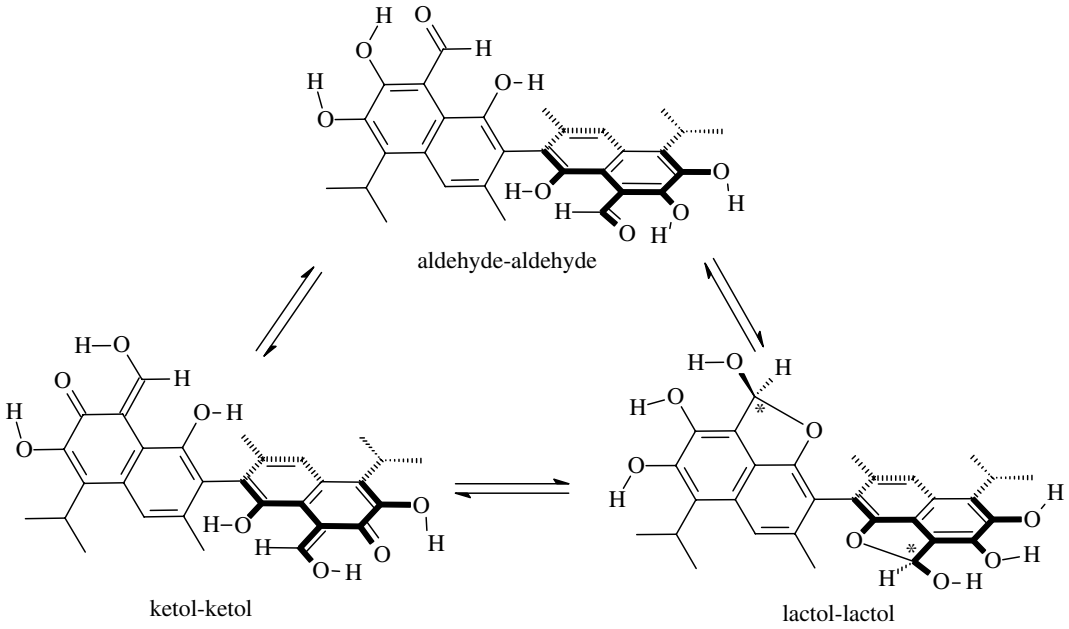
doi:10.1016/j.molstruc.2006.03.013



Scheme 1. Structures of tautomeric forms of gossypol.

pressure. Crude precipitate was recrystallised from absolute ethanol. Yield: 72.1%. Melting point 105–111 °C with the decomposition. Elementary analysis $C_{46}H_{64}N_2O_{10}$: Calculated: C = 68.63%, H = 8.01%, N = 3.48%; Found: C = 68.62%, H = 8.00%, N = 3.49%.

2.2. FT-IR measurements

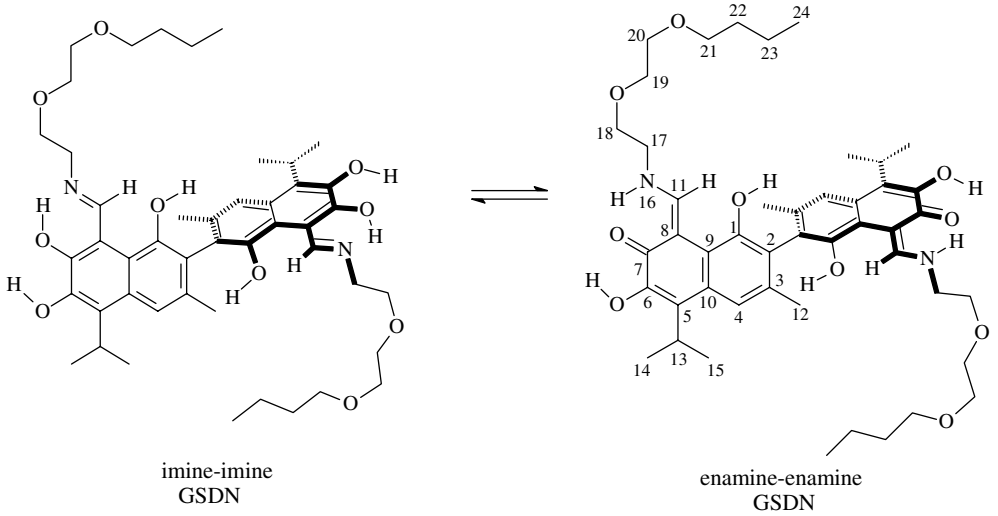
The FT-IR spectra of gossypol and GSDN were recorded in methylene chloride and chloroform (0.05 mol L^{-1}), respectively, at 300 K using a Bruker IFS 113v spectrometer. Chloroform and methylene chloride spectral-grade solvents were stored over 3 Å molecular sieves for several days.

A cell with Si windows and wedge-shaped layers was used to avoid interferences (mean layer thickness 170 μm). The spectra were taken with an IFS 113v FT-IR spectrophotometer (Bruker, Karlsruhe) equipped with a DTGS detector; resolution 2 cm^{-1}, NSS = 125. The Happ–Genzel apodization function was used.

2.3. NMR measurements

The NMR spectra of GSDN were recorded in $CDCl_3$ using a Varian Gemini 300 MHz spectrometer operating at 125.77 and 50.68 MHz for carbon and nitrogen, respectively. For the liquid phase experiments, the 5 mm inverse, variable temperature PFG probe was used. Internal TMS and external nitromethane were used as the references for proton and carbon as well as nitrogen spectra, respectively.

^1H NMR measurements were performed for 0.05 mol L^{-1} of GSDN chloroform solution as well as at the operating frequency 300.075 MHz; flip angle,



Scheme 2. The structures and the carbon atom numbering of two possible tautomeric forms of GSDN.