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Journal of Molecular Structure 832 (2007) 184–190
Journal of MOLECULAR STRUCTURE
www.elsevier.com/locate/molstruc

FT-Raman spectra of *n*-propanol and selected partially ^{2}H-labelled analogues

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Received 9 November 2005; received in revised form 18 August 2006; accepted 22 August 2006
Available online 5 October 2006

Abstract

Fourier-transform Raman spectra of $CH_3CH_2CH_2OH$ and some of its selectively deuteriated analogues have been obtained. Comparisons of the Raman spectra of the protiated and partially deuteriated species, in conjunction with polarization data, has enabled improved vibrational assignments to be made for the C–H modes. As a result, confirmation of some literature assignments of stretching and bending modes and revision of other tentative assignments for large biopolymer molecules have been proposed.

Keywords: Raman spectra; *n*-Propanol; Deuteriated analogues; Assignments

1. Introduction

In the assignment of the vibrational spectra of large complex molecules of biological interest including wool and cotton [1,2] and biopolymers, such as the human keratotic species skin, hair and nail [3,4], the unequivocal identification of important modes is often difficult because of overlapping spectroscopic features which arise from ν(CH), ν(CO) and ν(CN) bands which occur in similar wavenumber ranges. It is increasingly important for biomedical diagnostic applications of vibrational spectroscopy to be able to assign properly the vibrational bands in materials which have been modified by biological processes. Thus, recent Raman spectroscopic studies of diseased and healthy human tissues [4] revealed that some critical spectroscopic differences have been noted in the ν(CH) and $\delta(CH_2)$ regions. In some cases, it has been possible to relate the observed vibrational band changes to real biological effects such as the de-lipidization of human stratum corneum in the epidermis of diseased tissue samples. Likewise, the molecular basis for the observed role of chemical enhancing agents such as dimethyl sulphoxide on the mechanism of transdermal drug delivery is little understood [5,6] but is believed to involve a lipid transmission mechanism in which the role of water is crucial; this interpretation has yet to be related to the spectroscopic changes in the ν(CH) region of the Raman spectrum.

Further problems can arise in the vibrational assignment of large biological molecules when small molecular species are used as model compounds; in some cases, the rigidity imposed by tertiary skeletal structures can substantially alter the appearance of the spectra. This effect has been noted in previous work from our laboratories on cellulose [3] and bacterial cell walls [7], in which the importance of the β-glycosidic bonds on the biopolymeric structures have a controlling influence on the vibrational skeletal modes and their observed spectra.

We have initiated a programme designed particularly to provide initial identification of ν(CH) and δ(CH) modes of simple organic molecules, in order to assist in the assignment of vibrational bands in more complex biological materials. Improved assignments for the ν(CH) and $\delta(CH_2)$ regions will assist the identification of these features in biopolymers, lipids and proteins, thus improving the understanding of the vibrational modes of which the skeletal structures are composed. In this paper we have applied selective deuterium labelling in specially synthesised

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doi:10.1016/j.molstruc.2006.08.018

compounds to address the problems of assigning the ν(CH) and $\delta(CH_2)$ vibrational bands in a compound (*n*-propanol) containing the $CH_3CH_2CH_2$-moiety, in order to derive improved molecular vibrational assignments that can be assimilated into more complex species.

2. Experimental

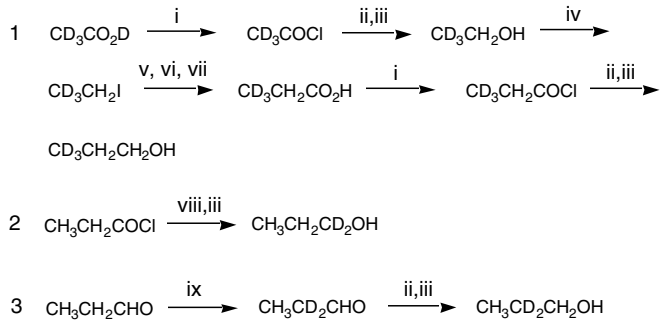
2.1. Origin of specimens

The compounds investigated in this study comprised unlabelled *n*-propanol, $CH_3CH_2CH_2OH$, together with three specifically deuteriated analogues, $CH_3CH_2CD_2OH$, $CH_3CD_2CH_2OH$ and $CD_3CH_2CH_2OH$.

All the unlabelled materials (including *n*-propanol) required for this work were high purity samples obtained from Aldrich or BDH. Isotopically labelled starting materials [D_2O, $LiAlD_4$ and CD_3CO_2D] were obtained from Aldrich and were used without further purification. The labelled alcohols were synthesised by the routes summarised in Scheme 1; details of the procedure for the synthesis of $CH_3CH_2CD_2OH$ and $CH_3CD_2CH_2OH$ are given below; the preparation of $CD_3CH_2CH_2OH$ has been described previously [8]. The isotopic purity of the partially labelled propanols was estimated from their mass spectra to be 96–99%.

2.1.1. $CH_3CH_2CD_2$ OH

A suspension of lithium aluminium deuteriide (5.0 g, 0.119 mol) in triglyme [triethylene glycol, dimethyl ether, $CH_3O(CH_2CH_2O)_3OCH_3$, (150 cm^3)] was stirred magnetically under a nitrogen atmosphere. The temperature was maintained between 30 and 50 °C by means of external cooling (ice/salt bath) during the dropwise addition over a period of 2 h of a solution of propionyl chloride (19 g, 0.205 mol) in triglyme (50 cm^3). Stirring was continued overnight, after which tetragol [tetraethylene glycol, $HO(CH_2CH_2O)_3OH$, (80 cm^3)] was added dropwise over 1 h. Careful distillation gave a colourless liquid product (12.1 g, 95%) having b.p. 96–99 °C; redistillation through a 5 cm helically packed column gave *n*-propanol-1,1-d_2 (10.4 g, 84%) having b.p. 98–99 °C.



Scheme 1. Reagents and conditions: (i) excess PhCOCl, distil., (ii) excess $LiAlH_4$, triglyme, stir 24 h, (iii) excess tetragol, (iv) I_2, red P, (v) Mg, $(C_2H_5)_2O$, (vi) excess CO_2, −78 °C, (vii) HCl/H_2O, (viii) excess $LiAlD_4$, triglyme, stir 24 h, (ix) excess D_2O, pyridine, reflux 72–96 h; repeat twice.

2.1.2. $CH_3CD_2CH_2$ OH

$CH_3CD_2CH{=}O$. A mixture of redistilled *n*-propionaldehyde (32 g, 0.55 mol), deuterium oxide (48 g, 2.4 mol) and pyridine (4 g, 0.05 mol) was refluxed in a nitrogen atmosphere for 72–96 h. The isotopically enriched aldehyde was removed by distillation through a 10 cm helix-packed column (b.p. 47–48 °C) and subjected to two further exchanges with fresh portions of deuterium oxide (35 g, 1.75 mol) and pyridine (4 g, 0.05 mol). The final yield of *n*-propionaldehyde-2,2-d_2 having b.p. 47–48 °C was 13.5 g (41%), but additional batches of aldehyde could be exchanged in somewhat higher yields using the deuterium oxide employed for the first batch of aldehyde.

2.1.3. $CH_3CD_2CH_2OH$

A solution of *n*-propionaldehyde-2,2-d_2 (18 g, 0.30 mol) in triglyme (50 cm^3) was added dropwise during a period of 1.3 h to a magnetically stirred suspension of lithium aluminium hydride (8.7 g, 0.23 mol) in triglyme (300 cm^3) under a nitrogen atmosphere. The temperature was kept below 40 °C by means of external cooling (cold water bath) during the early stages of the addition when the reaction was moderately vigorous. Stirring was continued overnight, after which tetragol (50 cm^3) was added dropwise over 1 h. Careful distillation gave an almost colourless liquid (16.6 g, 89%) having b.p. 95–101 °C (bulk 98–99 °C); redistillation through a 5 cm helix packed column gave *n*-propanol-2,2-d_2 (16.8 g, 89%) having b.p. 98–99 °C.

2.2. Raman spectroscopic instrumentation

Fourier-transform Raman spectra were recorded using a Bruker FRA106 Raman module attachment on an IFS66 infrared optics system. A Nd^{3+}/YAG laser operating at 1064 nm was used as an excitation source and the laser beam focussed to a 100 μm diameter spot at the sample. Samples of the propanols were contained in sealed capillary tubes mounted in a specially constructed holder. Laser powers of up to 500 mW were used with typically 2000 scans at 4 cm^{-1} spectral resolution being collected; the average spectral accumulation time was estimated as 60 min per specimen under these conditions. A liquid-nitrogen cooled germanium detector with extended spectral bandwidth was used over the normal scan range of 50–3500 cm^{-1}; spectra were corrected for the instrument response and the observed band wavenumbers, calibrated against the internal laser frequency, are correct to better than 1 cm^{-1}. The depolarization ratio measurements were made with an optical vector rotator (90°) in the incident laser beam.

3. Vibrational theory

For C_S molecular symmetry as indicated diagrammatically in Fig. 1, the vibrational modes may be classified as follows: