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HETCOR NMR study of poly(*rac*-lactide) and poly(*meso*-lactide)

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Abstract

The application of heteronuclear chemical shift correlation (HETCOR) NMR allowed us to correlate the homodecoupled methine proton with the methine carbon signals of poly(*rac*-lactide) and poly(*meso*-lactide), and made it possible to perform a detailed analysis of ^{1}H NMR spectra (homodecoupled) and to ascribe the signals to configurational pentads. The assumption made by Chisholm and coworkers [Chisholm et al., Chem. Comm. 1997, p. 1999] that the previous assignment of methine carbon signals in ^{13}C NMR spectra was incorrect appeared to be wrong. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Polylactide; Stereosequences; NMR

1. Introduction

Owing to its biocompatibility, non-toxicity and biodegradability, polylactide obtained via the ring cleavage of racemic lactide or *meso*-lactide is known to be a valuable material widely used in medicine (sutures, fibres, rods, drug delivery systems, artificial tissue matrices) and agriculture (plant growth promotion) [1–3]. Due to the chirality of two carbon atoms in the lactide molecule and a possibility of relatively easy preparation of both optically pure enantiomers and racemate, it is possible to obtain polylactide of desired structure, and consequently to control physical properties of the products derived from polylactide. It is thus essential to have a possibility to monitor the structure of polylactide chain; such a possibility is provided by HR-NMR. spectroscopy. The lactide molecule contains two equivalent asymmetric carbon atoms, thus existing in the form of RR and SS enantiomers, as well as *meso*-RS form. Polymerization of equimolar mixture of RR and SS enantiomers (racemic lactide) affords poly(*rac*-lactide) assuming that neither enantiomer is preferentially selected during polymerization (no stereoelection) and no transesterification occurs. The *meso*-form after polymerization gives poly(*meso*-lactide) provided that the transesterification processes do not take place. During polymerization of racemic lactide or *meso*-lactide simultaneous addition of the pair of asymmetric carbon atoms to the growing chain end occurs. When the configuration of the chain end does not affect the configuration of added monomer molecule, then the polymerization proceeds according to ‘pair addition Bernoullian statistics’. In the case of racemic mixture of lactide, under the aforementioned conditions, the structure of polylactide chain is ‘predominantly isotactic’ (using Vert’s terminology [4]). A consequence of the pair addition is a number of possible sequences present in the polymer chain. In poly(*rac*-lactide) chain three triads (ii, is, si), five tetrads (iii, isi, iis, sii, sis), seven pentads (iiii, iiis, siii, iisi, isii, isis, sisi), 11 hexads, etc. may be present; the *n*-ads containing ss structures are forbidden. By contrast, in poly (*meso*-lactide) chain the ii connections are not possible, and in consequence the following *n*-ads may be present: three triads (ss, is, si), five tetrads (sss, isi, sis, iss, ssi), seven pentads, etc.

In our previous work [5], we reported the analysis of microstructure from ^{13}C NMR spectra in the carbonyl carbon range on hexad level, and in the methine carbon range on tetrad level, where the individual lines in the NMR spectrum were ascribed to corresponding configurational sequences. Our results were confirmed by the studies of Kricheldorf [6] who presented in addition the analysis of poly(*meso*-lactide) based on the ^{13}C NMR. spectra, as well as the signal assignment of poly(*rac*-lactide) and poly(*meso*-lactide) in the ^{1}H NMR. (homodecoupled) spectra. In 1995, we demonstrated a possibility of the preparation of partially disyndiotactic polymers from racemic lactide by using lithium *tert*-butoxide as the initiator [7]. The structural analysis of polylactide chain performed by means of NMR was confirmed by later work of Vert [8], Spassky [9] and Thakur [10]. Using higher resonance frequencies the latter author observed hexad stereosequence sensitivity also in the methine range of the carbon spectra as well as in proton, homonuclear decoupled spectra. Chisholm et al. [11]

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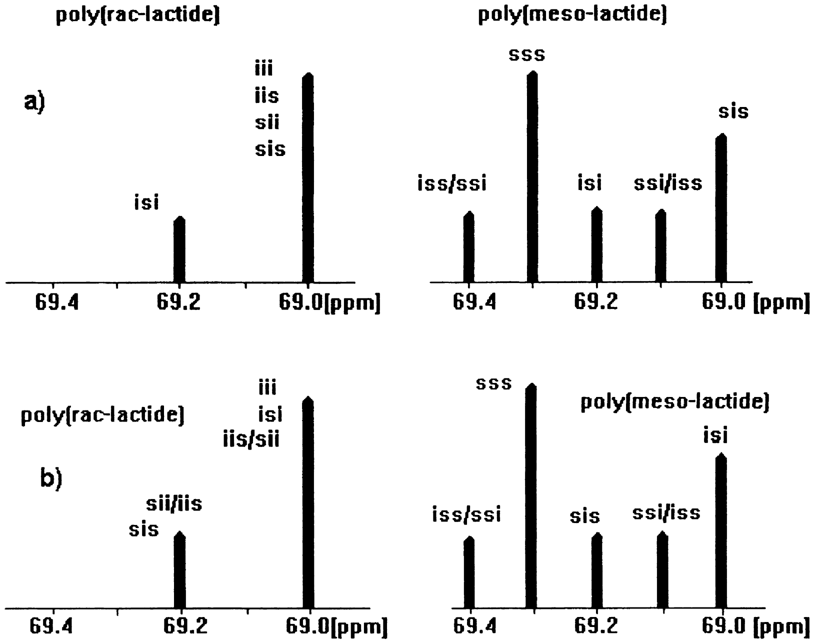

Fig. 1. The tetrads assignment of the methine carbon signals in the ^{13}C NMR. spectrum: (a) proposed by us [5] for poly(*rac*-lactide) and by Kricheldorf et al. [6] for poly(*meso*-lactide); (b) proposed by Chisholm [11].

recorded the HETCOR NMR. spectra of poly(*rac*-lactide) and poly(*meso*-lactide), and called in question the signal assignment in the methine carbon range of the ^{13}C NMR spectra. They proposed a new assignment changing the order of the signals due to *isi* and *sis* tetrads. In the present work we demonstrated that although the HETCOR NMR spectra are indeed helpful in ascribing the signals of the spectrum to individual configurational sequences, the tetrad assignment in the methine range of polylactide proposed by Chisholm et al. [11] is incorrect.

2. Experimental part

2.1. Polymerization procedure

The polymerization of racemic lactide or *meso* lactide were carried out in bulk, at 150°C using $Al(acac)_3$ as initiator. This initiator was a guarantee for lack of transesterification during the polymerization process [5]. Monomer-to-initiator mole ratio is 10^3:1. A conventional vacuum line method for degassing and sealing the ampoules was used.

2.2. NMR spectroscopy

The ^{13}C (75 MHz) and ^{1}H (300 MHz) NMR spectra were acquired on a varian Unity Inova spectrometer in 5 mm sample tubes using chloroform-d as a solvent and TMS as an internal standard. In ^{13}C spectra, 3.7 s acquisition time, 9 μs pulse width, 3 s pulse delay, digital resolution 64 K, spectral width 16 500 Hz and 3000 scans were used. In ^{1}H homonuclear decoupling spectra, methyl protons decoupled from the methine protons during the 1.8 s acquisition time, 9 μs pulse width, 3 s pulse delay, digital resolution 64 K, spectral width 4000 Hz and 64 scans were used. HETCOR (heteronuclear chemical shifts correlation) spectra were acquired using spectral width from methine region in ^{13}C spectrum and homodecoupled methine region in ^{1}H spectrum.

3. Results and discussion

Aside from the position of individual lines on the chemical shift scale of the ^{13}C NMR spectrum, also the differences in their intensity, which can be theoretically calculated [5,8], were used in order to ascribe the signals to respective configurational sequences. For the polymer chains obeying the pair-addition Bernoullian statistics in the case of poly (*rac*-lactide) the tetrad intensities were calculated to be [5–6]

iii (0.375); isi(0.25); iis = sii = sis(0.125).

In turn, for poly(*meso*-lactide) the calculated intensities are as follows [6,8]:

sss(0.375); sis(0.25); isi = iss = ssi(0.125).

Only two of the tetrads are identical in poly(*rac*-lactide) and poly(*meso*-lactide) chains, i.e. isi and sis, which obviously must exhibit the same chemical shift value in both cases. However, their intensities in the spectra of respective polylactides are different. In the experimental ^{13}C NMR spectrum of pure poly(*meso*-lactide), the intensity of the methine carbon signal at $\delta = 69.21$ ppm is twice lower than that of the signal at $\delta = 69.01$ ppm [6,10] (Fig. 1(a)). The higher intensity of the line owing to sis tetrad decisively determines

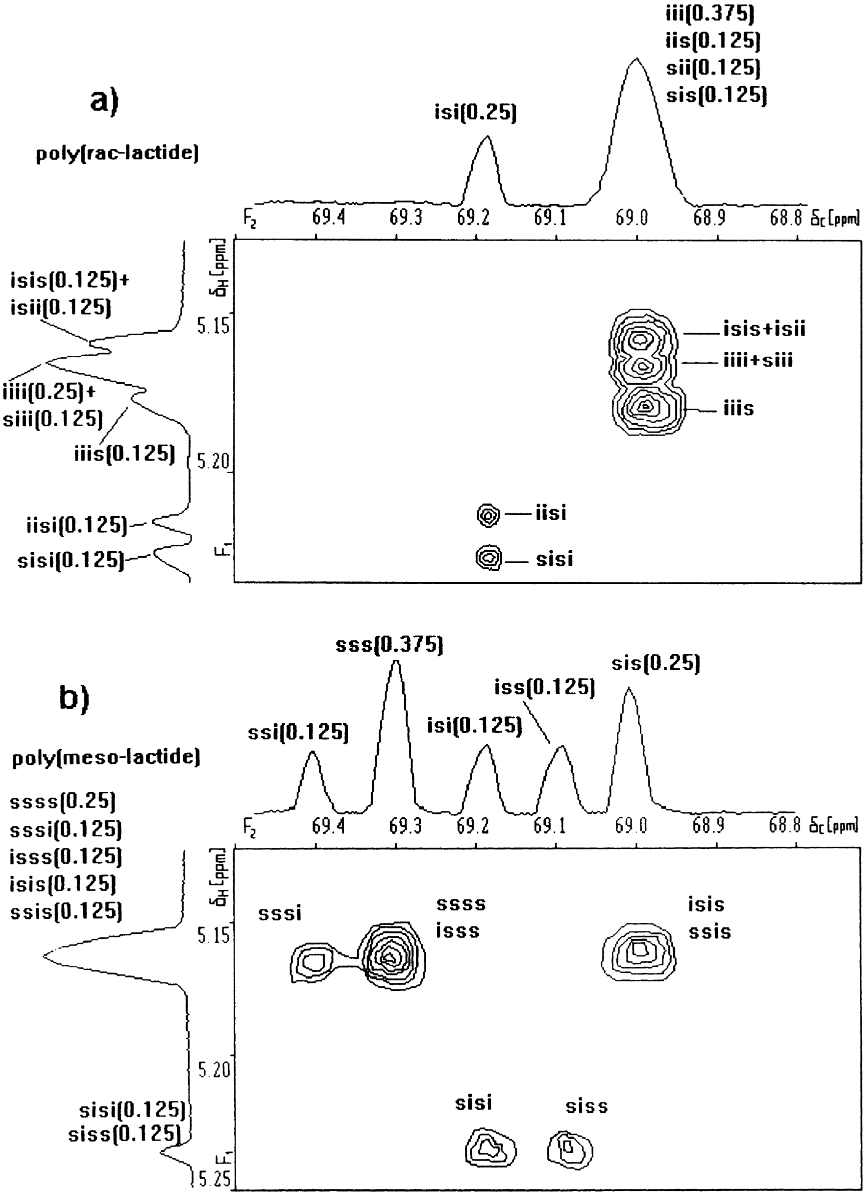

Fig. 2. HETCOR NMR spectrum of (a) poly(*rac*-lactide) and (b) poly(*meso*-lactide). Correlation of the homodecoupled methine proton with the methine carbon signal (theoretical, calculated intensities of the lines due to tetrads and pentads are given in brackets).

its position in the ^{13}C NMR spectrum, thus showing the ‘new assignment’ proposed by Chisholm et al. [11] to be incorrect (Fig. 1(b)).

The problem is to correlate the carbon and proton (homodecoupled) spectra on the basis of the HETCOR NMR spectra of poly(*rac*-lactide) and poly(*meso*-lactide). Assuming the signals in the ^{1}H (homodecoupled) NMR spectrum to arise from pentads (in a given pentad the methine proton is in between the remaining chiral carbon atoms separated by 3 and 6 bonds), and taking into account the theoretically calculated intensities of the signals corresponding to individual sequences, we performed the analysis of the HETCOR spectra. The results are presented in Fig. 2(a) for poly(*rac*-lactide), and in Fig. 2(b) for poly(*meso*-lactide). The analysis confirms the assignment of the signals at 69.2 and 69.0 ppm, respectively to isi and sis tetrads, and moreover demonstrates that the ssi and iss tetrads give the signals at 69.4 and 69.1 ppm, respectively (Fig. 3(a)). In addition, the analysis of the HETCOR spectra allowed us to assign the signals in ^{1}H (homodecoupled) NMR spectra of polylactide in the methine proton range to corresponding configurational pentads (Fig. 3(b)). Assignment is consistent with both the HETCOR NMR spectra (Figs. 2 and 3) and with the line intensities calculated theoretically for poly(*rac*-lactide) and poly(*meso*-lactide) assuming the pair-addition Bernoullian statistics.

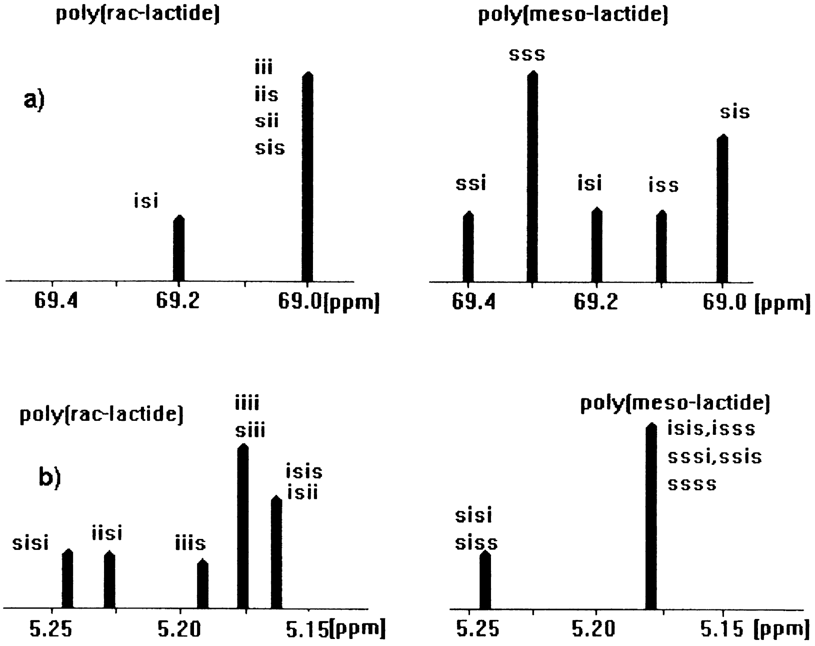

Fig. 3. The assignment of the lines to the configurational sequences (a) in the ^{13}C NMR. spectrum (methine carbon range) of poly(*rac*-lactide) and poly(*meso*-lactide); (b) in the ^{1}H NMR. spectrum (homodecoupled methine proton signal) of poly(*rac*-lactide) and poly(*meso*-lactide).

4. Conclusion

The HETCOR NMR spectra of poly(*rac*-lactide) and poly(*meso*-lactide) allowed us to correlate the homodecoupled methine proton spectrum with the methine carbon spectrum, and consequently to perform a more detailed analysis and unambiguous assignment of the signals at the pentad level in the ^{1}H (decoupled) NMR spectra, as well as to establish the positions of the lines due to isi, sis, ssi and iss tetrads in the methine region of ^{13}C NMR spectrum.

Acknowledgements

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