Synthesis of Model Molecules and NMR Analysis of Polymeric Reagents Based on Propane-1,3-dithiol and 1,3-Dithiane Systems

Francesco Lucchesini,*[a] Vincenzo Bertini,[a] Marco Pocci,[a] Eugenio Micali,[a] and Angela De Munno[b]

Keywords: NMR spectroscopy / Solid-phase synthesis / Polymers / Sulfur heterocycles

Purposely synthesized model compounds, one- and two-dimensional NMR spectra and simulations are used for a full ^{1}H and ^{13}C NMR spectroscopic investigation of soluble copolymeric reagents for supported organic syntheses containing (1,3-propanediyl)bis(benzenesulfonate), (1,3-propanediyl)bis(thioacetate), propane-1,3-dithiol, and 1,3-dithiane functions. The collected NMR spectroscopic data confirm the possibility of rapid and accurate assessments of preparations and applications of the newly prepared copolymeric reagents, without resorting to special equipment.

Introduction

In the field of combinatorial chemistry and, more generally of polymer-supported organic synthesis, NMR analysis is a rapid, reliable and nondestructive technique that plays a key role in monitoring the transformations of chemical structures bound to the polymeric support.[1] Functionalised insoluble swollen resins usually give broad NMR signals, although the introduction of the magic angle spinning technique has, in many cases, avoided such inconvenience, allowing the acquisition of ^{1}H and ^{13}C NMR spectra with line widths similar to those obtained with small molecules.[1] When such a technique is ineffective the application of more complex procedures is necessary.[2-4] Some solid-phase reactions have been monitored by ^{13}C, ^{19}F, ^{31}P and ^{15}N gel-phase NMR spectroscopy.[1] Without resorting to special equipment or specialized techniques, conventional NMR spectroscopy has revealed its general value for the analysis of soluble polymeric supports, for instance in the synthesis of prostaglandin E_2 methyl ester[5] on non-crosslinked polystyrene.

Recently, we reported reliable preparations of soluble copolymeric reagents for supported organic syntheses containing propane-1,3-dithiol functions, and we explored their effectiveness in the synthesis of ketones from aldehydes through the formation of 1,3-dithiane derivatives.[6,7]

In this paper we report a detailed ^{1}H and ^{13}C NMR study of our reagents and of purposely made model molecules, with the aim of designing simple methodologies for the control of their future preparations and applications.

Results and Discussion

The molecules **2**, **3**, **4a** and **4b** (Scheme 1), models for the copolymers **P2**−**P4**, (Scheme 2) were prepared as reported in the Exp. Sect. The dithianes **4a** and **4b** were obtained as a mixture of *cis* and *trans* isomers and could be separated by column chromatography. Monomer **1** was used as a model of the copolymer **P1**. To facilitate comparisons of NMR signals, the atom numbering of the model molecules was preserved as much as possible in the corresponding copolymers, using the indexes *c* for vinyl or polymer chain atoms and *s* for ring atoms of the comonomeric styrene units, as exemplified for **P1** (Scheme 1).

The ^{1}H and ^{13}C NMR spectra of the model compounds were adequately assigned with the use of correlation tables,[8] standard 1-D and 2-D NMR experiments and Bruker WIN-DAISY simulations. The ^{1}H NMR shifts of H(2′′) and H(3′′) in benzenesulfonate ester **1** were assigned by NOE difference experiments through the variation of the signal intensity upon saturation of H(1′) or H(1^{c}). The positions of the H(3′′′) and H(5′′′) signals (hidden by the signals of the phenyl protons) in the ^{1}H NMR spectrum of thienyldithianes *cis*-**4b** and *trans*-**4b** were determined by COSY-90 experiments through the coupling of such protons with the well-separated signals of H(4′′′). After assigning the ^{1}H NMR spectra, the assignment of the ^{13}C NMR shifts was performed on the basis of carbon-proton couplings between directly bonded atoms (HETCOR experiments), or long-range couplings through two or three bonds (COLOC experiments).

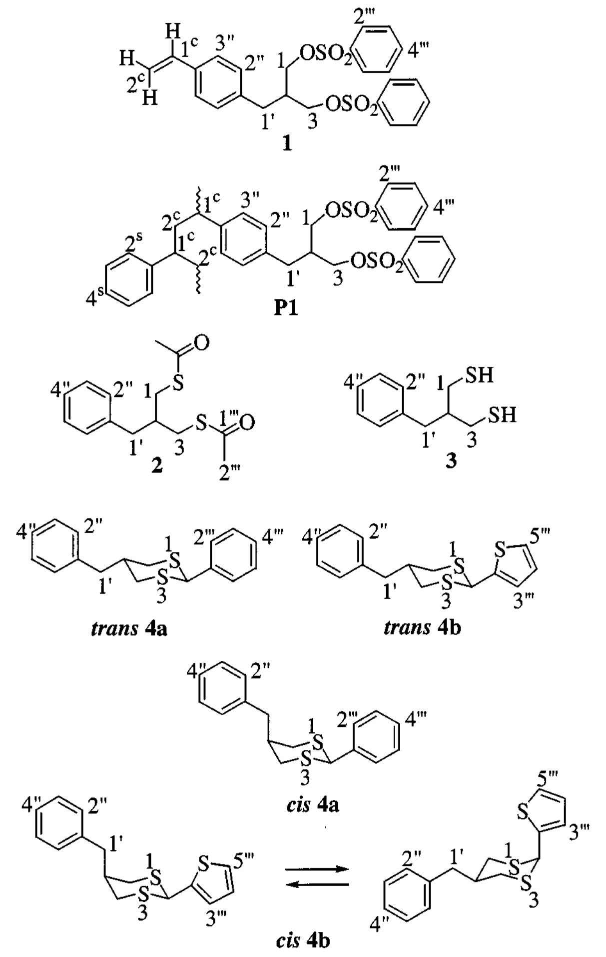
The copolymer **P1**, prepared from **1** and styrene under conditions that ensure a monomer content in the copolymer

---

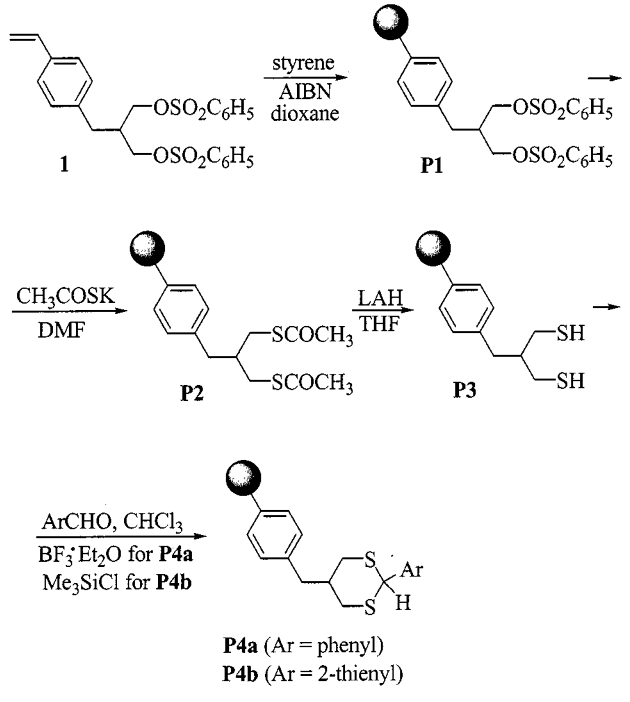
[a] Dipartimento di Chimica e Tecnologie Farmaceutiche ed Alimentari, Università di Genova,
Via Brigata Salerno, 16147 Genova, Italy
E-mail: lucchesini@dictfa.unige.it
[b] Dipartimento di Chimica e Chimica Industriale, Università di Pisa,
Via Risorgimento 35, 56126 Pisa, Italy

Supporting information for this article is available on the WWW under http://www.eurjoc.com or from the author.

1434−193X/02/0509−1546 $ 20.00+.50/0



Scheme 1



Scheme 2

not diverging by more than 0.5% from that of the feed[7] (see Exp. Sect.), and **P2**−**P4** obtained from **P1** (Scheme 2) afforded ^{1}H and ^{13}C NMR spectra with a satisfactory intensity of the signals of the functionalised monomeric units. The ^{13}C NMR spectra showed sufficiently well-resolved signals that they could be adequately assigned on the basis of model compounds, the ^{13}C NMR spectrum of atactic polystyrene[9] and correlation tables.[8] Since the ^{1}H NMR spectra showed broad lines, they could only be used profitably for those signals that could be identified unambiguously. The ^{1}H and ^{13}C NMR spectroscopic data of the models and the copolymers are collected in Table 1.

An initial inspection of these results indicates that each copolymer **P1**, **P2**, **P3**, **P4a** and **P4b** contains the functionalities of the corresponding model molecule as shown by the comparison between models and copolymers through all the assigned ^{1}H NMR lines in the copolymers and through the following ^{13}C signals. For **1** and **P1**: C(1′), C(2), C(1) + C(3), C(3‴), C(4‴), C(1‴), [C(2‴) in **P1** is hidden by the broad signal at δ = 127.2−128.7]; for **2** and **P2**: C(2‴), C(1), C(1′), C(2), C(1‴); for **3** and **P3**: C(1), C(1′), C(2); for *cis* **4a** and **P4a**: C(5), C(4), C(1′), C(2), C(1‴); for *trans* **4a** and **P4a**: C(4) + C(6), C(5), C(1′), C(2), C(1‴); for *cis* **4b** and **P4b**: C(4), C(5), C(1′), C(2), C(5‴), C(3‴), C(4‴), C(2‴); for *trans* **4b** and **P4b**: C(4) + C(6), C(5), C(1′), C(2), C(3‴), C(4‴), C(2‴).

An approximate evaluation of the yields of copolymer transformations from **P1** to **P4a** was carried out by comparing the integrals of the ^{13}C NMR signals of the carbon atoms not involved in the transformations and the carbon atoms connected to the formed functions. For the carbon atoms not involved in the transformations, the sum of the integrals of C(4″) and C(1^s), which were well separated in the ^{13}C NMR spectra of **P2**, **P3** and **P4a**, was used. For the carbon atoms connected to the formed functions the following integrals were used: for **P2** the sum of integrals of C(2‴) at δ = 30.7 and C(1) + C(3) at δ = 31.8, or the integral of C(1‴) at δ = 195.2; for **P3** the integral of C(1) + C(3) at δ = 26.5, the integral of C(1′) at δ = 37.3, or the integral of C(1″) at δ = 136.3; for **P4a** the sum of the integrals of *cis* C(4) + *cis* C(6) at δ = 35.6, *cis* C(1′) at δ = 35.8 and *trans* C(4) + *trans* C(6) + *trans* C(5) at δ = 37.3, or the integral of *cis* C(2) + *trans* C(2) at δ = 51.4, or the sum of the integrals of *trans* C(1″) at δ = 135.4, *cis* C(1″) at δ = 137.2, *trans* C(1‴) at δ = 138.5, and *cis* C(1‴) at δ = 139.3. For each copolymer **P2**, **P3** and **P4a** the ratios between the integrals of the signals of the two types of carbon compared with the values expected from the experimental monomer composition of the mixture producing **P1** indicated almost quantitative yields for the transformations **P1** → **P2** and **P1** → **P3** and yields higher than 90% for **P1** → **P4**.

Comparing the NMR spectra of phenyldithianes *cis*-**4a** and *trans*-**4a** it appears that for the two isomers the values of $\delta_{H(2)}$ (5.13 and 5.12, respectively) and $\delta_{C(2)}$ (both 51.4) are practically coincident, whereas for the isomeric thienyldithianes *cis*-**4b** and *trans*-**4b** (δ = 5.23 and 5.40 and 43.4 and 45.1, respectively) they are significantly different. The

Table 1. ^{1}H and ^{13}C NMR of model molecules and copolymers in $CDCl_3$

Compound	δ
1	δ_C = 32.9 (C-1′), 40.0 (C-2), 68.4 (C-1 + C-3), 113.8 (C-2^c), 126.5 (C-3′′), 127.9 (C-2′′′), 129.1 (C-2′′), 129.4 (C-3′′′), 134.0 (C-4′′′), 135.4 (C-1′′′), 136.2 (C-4′′), 136.3 (C-1^c), 136.8 (C-1′′); δ_H = 2.27 (m, 1 H, 2-H), 2.58 (d, *J* = 7.6 Hz, 2 H, 1′-H),3.94 (m, 4 H, 1-H + 3-H), 5.22 (dd, *J* = 10.9, 0.9 Hz, 1 H, 2^c-H*cis*), 5.69 (dd, *J* = 17.6, 0.9 Hz, 1 H, 2^c-H*trans*)), 6.65 (dd, *J* = 17.6, 10.9 Hz, 1 H, 1^c-H), 6.91 (m, 2 H, 2′′-H), 7.23 (m, 2 H, 3′′-H), 7.56−7.86 (m, 10 H, 2′′′-H + 3′′′-H + 4′′′-H)
2	δ_C = 30.6 (C-2′′′), 31.9 (C-1 + C-3), 39.1 (C-1′), 40.3 (C-2), 126.4 (C-4′′), 128.5 (C-2′′), 129.1 (C-3′′), 138.8 (C-1′′), 195.2 (C-1′′′); δ_H = 2.15 (m, 1 H, 2-H), 2.34 (s, 6 H, 2′′′-H), 2.67 (d, *J* = 7.1 Hz, 2 H, 1′-H), 2.82−3.02 (m, 4 H, 1-H + 3-H), 7.13−7.31 (m, 5 H, 2′′-H + 3′′-H + 4′′-H)
3	δ_C = 26.4 (C-1 + C-3), 37.7 (C-1′), 44.7 (C-2), 126.3 (C-4′′), 128.5 (C-2′′), 129.0 (C-3′′), 139.3 (C-1′′); δ_H = 1.24 (t, *J* = 8.4 Hz, 2 H, SH), 2.01 (m, 1 H, 2-H), 2.53−2.74 (m, 4 H, 1-H + 3-H), 2.72 (d, *J* = 7.2 Hz, 2 H, 1′-H), 7.15−7.32 (m, 5 H, 2′′-H + 3′′-H + 4′′-H)
***cis* 4a**	δ_C = 30.8 (C-5), 35.8 (C-4 + C-6), 36.0 (C-1′), 51.4 (C-2), 126.2, 127.9, 128.4, 128.5, 128.7, 129.3 (aromatic *C*−H), 139.2 (C-1′′′), 140.2 (C-1′′); δ_H = 2.19 (m, 1 H, 5-H), 2.74 (dd, *J* = 14.4, 4.1 Hz, 2 H, 4e-H + 6e-H), 3.24 (d, *J* = 7.6 Hz, 2 H, 1′-H), 3.25 (dd, *J* = 14.4, 3.0 Hz, 2 H, 4a-H + 6a-H), 5.13 (s, 1 H, 2-H), 7.18−7.40 (m, 8 H, aromatic protons), 7.57 (m, 2 H, aromatic protons)
***trans* 4a**	δ_C = 37.3 (C-4 + C-6), 37.6 (C-5), 43.0 (C-1′), 51.4 (C-2), 126.5, 127.8, 128.5, 128.6, 128.7, 129.2 (aromatic *C*−H), 138.3 (C-1′′′), 138.5 (C-1′′); δ_H = 2.23 (m, 1 H, 5-H), 2.64 (d, *J* = 7.4 Hz, 2 H, 1′-H), 2.74−2.85 (m, 4 H, 4-H + 6-H), 5.12 (s, 1 H, 2-H), 7.16−7.47 (m, 10 H, aromatic protons)
***cis* 4b**	δ_C = 33.7 (C-4 + C-6), 34.0 (C-5), 39.3 (C-1′), 43.4 (C-2), 126.1 (C-5′′′), 126.3 (aromatic *C*−H), 126.9 (C-3′′′), 127.0 (C-4′′′), 128.5, 129.3 (aromatic *C*−H), 139.3 (C-1′′), 144.0 (C-2′′′); δ_H = 2.22 (m, 1 H, 5-H), 2.73 (dd, *J* = 14.1, 7.2 Hz, 2 H, 4e-H +6e-H), 2.90 (d, *J* = 7.5 Hz, 2 H, 1′-H), 2.95 (dd, *J* = 14.1, 2.9 Hz, 2 H, 4a-H + 6a-H), 5.23 (s, 1 H, 2-H), 6.98 (dd, *J* = 5.1, 3.6 Hz, 1 H, 4′′′-H), 7.18−7.31 (m, 7 H, 2′′-H + 3′′-H + 4′′-H + 3′′′-H + 5′′′-H)
***trans* 4b**	δ_C = 36.7 (C-4 + C-6), 36.8 (C-5), 42.2 (C-1′), 45.1 (C-2), 125.6 (C-5′′′), 126.1 (C-3′′′), 126.5 (aromatic *C*−H), 126.7 (C-4′′′), 128.6, 129.2 (aromatic *C*−H), 138.6 (C-1′′), 141.2 (C-2′′′); δ_H = 2.23 (m, 1 H, 5-H), 2.68 (d, *J* = 7.3 Hz, 2 H, 1′-H), 2.72−2.88 (m, 4 H, 4-H + 6-H), 5.40 (s, 1 H, 2-H), 6.93 (dd, *J* = 5.1, 3.6 Hz, 1 H, 4′′′-H), 7.13−7.33 (m, 7 H, 2′′-H + 3′′-H + 4′′-H + 3′′′-H + 5′′′-H)
P1	δ_C = 32.6 (C-1′), 40.0 (C-2), 40.3 (C-1c), 40.6−46.3 (C-2c), 68.3 (C-1 + C-3), 125.6 (C-4s), 127.2−128.7 (C-2s + C-3s + C-2′′ + C-3′′ + C-2′′′), 129.3 (C-3′′′), 133.9 (C-1′′ + C-4′′′), 135.6 (C-1′′′), 143.6 (br, C- 4′′), 145.1 (br, C-1s); δ_H = 3.70−4.02 (H-1+ H-3), 7.39−7.89 (H-2′′′ + H-3′′′ + H-4′′′)
P2	δ_C = 30.7 (C-2′′′), 31.8 (C-1 + C-3), 38.6 (C-1′), 40.3 (C-2 + C-1c), 41.1−46.7 (C-2c), 125.6 (C-4s), 127.0−128.6 (C-2′′ + C-3′′ + C-2s + C-3s), 135.7 (C-1′′), 143.4 (br, C-4′′), 145.3 (br, C-1s), 195.2 (C-1′′′); δ_H = 2.34 (H-2′′′)
P3	δ_C = 26.5 (C-1 + C-3), 37.3 (C-1′), 40.4 (C-1c), 41.0−46.8 (C-2c), 44.6 (C-2), 125.6 (C-4s), 126.8−129.2 (C-2′′ + C-3′′ + C-2s + C-3s), 136.3 (C-1′′), 143.2 (br, C-4′′), 145.3 (br, C-1s)
P4a	δ_C = 30.8 (*cis*, C-5), 35.6 (*cis*, C-4 + *cis*, C-6), 35.8 (*cis*, C-1′), 37.3 (*trans*, C- 4 + *trans*, C-6 + *trans*, C-5), 40.3 (C-1c), 41.1−47.1 (C-2c), 42.6 (*trans*, C-1′), 51.4 (*cis*, C-2 + *trans*, C-2), 125.6 (C-4s), 127.0−129.2 (C-2s + C-3s + C-2′′ + C-3′′ + C- 2′′′ + C-3′′′ + C- 4′′′), 135.4 (*trans*, C-1′′), 137.2 (*cis*, C-1′′), 138.5 (*trans*, C-1′′′), 139.3 (*cis*, C-1′′′), 143.3 (br, C-4′′), 145.3 (br, C-1s); δ_H = 5.12 (H-2)
P4b	δ_C = 33.6 (*cis*, C-4 + *cis*, C-6), 34.0 (*cis*, C-5), 36.8 (*trans*, C-4 + *trans* C-6 + *trans*, C-5), 39.0 (*cis*, C-1′), 40.4 (C-1c), 41.1−46.8 (C-2c), 41.9 (*trans*, C-1′), 43.4 (*cis*, C-2), 45.2 (*trans*, C-2), 125.6 (C-4s + *trans*, C-5′′′), 126.1 (*cis*, C-5′′′ + *trans*, C-3′′′), 126.7 (C-4′′′), 126.9 (*cis*, C-3′′′), 127.1 (*cis*, C- 4′′′), 127.3−129.3 (C-2′′ + C-3′′ + C-2s + C-3s), 135.5 (*trans*, C-1′′), 136.2 (*cis*, C-1′′), 141.4 (*trans*, C-2′′′), 143.2 (br, C-4′′), 144.2 (*cis*, C-2′′′), 145.3 (br, C-1s); δ_H = 5.22 (*cis*, H-2), 5.41 (*trans*, H-2)

behaviour of **4a** parallels that of several 5-substituted 1,3-dithianes bearing a *tert*-butyl group in the 2-position,[10] for which the conformational equilibrium either in the *cis* or *trans* isomers always arranges the bulky *tert*-butyl group in the equatorial position, entailing a basically unchanged environment around C(2) or H(2). Furthermore, it is known from a series of 2-aryl-5-alkyl-1,3-dithianes[11] that *cis* and *trans* isomers differ much more in their $\delta_{C(5)}$ than $\delta_{C(2)}$ values. It can therefore be concluded that the phenyl group is arranged equatorially in both *cis*-**4a** and *trans*-**4a**, while the benzyl group is axial in the *cis*- and equatorial in the *trans* isomer. The observed differences in $\delta_{H(2)}$ and $\delta_{C(2)}$ for *cis*-**4b** and *trans*-**4b**, and the comparison with the isomers of **4a**, indicate that the thienyl and benzyl groups, which are both equatorial in *trans*-**4b**, are competitive in assuming the equatorial position in *cis*-**4b**. These conclusions for compounds **4a** and **4b** were confirmed by determining their $^3J_{4,5}$ H−H coupling constants from their ^{1}H NMR spectra using WIN-DAISY simulations. These coupling constants are very sensitive to conformational effects, and are compared to those of 2-phenyl-1,3-dithiane[12] in Table 2. As expected the obtained couples of $^3J_{4,5}$ values agreed with the H(5) proton occupying an axial position for *trans*-**4a** and *trans*-**4b**, an equatorial position for *cis*-**4a**, and undergoing a conformational equilibrium between axial and equatorial for *cis*-**4b** (Table 2, rows 9 and 12).

A comparison of the ^{1}H and ^{13}C NMR spectra of **P4a** and **P4b** with those of the model molecules confirms the presence in the copolymers of 2,5-disubstituted-1,3-dithiane rings both as *cis* or *trans* isomers, and the absence of any restriction to their conformational freedom by the polymer chain. Both the copolymers and models show similar conformational equilibria. The signals of *cis*-**4a** [C(2) at δ = 51.4 and H(2) at δ = 5.13] and *trans*-**4a** [C(2) at δ = 51.4 and H(2) at δ = 5.12] correspond to those in **P4a** at δ = 51.4 and δ = 5.12, respectively. The signals of *cis*-**4b**

Table 2. Proton NMR values and coupling constants (Hz) from WIN-DAISY simulations on the examined model compounds compared with known 2-phenyl-1,3-dithiane[12]

	2-Phenyl-1,3-dithiane	***trans*-4a**	***trans*-4b**	***cis*-4a**	***cis*-4b**
$\delta_{4a} = \delta_{6a}$		2.78	2.75	3.24	2.94
$\delta_{4e} = \delta_{6e}$		2.82	2.84	2.72	2.73
δ_{5e}				2.18	
δ_{5a}		2.23	2.23		
δ_{5}					2.22
$\delta_{1'}$		2.63	2.68	3.23	2.89
$^{2}J_{4a,4e}$		−14.0	−14.2	−14.3	−14.2
$^{3}J_{4a,5a}$	12.4	11.2	10.5		
$^{3}J_{4a,5}$					7.3
$^{3}J_{4a,5e}$	2.4			2.9	
$^{3}J_{4e,5a}$	2.9	2.7	2.8		
$^{3}J_{4e,5}$					2.9
$^{3}J_{4e,5e}$	4.6			4.2	
$^{4}J_{4e,6e}$	1.4	1.3	1.2	1.6	0.9
$^{3}J_{1',5a}$		7.4	7.4		
$^{3}J_{1',5}$					7.5
$^{3}J_{1',5e}$				7.5	

[C(2) at δ = 43.4 and H(2) at δ = 5.23, due to the conformational equilibrium distributing thienyl and benzyl groups between axial and equatorial positions (see above)], and those of *trans*-**4b** [C(2) at δ = 45.1 and H(2) at δ = 5.40] unequivocally correspond to the broad signals in **P4b** at δ = 43.4/45.2 and δ = 5.22/5.41.

The *trans*:*cis* ratio of the phenyl-substituted 1,3-dithiane rings in **P4a**, determined from the integrals of the signals of *trans* C(1′′) at δ = 135.4 and *cis* C(1′′) at δ = 137.2, or *trans* C(4) + *trans* C(6) + *trans* C(5) at δ = 37.3 and *cis* C(4) + *cis* C(6) at δ = 35.6 + *cis* C(1′) at δ = 35.8, gave the average value of 2.9. The *trans*:*cis* ratio of the thienyl-substituted 1,3-dithiane rings in **P4b**, determined from the integrals of the signals of *trans* C(4) + *trans* C(6) + *trans* C(5) at δ = 36.8 and *cis* C(4) + *cis* C(6) at δ = 33.6 + *cis* C(5) at δ = 34.0, gave the value of 1.5 confirmed by a further determination from the integrals of the signals of *trans* H(2) at δ = 5.41 and *cis* H(2) at δ = 5.22 giving the value 1.4.

In order to obtain configurational and compositional information on the obtained copolymer chains, samples of **P1** prepared with monomer molar ratios from 1:1 to 1:19 (monomer **1**:styrene) and polymerisation conversions lower than 10%, were carefully explored by ^{1}H and ^{13}C NMR spectroscopy to determine the reliable integrals of the ^{13}C NMR signals. The narrow signal of C(1^{c}) at δ = 40.3, partially hidden by C(2), and the broad one of C(2^{c}) at δ = 41−47 were in accordance with the expected presence in **P1** of an atactic polystyrene chain.[13] The broad signals of C(4′′) (δ = 143.6) and C(1^{s}) (δ = 145.1) [sufficiently separated from C(4′′)[8] due to the effect of alkyl substitution at the *para* position] confirmed the atacticity of the polymer chain and, on the basis of their relative areas, also afforded a visible indication of the copolymer composition.

In the ^{1}H NMR spectra of **P1** broad isolated signals were observed at δ = 3.89−4.02 due to H(1) + H(3) and δ = 7.39−7.89 due to H(2′′′) + H(3′′′) + H(4′′′). The signal at δ = 3.89−4.02 could be integrated with respect to CH_2Br_2 as internal standard (δ = 4.93) affording a measure of the composition of copolymers obtained from different feeds at low polymerisation conversions. Some preliminary measurements indicated that for low concentrations of **1** in the feed, copolymer and feed have nearly the same composition.

Experimental Section

General: ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX spectrometer at 300 and 75.5 MHz, respectively. Chemical shifts (δ) were referred to TMS as internal standard, *J* values are given in Hz. Routine ^{13}C NMR spectra of the copolymers were acquired at concentrations of about 60 mg/mL in $CDCl_3$ with a digital resolution of approximately 1 Hz/pt using a WALTZ 16 decoupling sequence. Reliable integrals of ^{13}C NMR signals were carried out with copolymer concentrations of about 200 mg/mL using an inverse gated decoupling sequence with a 25 sec delay, applicable to carbon atoms having T_1 values up to 5 sec. ^{1}H NMR spectrum simulations with R-factor values better than 1% were performed with the Bruker WIN-DAISY 3.0 program starting from experimental spectra acquired with at least 0.1 Hz/pt digital resolution. IR spectra were run on a Perkin−Elmer System 2000 FTIR instrument. Mass spectra were obtained with a GC-MS Ion Trap Varian Saturn 2000 instrument (EI mode or CI when indicated; filament current: 10 μA) equipped with a DB-5MS (J&W) capillary column. Flash-chromatography was performed on Merck silica gel (0.040−0.063 mm). Commercial chemicals were from Sigma-Aldrich. Styrene, azo bis-isobutyronitrile (AIBN) and solvents were treated as reported elsewhere.[7] Monomer **1** was prepared according to a previous study.[6] Soluble copolymers **P1**−**P4** were prepared as previously described.[7] **P1** was obtained from solutions of **1** and styrene in dioxane with a nominal molar ratio of the monomers of 1:5, a nominal concentration of 8.5 M and polymerisation conversion higher than 98% unless otherwise stated. For the transformation **P3** → **P4** an excess (1:1.3) of the appropriate aldehyde was used to avoid the presence of unchanged thiol functions and their capping with an excess of acetone.[6,7] 2-Benzyl(1,3-propanediyl)bismethanesulfonate was prepared according to the literature.[14] Figures showing the ^{1}H and ^{13}C NMR spectra of the prepared model compounds and copolymers, and showing the diagnostic signals of the conformational equilibrium in 1,3-dithianes or of the atactic polystyrene chain are provided in the Supplementary Information (see also footnote on the first page of this article).

***S,S′*-2-Benzyl(1,3-propanediyl)bis(thioacetate) (2):** A solution of 2-benzyl(1,3-propanediyl)bis(methanesulfonate)[14] (5.00 g, 15.5 mmol) in dry DMF (15 mL) was added under nitrogen to a stirred solution of potassium thioacetate (4.45 g, 40.0 mmol) in dry DMF (40 mL). The mixture was stirred at 70 °C for 75 min, diluted with water (100 mL) and extracted with diethyl ether. The extracts were washed with water, dried with anhydrous Na_2SO_4 and evaporated under vacuum until complete removal of the solvent. The oily residue was flash-chromatographed using a mixture of petroleum ether (boiling range 40−60 °C)/acetone, 100:3, as eluent to yield **2** (3.83 g, 87%) as a pale yellow oil. $C_{14}H_{18}O_2S_2$ (282.42): calcd. C 59.5, H 6.4, S 22.7; found C 59.6, H 6.5, S 22.6. IR (film): $\tilde{\nu}_{max}$ = 1695vs (C=O), 746 and 701 (phenyl ring) cm^{-1}. MS (CI): *m*/*z* (%) = 283 (6) [M^{+} + 1].

2-Benzyl-1,3-propanedithiol (3): A solution of **2** (0.90 g, 3.2 mmol) in dry THF (15 mL) was treated at 0 °C with LAH (0.32 g, 8.5 mmol). The mixture was allowed to reach room temperature whilst stirring for about 12 h, then it was cooled to 0 °C, treated carefully with deoxygenated 5 M HCl (10 mL) and extracted with CH_2Cl_2. The extracts, after a rapid washing with deoxygenated water, drying with anhydrous Na_2SO_4 and removal of the solvent at reduced pressure, yielded **3** as an oil (0.63 g, 99%), which was not submitted to elemental analysis due to its unpleasant smell. MS (EI): *m/z* (%) = 198 (100) [M^+].

Preparation of the Dithianes *cis*-4a, *trans*-4a, *cis*-4b and *trans*-4b. General Procedure: A solution of **3** in dry $CHCl_3$ was treated with the appropriate carbonyl compound (benzaldehyde for **4a**, 2-thiophenecarboxaldehyde for **4b**) and chlorotrimethylsilane at room temperature (reagent molar ratio 1:1.4:4). The mixture was stirred at the same temperature for about 12 h then it was diluted with CH_2Cl_2, washed with water, 10% NaOH and water again, dried with anhydrous Na_2SO_4 and evaporated under vacuum until complete removal of the solvent. The residue was flash-chromatographed with a mixture of petroleum ether (boiling range 40−60 °C)/benzene, 10:4, as eluent, to afford the expected products. The *cis* isomers of **4a** and **4b** eluted faster than the *trans* ones.

***cis*-5-Benzyl-2-phenyl-1,3-dithiane (*cis*-4a):** Yield 17%. M.p. 115−116 °C (from diethyl ether/hexane). $C_{17}H_{18}S_2$ (286.46): calcd. C 71.3, H 6.3, S 22.4; found C 70.9, H 6.1, S 22.7. MS (EI): *m/z* (%) = 286 (100) [M^+].

***trans*-5-Benzyl-2-phenyl-1,3-dithiane (*trans*-4a):** Yield 42%. M.p. 135−137 °C (from ethanol). $C_{17}H_{18}S_2$ (286.46): calcd. C 71.3, H 6.3, S 22.4; found C 70.9, H 6.2, S 22.7. MS (EI): *m/z* (%) = 286 (100) [M^+].

***cis*-5-Benzyl-2-(2-thienyl)-1,3-dithiane (*cis*-4b):** Yield 27%. M.p. 96−97 °C (from diethyl ether/hexane). $C_{15}H_{16}S_3$ (292.49): calcd. C 61.6, H 5.5, S 32.9; found C 61.2, H 5.3, S 33.2. MS (EI): *m/z* (%) = 292 (100) [M^+].

***trans*-5-Benzyl-2-(2-thienyl)-1,3-dithiane (*trans*-4b):** Yield 46%. M.p. 103−104 °C (from ethanol). $C_{15}H_{16}S_3$ (292.49): calcd. C 61.6, H 5.5, S 32.9, found C 61.4, H 5.4, S 33.8. MS (EI): *m/z* (%) = 292 (100) [M^+].

Acknowledgments

This work was financially supported by Italian MIUR, CNR and University Funds.

---

[1] M. J. Shapiro, J. S. Gounarides, *Prog. Nucl. Magn. Res. Spectrosc.* **1999**, *35*, 153−200.

[2] J. Chin, B. Fell, S. Pochapsky, M. J. Shapiro, J. R. Wareing, *J. Org. Chem.* **1998**, *63*, 1309−1311.

[3] M. J. Shapiro, J. Chin, R. E. Marti, M. A. Jarosinski, *Tetrahedron Lett.* **1997**, *38*, 1333−1336.

[4] R. S. Garigipati, B. Adams, J. L. Adams, S. K. Sarkar, *J. Org. Chem.* **1996**, *61*, 2911−2914.

[5] [5a] S. Chen, K. M. Janda, *J. Am. Chem. Soc.* **1997**, *119*, 8724−8725. [5b] S. Chen, K. M. Janda, *Tetrahedron Lett.* **1998**, *39*, 3943−3946.

[6] V. Bertini, F. Lucchesini, M. Pocci, A. De Munno, *Tetrahedron Lett.* **1998**, *39*, 9263−9266.

[7] V. Bertini, F. Lucchesini, M. Pocci, A. De Munno, *J. Org. Chem.* **2000**, *65*, 4839−4842.

[8] E. Pretsch, T. Clerc, J. Seibl, W. Simon, Tabellen zur Strukturaufklärung Organischer Verbindungen mit Spektroskopischen Methoden, Springer-Verlag, Berlin, **1990**, p. C120−C125.

[9] W. T. Ford, T. Balakrishnan, *Macromolecules* **1981**, *14*, 284−288.

[10] [10a] E. L. Eliel, R. O. Hutchins, *J. Am. Chem. Soc.* **1969**, *91*, 2703−2715. [10b] E. L. Eliel, V. S. Rao, F. G. Riddell, *J. Am. Chem. Soc.* **1976**, *98*, 3583−3590.

[11] Y. Haramoto, H. Kamogawa, *Bull. Chem. Soc. Jpn.* **1985**, *58*, 477−480.

[12] T. Schaefer, J. P. Kunkel, R. W. Schurko, G. M. Bernard, *Can. J. Chem.* **1994**, *72*, 1722−1727.

[13] J. C. Randall, *J. Polymer Sci., Polym. Phys. Ed.* **1975**, *13*, 889−899.

[14] M. S. Newman, G. S. Cohen, R. F. Cunico, L. W. Dauernheim, *J. Org. Chem.* **1973**, *38*, 2760−2763.

Received October 31, 2001
[O01531]