$$Cu(H_2O)_6^{2+} + RNH_2 = Cu(H_2O)_5(RNH_2)^{2+} + H_2O \quad (1)$$

$$Cu(H_2O)_5(RNH_2)^{2+} + RNH_2 = Cu(H_2O)_4(RNH_2)_2^{2+} + H_2O \quad (2)$$

$$Cu(H_2O)_4(RNH_2)_2^{2+} + RNH_2 = Cu(H_2O)_3(RNH_2)_3^{2+} + H_2O \quad (3)$$

$$Cu(H_2O)_3(RNH_2)_3^{2+} + RNH_2 = Cu(H_2O)_2(RNH_2)_4^{2+} + H_2O \quad (4)$$

$$Cu(H_2O)_2(RNH_2)_4^{2+} + RCONHR + OH^- = Cu(H_2O)_2(RNH_2)_3(RCONR)^+ + RNH_2 + H_2O \quad (5)$$

$$Cu(H_2O)_2(RNH_2)_3(RCONR)^+ + RCONHR + OH^- = Cu(H_2O)_2(RNH_2)_2(RCONR)_2 + RNH_2 + H_2O \quad (6)$$

In these equilibria the axial ligands are represented as water molecules although the EPR spectra give no information about the nature of the axial ligands. Steric constraints on the polymer make it unlikely, however, that nitrogen atoms are also present at the axial sites. Our results show Cu(II) to be bound in a tetragonally elongated octahedral geometry in all compounds and not in a square-based pyramidal geometry as has been suggested[8] for the compounds present at pH >10.

The peptide coordination at high pH confers dichroism to the copper d–d band. Although $(Lys)_n$ has an α-helical structure in aqueous solution at high pH, it has been found that Cu(II) destroys this structure,[6] and thus early explanations[2] of the asymmetric oxidation of DOPA cannot be correct. The binding of two peptide nitrogen atoms of the backbone at high pH does, however, confer a high degree of organization upon the $(Lys)_n$ chain which may enable D-DOPA to bind preferentially. It would be of interest to investigate the catalytic specificity of Cu(II) $(D\text{-}Lys)_n$ or $(DL\text{-}Lys)_n$.

At neutral pH, $Cu(Lys)_n$ catalyzes the decomposition of H_2O_2, and it has been suggested[5] that the catalytic site has two replaceable ligands on the Cu(II). Our results are consistent with this structure. Below pH 8 the amine and water ligands are both quite labile and several complexes exist in equilibrium. The sensitivity of the nature of the species present in solution to pH, to the Cu:Lys ratio, and to concentration observed by others are all due to the complexity of the equilibria. Although we have not measured equilibrium constants, it is clear that they are not widely separated in magnitude. This also explains the discrepancy of the NMR results[10,11] with the results of other types of experiment, since the NMR data were obtained at very low Cu:Lys ratios, which shifts the equilibria 5 and 6 to the left, resulting in less peptide coordination.

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Isomerization Reactions in the Polymerization of Alicyclic Dithiols with Aldehydes

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Owing to the conformational wealth of the cyclohexane ring,[1] its incorporation in molecular chains may affect in a significant way the properties of the resulting polymers. Thus the alicyclic polyformal prepared from *trans*-1,4-bis(hydroxymethyl)cyclohexane and paraformaldehyde melts at higher temperature than its aliphatic counterpart. In general, the cis isomers of alicyclic polyesters and polyformals either are amorphous or melt at lower temperatures than the corresponding trans isomers.[2-5]

Isomerization processes in the synthesis of alicyclic polyformals were not detected.[6] In general, the cis/trans composition of the polymers coincides with the cis/trans content of the glycol used in the preparation of the polymers. However, isomerization interconversion in disubstituted cyclohexanes may occur. Thus, although compounds with equatorial substituents have less steric crowding and therefore are more stable than the compounds with corresponding axial substituents, trans–cis interconversion was reported for some disubstituted cyclohexanes. For example, the equilibrium of *cis*- and *trans*-4-*tert*-butylcyclohexanol, obtained by treating either isomer with an aluminum isopropoxide–isopropyl alcohol–acetone mixture, contains four parts of the trans isomer to one part of the cis isomer. It should be pointed out that in all the isomeric interconversions, the trans isomer is predominant. Thus the isomeric interconversion of polyesters containing cyclohexane dicarboxylate groups seems to be the same whether the polymer is prepared from cis or trans isomers.[7] In both cases the cis/trans ratio obtained in the polymers is 0.66.

In the present work the synthesis of alicyclic poly(thioformals) is described. The possibility of cis–trans interconversion in the disubstituted cyclohexanes is studied by ^1H and ^{13}C NMR spectroscopy.

Experimental Part

Materials. Cis/trans mixtures of 1,4-bis(hydroxymethyl)-cyclohexane were used to obtain the corresponding alicyclic dithiols. The cis/trans isomer ratio was determined by ^1H NMR spectroscopy. Thiourea, bromhydric acid, paraformaldehyde, and propionaldehyde were used as received. Benzene and *p*-toluenesulfonic acid were purified by methods described elsewhere.

Synthesis of *cis*/*trans*-1,4-Bis(mercaptomethyl)cyclohexane. The preparation of this product was carried out by reaction of *cis*/*trans*-1,4-bis(bromoethyl)cyclohexane (previously obtained by reaction of the alicyclic glycol with bromhydric acid) and thiourea, followed by hydrolysis of the resulting thiouronium salt.

Polymerization Reactions. Two polymers were obtained by condensation polymerization of *cis*/*trans*-1,4-bis(mercaptomethyl)cyclohexane with paraformaldehyde (polymer A) and propionaldehyde (polymer B). The reactions were carried out

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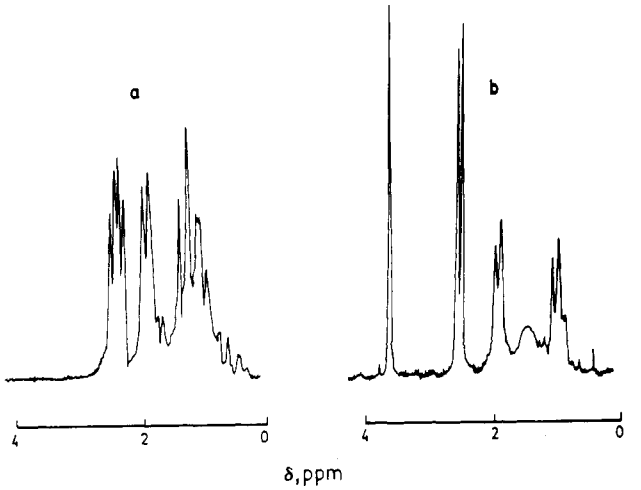


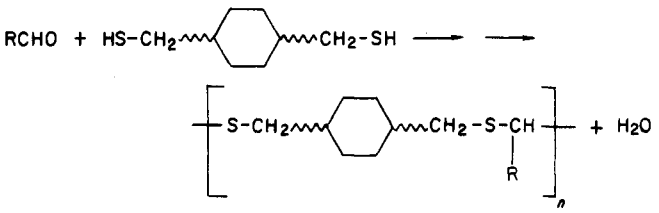
Figure 1. ^1H NMR spectra of *cis/trans*-1,4-bis(mercaptomethyl)cyclohexane (a) and of polymer A (b).

at the temperature of refluxing benzene and under a nitrogen atmosphere in the former case and at room temperature in the latter, using *p*-toluenesulfonic acid (1%) as catalyst and reaction times of 24 h. In the preparation of polymer A the water produced in the polymerization was separated by means of a Dean–Stark distillation trap.

Characterization of the Polymers. ^1H and ^{13}C NMR spectra of the polymers were registered at room temperature with a Bruker WP80SV spectrometer working at 80 and 20.1 MHz, respectively. Both carbon tetrachloride and deuterated chloroform were used as solvents and tetramethylsilane was used as internal standard. The value of the melting point of the crystalline polymer (polymer A), determined in a Tottoli-type Buchi apparatus at a heating rate of 2 °C/min, was found to be 165 °C.

Results and Discussion

The condensation reaction between the alicyclic dithiol and the aldehydes used in this work gives rise to the following global structure:



polymer A, R = H
polymer B, R = C_2H_5

In the case of polymer A, obtained by reaction between the dithiol and paraformaldehyde, both the starting alicyclic dithiol and the polymer were analyzed by ^1H NMR spectroscopy; their spectra are shown in Figure 1. The chemical shifts were assigned by considering the resonance signals that appear in the ^1H NMR spectra of alicyclic diols (cis and trans isomers of 1,4-bis(hydroxymethyl)cyclohexane) used in the synthesis of the corresponding dithiol. The analysis of the spectra clearly shows the differences between them; the starting alicyclic dithiol presents four resonance signals between 2.35 and 2.52 ppm (two doublets) belonging to the external axial (2.52 ppm) and equatorial (2.35 ppm) methylene groups of the cyclohexane ring. The areas of these peaks allow the determination of the ratio in cis/trans units in the dithiol, which was found to be 0.9. In the spectrum of polymer A only two signals appear (doublet at 2.55 ppm) for the resonance of the same methylene protons, suggesting that the configuration of the substituents in the cyclohexane rings of the polymer is 100% cis or 100% trans. On the other hand, in the

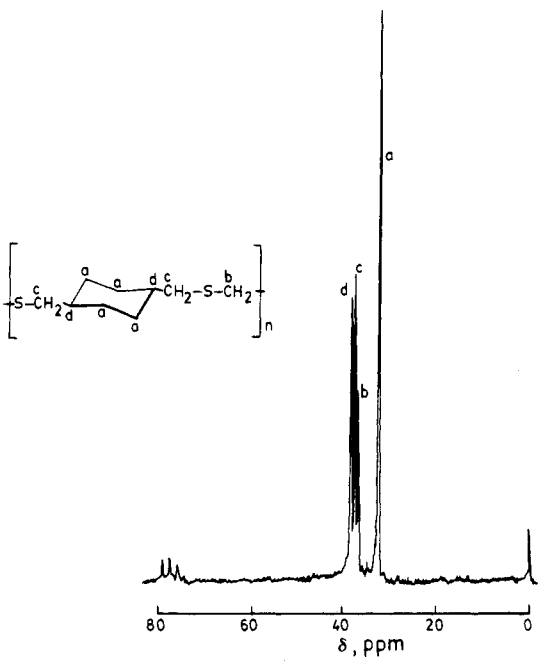


Figure 2. ^{13}C NMR spectrum of polymer A.

spectrum of the poly(thioformal) only the signals corresponding to the equatorial (1.95 ppm) and axial protons (1.05 ppm) of the cyclohexane ring in the 1,4-trans structure appear. The peaks corresponding to the resonance of the protons in the 1,4-cis structure, which should appear at intermediate chemical shifts between the resonances of the axial and equatorial protons as a consequence of the rapid chair–chair interconversion, are absent. All these considerations lead us to conclude that the structure of the alicyclic poly(thioformal) corresponds to that of polymers in which the configuration of the cyclohexane ring is 1,4 trans. This result is surprising since no isomerization reactions occur in the synthesis of polyformals derived from *cis/trans*-1,4-bis(hydroxymethyl)cyclohexane.[6] It should be pointed out, however, that isomerization reactions have been reported in the polymerization of *cis*- and *trans*-1,4-cyclohexanedicarboxylic esters with ethylene glycol.[7]

In order to confirm these results, the ^{13}C NMR spectrum of polymer A, shown in Figure 2, was analyzed. The spectrum presents only four signals, whose assignments to the different carbons are indicated in the same figure. If there were cis and trans stereoisomeric units in the polymer, the methylene substituents in axial and equatorial positions would give rise to a more complex spectrum, like that observed in polyesters derived from sebacic acid and *cis*- or *trans*-1,4-bis(hydroxymethyl)cyclohexane.[4] All these results clearly show that isomerization reactions occur during the condensation polymerization of these alicyclic dithiols and paraformaldehyde.

The possible influence of temperature in the isomerization process was studied by analyzing the spectra of polymers prepared at room temperature with the same mixture of dithiols and propionaldehyde. Due to the high reactivity of the thiol group, these reactions occur at very high rates giving high yields and relatively high molecular weights. ^1H and ^{13}C NMR spectra of this polymer (polymer B) are shown in Figures 3 and 4, respectively. The proton resonance that appears as a doublet centered at 2.60 ppm is attributed to the exocyclic methylene groups in 1,4-trans configuration because of similar reasons indicated in the spectral analysis of polymer A. In the ^{13}C NMR spectrum of polymer B, six signals appear, corresponding

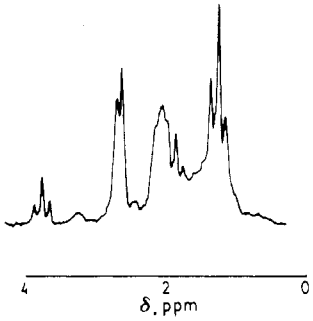


Figure 3. ^{1}H NMR spectrum of polymer B.

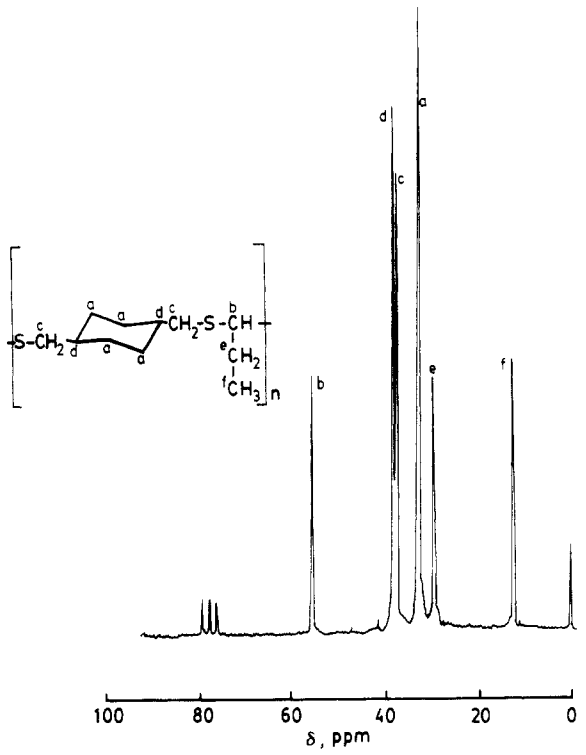


Figure 4. ^{13}C NMR spectrum of polymer B.

to the resonances of the six different carbons of the structural unit with the CH_2 substituents in 1,4-trans configuration. Therefore, isomerization is not apparently influenced by the reaction temperature.

Additional evidence that isomerization reactions take place in the polymerization of *cis*/*trans*-1,4-bis(mercaptomethyl)cyclohexane and paraformaldehyde is that polymer A is a crystalline material whose melting point (165 °C) is similar to that of the polymer obtained from 100% *trans*-1,4-bis(mercaptomethyl)cyclohexane and paraformaldehyde.[8]

Registry No. *cis*-1,4-Bis(bromomethyl)cyclohexane, 15898-77-8; *trans*-1,4-bis(bromomethyl)cyclohexane, 57702-84-8; thiourea, 62-56-6; *cis*-1,4-bis(mercaptomethyl)cyclohexane, 78307-98-9; *trans*-1,4-bis(mercaptomethyl)cyclohexane, 99113-60-7; (*cis*-1,4-bis(mercaptomethyl)cyclohexane)·(*trans*-1,4-bis(mercaptomethyl)cyclohexane)·(formaldehyde) (copolymer), 99559-85-0; (*cis*-1,4-bis(mercaptomethyl)cyclohexane)·(*trans*-1,4-bis(mercaptomethyl)cyclohexane)·(propionaldehyde) (copolymer), 99559-86-1.

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Determination of a Θ-Temperature Using Low-Angle Light Scattering

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The Flory Θ-temperature (T_Θ), where the excluded volume of the chain is just balanced by the attractive interactions and the polymer chain assumes its unperturbed dimensions, must be determined before measurements can be made at Θ conditions. The most common method of determination is extrapolation of cloud point temperatures to infinite molecular weight. Alternatively, the temperature where the second virial coefficient, A_2, vanishes can be determined by light scattering or osmotic measurements:[1]

$$Kc/R_{0,T} = (d\Pi_T/dc)/RT = 1/M + 2A_{2,T}c + 3A_{3,T}c^2 + \ldots \quad (1)$$

Here, c is the concentration, Π is the osmotic pressure, T is the absolute temperature, M is the molecular weight, and K is equal to $4\pi^2n^2(dn/dc)^2/\lambda^4N_A$, where n is the refractive index of the solution, dn/dc is the differential refractive index increment, λ is the wavelength of incident light, and N_A is Avogadro's number. The temperature dependence of n ($dn/dT = 0.00054$ °C^{-1} for cyclohexane in the range of T used here[2]) and dn/dc are considered in the determination of K at a given temperature. The Rayleigh factor (R_θ) measured at scattering angle θ extrapolated to $\theta = 0$ is indicated by R_0, and the temperature dependence of R_0, Π, and A_2 have been explicitly indicated by the subscript T. For polydisperse samples, the molecular weight M will be the weight-average molecular weight, M_w, and the number-average molecular weight, M_n, for light scattering and osmometry, respectively. The Rayleigh factor, R_0, where the subscript zero indicates zero scattering angle, must be determined by extrapolation of R_θ measured at higher scattering angles θ for polymers which are large enough ($>\lambda/20$) to have significant intramolecular interference at $\theta > 0$. The large sample volume used in most classical light scattering instruments increases the time required for equilibration at each temperature for scattering measurements. These constrainsts have made the determination of Θ-temperatures by light scattering time-consuming and subject to errors of extrapolation. We wish to report measurements on poly(α-methylstyrene) in cyclohexane where we have been able to measure the Θ-temperature very quickly using the technique of low-angle light scattering. This technique is more accurate than extrapolation of data from higher scattering angles and allows continuous monitoring of the scattering intensity as the temperature is raised or lowered. The time fluctuation of the scattered light intensity, which increases dramatically as the critical solution temperature is approached, can also be observed and studied simultaneously.

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