

Conformational Analysis of Alkylated Biuret and Triuret: Evidence for Helicity and Helical Inversion in Oligoisocyanates

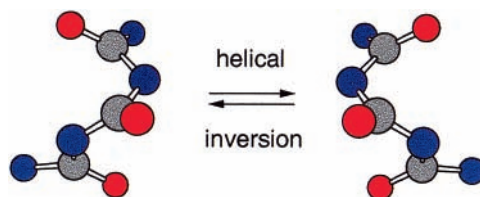
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ABSTRACT



The conformations of several oligoisocyanates have been investigated by NMR in order to study the onset and dynamics of helicity in polyisocyanates. Pentaethylbiuret and hexaethyltriuret were found to adopt turns and helices in solution. For hexaethyltriuret, symmetric and asymmetric helices are present. Not only is an interconversion of these forms observed ($\Delta G_{SA}^\ddagger = 9.3 \pm 0.4$ kcal/mol) but also a reversal of helicity ($\Delta G_{PM}^\ddagger = 9.0 \pm 0.4$ kcal/mol). The coalescence pattern for the latter process provides direct evidence for a concerted, conrotatory helical inversion.

The well-established helicity in polymeric isocyanates arises from a competition between the planarity of amide C–N bonds and the distortions from planarity that result from the steric bulk of the alkyl groups.¹ Studies of polyisocyanates have revealed intriguing cooperative effects linking side chain chirality with the preferred helical sense.^{2,3} In an effort to explore the onset and dynamics of helicity in polyisocyanates, we have studied the preferred conformations of well-defined

oligomers of polyisocyanates: tetraethylurea (**1**), pentaethylbiuret (**2**), and hexaethyltriuret (**3**).⁴ In this Letter we now report NMR data showing that even the short oligoisocyanate biuret and triuret form turns and helices in solution, that the handedness undergoes rapid inversion on the NMR time

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(1) (a) Bur, A. J.; Fetters, L. J. *Chem. Rev.* **1976**, *76*, 727. (b) Cook, R.; Johnson, R. D.; Wade, C. G.; O'Leary, D. J. Muñoz, B. Green, M. M. *Macromolecules* **1990**, *23*, 2223.

(2) (a) Green, M. M.; Andreola, C.; Muñoz, B.; Reidy, M. P.; Zero, K. *J. Amer. Chem. Soc.* **1988**, *110*, 4063. (b) Green, M. M.; Reidy, M. P.; Johnson, R. D.; Darling, G.; O'Leary, D. J.; Willson, C. G. *J. Am. Chem. Soc.* **1989**, *111*, 6452. (c) Lifson, S.; Felder, C. E.; Green, M. M. *Macromolecules* **1992**, *25*, 4142. (d) Green, M. M.; Peterson, N. C.; Sato, T.; Teramoto, A.; Cook, R. Lifson, S. *Science* **1995**, *268*, 1860.

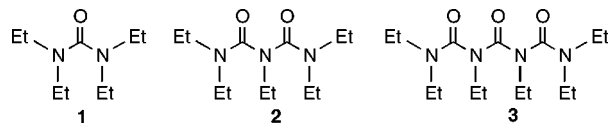
(3) A number of other synthetic polymers also adopt helical structures. (a) Kramer, P. C.; Nolte, R. J. M.; Drenth, W. *J. Am. Chem. Soc.* **1988**, *110*, 6818 (polyisocyanides). (b) Ute, K.; Hirose, K.; Kashimoto, H.; Nakayama, H.; Hatada, K.; Vogl, O. *Polym. J.* **1993**, *25*, 1175 (polychlorals). (c) Okamoto, Y.; Suzuki, K.; Ohta, K.; Hatada, K.; Yuki, H. *J. Am. Chem. Soc.* **1979**, *101*, 4763 (polymethacrylates). (d) Gellman, S. *Acc. Chem. Res.* **1998**, *31*, 173 (poly(β -amino acid) foldamers). (e) Engelkamp, H.; Middlebeek, S.; Nolte, R. J. M. *Science* **1999**, *284*, 785 (self-assemblies with tunable helicity). (f) Yashima, E.; Maeda, K.; Okamoto, Y. *Nature* **1999**, *399*, 449 (memory effects in polyacetylenes). (g) Fujiki, M. *J. Amer. Chem. Soc.* **2000**, *122*, 3336 (chiroptical switching in helical polysilylenes).

(4) Oligomers **2** and **3** were synthesized using established procedures. Details of these syntheses will be described elsewhere.

(5) ΔG_{rot}^\ddagger for neat tetramethylurea is estimated at 6.1 kcal/mol. Stilbs, P.; Moseley, M. E. *J. Magn. Reson.* **1978**, *31*, 55.

(6) Stewart, W. E.; Siddall, T. M. *Chem. Rev.* **1970**, *70*, 517.

scale, and that not one but two distinct mechanisms contribute to this inversion.



The methyl and methylene ^{13}C peaks of tetraethylurea in Freon-21 show no sign of decoalescing even at 150 K, thereby placing an upper bound of 5.3 kcal/mol on the barrier to hindered rotation.⁵ By contrast, the methyl carbons of **2** in THF are well resolved at 164 K in the expected 2:2:1 ratio. As the temperature is increased the EZ methyls broaden and coalesce at about 185 K. A similar pattern is observed for the outer methylene carbons. On the basis of these reporter nuclei, an average ΔG^\ddagger of 9.1 ± 0.1 kcal/mol at 200 K is calculated. Likewise, the hexaethyltriuret **3** shows an averaged barrier of 11.4 ± 0.4 kcal/mol. Thus, the rotational barriers increase across the series **1**, **2**, and **3**. This runs counter to the trend where increasing steric bulk in ureas lowers rotational barriers by destabilization of the planar ground state.⁶ On the basis of our observed increase in barrier heights, we postulate that the biuret and triuret must adopt some conformation that turns around on itself, leading to a mutual hindering of the rotation of the end groups through steric interactions. Alternatively, the terminal amides may be better able to achieve planarity at the expense of the inner amides by twisting about those inner C–N bonds.

Supporting evidence for the turn in biuret **2** comes from the ^1H NMR (Figure 1). The methyl-decoupled methylene hydrogens of **2** at high temperature show two singlets in a ratio of 4:1 corresponding to the outer and inner CH_2 's, respectively. Cooling the sample to 158 K did not give the expected singlet for each of the E, Z, and inner CH_2 's but rather a complicated set of overlapping AB patterns. The observation of diastereotopic hydrogens is consistent with the asymmetry that arises from a turn. Moreover, the coalescence of the AB pattern at higher temperatures implies a loss in diastereotopicity caused by a rapid interconversion of enantiomeric turns. On the basis of line shape analysis of the AB pattern of the inner CH_2 , we estimate an inversion barrier ΔG^\ddagger of 8.2 ± 0.4 kcal/mol at 173 K in THF- d_8 . This barrier is well below the 19.6 kcal/mol barrier recently reported for helix reversal in poly(2-butylhexylisocyanate).⁷ The larger barrier in this polymer may be due to increased chain length or due to substitution at the 2 position which is known to strongly influence the conformational preference of the polymer.^{2a,b}

Since the diastereotopic methylene H's are consistent with any number of conformers (not necessarily helical), modeling studies were undertaken to explore its conformational behavior. A conformational search of **2** was carried out using the Monte Carlo searching algorithm with the Merck molecular force field,⁸ followed by refinement of the energies

(7) Ute, K.; Fukunishi, Y.; Jha, S. K.; Cheon, K.-S.; Munoz, B.; Hatada, K.; Green, M. M. *Macromolecules* **1999**, *32*, 1304.

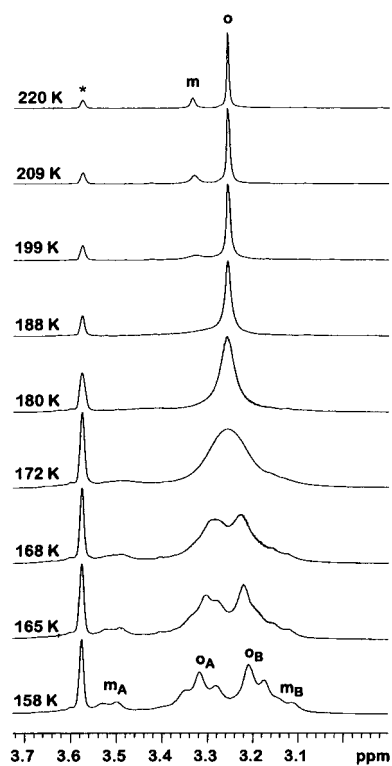


Figure 1. Variable temperature ^1H NMR of the CH_3 -decoupled methylene region of pentaethylbiuret **2** in THF- d_8 at 400 MHz. m = middle methylene hydrogens, o = outer methylene hydrogens, * = residual THF- d_7 .

using Hartree–Fock theory and the 6-31G* basis set. The lowest energy conformer is indeed a C_2 -symmetric turn with both C=O's directed away from the helix axis as in the polyisocyanates. A second, higher energy conformer has one carbonyl pointing “in”. We see no evidence of this C_1 -asymmetric helix in the NMR; either it is present in very small amounts or it is in rapid exchange with the C_2 conformer. Similar computational studies on **3** indicate again that there are two conformers: a lower energy, helical C_2 symmetric conformer and a higher energy, helical C_1 conformer. Surprisingly, the C_2 structure has the two end carbonyls pointing “in”, aligned along the helix backbone, rather than radiating out from the helix axis, as in the polymer. This unexpected conformation presumably arises because oxygen is substantially smaller than diethylamino, thereby minimizing steric interactions along the crowded backbone. In the asymmetric conformer of **3**, one carbonyl points in, while the other two point out. The deviation of the lone pair from perpendicularity at the terminal amide of **3**, as given by the torsional angle $\tau(\text{N}-\text{C}_{\text{sp}^2})$,⁹ is 24° , modestly smaller than the 29° deviations from planarity seen in **1**. This is consistent with the higher barrier observed for rotation in **3**.

(8) SPARTAN Version 5. Wavefunction, Inc. 18401 Von Karman Avenue, Suite 370, Irvine, CA 92612.

(9) This torsional angle is the mean value of two dihedral angles, $\phi_1(\text{O}_1-\text{C}_1-\text{N}_1-\text{C}_2)$ and $\phi_2(\text{N}_2-\text{C}_1-\text{N}_1-\text{C}_3)$. Trautner, F.; Reinemann, S.; Minkwitz, R.; Oberhammer, H. *J. Am. Chem. Soc.* **2000**, *122*, 4193.

In contrast to **2** an asymmetric conformer does appear in the ^{13}C NMR spectra of **3** (Figure 2). At temperatures below

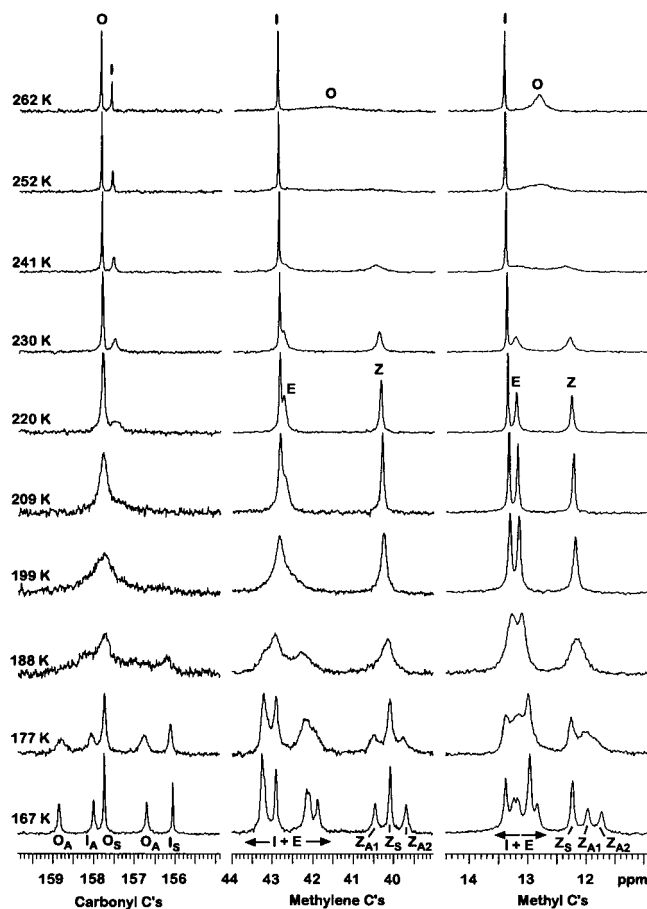


Figure 2. Selected variable temperature 100 MHz ^{13}C NMR spectra of hexaethyltriuret **3** in Freon-21-*d* measured on a Varian INOVA-400. I = inner carbonyl, O = outer carbonyl, S = symmetric conformer, A = asymmetric conformer, E = trans to carbonyl, Z = cis to carbonyl.

220 K each of the eight ^{13}C signals undergoes a complex decoalescence that gives rise to a total of 21 (!) peaks. At 167 K the carbonyl region clearly shows two sharp peaks in a ratio of 2:1, corresponding to the C_2 -symmetric helix, and three broader peaks in a ratio of 1:1:1, corresponding to the asymmetric helix. In THF the C_2 helix is dominant (66%), while in Freon-21 it is slightly disfavored (46%). As the temperature is raised, peaks of the symmetric and asymmetric forms exchange.

To account for the symmetric–asymmetric interconversion (SA) as well as the helical inversion (PM), we propose three mechanisms depicted schematically in Figure 3. A simple rotation of one arm of the helix backbone interconverts the symmetric and asymmetric forms without inverting the helicity ($M_{\text{asym}} \rightleftharpoons M_{\text{sym}}$) via a transition state in which the terminal amides are perpendicular. Inversion of helicity (P \rightleftharpoons M) on the other hand requires rotation of both halves of the helix backbone, and this can be accomplished by two

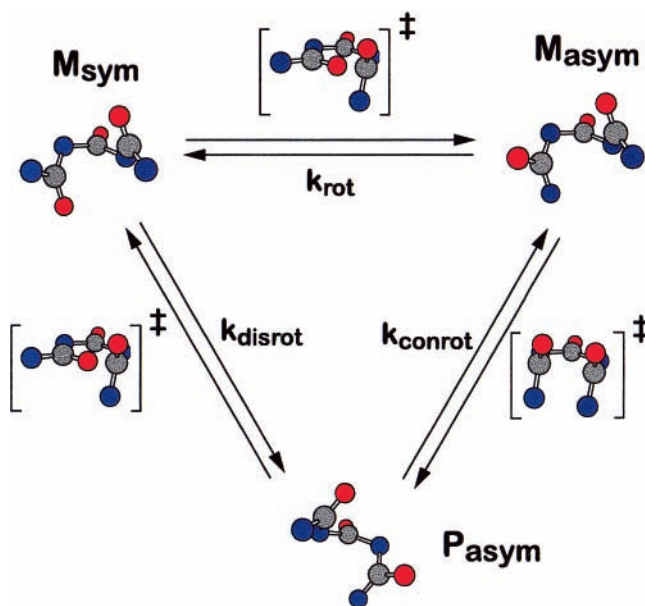


Figure 3. Mechanisms for helical inversion and symmetric–asymmetric interconversion in **3**. For simplicity, pendant ethyl groups are not shown. k_r = rotation of one end group, k_{conrot} = rotation of two end groups in same direction, and k_{disrot} = rotation of two end groups in the opposite direction.

distinct mechanisms. First, a concomitant reversal of helicity and symmetry ($P_{\text{asym}} \rightleftharpoons M_{\text{sym}}$ of Figure 3) can be achieved by a stepwise, disrotatory motion of both end groups and proceeds through a transition state similar to that of the $M_{\text{asym}} \rightleftharpoons M_{\text{sym}}$ interconversion with perpendicular end groups. This is essentially the mechanism observed in the racemization of helicenes.¹⁰ Alternatively, helicity can be inverted while maintaining the asymmetry ($P_{\text{asym}} \rightleftharpoons M_{\text{asym}}$ of Figure 3). In this case a C_s transition state is achieved by a novel concerted, conrotatory twisting of the two halves of the helix backbone.

Evidence for the conrotatory helical inversion is found in the three ^{13}C Z-methyl peaks near 12 ppm (Figure 2). The two diastereotopic methyl carbons of the asymmetric form (Z_{A1} and Z_{A2} of Figure 2) coalesce with each other near 175 K and then with the symmetric carbons (Z_S) at 184 K. Thus, Z_{A1} and Z_{A2} exchange slightly faster with each other than with the symmetric form. On the basis of line shape analysis of the three-site system, we estimate $k_{\text{PM}} = 17 \pm 0.5 \text{ s}^{-1}$ and $k_{\text{SA}} = 38 \pm 2 \text{ s}^{-1}$, corresponding to $\Delta G_{\text{PM}}^\ddagger = 9.1 \pm 0.4$ and $\Delta G_{\text{SA}}^\ddagger = 9.3 \pm 0.4 \text{ kcal/mol}$ at 180 K. The barrier heights for the two processes appear equal within experimental error, but the qualitative line shapes seen in both the methyl and methylene regions clearly differentiate the two processes and show that the helical inversion in the asymmetric form is indeed faster. Z_{A1} and Z_{A2} can exchange indirectly via Z_S , but if that indirect process were fast compared to the direct exchange of Z_{A1} and Z_{A2} , a very

(10) Laarhoven, W. H.; Prinsen, W. J. C. *Top. Curr. Chem.* **1984**, *125*, 63.

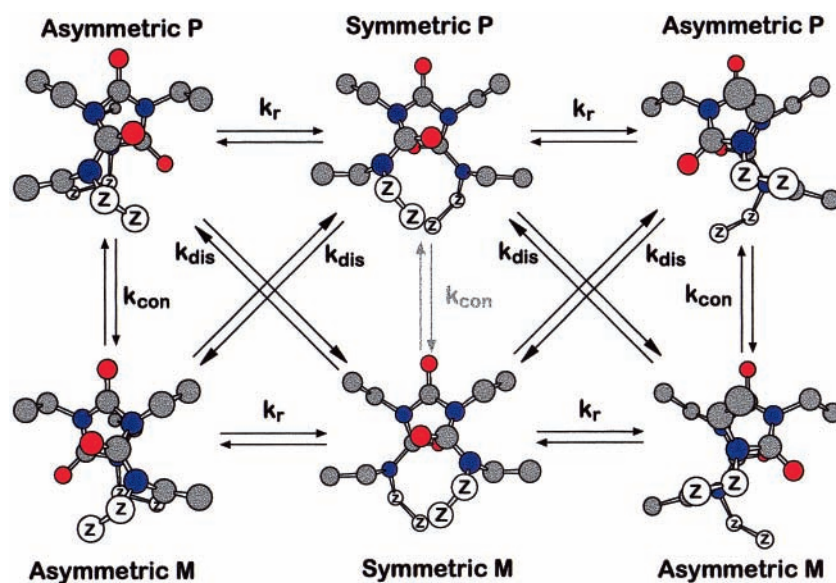


Figure 4. Conformations of hexaethyltriuret. Z carbons are labeled. Labels and arrows in gray correspond to a process not visible in the ^{13}C NMR due to the homotopicity of the reporter nuclei.

different line shape would result, one easily distinguishable from the fast, direct exchange. Figure 4 shows that the concerted, conrotatory interconversion of P_{asym} and M_{asym} directly exchanges $\text{Z}_{\text{A}1}$ and $\text{Z}_{\text{A}2}$ due to a concomitant reorientation of the ethyl group.

The ^{13}C spectra clearly show an exchange between symmetric and asymmetric forms but not whether it proceeds via a simple rotation of one arm ($\text{M}_{\text{asym}} \rightleftharpoons \text{M}_{\text{sym}}$) or a disrotatory motion of both arms ($\text{P}_{\text{asym}} \rightleftharpoons \text{M}_{\text{sym}}$). Because their transition states are probably quite similar, both are likely to contribute to $\text{S} \rightleftharpoons \text{A}$. Furthermore, we propose that the disrotatory mechanism must contribute to the overall helical inversion because the barrier for the symmetric–asymmetric conversion ($\Delta G_{\text{SA}}^\ddagger$), which encompasses the disrotatory mechanism, is so similar to the conrotatory helical inversion ($\Delta G_{\text{PM}}^\ddagger$). Interestingly, the helicity reversal shows remarkably large negative entropies of activation (-13 ± 1 and -17 ± 1 eu for the CH_3 and CH_2 reporter nuclei, respectively), as does the SA interconversion (-16 ± 2 and -18 ± 2 eu), indicating a high degree of organization in the transition states for these processes.

Through NMR and molecular modeling studies we conclude that even very short oligoisocyanates adopt helical conformations in solution. Additionally, we see very complex conformational dynamics in triurets involving interconversion of a symmetric and asymmetric form. We have found evidence supporting the concerted, conrotatory helical inversion and postulate a disrotatory mechanism as well. We plan to study the effect of increased chain length on the helix inversion dynamics and to study the effect of side groups to see which might be “helix-makers” or “helix-breakers”, and these results will be communicated in due course.

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