Notes

Surprising Isomer Effect in Knoevenagel Condensations: Ortho Isomer Yields Polymer and Meta Isomer Yields Cyclomer

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Introduction

Polymers containing asymmetric chromophores are currently of great interest for second-order nonlinear optical applications (NLOP).[1] Mainchain polymers comprised of 4-amino-α-cyanocinnamoyl chromophores prepared via a Knoevenagel condensation and linked in the syndioregic configuration (head to head and tail to tail, see Figure 1) are under investigation in this laboratory for nonlinear optical films.[2,3] Details of the preparation of this type of polymer, in which *o*-xylylene groups link the electron-donating amine ends of chromophore pairs, and 1,2-diamidocyclohexyl groups link the electron-acceptor carbonyl ends of chromophore pairs, have already been reported.[4] (See Figure 1 for the chemical structure)

We have previously explored the effects of the cis and trans isomers of the 1,2-diamidocyclohexyl bridging group (spacing group B, Figure 1) on the properties of the resulting polymers. When comparing polymers at approximately the same molecular weight, the trans-isomer yields a polymer having a 15 °C higher glass transition temperature (T_g), and a lower sub-T_g relaxation rate.[3] Molecular orbital calculations on a *trans*-1,2-diamidocyclohexyl chromophore pair (a model compound) indicate that the diequatorial conformation is 7 kcal/mol lower in energy than the diaxial conformation;[5] this preferred diequatorial conformation is calculated to have a molecular quadratic hyperpolarizability two times greater than the diaxial conformation.

In syndioregic polymers such as these, poling is believed to result in a folding of the polymer chain and alignment of the dipoles. It is thus not necessary to align the entire polymer chain as in isoregic (head to tail) NLO polymers. It was felt that a substitution of *m*-xylylene for *o*-xylylene (spacing group A, Figure 1) might help to increase the final alignment. However, we were surprised to find only 1:1 cyclomer formation and no polymer.

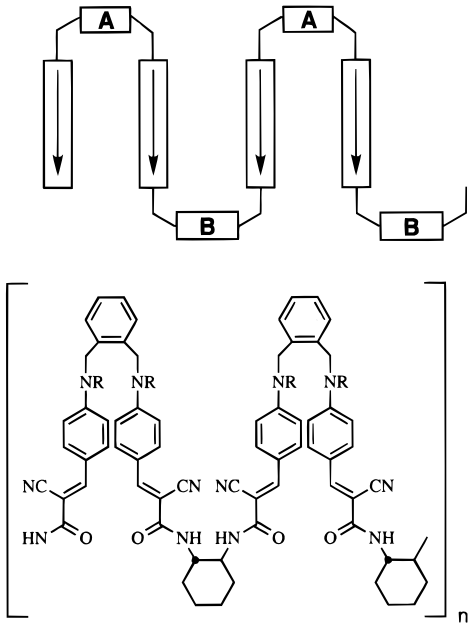

Figure 1. Syndioregic accordion polymer.

Experimental Section

α,α′-Bis(*N*-ethylanilino)-*o*-xylene, α,α′-Bis(*N*-ethyl-4-formylanilino)-*o*-xylene (1, R = Et), and *trans*-1,2-Bis-(cyanoacetamido)cyclohexane (2). These compounds were synthesized by the method described in the literature.[4]

α,α′-Bis(*N*-methylanilino)-*m*-xylene. A 5.00 g amount of α-α′-dichloro-*m*-xylene (29 mmol) was added to a mixture of 6.2 mL of *N*-methylaniline (57 mmol) and 7.9 g of K_2CO_3 (58 mmol) in 100 mL of DMF. The mixture was placed in an oil bath at 90°C and stirred for 48 h. The blue-green mixture was cooled and poured into 300 mL of H_2O and extracted with 2 × 75 mL of CH_2Cl_2. The combined extracts were dried over $MgSO_4$ and concentrated in vacuum to give 9.12 g of a thick blue green oil (99%). This material was used without purification in the following step.

α,α′-Bis(*N*-methyl-4-formylanilino)-*m*-xylene (6, R = Me). A 5.8 mL amount of $POCl_3$ (62 mmol) was added to 200 mL of DMF with cooling (water bath). The solution was then heated to 50 °C briefly and cooled to 5 °C. A solution of 9.12 g of α,α′-*bis*(*N*-methylanilino)-*m*-xylene (29 mmol) in 50 mL of DMF was added dropwise with cooling (ice bath). The cooling bath was removed and the solution stirred for 30 min. The solution was then heated to 70−90°C and stirred for 2 h. The clear green solution was cooled and poured into 500 mL of H_2O. A 40 mL amount of a 4 M aq. NaOH solution was added, and the mixture was extracted with 3 × 75 mL of CH_2Cl_2. The combined extracts were washed with 3 × 600 mL of H_2O and then dried over $MgSO_4$ and concentrated in vacuum to give 9.60 g of an oily green solid (89%) which was recrystallized from 400 mL of abs EtOH to give 5.34 g of light green crystals (49%). Mp 140−142.5 °C. ^{1}H NMR (acetone-d_6): 9.69 (2H), 7.63 (d, 4H), 7.30 (1H), 7.13 (d, 2H), 7.10 (1H), 6.77 (d, 4H), 4.71 (s, 4H), 3.10 (s, 6H); ^{13}C NMR (acetone-d_6): 190.02, 154.35, 139.10, 132.09, 129.62, 126, 125.94, 125.30, 111.97, 55.74, 39.08.

9,20-Dicyano-3,26-dimethyl-10,19-dioxo-3,11,18,26-tetraazapentacyclo[24.3.1.2^{4,7}.2^{22,25}. 0^{12,17}]hexatriaconta-1(31),4,6,8,20,22(35),23,25(36),28(32),29-undecaene (8, R = Me). A 1.36 g amount of α,α′-*bis*(*N*-methyl-4-formylanilino)-*m*-xylene (**6**, R = Me) (3.65 mmol), 0.91 g of *trans*-1,2-*bis*(cyanoacetamido)cyclohexane (**2**) (3.65 mmol), and 1 mL of piperdine were added to 15 mL of dry pyridine and heated to reflux. After 4 h at reflux, a precipitate was observed and 10 mL of chlorobenzene was added. The addition of the chlorobenzene dissolved most of the solid. After 2 days of continued heating, no aldehyde end groups were present as indicated by ^{1}H NMR analysis. The solution was cooled, and 200 mL of methanol was added, precipitating out the product. The solids were filtered and dried to yield 1.2 g (56%). The resulting material was insoluble in chloroform and slightly

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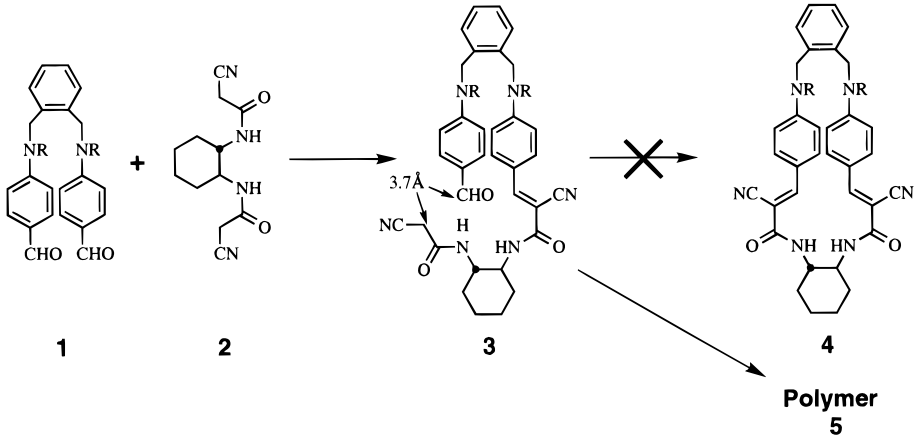
Scheme 1. Synthesis of Ortho-Bridged Polymer



soluble in pyridine (more soluble in hot pyridine). ^{1}H NMR (DMSO-d_6): 7.63 (s, 2H), 7.43 (d, 4H), 7.28 (m, 2H), 7.23 (bm, 2H), 6.58 (d, 4H), 4.65 (dd, 4H), 3.80 (m, 2H), 3.15 (s, 6H), 1.25−1.9 (bm, 8H); ^{13}C NMR (DMSO-d_6): 163.00, 151.45, 150.17, 137.88, 132.13, 128.97, 126.10, 124.29, 118.56, 117.74, 111.65, 97.43, 54.61, 53.85, 31.43, 24.71; MS (*m*/*z*): 584; TGA-(10 °C/min): 5% wt loss at 376 °C.

9,20-Dicyano-3,26-diethyl-10,19-dioxo-3,11,18,26-tetraazapentacyclo[24.3.1.2^{4,7}.2^{22,25}.0^{12,17}]hexatriaconta-1-(31),4,6,8,20,22(35),23,25(36),28(32),29-undecaene (8, R = Et). A 0.50 g amount of α,α′-*bis*(*N*-ethyl-4-formylanilino)-*m*-xylene (**6**, R = Et) (1.23 mmol), 0.31 g of of *trans*-1,2-*bis*(cyanoacetamido)cyclohexane (**2**) (1.24 mmol), and 0.35 g of 4-(dimethylamino)pyridine were added to 15 mL of dry pyridine. After 24 h at reflux, no aldehyde peaks were present according to ^{1}H NMR analysis. The product was precipitated twice into methanol, and the yield was 0.46 g (60%). The product was fairly soluble in chloroform and soluble in pyridine. Mp 164 °C ^{1}H NMR($CDCl_3$): 8.02 (s, 2H), 7.53 (d, 4H), 4.39 (t, 1H), 7.20 (d, 2H), 6.80 (s, 1H), 6.40 (d, 4H), 6.00 (d, 2H), 4.55 (dd, 4H), 4.07 (m, 2H), 3.45 (q, 4H), 2.03 (m, 2H), 1.87 (m), 1.49 (m), 1.22 (t, 6H); ^{13}C NMR ($CDCl_3$): 163.52, 152.64, 150.90, 137.90, 133.32, 129.23, 125.84, 123.06, 119.85, 117.96, 111.13, 95.68, 56.07, 53.40, 45.87, 31.47, 25.17, 12.51; MS (*m*/*z*): 612; TGA(10 °C/min): 5% wt loss at 359 °C.

Results and Discussion

Using the *trans*-1,2-diamidocyclohexyl bridging group, we attempted to make a polymer from the *m*-xylylene dialdehyde (**6**, R = Me, Scheme 2) analogously to the ortho polymer[4]. However, the ^{1}H NMR of this material was quite unusual for a polymer; the lines were very sharp and there was no indication of any aldehyde end groups (which were used to estimate molecular weight in the ortho polymer[4]). In addition, the benzylic protons were now diastereotopic (doublet of doublets in the ^{1}H NMR) which is diagnostic of a constrained conformation. In the ortho polymer the benzylic protons are a broad singlet. We were thus forced into considering the cyclic product (**8**, R = Me). This was confirmed by mass spectroscopy which showed a molecular ion at 584 *m*/*z*. Similarly, only cyclization was observed with the ethyl-substituted dialdehyde (**6**, R = Et).

Surprisingly, the material with the *m*-xylylene bridging group showed no evidence of polymer formation, and the polymer made with the *o*-xylylene bridging group showed no evidence of cyclic products by GPC, NMR, or MS.

Others have also found systems in which there is a clear change in product for what appear to be minor changes in substrate.[6,7] In our efforts to understand this change in behavior we examined both kinetic and thermodynamic possibilities, hoping to find a method of predicting whether or not polymer is formed before the actual synthesis.

It can be safely inferred that the compounds **3** and **7** are intermediates in the condensation reaction between **1** with **2** and **6** with **2**, respectively. It is at this point in the reaction pathway when the paths leading to polymer or cyclomer diverge. If the difference in path-ways is due to a kinetic effect, then the approach of the aldehyde to the methylene carbon in the ortho compound **3** should be retarded in some manner in relation to the corresponding carbon and aldehyde in **7**.

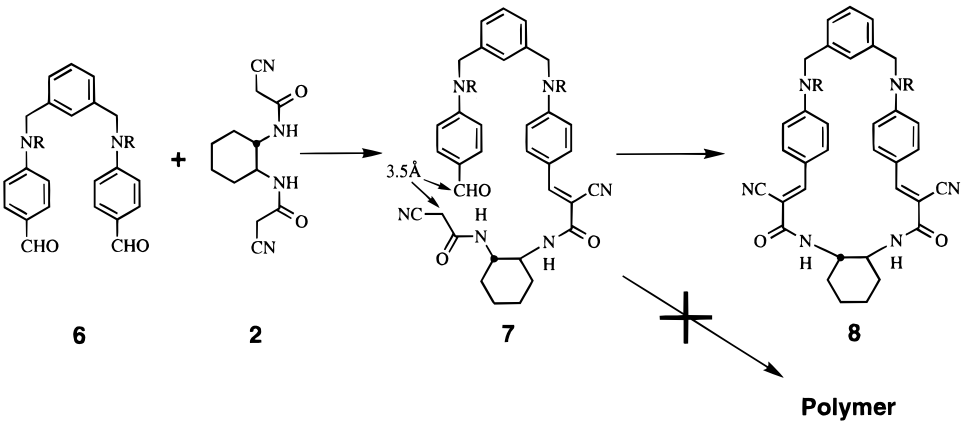
We used the computer program MOPAC[8−10] to examine the conformation space of the two intermediates (**3** and **7**). Due to the size of these molecules, an exhaustive conformational search was not undertaken. In both cases the lowest energy conformation found was approximately linear (**3**: 34.2 kcal/mol and **7**: 41.3 kcal/mol). Both compounds also had a conformation in which the cyanoacetamide methylene carbon approaches the aldehyde carbon. In **3** the energy of this conformation was 39.7 kcal/mol, and the two carbon atoms were 3.7 Å apart. In **7** the energy was 45.0 kcal/mol, and the atoms were 3.5 Å apart. The energy difference between the lowest energy conformation and conformations **3** (ΔH = 5.5 kcal/mol) and **7** (ΔH = 3.7 kcal/mol) is not enough to explain the reaction difference between these two compounds. There appears to be no kinetic reason for the difference in products. We thus turn to thermodynamics for our answer.

The strain energy of a cyclic molecule can be estimated by means of an isodesmic reaction scheme.[11] In this imaginary reaction the kinds and number of bonds on both sides of the scheme are the same (i.e. the number of C−H, N−H, and C=O are conserved). The difference in energy between the two sides is the deviation from simple bond additivity or the strain energy.

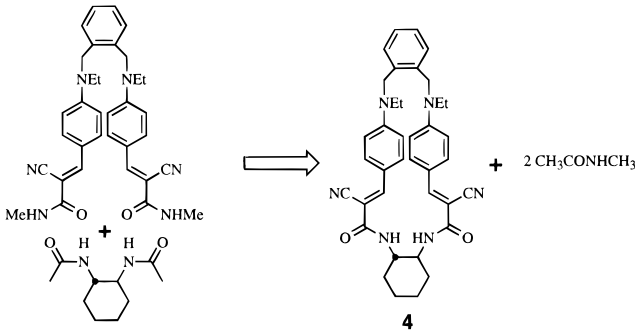
Both cyclic compounds (**4** and **8**) adopted nearly C_{2v} symmetry in their optimized form. The conjugated phenyl rings are approximately parallel with the ortho compound having a considerably larger twist between the phenyl ring and the conjugated double bond.

The strain energy of the cyclomer is ΔH for the reaction $R_n \rightarrow n(R)$ (n is the number of repeat units, ΔH is in kcal/repeat unit). In order to estimate an equilibrium constant we also need to calculate ΔS for the same reaction. The entropy can be divided into internal and translational (rotational) entropies. The internal entropy includes the number of accessible config-

Scheme 2. Synthesis of Meta-Bridged Cyclomer

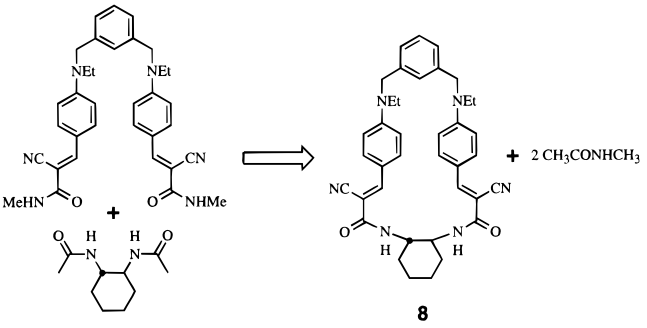


Scheme 3. Isodesmic Reaction Forming Ortho Cyclomer



ΔH = 10.6 kcal/mol

Scheme 4. Isodesmic Reaction Forming Meta Cyclomer



ΔH = 0.6 kcal/mol

urational states and vibrational modes and is negative for all $R_n \rightarrow n(R)$. This is a consequence of the loss of conformational flexibility on going from the chain to the cyclomer. However, it has been shown that the translational contribution to the entropy (due to the change in the number of molecules is positive and close to 29cal/K/mol)[12] is usually much greater than the internal contribution. ΔS for a range of polymer/cyclomer systems generally lay between 10 and 25 cal/K/mol.[13] Taking a value for ΔS of 20 cal/K/mol and the boiling point of pyridine (115 °C), $T\Delta S$ is around 7−8 kcal/mol. A strain energy less than this will favor cyclic products.

The lowest energy conformation for the open chain meta compound was less than 1 kcal/mol lower in energy than the cyclic compound. The cyclic meta compound **8** is essentially strainless and is therefore favored over the polymer. The cyclic ortho compound **4**, however, was found to have a strain energy in excess of 10 kcal/mol. This is larger than the gain in entropy on cyclization (depolymerization) and, therefore, polymer is formed.

Summary

α,α′-(4-Formylanilino)xylenes when linked via a Knoevenagel condensation with a *bis*-cyanoacetamide give polymeric products in the case of *o*-xylene and cyclic products when the xylene is meta. The surprising isomer effect can be explained by the fact that the meta cyclic compound is of similar energy to the open chain polymer. When entropy is considered, the cyclic product is, therefore, favored over the polymer. The ortho cyclic compound is strained relative to the polymer and, therefore, polymer is formed in this case.

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References and Notes

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