the helices and loops indicate very similar amplitudes of motion, while the linker segment and the N- and C-termini have higher flexibility (Figure 2). This general trend is reproduced by the simulations. To simplify comparison, experimental and simulated S^2 values are averaged over secondary structure elements[18] and presented in Table II. Agreement with experiment is better for the all atom model A than for the united atom model U. The modified all atom model N gives lower order parameters than A, but reproduces, contrary to the other two models, the dip in S^2 values for the linker segment. The A and U runs show unconverged correlation functions for some of the residues in this linker segment. Continuation of the A and U simulations would lead to convergence in the correlation functions and better agreement between the experimental and simulated order parameters. Other conceivable causes for the increased mobility in the simulations are that approximations in the potential surface may make it too flat or that the truncation of nonbonded forces may cause an uneven temperature distribution with surplus thermal motion in the amide protons.

In summary, simulation reproduces well the main features of the NMR results, namely, the increased amplitudes of motion for both termini and a few residues around position 43. Thus the MD time scale is sufficient, once equilibration is achieved, to correctly reproduce the fast reorientation dominating ^{15}N relaxation. The order parameters are approximately 10% lower in all three simulations, which is a substantial improvement from the pioneering work by Lipari et al.[6] where the calculated order parameters for ^{13}C–H bonds in methyl groups are on the average 50% *higher* than the experimentally measured values. The difference between experimental and simulation order parameters will also aid the interpretation of simulation data on protein dynamics, and we expect that further refinement of computational methods will eventually bring simulation and experiment into full agreement.

Acknowledgment. J.K. acknowledges a graduate scholarship from the Swedish Natural Science Research Council, and we thank Drs. Walter Chazin and Arthur Palmer for helpful discussions. We are also grateful for a generous allocation of computer time by the Supercomputer Centre North, Skellefteå, Sweden.

Stereochemical Studies of Ziegler–Natta Alkene Insertion through Intramolecular Formation of Dimethylcyclohexanes

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Received August 23, 1991

Recently, we reported the titanium-mediated regioselective[1] and stereoselective[2] formation of five-membered rings, which provided a model for Ziegler–Natta polymerization[3] of 1,5-hexadiene substrates by titanium and zirconium catalysts.[4] Corresponding six-membered-ring formation mediated by early transition metals was first demonstrated by the analogous polymerization of 1,6-heptadiene.[5] This alternating intermolecular/intramolecular insertion of each monomer produced repeating units of 1,3-disubstituted cyclohexane rings bridged by methylene groups. Although studies of related 1,6-heptadiene polymerizations[6] and monomeric intramolecular insertions by Ziegler–Natta catalysts followed,[7] stereochemical features of this ring-forming reaction have not been addressed.

Scheme I.

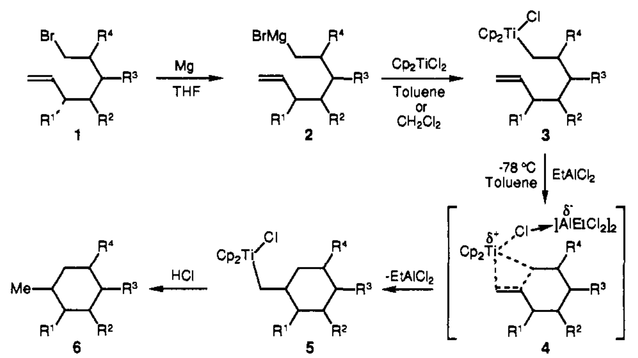

Table I. Substituent Effects on the Stereoselectivity of Ziegler–Natta Ring Formation

substrate	substituents				yield, %^{a}		product ratio
	R^1	R^2	R^3	R^4	**1** to **3**	**3** to **6**	*trans*-**6**:*cis*-**6**
a	H	H	H	H	73	76	
b	Me	H	H	H	b	89^c	99:1
c	H	Me	H	H	82	91	3:97
d	H	H	Me	H	65	63^d	50:50
e	H	H	iPr	H	50	91	23:77
f	H	H	H	Me	97	72	81:19
g	H	H	H	iPr	74^e	88^d	92:8

^{a}All reactions were run on a 2-mmol scale except in the case of **e** (0.6 mmol). Unless otherwise noted, the transformation of **2** to **3** was performed in THF/CH$_2$Cl$_2$ and the reaction of **3** to **6** in toluene. Yields were determined by capillary gas chromatographic analysis (ref 10). ^{b}Could not be accurately determined due to incomplete solubility. ^{c}Reflects the yield from **1** to **6**. ^{d}Reaction performed in CH$_2$Cl$_2$. ^{e}Reaction performed in toluene.

With the use of substrates **b** through **g**, the stereochemical selectivity of dialkyl-substituted cyclohexane formation has been determined. Grignard formation from **1** followed by transmetalation of the alkenyl ligand to titanium produced **3** (Scheme I).[8] The reaction mixture was then evaporated to an oil and extracted from the magnesium salts with a toluene/hexane mixture to produce a solution of **3**[9] in 65–97% yield.[10] Although five-membered-ring formation was promoted with as little as 0.5 equiv of EtAlCl$_2$,[2] cyclohexane formation required 1.75–2.25 equiv of EtAlCl$_2$ to reach >97% conversion to **5** within 4–6 h at -78 °C.[11] Under these Ziegler–Natta conditions, titanium catalysts interact

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(8) Prepared by previously reported procedures.[1,2] During typical formation of **3** from **1**, ligand cyclization (**5**) did not exceed 4% of the product mixture.

(9) Compound **3** was a stable, isolable mixture of the Ti–Cl and Ti–Br species resulting from halide exchange with ClMgBr.

(10) Product distribution and yields for these volatile compounds were determined by capillary gas chromatographic analysis of the quenched reaction mixture (HCl/Et$_2$O) using internal standards and correcting for detector response.

(11) Polymerization by Cp$_2$TiEtCl/EtAlCl$_2$ was found to be second order in aluminum cocatalyst: Waters, J. A.; Mortimer, G. A. *J. Polym. Sci., Polym. Chem. Ed.* **1972**, *10*, 895.

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with the Lewis acid cocatalyst and develop extensive positive charge at the metal center. Ligand cyclization of **3a**, followed by protonolysis, produced **6a** in 76% yield with complete regioselectivity, as evidenced by the absence of cycloheptane (Table I).[10] Methyl substitution on the tether at the allylic (**b**) or homoallylic (**c**) position gave high yields of dimethylcyclohexane products with 99:1 and 3:97 trans:cis selectivity, respectively. Although the cyclization of **3d** to **6d** did not result in product selectivity (50:50), further increase in the size of the tether substituent (**3e**) produced a 23:77 trans:cis ratio of products **5e**.

The cyclization of substrate **3f**, analogous in substitution pattern to the α, β, and γ carbons of a Ziegler–Natta catalyst with a growing polypropylene chain, differed from those substrates having R^4 = H. Although a trans:cis selectivity of 81:19 was observed, the generation of 3-methyl-1-methylenecyclohexane (**7**), resulting from β-hydride elimination of **5f**, occurred to an extent of 9%. Formation of **7** occurred exclusively from *trans*-**5f**, the product requiring one axial substituent on the cyclohexane ring. Warming the reaction mixture to 0 °C prior to quenching produced a decrease in the amount of *trans*-**6f** and no change in the quantity of *cis*-**6f**. Further, generation of a 3:97 trans:cis mixture of **5c** (**5c** = **5f**) did not produce detectable amounts of **7**. Formation of this common intermediate (**5c**/**f**) from two different substrates (**3c**/**3f**) to give opposite trans:cis preferences demonstrated that alkene insertion was not reversible under these reaction conditions.

With the use of a β-isopropyl substituent, analysis of the cyclization process became more complex. Although Grignard formation from **1g** produced **2g** with only 4% cyclization, subsequent treatment with Cp_2TiCl_2 produced an 83:6:11 ratio of **3g**:*trans*-**5g**:*cis*-**5g**. This unavoidable 17% conversion to cyclic products during transmetalation differed significantly from the 2–4% observed for all other substrates.[12] Treatment of this mixture with $EtAlCl_2$ produced 98% conversion to a 70:19 mixture of *trans*-**6g**:*cis*-**6g**. As was found for **3f**, 9% of the β-hydride elimination product was generated as well. Correcting for the amount of **5** generated prior to the addition of $EtAlCl_2$, the trans selectivity of the ring-forming process promoted by $EtAlCl_2$ was 92:8. The product ratio obtained during transmetalation (6:11), as a result of insertion promoted by MgX_2, was opposite and less selective than that observed for the cyclization promoted by $EtAlCl_2$ (92:8).

In addition to the efficient six-membered-ring formation of unactivated alkenes with sp^3-hybridized carbons,[13] these studies have provided insight into the titanocene-mediated Ziegler–Natta polymerization process through the analysis of monomeric products. As evident from the cyclization of **3d**, a methyl substituent appeared to have little effect on the transition state during the syn coplanar alkene insertion due to the conformational flexibility allowed by the tether. Stereoselectivity observed for the intramolecular insertion of **3b**, **3c**, and **3d** paralleled the intermolecular polymerization of either racemic or optically active α-olefins.[14] In these studies, a high degree of stereoelection was demonstrated through predominant polymerization of similar antipodes of 3-methyl-1-pentene and 4-methyl-1-hexene, while 5-methyl-1-heptene produced low alkene facial selectivity. Conformational control did play a role in the intramolecular insertion of **3f** resulting from β-substituent interaction with the active catalyst species. The resulting 81:19 *trans*-**5f**:*cis*-**5f** product ratio implies that the stereochemical microstructure of poly(1,6-heptadiene) produced by Ziegler–Natta catalysts and alkylaluminum cocatalysts is predominantly trans. The stereoselectivity obtained for formation of poly(1,6-heptadiene) should be much less than that obtained for poly(1,5-hexadiene),[2,4] but could be significantly influenced by the nature of the Lewis acid cocatalyst. This dependence of the resulting stereoselectivity on the Lewis acid cocatalyst ($EtAlCl_2$ or MgX_2) suggests an intimate catalyst–cocatalyst interaction rather than simple generation of a $[Cp_2TiR^+]$ species. Further investigation into the role of the cocatalyst on the chain-end control of propylene polymerization is currently underway.

Acknowledgment. We are grateful to the donors of the Petroleum Research Fund, administered by the American Chemical Society, to the National Institutes of Health (GM44163), and to Michigan State University for support of this research.

Registry No. 1a, 4117-09-3; **1b**, 140661-05-8; **1c**, 140661-06-9; **1d**, 140661-07-0; **1e**, 140661-08-1; **1f**, 140661-09-2; **1g**, 140661-10-5; **3a**, 96228-19-2; **3b**, 140661-11-6; **3c**, 140661-12-7; **3d**, 140661-13-8; **3e**, 140661-14-9; **3f**, 140661-15-0; **3g**, 140661-16-1; **5a**, 96228-21-6; **5b**, 140661-17-2; **5c**, 140661-18-3; *trans*-**5d**, 140661-19-4; *cis*-**5d**, 140661-20-7; *trans*-**5e**, 140661-21-8; *cis*-**5e**, 140661-22-9; *trans*-**5g**, 140661-23-0; *cis*-**5g**, 140661-24-1; **6a**, 108-87-2; **6b**, 6876-23-9; **6c**, 638-04-0; *trans*-**6d**, 2207-04-7; *cis*-**6d**, 624-29-3; *trans*-**6e**, 1678-82-6; *cis*-**6e**, 6069-98-3; *cis*-**6f**, 638-04-0; *trans*-**6g**, 17066-66-9; *cis*-**6g**, 17066-65-8; **7**, 3101-50-6.

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[12] In the case of substrate **g**, intramolecular insertion could not be avoided during the transmetalation step using either toluene (7–17% **5g**) or CH_2Cl_2 (32% **5g**), and when allowed to proceed, cyclization has reached >90% conversion to **5** when R^4 = alkyl (1:2 ratio of *trans*-**5**:*cis*-**5**). Coincidently, free radical cyclization of **1g** (0.05 M/nBu$_3$SnH/AIBN/PhH/80 °C) produced 31% conversion to cyclic products composed of the same 10:20 ratio of *trans*-**6g**:*cis*-**6g**.

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^{13}C NMR Spectroscopic Determination of the Magnitude of the β-Silyl Stabilization Effect in 1-Mesitylvinyl Cations

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Received March 2, 1992

Computational and experimental evidence demonstrates the stabilizing effect of β-silyl groups in carbocations.[1] The hyperconjugational origin of the effect leads to a pronounced dihedral dependence and bond angle distortions. This has recently been proven by dynamic ^{13}C NMR spectroscopy and by IGLO calculations of chemical shifts.[2,3]

Vinyl cations are especially well suited to study β-hyperconjugation. The $C^+{=}C_\beta$ bond is shorter than a single bond, and the σ bond of a β-substituent to C_β is in the plane of the "vacant" 2p orbital on C^+, thus allowing maximum overlap for hyperconjugation. 1-Arylvinyl cations, first postulated in 1964,[4] have been rather elusive toward NMR spectroscopic observation. Heterolytic cleavage of sp^2-C–halogen bonds in 1-arylvinyl halides[5] as well as protonation of alkynes,[6] except for 1-ferrocenylalkynes,[7] has

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[3] (a) In contrast to our findings[2] in a recent study[3b] of 1-adamantyl-2-(trimethylsilyl)allyl cation, no stabilization but some destabilizing influence of a β-silyl substituent was inferred from ^{13}C-NMR data. This is due to the orthogonal alignment of the β-C–Si bond and the "vacant" 2p orbital on C^+ and to steric perturbation of allyl resonance in this cation. (b) Prakash, G. K. S.; Reddy, V. P.; Rasul, G.; Casanova, J.; Olah, G. A. *J. Am. Chem. Soc.* **1992**, *114*, 3076.

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