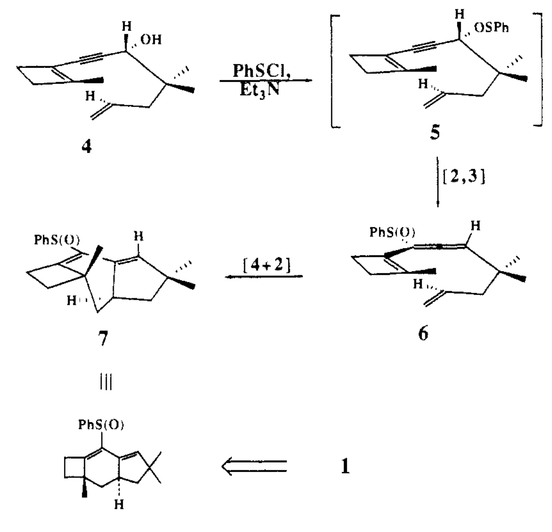
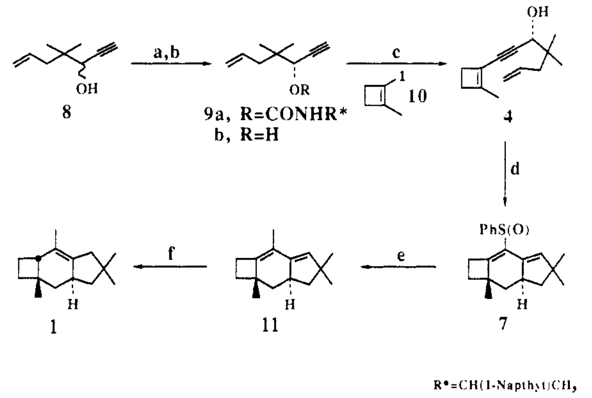
Scheme II



Scheme III



(a) (*S*)-(+)-1-(1-naphthyl)ethyl isocyanate, $Me_2NCH_2CH_2OH$, PhH, reflux, 48 h (81%). (b) $HSiCl_3$, Et_3N, PhH, room temperature, 48 h (76%). (c) **10**, $Pd(PPh_3)_2Cl_2$, CuI, Et_2NH, room temperature, 6 h (77%). (d) PhSCl, Et_3N, CH_2Cl_2, -78 °C, 2 h; room temperature, 38 h (70%). (e) MeMgBr, Ni(dppp)Cl_2, THF, reflux, 18 h (62%). (f) Na/NH_3, *t*-BuOH, -78 °C, 3 h (69%).

(+)-sterpurene, identical by high-field ^1H NMR with the natural product. The observed optical rotation, $[\alpha]_D$ +64.9 (*c* 1.54, $CHCl_3$), was identical within experimental error with that of natural sterpurene, $[\alpha]_D$ +65.3 (*c* 0.87, $CHCl_3$),[20] thus demonstrating that the central-axial-central chiral element transfer process, including the intramolecular Diels-Alder reaction, proceeded with complete enantio- and diastereoselectivity and also that the absolute stereochemistry of (+)-sterpurene is that which is shown.[21]

Acknowledgment. This study was supported by NSF Grant CHE-8518801. R. G. acknowledges receipt of a Chancellor's Patent Fund grant from UC Riverside for partial support. We are very grateful to Professor W. A. Ayer for providing the optical rotation of sterpurene and to Dr. C. Abell for informing us of his results prior to publication. We also thank Professor R. D. Little and Professor E.-I. Negishi for providing us with additional experimental details. Finally, we thank Dr. K. Bartels for performing preliminary experiments in this area.

Supplementary Material Available: Spectral data for selected compounds (3 pages). Ordering information is given on any current masthead page.

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(20) Ayer, W. A., personal communication.

(21) While this work was being carried out, Dr. C. Abell (Cambridge University) informed us that the absolute configuration of 7,12-dihydroxysterpurene is the same as we have determined for sterpurene itself.

Macromolecular Stereochemistry: A Cooperative Deuterium Isotope Effect Leading to a Large Optical Rotation

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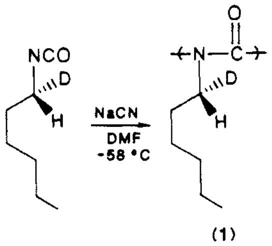
Poly((*R*)-1-deuterio-*n*-hexyl isocyanate) (**1**),[1-3] a macromolecule configurationally chiral only by virtue of deuterium substitution, exhibits a surprisingly high[4] D-line specific rotation of −367° in dilute solution in chloroform at 25 °C.



(1)

The source of the optical activity for **1** can be traced, by inspection of the ultraviolet and circular dichroism spectra exhibited in Figure 1, to electronic absorption bands associated with the recurring amide group backbone structure.[5] This is confirmed by comparison of these spectral characteristics for **1** (Figure 1) with those of poly((*R*)-2,6-dimethylheptyl isocyanate) (**2**)[6] ($[\alpha]^{21}_D$

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(1) Prepared from (*R*)-1-deuterio-*n*-hexyl isocyanate (see ref 2 below) by anionic polymerization following: Shashoua, V. E.; Sweeny, W.; Tietz, R. F. *J. Am. Chem. Soc.* **1960**, *82*, 866.

(2) The precursor (*R*)-1-deuterio-*n*-hexylamine preparation parallels: Streitweiser, A., Jr.; Schaeffer, W. D. *J. Am. Chem. Soc.* **1956**, *78*, 5597. Streitweiser, A., Jr.; Wolfe, J. R. *J. Org. Chem.* **1963**, *28*, 3263. Deuterium coupling in the ^{13}C NMR specified the isotopic site at C-1. The isocyanate was prepared following: Farlow, M. W. *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. IV, p 521.

(3) The Fourier transform infrared spectra of cast films of **1** and poly(*n*-hexyl isocyanate), with the exception of the carbon-deuterium stretching mode at 2221 cm^{-1} were identical from 4000 to 1500 cm^{-1}. Weight average molecular weight of **1**, M_w, determined by low angle light scattering, 870 000; radius of gyration $\langle R_G^2\rangle^{1/2}$: 1680 Å in tetrahydrofuran (THF). Intrinsic viscosity of **1** $[\eta]$, uncorrected for shear, 37 dlg^{-1} (THF). Polydispersity estimated by gel permeation chromatography on three Ultrastyragel columns (100 Å, 10^3 Å, 10^5 Å) with a universal calibration curve, M_w/M_n = 1.27. See: Yau et al. (Yau, W. W.; Kirkland, J. J.; Bly, D. D. *Modern Size Exclusion Liquid Chromatography*; Wiley-Interscience: New York, 1979) for explanations of these terms.

(4) For early literature in the area of optically active isotopically substituted molecules, see: Loewus, F. A.; Westheimer, F. H.; Vennesland, B. *J. Am. Chem. Soc.* **1953**, *75*, 5018. Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1953**, *75*, 5014. Levy, H. R.; Loewus, F. A.; Vennesland, B. *J. Am. Chem. Soc.* **1957**, *79*, 2949. Althouse, V. E.; Feigl, D. M.; Sanderson, W. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1966**, *88*, 3595. For reviews, see: Arigoni, D.; Eliel, E. L. In *Topics in Stereochemistry*; Wiley: 1969; Vol. 4, p 127ff. Verbit, L. In *Progress in Physical Organic Chemistry*; Wiley-Interscience: 1970; Vol. 7, p 51ff; Barth, G.; Djerassi, C. *Tetrahedron* **1981**, *37*, 4123.

(5) Troxell, T. C.; Scheraga, H. A. *Macromolecules* **1971**, *4*, 528. Milstein, J. B.; Charney, E. *Macromolecules* **1969**, *2*, 678.

(6) The monomeric isocyanate was obtained from the carboxylic acid following Kaiser and Weinstock (Kaiser, C.; Weinstock, J. *Org. Synth.* **1971**, *51*, 48). The acid was prepared via hydrogenation of citronellic acid obtained from (*R*)-(+)-pulegone. See: Lukěs, R.; Zobácŏvá, A.; Plešek, J. *Croat. Chem. Acta* **1957**, *29*, 201. Plešek, J. *Chem. Listy.* **1956**, *50*, 1854. Chan, K. K.; Cohen, N.; DeNoble, J. P.; Specian, A. C., Jr.; Saucy, G. *J. Org. Chem.* **1976**, *41*, 3497. Elemental analysis for **2** calcd C, 70.96; H, 11.31; N, 8.27. Found: C, 70.99; H, 11.83; N, 8.21. The enantiomeric excess of the starting (*R*)-(+)-pulegone is 92–94% based on the observed optical rotation. See: Valentine, D., Jr.; Chan, K. K.; Scott, C. G.; Johnson, K. K.; Toth, K.; Saucy, G. *J. Org. Chem.* **1976**, *41*, 62. $[\alpha]_D$ = 8.4° (neat, 1 = 1) for the derived (*R*)-(+)-citronellic acid. The intrinsic viscosity and weight average molecular weight of **2** were $[\eta]$ = 9.5 dlg^{-1} in $CHCl_3$ and M_w = 300 000 in $CHCl_3$, respectively. Radius of gyration $\langle R_G^2\rangle^{1/2}$ in $CHCl_3$ was 540 Å.

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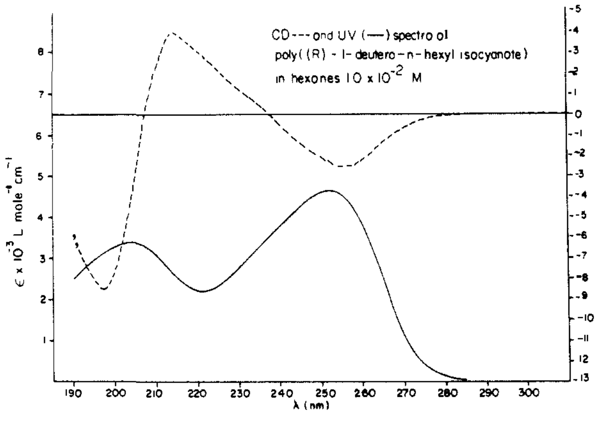


Figure 1.

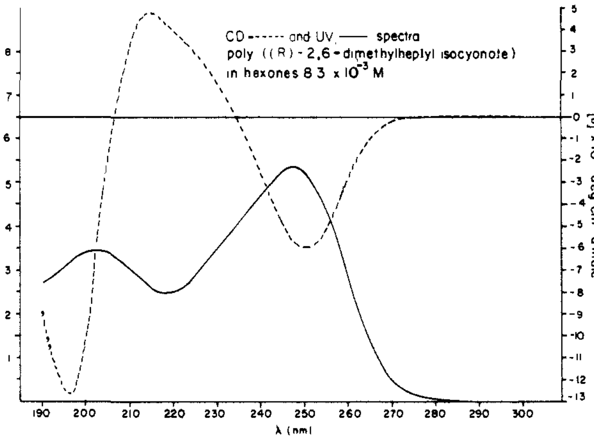
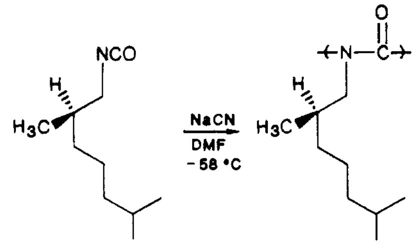


Figure 2.

−485° (CHCl$_3$)) presented in Figure 2 and as well by the literature of various optically active polyisocyanates,[7,8] which shows analogous circular dichroic activity for the higher wavelength band (Figures 1 and 2).



(**2**)

Poly(*n*-alkyl isocyanates) are well known to adopt stiff helical conformations in solution.[9] This fact suggests that the optical activity associated with the backbone chromophore in **1** and **2** may arise from an excess of one of the helical senses[10] now cast into diastereomeric states as a consequence of the chiral stereogenicity of the pendant groups. This interpretation is supported by the large negative increase in D-line optical rotation on formation of the polyisocyanates **1** and **2**[11] and the same-signed exciton-like couplet clearly associated with the higher energy absorption maximum in both polymers (Figures 1 and 2).[12]

Consistent with the higher optical activity of **2** compared to **1**, we have found a strong temperature dependence of the $[\alpha]_D$ of **1** but not of **2** suggesting that the helix excess is smaller in **1** than in **2**. Thus at approximately 47 °C the $[\alpha]_D$ for **1** and **2** are −258° and −480°, while the values at 10 °C are −450° and −498°, respectively. All values, highly reproducible, were determined in dilute solution in chloroform and were rapidly and fully reversible.[13]

Although the high optical activity seen for **1** is certainly unusual, the real importance of this work lies in the surprising influence of the isotope on the ratio of the helical senses. We have determined that the ultraviolet spectra of **1** and of identically prepared but optically inactive poly(*n*-hexyl isocyanate) are exactly the same over their accessible absorption region in hexane (290–190 nm) demonstrating that the isotope causes no detectable structural or conformational perturbation outside of influencing the helix sense. This influence is a conformational equilibrium isotope effect and in contrast to primary kinetic isotope effects[14] is not expected to involve a large energy difference per deuterium.[15] It is therefore impossible to understand the influence of the isotope on the helix sense excess in **1** required by the data above, without considering cooperation among many residues of the polymer chain. Such a cooperative mechanism can be understood by considering the conformational characteristics of poly(*n*-alkyl isocyanates).

Poly(*n*-butyl isocyanate) forms an 8/3 helix with a pitch of 5.14 Å in the solid crystal,[16] and this structure is also close to the minimum energy conformation predicted by force field calculations for poly(*n*-alkyl isocyanates).[17] On the basis of much evidence, this helix is considered to persist in the dissolved state[9] where the dimensional characteristics[18] have been hypothesized to arise from torsional motions in combination with occasional helix reversals.[19] In such a model where at least several hundred residues are proposed[19] to follow each other in a single helical sense sequence, one can understand an excess of one helical sense among these sequences by an energy difference arising from the excess energy

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[7] Goodman, M.; Chen, S. *Macromolecules* **1970**, *3*, 398; **1971**, *4*, 625.

[8] Green, M. M.; Gross, R. A.; Cook, R.; Schilling, F. C. *Macromolecules* **1987**, *20*, 2636. Green, M. M.; Gross, R. A.; Crosby, III, C.; Schilling, F. C. *Macromolecules* **1987**, *20*, 992.

[9] A critical review is as follows: Bur, A.; Fetters, L. J. *Chem. Rev.* **1976**, *76*, 727. See, also: Berger, M. N.; Tidswell, B. M. *J. Polym. Sci. Polym. Symp.* **1973**, *No. 42*, 1063.

[10] The helix sense in excess in **1** and **2** could be known by a theoretical analysis of the circular dichroism spectra which is underway by Professor R. Woody and Dr. T. Cooper in the Department of Biochemistry, Colorado State University.

[11] See: Morawetz, H. *Macromolecules in Solution*; 2nd ed.; Wiley-Interscience: New York, 1975; p 242ff. Selegny (*Optically Active Polymers*; Selegny, E., Ed.; Reidel: Boston, 1979) gives many examples of this phenomenon in vinyl polymers. See especially the article by Selegny and Merle-Aubry (Selegny, E.; Merle-Aubry, L. p 15ff). Farina, M. In *Topics in Stereochemistry*; Eliel, E. L., Wilen, S. H., Eds.; 1987; Vol. 17, pp 1ff, 77, and 78, and references therein in particular.

[12] For a general discussion of the circular dichroism characteristics of polymers, see: Sears, D. W.; Beychok, S. *Physical Properties and Techniques of Protein Chemistry*; Leach, S. J., Ed.; Academic Press: New York, 1973; Chapter 23, Part C, p 446ff. Tinoco, I., Jr. In *Optically Active Polymers*; Selegny, E., Ed.; Reidel: Boston, 1979; pp 1–13. See, also: *Circular Dichroic Spectroscopy, Exciton Coupling in Organic Stereochemistry*; Harada, N., Nakanishi, K., Eds.; University Science Books: Mill Valley, CA, 1983; references to Chapter 1 therein.

[13] Thermal dependence of electronic spectral characteristics are also found in other conjugated polymers. See: Miller, R. D.; Hofer, D.; Rabolt, J.; Fickes, G. N. *J. Am. Chem. Soc.* **1985**, *107*, 2172. Miller, R. D.; Farmer, B. L.; Fleming, W.; Sooriyakumaran, R.; Rabolt, J. *J. Am. Chem. Soc.* **1987**, *109*, 2509.

[14] For a recent paper in this area and leading references, see: Green, M. M.; Boyle, B. A.; Vairamani, M.; Mukhopadhyay, T.; Saunders, W. H., Jr.; Bowen, P.; Allinger, N. L. *J. Am. Chem. Soc.* **1986**, *108*, 2381.

[15] Anet, F. A. L.; Kopelevich, M. *J. Am. Chem. Soc.* **1986**, *108*, 1355, 2109. Anet, F. A. L.; Kopelevich, M. *J. Chem. Soc., Chem. Commun.* **1987**, 595. Servis, K. L.; Domenick, R. L.; Forsyth, D. A.; Pan, Yi. *J. Am. Chem. Soc.* **1987**, *109*, 7263. Forsyth, D. A.; Botkin, J. H.; Puckace, J. S.; Servis, K. L.; Domenick, R. L. *J. Am. Chem. Soc.* **1987**, *109*, 7270. Forsyth, D. A.; Hanley, J. A. *J. Am. Chem. Soc.* **1987**, *109*, 7930. For a review of the earlier literature, see: Melander, L.; Saunders, W. H., Jr. *Reaction Rates of Isotopic Molecules*; Wiley-Interscience: New York, 1980; pp 189–201.

[16] Shmueli, K.; Traub, W.; Rosenheck, K. *J. Polym. Sci. Part A-2* **1969**, *7*, 515.

[17] See ref 5 above and Tonelli (Tonelli, A. *Macromolecules* **1974**, *7*, 628).

[18] *Molecular Motion in High Polymers*, Bailey, R. T., North, A. M., Pethrick, R. A., Eds.; Clarendon Press: Oxford, 1981; pp 67 and 203 and references therein.

[19] See ref 5, 9, and 17 above and the following: Cook, R. *Macromolecules* **1987**, *20*, 1961. Bur, A. J.; Roberts, D. E. *J. Chem. Phys.* **1969**, *51*, 406.

per residue for one of the helical senses multiplied by the number of residues in the sequence. By this amplification mechanism, very small energy differences per residue can cooperatively lead to large differences in the ratio of right- and left-handed helical sequences and thereby to large optical rotations, as observed here.

Experiments are in progress to reveal the per deuterium energy difference favoring one helical sense.[20] Such information will be helpful to understanding the structural forces behind the conformational equilibrium isotope effect reported in this work. Diastereotopic carbon hydrogen stretching frequency differences could play a role,[15] and their contribution could be evaluated by spectroscopic experiments also in progress.

Acknowledgment. Work at the Polytechnic University was supported by the National Science Foundation (CHE-8615872) and by the Petroleum Research Fund administered by the American Chemical Society. We are grateful to these organizations and as well to Professors H. Morawetz (Polytechnic University) and S. Lifson (Weizmann Institute) for helpful discussions. We also thank Prof. W. Agosta for allowing use of the circular dichroism spectrometer at Rockefeller University (purchased with the support of the National Science Foundation). This paper is dedicated to our teacher Professor Kurt Mislow on the occasion of his 65th birthday.

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(20) Professor S. Lifson of the Weizmann Institute has completed a statistical mechanical analysis (to be published) which is consistent with the cooperative effect proposed here and makes predictions of the relationship between the energy difference per deuterium favoring one helical sense and the temperature dependence of the optical rotation. He has also made the challenging suggestion that the energy difference per residue in **1** could arise, at least in part, from an electrostatic interaction between the dipole of the C-H(D) bond α to nitrogen and one of the carbonyl oxygens. In such an interaction which could be described as a C-H to oxygen hydrogen bond, deuterium will differ, however slightly, from hydrogen. See: Melander and Saunders in ref 15 above, pp 197-198. Katz, J. J.; Crespi, H. L. In *Isotope Effects in Chemical Reactions*; ACS Monograph 167; Van Nostrand Reinhold: New York, 1970; Chapter 5. This idea could find support in the following: Taylor, R.; Kennard, O. *J. Am. Chem. Soc.* **1982**, *104*, 5063 and references therein. See, also: Seiler, P.; Weisman, G. R.; Glendening, E. D.; Weinhold, F.; Johnson, Van B.; Dunitz, J. D. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1175.

Intermolecular Hetero-Diels-Alder Reactions of Enamino Ketones at High Pressure. The First Significant Pressure-Induced Diastereoselectivity in Organic Transformations[1]

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Stereoselectivity[2] is today one of the main goals in the development of new synthetic methods in organic chemistry. It is therefore of great interest to explore the potential of applying high pressure to increase the diastereoselectivity of chemical transformations. The first attempts, however, to use this method for diastereoselective synthesis[3,4] were not very promising as the observed $\Delta\Delta V^{\ddagger}$ values did not exceed ±1 $cm^3 \cdot mol^{-1}$. Sera[5] found for the cycloaddition of various dienophiles and cyclopentadienes values of $\Delta V^{\ddagger}_{exo} - \Delta V^{\ddagger}_{endo}$ between 1.0 and −0.5 $cm^3 \cdot mol^{-1}$. We have now shown for the *hetero*-Diels-Alder reaction[6] of the enamino ketone **1** and ethyl vinyl ether (**2**)[7] that a significant increase of diastereoselectivity can be obtained by applying high pressure.

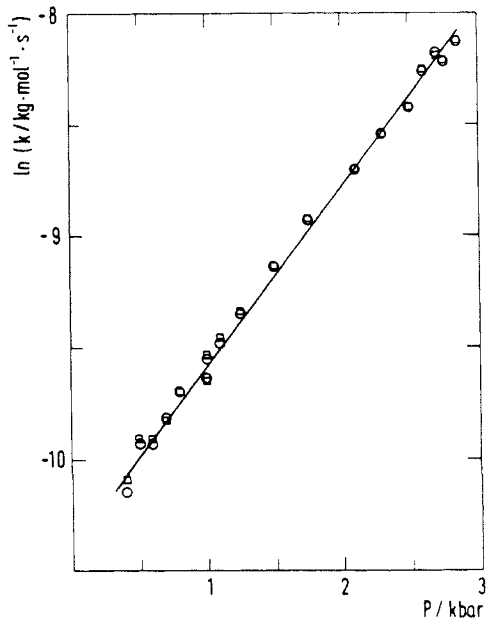
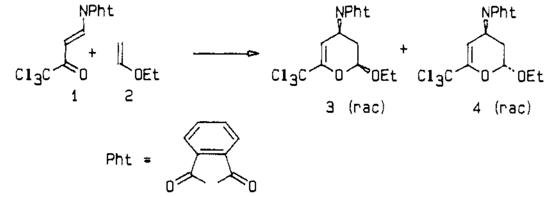


Figure 1. Pressure dependence of the rate coefficient k for the Diels-Alder reaction of **1** and **2** in CH_2Cl_2 solution at 90 °C: The symbols ○ and □ refer to kinetic analysis with two different regions in the spectrum of the C=O fundamentals of the educt **1** around 1740 cm^{-1}.



We assume that **1** reacts in the shown (*E*)-configuration giving the cis-adduct **3** via an endo orientation and the trans-adduct **4** via an exo orientation in the transition state. The reaction of **1** and **2** is of considerable interest as it allows an easy access to 3-amino sugars.[7,8] The kinetics of the cycloaddition of **1** and **2** in CH_2Cl_2 solution was directly measured under high pressure by Fourier transform infrared spectroscopy on the characteristic educt and product C=O stretching fundamentals. The reaction mixture was contained within a closed thin-walled Teflon bag which is transparent to IR light. The Teflon bag was positioned between the silicon windows of an optical cell for operation up to 3 kbar.[9] The cycloadditions were performed with the con-

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[†] Institut für Organische Chemie.

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(1) Intra- and Intermolecular Hetero-Diels-Alder Reactions. 23. This work was generously supported by the Deutsche Forschungsgemeinschaft (SFB 93 "Photochemie mit Lasern") and by the Fonds der Chemischen Industrie. Part 22: Buback, M.; Tost, W.; Tietze, L. F.; Voss, E. *Chem. Ber.* **1988**, *121*, 781.

(2) (a) For selective reviews, see: *Selectivity-A Goal for Synthetic Efficiency*; Bartmann, W., Trost, B. M., Eds.; VCH Verlagsgesellschaft: Weinheim, 1984. (b) *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1983-1987.

(3) For recent excellent reviews, see: Asano, T.; le Noble, W. J. *Chem. Rev.* **1978**, *78*, 4. Matsumoto, K.; Sera, A. *Synthesis* **1985**, 999. Isaacs. N. S.; George, A. V. *Chem. Brit.* **1987**, 47. Eldik, R. van; Jonas, J. *High Pressure Chemistry and Biochemistry*; D. Reidel: Dordrecht, 1987. Jurczak, J. *J. Physica Status Solidi* [*Sectio*] *B* **1986**, *139/140*, 709.

(4) Dauben, W. G.; Gerdes, J. M.; Look, G. C. *Synthesis* **1986**, 532.

(5) Seguchi, K.; Sera, A.; Marayuma, K. *Tetrahedron Lett.* **1973**, *17*, 1585.

(6) Boger, D. L.; Weinreb, S. M. *Hetero-Diels Alder Methodology in Organic Synthesis*; Academic: New York, 1987. L. F. Tietze in ref 2a, p 299.

(7) Tietze, L. F.; Voss, E. *Tetrahedron Lett.* **1986**, *27*, 6181. See Also: Tietze, L. F.; Voss, E.; Harms, K.; Sheldrick, G. M. *Tetrahedron Lett.* **1985**, *26*, 5273.

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