New asymmetric Diels–Alder cycloaddition reactions. Chiral α,β-unsaturated carboximides as practical chiral acrylate and crotonate dienophile synthons

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in $[\eta^5\text{-}(C_6H_5)_5C_5)Ni\text{-}(\eta^3\text{-}C_3(C_6H_5)_3)\text{-}Ni(C_4(C_6H_5)_4\text{-}\eta^4)$ (1.41–1.48 and 1.44 Å).[20] The average d(Sn–C) values are 2.67 and 2.70 Å for R = H[5] and 2.675 and 2.678 Å for R = CH_3[6] (two independent molecules in each) vs. 2.692 (8) Å for decaphenylstannocene.

We are now attacking the opposite problem, that of producing a severely bent angle so that the lone-pair electrons will be both chemically (as a base) as well as stereochemically active. Our recent metallocenophane syntheses[31,32] are steps in this direction.

Acknowledgment. Our work is supported by the Office of Naval Research. We thank the University of Oklahoma for providing computer time and S.-W. Ng for helpful discussions. C.J. was supported by the University of Oklahoma-Technical University of Berlin Exchange Program.

Registry No. $[\eta^5\text{-}(C_6H_5)_5C_5]_2Sn^{II}$, 90481-28-0; CpSnCl, 54067-91-3; $SnCl_2$, 7772-99-8; $[\eta^5\text{-}(C_6H_5)_5C_5]CpSn^{II}$, 90461-74-8; tetraphenylcyclopentadienone, 479-33-4; pentaphenylcyclopentadenol, 2137-74-8; bromopentaphenylcyclopentadiene, 56849-84-4; pentaphenylcyclopentadiene, 2519-10-0.

Supplementary Material Available: Listing of crystal data (Table I), data collection parameters (Table II), atomic positional parameters (Table III), least-squares planes and dihedral angles (Table VI), hydrogen-atom parameters (Table VII), thermal parameters (Table VIII), and observed and calculated structure factors. (17 pages). Ordering information is given on any currect masthead page.

(31) Dory, T. S.; Zuckerman, J. J. *J. Organomet. Chem.* **1984**, *264*, 295.
(32) Molloy, K. C.; Nasser, F. A. K.; Zuckerman, J. J., unpublished results.

New Asymmetric Diels–Alder Cycloaddition Reactions. Chiral α,β-Unsaturated Carboximides as Practical Chiral Acrylate and Crotonate Dienophile Synthons

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The achievement of abolute stereochemical control in the Diels–Alder reaction has been the focus of numerous of investigations spanning a period of more than 20 years. Recently, several examples of highly diastereoselective cycloadditions employing chiral dienophilic esters,[1,2] ketones,[3] and chiral dienes[4] have been reported. Nonetheless, issues associated with absolute stereochemical control in this reaction continue to pose an important challenge in the area of reaction design. The purpose of this communication is to describe our own studies directed at the development of the α,β-unsaturated carboximides **1–3** as practical chiral dienophiles in the Diels–Alder process.

The requisite dienophiles **1–3** were prepared by N-acylation of the illustrated chiral 2-oxazolidones derived from (*S*)-valinol, (*S*)-phenylalanol, or (1*S*,2*R*)-norephedrine.[5] Specifically, the crystalline crotonate imides **1b–3b** were obtained in 80–90% yields from the lithiated 2-oxazolidones and (*E*)-2-butenoyl chloride in direct analogy with previously reported N-acylation procedures:[5] **1b**, mp 56–56.5 °C; **2b**, mp 85–86 °C; **3b**, mp 66–66.5 °C.[6] The more sensitive acrylate carboximides **1a**, mp 44–45 °C; **2a**, 73.5–74.5 °C, and **3a** (oil) were prepared in 50–60% yields from the respective *N*-bromomagnesium 2-oxazolidones and propenoyl chloride (THF, 0 °C, 5 min) under carefully defined conditions.[6,7] Our preliminary evaluation of the synthetic utility of these dienophiles was made in conjuction with the Lewis acid promoted Diels–Alder process with cyclopentadiene (Scheme I). After an extensive survey of Lewis acid addends, we discovered that diethylaluminum chloride (DEAC) or dimethylaluminum chloride (DMAC), employed in excess of 1 equiv relative to dienophile, is *essential* to the realization of high reaction diastereoselectivity. In a typical experiment, a solution of crotonate imide **1b** in CH_2Cl_2 (0.5 M) and cyclopentadiene (20 equiv) was cooled to −100 °C and 1.4 equiv of precooled DEAC (1.8 M in toluene) was added via cannula.[8] After a reaction time of approximately 2 min, the reaction was quenched via transfer to an aqueous ammonium chloride solution. Conventional product isolation afforded adduct **4b** ($X_C = X_V$)[9] along with minor amounts of other product diastereomers in 99% yield. Recrystallization provided the diastereometrically pure adduct in 82% yield as colorless prisms, mp 96–98 °C (Table I, entry D). The data included in Table I indicate that both chiral acrylates **1a–3a** and crotonates **1b–3b** are excellent chiral dienophiles which undergo exceptionally high-yield cycloaddition reactions. Most significantly, the levels of asymmetric induction in these systems are consistantly good. From the standpoint of practicality, we have found that purification of the major Diels–Alder cycloadduct to high diastereomeric purity may be *routinely* achieved by either recrystallization or chromatography.[10] In this study (see Tables I and II), as in earlier investigations,[5,11] the high incidence of product crystallinity associated with these carboximide systems greatly enhances the practical utility of these dienophiles. The nondestructive removal of the 2-oxazolidone auxiliaries through lithium benzyloxide transesterification (1.5 equiv ROLi:, THF, 0 °C 3 h) proceeds in excellent yields (85–95%) and is currently the method of choice for auxiliary cleavage.[11] Accordingly, transesterification of cy-

Table I. Et_2AlCl-Promoted Diels–Alder Reactions of Dienophiles **1–3** and Cyclopentadiene (Scheme I)[6]

entry	dienophile	diastereoselection[a] endo:exo	diastereoselection[a] endo (4:5)	purified ratio (4:5)	isolated yield, %[b]	mp, °C
A	**1a**, R_1 = H	>100:1	93:7	>99:1	81	59.2–61
B	**2a**, R_1 = H	>100:1	95:5	97:3	78	120–121
C	**3a**, R_1 = H	100:1	5:95	<1:99	82	91–92
D	**1b**, R_1 = Me	48:1	95:5	>99:1	82	96–98
E	**2b**, R_1 = Me	55:1	97:3	99:1	83	oil
F	**3b**, R_1 = Me	60:1	2:98	<1:99	88	oil

[a] Reference 10; reaction temperature, −100 °C. [b] Yield refers to isolated material with the indicated diastereomer purity.

(1) (a) Walborsky, H. M.; Barash, L.; Davis, T. C. J. *Tetrahedron* **1963**, *19*, 2333. (b) Ensley, H. E.; Parnell, C. A.; Corey, E. J. *J. Org. Chem.* **1978**, *43*, 1610. (c) Oppolzer, W.; Chapuis, C.; Kelley, M. *Helv. Chim. Acta* **1983**, *66*, 4781 and references cited therein.
(2) Rousch, W. R.; Gillis, H. R.; Ko, A. I. *J. Am. Chem. Soc.* **1982**, *104*, 2269 and references cited therein.
(3) Reed, L. A., III; Davis, J.; Choy, W.; Masamune, S. *J. Org. Chem.* **1983**, *48*, 4441–4444 and references cited therein.
(4) (a) Trost, B. M.; O'Krongly, D.; Belletire, J. L. *J. Am. Chem. Soc.* **1980**, *102*, 7595. (b) David, S.; Eustache, J.; Luvineau, J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1795. (c) Dauben, W. A.; Bunce, R. A. *Tetrahedron Lett.* **1982**, 4875.
(5) Evans, D. A.; Bartroli, J.; Shih, T. *J. Am. Chem. Soc.* **1981**, *103*, 2127–2129.
(6) Satisfactory elemental analysis and spectral data were obtained for all compounds reported herein.
(7) Specific experimental conditions for the synthesis of **1a–3a** are provided in the supplementary material. It is recommended that these conditions be followed precisely.
(8) The general cyclopentadiene cycloaddition procedure for the acrylate imides **1a–3a** requires the addition of DEAC to a solution at −100 °C of dienophile prior to the addition of diene. A detailed experimental is provided in the supplementary material.
(9) For the purpose of brevity, the chiral auxiliaries derived from (*S*)-valinol, (*S*)-phenylalanol, and (1*S*,2*R*)-norephedrine will be abbreviated as X_V, X_P, and X_N, respectively.
(10) All product diastereomer analyses were carried out by either capillary gas chromatography or high-pressure liquid chromatography. The diastereomerically pure (≥99%) adducts were obtained either by recrystallization or medium-pressure liquid chromatography using Merck Lobar silica gel columns.
(11) For racemization control experiments for these transesterification conditions, see: Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737.

0002-7863/84/1506-4261$01.50/0

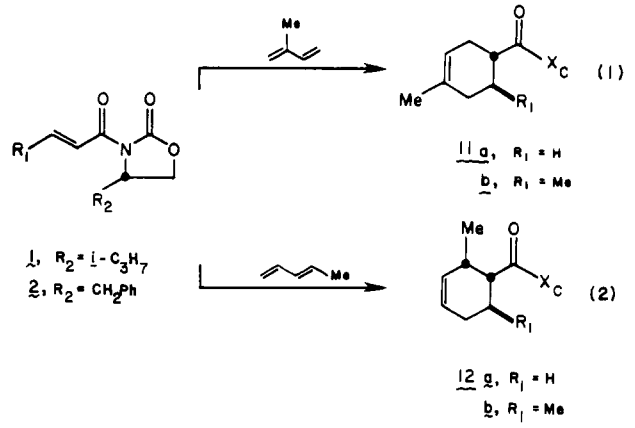
Table II. Et_2AlCl-Promoted Diels–Alder Reactions of Dienophiles **1** and **2** with Acyclic Dienes (eq 1 and 2)[6]

entry	dienophile[a]	diene	diastereoselection[b]	purified ratio[c]	isolated yield, %	mp, °C
A	**1a**, R_1 = H	isoprene	83:17	>99:1	36 (**11a**)	76.2–77.5
B	**2a**, R_1 = H	isoprene	95:5	>99:1	85 (**11a**)	85.7–86.6
C	**2a**, R_1 = H	piperylene	>100:1	>99:1	84 (**12a**)	165–167
D	**2b**, R_1 = Me	isoprene	94:6	>99:1	83 (**11b**)	58.8–60.0
E	**2b**, R_1 = Me	piperylene	95:1:2:2[d]	>99:1	77 (**12b**)	66–67.3

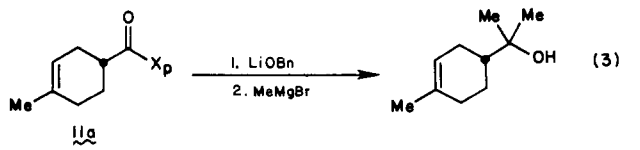
[a] Entries A–C carried out at −100 °C; entries D and E carried out at −30 °C. [b] Reference 10. [c] Diastereomeric purity of purified cycloadduct (ref 10). [d] No attempt was made to assign all endo and exo diastereomers.

cloadducts **4a** and **4b**, derived from the four dienophiles **1a**, **1b**, **2a**, and **2b**, afforded the benzyl esters (+)-**6a**, $[\alpha]_D$ +133.9° (*c* 1.37, $CHCl_3$), and (+)-**6b**, $[\alpha]_D$ +132.0° (*c* 2.08, $CHCl_3$). Subsequent hydrogenations of (+)-**6a** and (+)-**6b** to the carboxylic acids (+)-**7a**, $[\alpha]^{22}_D$ +33.9° (*c* 1.06, 95% EtOH), and (+)-**7b**, $[\alpha]^{22}_D$ +45.9° (*c* 5.42, 95% EtOH), of known absolute configuration unequivocally establish the stereochemistry of cycloadducts **4a** and **4b** ($X_C = X_V, X_P$).[9,12,13] Similarly, cycloadducts **5a** and **25b** ($X_C = X_N$) afforded the enantiomeric benzyl esters (−)-**6a** and (−)-**6b** whose rotations are equal in magnitude and opposite in sign to those values reported above.

The exceptional reactivity of these dienophile–Lewis acid complexes has enabled us to include less reactive acyclic dienes on the list of useful diastereoselective cycloadditions (eq 1 and 2). For example, the chiral acrylate **2a** (R_1 = H) undergoes

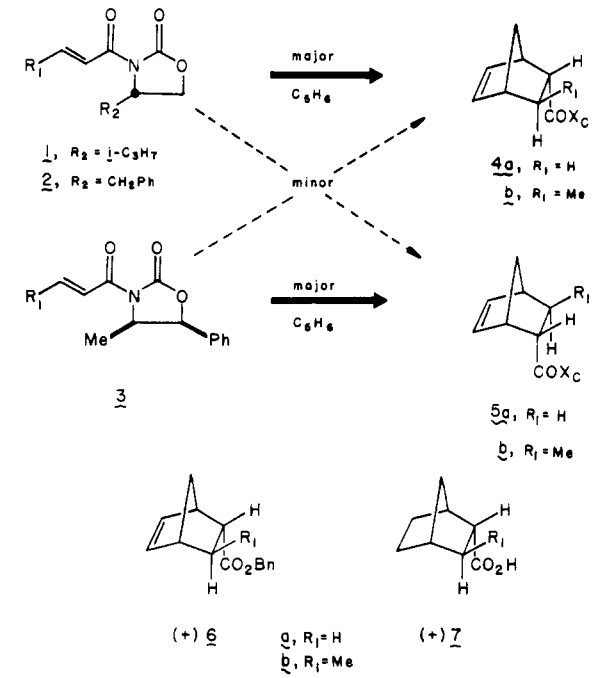


cycloaddition even at −100 °C with both isoprene (15 min) and piperylene (45 min) under the reaction conditions described above for cyclopentadiene[8] to give the illustrated crystalline cycloadducts **11a** and **12a** ($X_C = X_P$), respectively (Table II, entries B and C). Even the less reactive crotonate dienophile **2b** (R_1 = Me) undergoes cycloaddition with these same dienes at −30 °C (6 h) to again afford cycloadducts **11b** and **12b** ($X_C = X_P$) each of which is readily obtained in high diastereomeric purity (Table II, entries D and E).[9] We verified the sense of asymmetric induction in these reactions by correlating cycloadduct **11a** ($X_C = X_P$) with (*R*)-(+)-α-terpineol (eq 3). Transesterification (1.5 equiv of LiOBn,



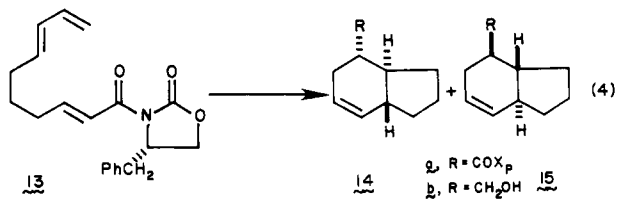
THF 0 °C, 3 h) of **11a** to the corresponding benzyl ester (93%) followed by subsequent treatment with methylmagnesium bromide afforded synthetic (+)-terpineol, $[\alpha]^{22}D$ +94.1° (neat), whose rotation is in excellent agreement with that reported for the natural

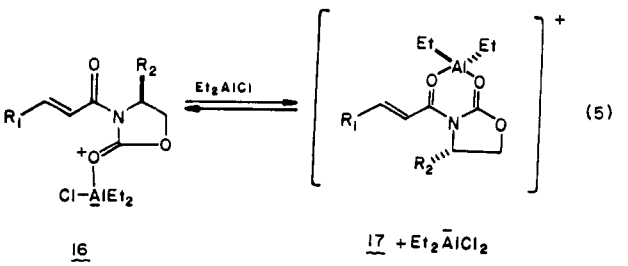
Scheme I



product, $[\alpha]^{22}_D$ +92.45° (neat).[14]

To further demonstrate the utility of these cycloadditions we have examined the intramolecular Diels–Alder reaction shown in eq 4. The requisite trienic acid was synthesized according to





the published procedure[2] and converted, via the derived acid chloride, to the illustrated carboximide **13**. Treatment of **13** with DMAC (1.4 equiv, CH_2Cl_2, −30 °C, 5 h) afforded a quantitative yield of **14a** and the associated endo diastereomer **15a** (**14a**:**15a** = 95:5).[10] The major diastereomer **14a** was conveniently purified by flash chromatography (**14a**:**15a** > 99:1) in 73% isolated yield. The absolute configuration of **14a** was established lithium ben-

(12) (a) Berson, J. A.; Ben-Efraim, D. A. *J. Am. Chem. Soc.* **1959**, *81*, 4083. (b) Berson, J. A.; Walia, J. S.; Remanick, A.; Suzuki, S.; Reynolds-Warnhoff, P.; Willner, D. *Ibid.* **1961**, *83*, 3986. The maximum rotation of enantiomer (−)-**7a**: $[\alpha]^{26}_D$ −30.6° (95% EtOH).

(13) Berson, J. A.; Hammons, J. H.; McRowe, A. W.; Bergman, R. G.; Remanick, A.; Houston, D. *J. Am. Chem. Osc.* **1967**, *89*, 2590. The rotation of enantiomer (−)-**7b**: $(\alpha)^{24}_D$ −40.5° (*c* 10.8, 95% EtOH).

(14) Henbest, H. B.; McElhinney, R. S. *J. Chem. Soc.* **1959**, 1834.

zyloxide transesterification followed by reduction ($LiAlH_4$) to the alcohol **14b**, $[\alpha]^{22}_D$ +43.3° (*c* 0.78, CCl_4), whose absolute configuration has been previously established, $[\alpha]^{22}_D$ +41.0° (*c* 1.94, CCl_4).[2]

From a mechanistic standpoint the actual structure of the Lewis acid–dienophile complex is of considerable interest. We are currently operating on the premise that the complexed ion pair **17** is the putative species exhibiting good levels of π-facial selectivity during the cycloaddition process. The stereochemical course of all preceeding cycloadditions can be readily rationalized assuming that the C_4 substituent, R_2, directs the cycloaddition process to the opposite face of the cisoid dienophile complex **17**.

Acknowledgment. This research was supported by the National Science Foundation and the Eli Lilly Co.

Supplementary Material Available: Synthesis of **1a,b**, **2a,b**, and **3a,b** and experimental conditions for individual diastereomer resolutions (11 pages). Ordering information is given on any current masthead page.

Alkynyl Sulfenylation. A Direct Approach for Nucleophilic Addition and Substitution of Olefins by Carbanions

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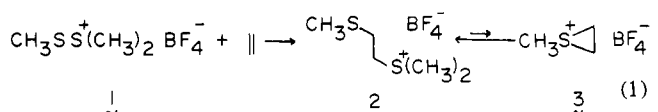
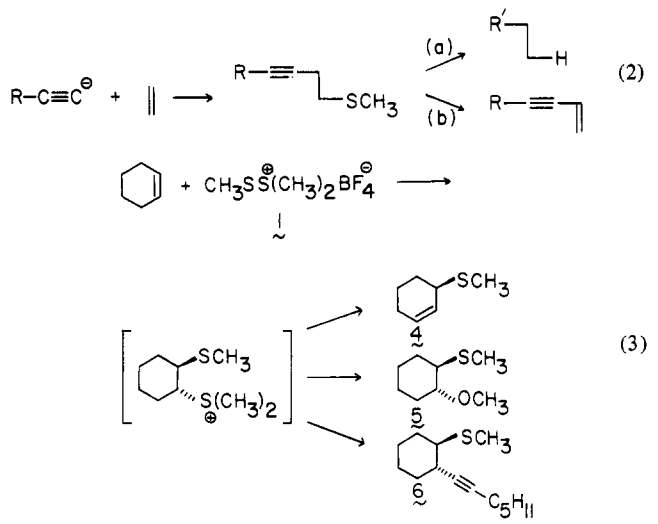
In exploring the concept of nucleophilic addition and substitution of olefins initiated by DMTSF (**1**), the question of the choice of nucleophile is of paramount importance.[1-4] The difficulty arises from the fact that the species present is the adduct **2**, which must be coaxed to solvolyze to the episulfonium ion **3** prior to nucleophilic attack. Thus, the nature of the nucleophile that can



(1)

exercise such discrimination without simply decomposing **2** becomes critical. Use of simple carbon nucleophiles would appear to be incompatible with such a reaction because of their basicity. Nevertheless, the importance of such carbon–carbon bond-forming reactions in organic synthesis and the importance of acetylenes for further structural elaboration[5] led us to examine an alkynyl sulfenylation as in eq 2. However, we were not surprised that use of a plethora of nucleophilic acetylide species failed. To illustrate (see eq 3), simple acetylide anions either failed to react



(2)

(3)

or produced complex mixtures or the elimination product **4**. In fact, with lithium heptynylide, this sequence constitutes a useful allylic sulfenylation. Attenuating the basicity but hopefully retaining nucleophilicity with boron compounds led to complex mixtures with trialkyl "ate" complexes (in part due to the oxidative workup required), preferential transfer of a methoxy group to give **5** (67% yield) with trimethyl borate "ate" complexes, or elimination to **4** in addition to **6** (43% yield) if a poorer migrating group, isopropoxy, is substituted for methoxy. Believing that use of a reagent that could complex dimethyl sulfide would facilitate formation of the reactive episulfonium salt intermediate and still possess a nucleophilic acetylide led us to explore the aluminum derivatives of acetylides.[6] The "ate" complex with triethylaluminum and lithium heptynylide (reagent B) gave up to 92% yields of **6** but with some competing ethyl transfer (0–20%). The dialkynylethylalane (reagent A, from 2 equiv of lithium heptynylide and 1 equiv of $(C_2H_5)_2AlCl$) and the lithium dialkynyldiethylaluminate (from 2 equiv of lithium heptynylide and 1 equiv of $(C_2H_5)_2AlCl$) gave clean reaction to produce **6** in 63% and 88% distilled yields, respectively.[7] Table I summarizes the results.[8]

The reaction is stereospecific (entries 1, and 3–6). The trans addition stems from the spectroscopic data, reasonable analogy

(1) For other types of nucleophiles, see: (a) Trost, B. M.; Shibata, T. *J. Am. Chem. Soc.* **1982**, *104*, 3225. (b) Trost, B. M.; Shibata, T.; Martin, S. J. *Ibid.* **1982**, *104*, 3228. (c) Caserio, M. C.; Kim, J. K. *Ibid.* **1982**, *104*, 3231.

(2) For reviews on episulfonium ions, see: Schmid, G. H. *Top. Sulfur Chem.* **1977**, *3*, 101. Smit, W. A.; Zefirov, N. S.; Bodrikov, I. V.; Krimer, M. Z. *Acc. Chem. Res.* **1979**, *12*, 282. For leading references to metal-initiated nucleophilic attack on olefins see ref 1a.

(3) For independent investigations of the application of the adducts of benzenesulfenyl chloride and olefins, see: Ibragimov, M. A.; Smit, W. A. *Tetrahedron Lett.* **1983**, *24*, 961. Patel, S. K.; Paterson, I. *Ibid.* **1983**, *24* 1315. Alexander, R. P.; Paterson, I. *Ibid.* **1983**, *24*, 5911.

(4) DMTSF = *d*imethyl(*m*ethylthio)sulfonium *f*luoroborate. Meerwein, H.; Zenner, K. F.; Gipp, R. *Liebigs Ann. Chem.* **1965**, *688*, 67. Helmkamp, G. K.; Cassey, H. N.; Olsen, B. A.; Pettitt, D. J. *J. Org. Chem.* **1965**, *30*, 933. Smallcombe, S. H.; Caserio, M. C. *J. Am. Chem. Soc.* **1971**, *93*, 5826.

(5) For a review, see: Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841. Negishi, E. "Organometallics in Organic Synthesis"; Wiley Interscience: New York, 1980; Vol. 1, Chapter 5. For some very recent examples, see: Miller, R. B.; Al-Hassan, M. I. *Tetrahedron Lett.* **1983**, *24*, 2055. Yoshida, T. *Chem. Lett.* **1982**, 293. Pelter, A.; Singarem, S.; Brown, H. C. *Tetrahedron Lett.* **1983**, *24*, 1433. Brown, H. C.; Basavarah, D. *J. Org. Chem.* **1982**, *47*, 5407, 3808, 3806.

(6) Kanemoto, S.; Morizawa, Y.; Oshima, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3941. Negishi, E.; Baba, S. *J. Am. Chem. Soc.* **1975**, *97*, 7385. Also see: Fried, J.; Sih, J. C. *Tetrahedron Lett.* **1973**, 3899. Murray, T. F.; Samsel, E. G.; Varma, V.; Norton, J. R. *J. Am. Chem. Soc.* **1981**, *103*, 7520.

(7) Typical procedures: (Reagent A) In a centrifuge tube, 0.728 mL (1.31 mmol) of a 1.8 M solution of diethylaluminum chloride in toluene was added to 1-lithio-1-heptyne (from 252 mg, 2.62 mmol of 1-heptyne and 1.69 mL, 2.62 mmol, of a 1.55 M solution of *n*-butyllithium in hexane) and 0.2 mL of dry THF. The resultant suspension was centrifuged to settle the lithium chloride. In a separate flask, cyclohexene (54 mg, 0.657 mmol) was added to 128.5 mg (0.655 mmol) of DMTSF in 0.8 mL of 1,2-dichloroethane at room temperature. After 15 min, the aluminate solution was cannulated away from the lithium chloride into the resultant mixture. After the mixture was heated for 2 h at 80 °C, the solution was diluted with methylene chloride, washed with aqueous sodium bisulfate and then sodium bicarbonate, and dried. After concentration, the crude product was distilled in a Kugelrohr apparatus to give 129 mg (88%) of product. (Reagent B) To 1.8 mL (2.79 mmol) of *n*-butyllithium in hexane (1.55 M) and 0.1 mL of THF at 0 °C was added 593 mg (2.79 mmol) of 1-*tert*-butyldimethylsiloxy-5-hexyne. After 15 min of stirring at room temperature, the solution was recooled to 0 °C and 1.47 mL (1.9 M, 2.79 mmol) of triethylaluminum in toluene added. In a separate flask, a solution of 118 mg (1.40 mmol) of 1-hexene in 1.4 mL of 1,2-dichloroethane was stirred at room temperature with 274 mg (1.40 mmol) of DMTSF for 90 min. The solution of the DMTSF/olefin adduct, cooled to 0 °C, was cannulated into a solution of the aluminate also at 0 °C. After the mixture was stirred for 3 h at room temperature, slow addition of aqueous sodium bisulfate quenched the reaction. Partitioning between ether and water was followed by washing the ether layer with aqueous sodium bisulfate and saturated aqueous sodium bicarbonate and then drying ($MgSO_4$). Evaporation of the solvent in vacuo and Kugelrohr distillation gave two fractions. The first fraction, bp 60–80 °C (0.1 mm), yielded 421 mg (71% recovery) of starting alkyne which accounts quantitatively for all the alkyne. Fraction two, bp 90–140 °C (0.1 mm), yielded 255.6 mg (53%) of 1-*tert*-butyldimethylsiloxy-8-methylthiododec-5-yne.

(8) All new compounds have been fully characterized by spectral means and have satisfactory combustion analysis or high-resolution peak matching.

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