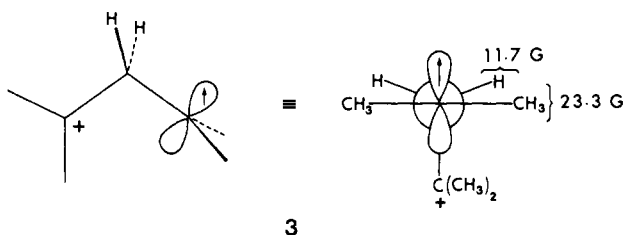


**Figure 2.** Observed (upper spectrum) and computer-simulated (lower spectrum) first-derivative ESR spectra of the ring opened form of the radical cation of 1,1,2,2-tetramethylcyclopropane in  $\text{CF}_2\text{ClCFCl}_2$ . The upper spectrum was recorded at 117 K after a  $\gamma$ -irradiated 0.8 mol % solution of the parent compound in this matrix was thermally annealed above 110 K. Irradiation was carried out at 77 K for a dose of 0.4 Mrad. The lower spectrum was simulated by using the ESR parameters in Table I and a Lorentzian line width of 2.5 G.

consists of 15 evenly spaced lines with an apparent splitting of 11.7 G but the intensity ratios do not correspond to a binomial distribution. A clue to the analysis is provided by the relative intensity of the two outermost components in each wing, and the spectrum is satisfactorily simulated by the hyperfine parameters  $a(6\text{ H}) = 23.3\text{ G}$  and  $a(2\text{ H}) = 11.7\text{ G}$ , as shown in the lower half of Figure 2. The 23.3-G coupling to six equivalent hydrogens is characteristic of a simple  $\alpha,\alpha$ -dimethyl-substituted alkyl radical, and we assign the ESR parameters to structure 3. All the



interacting protons are in  $\beta$  positions and both sets of couplings are in exact agreement with the  $\cos^2 \theta$  angular dependence.<sup>13</sup> Moreover, since the positively charged  $\text{Me}_2\text{C}^+$  group should be similar in many respects to the electron-withdrawing  $\text{CCl}_3$  group, the assignment is strongly supported by the fact that the hyperfine parameters are virtually identical with those of the  $\text{CCl}_3\text{CH}_2\text{CMe}_2$  radical ( $a(6\text{ H}) = 23.52\text{ G}$  and  $a(2\text{ H}) = 11.61\text{ G}$ ), which also possesses an eclipsed conformation at the radical center.<sup>14</sup> Evidently the thermal reaction described here is a simple isomerization,<sup>15,16</sup> a monorotatory ring opening at the weakened C(1)-C(2) bond of 2 giving rise to the orthogonal structure 3.<sup>17</sup>

(13) Heller, C.; McConnell, H. M. *J. Chem. Phys.* **1960**, *32*, 1535.

(14) Chen, K. S.; Tang, D. Y. H.; Montgomery, L. K.; Kochi, J. K. *J. Am. Chem. Soc.* **1974**, *96*, 2201.

**Acknowledgment.** This research has been supported by the Division of Chemical Sciences, U.S. Department of Energy (Report DOE/ER/02968-154).

**Registry No.** 1, 56324-44-8; 3, 93000-46-5.

(15) (a) The only other reasonable candidate for the radical product of the thermal reaction would seem to be the (1,1,3-trimethylallyl)carbinyl species  $\text{CH}_2=\text{C}(\text{Me})\text{CH}_2\text{CMe}_2$ , which could be formed via ring opening followed by proton loss from the carbonium ion center in 3. However, the methylene  $\beta$ -hydrogens in this radical are inequivalent below 170 K and give a triplet splitting of 17.5 G in the fast-exchange limit: Chen, K. S.; Edge, D. J.; Kochi, J. K. *J. Am. Chem. Soc.* **1973**, *95*, 7036. (b) The ESR parameters for the secondary radical also appear to exclude the 2,4-dimethyl-2-pentene radical cation,  $i\text{-PrCH}=\text{CMe}_2^+$ , which could arise from 3 by a 1,2-hydride shift. Thus, the values of  $a(6\text{ H})$  from the  $\text{CMe}_2$  group in the radical cations of isobutene, trimethylethylene, and tetramethylethylene are all lower than 23 G and lie in a narrow range between 16.5 and 17.2 G; Toriyama, K.; Nunome, K.; Iwasaki, M. *Chem. Phys. Lett.* **1984**, *107*, 86 and references therein.

(16) The ring opening of 2 has also been proposed to explain the formation of products upon electrochemical oxidation: Shono, T.; Matsumura, Y. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 2861.

(17) **Note Added in Proof:** Recent work<sup>18</sup> has shown that the parent cyclopropane radical cation also isomerizes in the  $\text{CF}_2\text{ClCFCl}_2$  matrix to a ring-opened orthogonal structure. However, the derived trimethylene radical cation adopts a bisected conformation at the radical center.

(18) Qin, X.-Z.; Williams, F. *Chem. Phys. Lett.*, in press.

## Tandem Alkylation-Cycloadditions. Control by Transition-Metal Templates

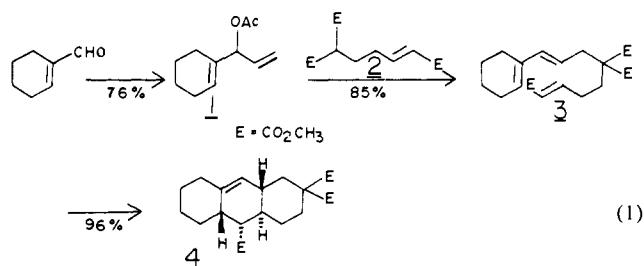
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Received July 30, 1984

The intramolecular Diels-Alder reaction has become an exceedingly powerful tool in the total synthesis of natural products.<sup>1</sup> Limited methods exist for the synthesis of the requisite substrate; olefination reactions constitute the most important. Recent developments in controlling regioselectivity in allylic alkylations by variation of the metal templates<sup>2-4</sup> offer a versatile strategy to conjugated polyenes and consequently substrates for intramolecular Diels-Alder reactions. We wish to report a convergent approach in which the dienophile and diene fragments are joined using alkylations mediated by transition metals and the flexibility offered by the ability to manipulate the regioselectivity of alkylation.

The simplicity of this approach derives, in part, from the ready availability of the allylic carboxylates. For example, addition of vinylmagnesium bromide to an  $\alpha,\beta$ -unsaturated aldehyde such



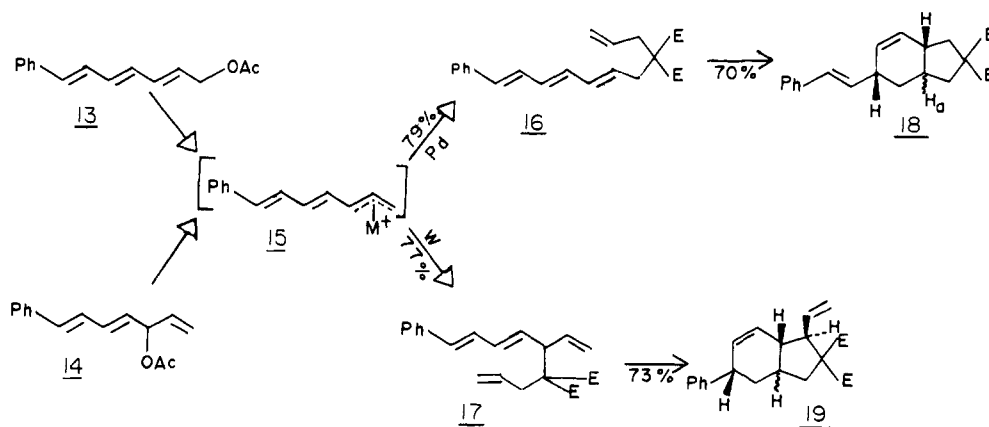
(1) For recent review, see: Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10. Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63. Fallis, A. G. *Can. J. Chem.* **1984**, *62*, 183. Taber, D. F. "Intramolecular Diels-Alder and Alder Ene Reaction"; Springer-Verlag: Berlin, 1984.

(2) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1976**, *98*, 630. Akermark, B.; Hansson, S.; Krakenberger, B.; Vitagliano, A.; Zetterberg, K. *Organometallics* **1984**, *3*, 679. Keinan, E.; Sahai, M. *J. Chem. Soc., Chem. Commun.* **1984**, 648. Curtis, M. D.; Eisenstein, O. *Organometallics* **1984**, *3*, 887.

(3) Trost, B. M.; Lautens, M. *Organometallics* **1983**, *2*, 1687; *J. Am. Chem. Soc.* **1983**, *105*, 3343; **1982**, *104*, 5543.

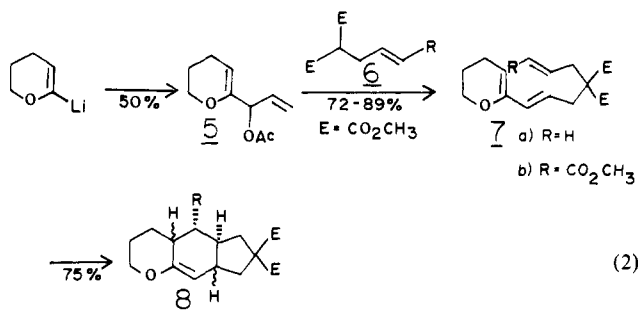
(4) Trost, B. M.; Hung, M.-H. *J. Am. Chem. Soc.* **1983**, *105*, 7757.

Scheme I



as cyclohexene-1-carboxaldehyde and quenching with acetic anhydride gives the diallylic acetate **1** in one pot (eq 1). To create a conjugate diene, terminal alkylation of the allylic acetate is required. Since the nucleophilic partner bearing the dienophile is a substituted malonate, a catalyst whose regioselectivity is dominated by steric factors such as a palladium<sup>2</sup> or molybdenum<sup>3</sup> complex is required. The limited stability of the acrylate **2** leads us to select a palladium-catalyzed reaction [BSA, 5 mol % (Ph<sub>3</sub>P)<sub>4</sub>Pd, THF, reflux], which gives a single regioisomeric product **3**<sup>5,6</sup> in excellent yield. Warming this product in refluxing toluene gives a nearly quantitative yield of the anticipated Diels–Alder product **4**<sup>5</sup> as a single isomer.<sup>7</sup> Thus, in a three-step operation, a simple  $\alpha,\beta$ -unsaturated aldehyde is converted into the tricycle **4** in 62% overall yield!

The sequence of lithiation of dihydropyran,<sup>8</sup> subsequent condensation with acrolein, and acetylation gives the diallylic acetate **5**. Palladium-catalyzed alkylation as before using **6**, R = H or CO<sub>2</sub>CH<sub>3</sub>, smoothly generates **7**.<sup>5</sup> With the activated dienophile **7b**, heating in toluene suffices to give **8b** (eq 2).<sup>5,9</sup> Only mod-



erately higher temperatures (refluxing mesitylene) are required for the intramolecular Diels–Alder reaction with the unactivated dienophile **7a** to give **8a**.<sup>5,9</sup>

In the case of allyl acetate **9**, prepared from furfuraldehyde in identical fashion with **1**, alkylation at the internal position was desired to allow the furan moiety to serve as the diene partner.<sup>11</sup>

(5) All new compounds have been characterized spectrally and elemental composition determined by combustion analysis and/or high-resolution mass spectrometry.

(6) The *E,E* stereochemistry of **3** is established by NMR:  $\delta$  6.92 (1 H, dt,  $J = 15, 6$  Hz), 6.05 (1 H, d,  $J = 16$  Hz), 5.84 (1 H, d,  $J = 15$  Hz), 5.28 (1 H, dt,  $J = 16, 7$  Hz).

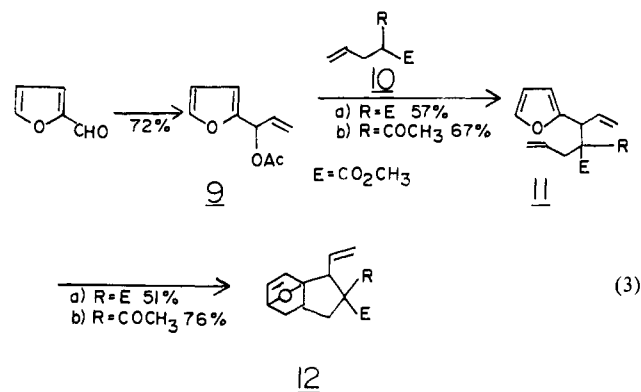
(7) <sup>1</sup>H and <sup>13</sup>C NMR establish the stereohomogeneity. The relative stereochemistry is assigned by analogy.<sup>1</sup>

(8) **7a** partial <sup>1</sup>H NMR  $\delta$  6.15 (1 H, dt,  $J = 15, 7$  Hz), 5.85 (1 H, d,  $J = 15$  Hz). **7b**  $\delta$  5.78 (1 H, d,  $J = 15$  Hz), 5.67 (1 H, dt,  $J = 15, 7$  Hz).

(9) For **8a** <sup>1</sup>H NMR indicates a 2:1 mixture (e.g., vinyl proton at  $\delta$  5.23, 0.33 H, and  $\delta$  5.08, 0.67 H); for **8b** a 4.8:1 mixture resulted (e.g., vinyl proton at  $\delta$  5.30, 0.83 H, and 5.09, 0.17 H). The stereochemistry of the major isomer of **8b** is assigned as *trans,anti* in analogy to ref 1 and 10.

(10) Boeckman, R. K., Jr.; Ko, S. S. *J. Am. Chem. Soc.* **1982**, *104*, 1033.

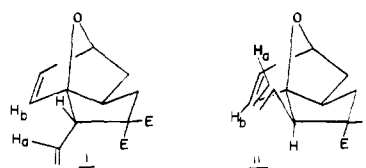
For such regioselectivity ( $\geq 95\%$ ), tungsten<sup>3</sup> is the catalyst of choice [15–30 mol % (CH<sub>3</sub>CN)<sub>3</sub>W(CO)<sub>3</sub>, 15–30 mol % bpy, THF, reflux] using the salt of **10**, R = CO<sub>2</sub>CH<sub>3</sub> or COCH<sub>3</sub>, generated with sodium hydride. Thus,  $\beta$ -keto esters and malonates which give **11a**<sup>5</sup> and **11b**,<sup>5</sup> respectively, participate equally well. Intramolecular Diels–Alder reaction is best accomplished by refluxing a 2:5 (v/v) ethanol–water solution<sup>11c</sup> of **11** to give a stereoisomeric mixture of **12** (eq 3).<sup>5,12</sup>



The polyene systems particularly highlight the virtue of these metal-catalyzed reactions. The  $\pi$ -allylmatal intermediate **15** suffers exclusive terminal attack to give **16**<sup>5</sup> with the anion of **6** (R = H) generated with sodium hydride in a palladium-catalyzed reaction [2 mol % Pd(OAc)<sub>2</sub>, 12.5 mol % dppb, 1-hexene, 5 mol % *n*-C<sub>4</sub>H<sub>9</sub>Li, THF, reflux]<sup>13a</sup> but exclusive internal attack to give

(11) Cf.: (a) Takebayashi, T.; Iwasawa, N.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1107. (b) Grootaert, W. M.; De Clercq, P. J. *Tetrahedron Lett.* **1982**, *23*, 329. (c) Sternbach, D. D.; Rossana, D. M. *Tetrahedron Lett.* **1982**, *23*, 303. (d) Torosyan, G. H.; Paravyan, S. L.; Mkrtchyan, R. S.; Tagmazyan, K. T.; Babayan, A. T. *Arm. Khim. Zh.* **1979**, *32*, 182; *Chem. Abstr.* **1980**, *92*, 76234z. (e) Gschwend, H. W.; Hillman, M. J.; Visis, B.; Rodenbaugh, R. K. *J. Org. Chem.* **1976**, *44*, 104. (f) Klepo, Z.; Jacopic, K. *Croat. Chem. Acta* **1975**, *47*, 45. (g) Parker, K. A.; Adamchuck, M. R. *Tetrahedron Lett.* **1978**, 1689. (h) Bilovic, D. *Croat. Chim. Acta.* **1968**, *40*, 15.

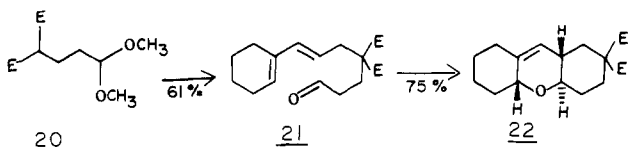
(12) For example, a 2:8:1 ratio of i and ii was obtained in the case of **12a**. Difference NOE shows a 6% enhancement between H<sub>a</sub> and H<sub>b</sub> in i (5.69, dt,  $J = 17, 9.9$  Hz, 1 H; 6.25, dm,  $J = 5.8$  Hz, 1 H; 6.33, d,  $J = 5.8$  Hz, 1 H) but no enhancement in ii (5.69, dt,  $J = 17.0, 10.1$  Hz, 1 H; 6.29, m, 2 H).



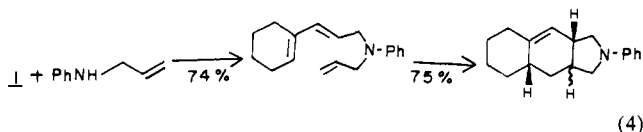
(13) (a) An in situ generation of the palladium(0) catalyst using 1-hexene and *n*-butyllithium in the presence of 1,4-bis(diphenylphosphino)butane (dppb) was employed in this case. Synthetically, this in situ generation method is quite convenient. (b) Trost, B. M.; Hung, M.-H., unpublished results.

17<sup>5</sup> in a tungsten-catalyzed reaction [30 mol % (CH<sub>3</sub>CN)<sub>3</sub>W(CO)<sub>3</sub>, 30 mol % bpy, THF, reflux] (Scheme I). The trienyl acetate **13** serves as the best precursor for the Pd-catalyzed reaction to ensure formation of only the terminal  $\pi$ -allylpalladium intermediate. On the other hand, the better kinetics of internal acetates in tungsten-catalyzed reactions and the higher intrinsic chemo-selectivity in  $\pi$ -allyltungsten formation<sup>13b</sup> dictate **14** as the preferred precursor for the tungsten reaction. As a result of the complementarity in the regioselectivity of the alkylation, grossly different substitution patterns result in the tetrahydroindanes **18**<sup>5,14</sup> and **19**<sup>5,15</sup> that result from the subsequent Diels-Alder reaction (mesitylene, reflux).

Modified nucleophiles extend this sequence to a synthesis of heterocycles. For example, **1** reacts with the malonate **20** in a Mo-catalyzed reaction [20 mol % Mo(CO)<sub>6</sub>, BSA, toluene, reflux, 81%] to give **21**<sup>5,16</sup> after hydrolysis [PPTS, acetone, 75%]. Addition of a Lewis acid<sup>17</sup> to **21** [1 equiv of CH<sub>3</sub>AlCl<sub>2</sub>, 1 equiv of (CH<sub>3</sub>)<sub>2</sub>AlCl, methylene chloride, room temperature] effects a heteroatom Diels-Alder reaction to give a single adduct **22**.<sup>5,7,18</sup>



To our knowledge, this example is the first report of an aldehyde as the dienophile in an intramolecular Diels-Alder reaction.<sup>19</sup> Alternatively, a heteroatom can serve as the nucleophile<sup>20</sup> as shown in eq 4.<sup>21</sup> Only palladium catalysts [5 mol % (Ph<sub>3</sub>P)<sub>4</sub>Pd, (*i*-



C<sub>3</sub>H<sub>7</sub>)<sub>2</sub>N C<sub>2</sub>H<sub>5</sub>, THF, reflux] succeed at present with heteroatom nucleophiles.

This convergent approach joins a masked conjugated diene with a potential dienophile in a metal-catalyzed alkylation reaction. Thus, each partner can be readily assembled individually and the sensitive substrate generated under very mild conditions immediately prior to intramolecular cycloaddition. The mildness of the conditions is emphasized by the successful utilization of the acrylates **2** and **6** (R = CO<sub>2</sub>CH<sub>3</sub>) since their anions are very unstable. The metal template provides a powerful steering mechanism in this cojoining. The regioselectivity of the alkylation dictates the nature of the Diels-Alder reaction. The types of skeletons that result from this rapid construction of polycyclic systems relate to such diverse natural products as the gibberellins<sup>11b</sup>

(14) A 2:1 mixture at the ring fusion with the *E* isomer dominating is assigned on the basis of the olefin region in the <sup>1</sup>H NMR and analogy.<sup>1</sup> Partial <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>)  $\delta$  6.34 (0.38 H, d, *J* = 16.4 Hz), 6.31 (0.62 H, d, *J* = 15.5 Hz), 6.11 (0.62 H, dd, *J* = 15.5, 7.5 Hz), 6.02 (0.38 H, dd, *J* = 16.4, 8 Hz).

(15) A 45:55 mixture of the *E* and *Z* ring-fusion isomers as determined by the methyl ester signals in the <sup>1</sup>H NMR spectrum (minor isomer at  $\delta$  3.72 and 3.69, major isomer at  $\delta$  3.69 and 3.65) is assigned by analogy.<sup>1</sup>

(16) Partial <sup>1</sup>H NMR  $\delta$  6.15 (1 H, dt, *J* = 15, 7 Hz), 5.85 (1 H, d, *J* = 15 Hz), 5.72 (1 H, ddt, *J* = 15, 8, 3 Hz), 5.05 (1 H, d, *J* = 15 Hz), 4.98 (1 H, d, *J* = 8 Hz), 4.60 (1 H, t, *J* = 3 Hz).

(17) Snider, B. B.; Phillips, G. B.; Cordova, R. *J. Org. Chem.* **1983**, *48*, 3003.

(18) <sup>1</sup>H NMR analysis allows assignment of the *trans,anti* stereochemistry. Partial <sup>1</sup>H NMR  $\delta$  4.03 (dm, *J* = 9.5 Hz), 3.14 (tm, *J* = 9.4 Hz).

(19) For a quasiintramolecular case, see ref 17. For intermolecular cases, see ref 17 and: Bednarski, M.; Danishefsky, S. *J. Am. Chem. Soc.* **1983**, *105*, 3716. Jurczak, J.; Bauer, T.; Filippek, S.; Tkacz, M.; Zygo, K. *J. Chem. Soc., Chem. Commun.* **1983**, 540 and references cited therein.

(20) Trost, B. M.; Keinan, E. *J. Org. Chem.* **1979**, *44*, 3451; *J. Am. Chem. Soc.* **1978**, *100*, 7779. Trost, B. M.; Genet, J. P. *Ibid.* **1976**, *98*, 8516.

(21) For related intramolecular Diels-Alder reactions, see: Babayam, A. T.; Melikyan, T. R.; Torosyan, G. H.; Mkrtchyan, R. S.; Tagmazyan, K. T. *Arm. Khim. Zh.* **1976**, *29*, 388; *Chem. Abstr.* **1976**, *85*, 143012.

(cf. **12**) and antibiotics represented by X-14547A<sup>22</sup> (cf. **18** and **19**).

**Acknowledgment.** We thank the National Institutes of Health and the National Science Foundation for their generous support of our work. M.L. gratefully acknowledges a predoctoral fellowship from NSERC of Canada. We thank Englehardt and Johnson Matthey for supplies of palladium salts and Pressure Chemical and Climax Molybdenum Corp. for molybdenum hexacarbonyl.

(22) Nicolaou, K. C.; Magolda, R. L. *J. Org. Chem.* **1981**, *46*, 1506. Roush, W. R.; Myers, A. G. *Ibid.* **1981**, *46*, 1509.

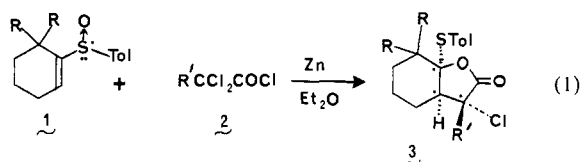
## Enantiospecific Lactonizations of Chiral 1-(Arylsulfinyl)cyclohexenes with Chloroketenes<sup>1</sup>

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The use of an enantiomerically pure sulfinyl group to activate a carbon-carbon double bond toward nucleophilic addition has only met with limited success to date due to the diminished Michael-reactivity of 1-alkenyl sulfoxides. Tsuchihashi was the first to add a carbon nucleophile to an optically pure styryl sulfoxide with significant asymmetric induction (60% ee).<sup>2</sup> More recently, Posner has shown that simple 1-alkenyl sulfoxides do not undergo conjugate additions with common organometallics.<sup>3</sup> However, when an additional activating group is present at the  $\alpha$  position of chiral 1-alkenyl sulfoxides, conjugate additions do indeed occur with a high degree of asymmetric induction.<sup>3,4</sup> Several years ago, we described a unique stereospecific cyclization of dichloroketene with simple 1-alkenyl sulfoxides.<sup>5</sup> *At this time, we wish to report that this reaction, when applied to enantiomerically pure 1-(arylsulfinyl)cyclohexenes, leads to optically pure  $\gamma$ -butyrolactones 3 with complete enantiospecificity. We have, in fact, assembled as many as three contiguous chiral centers from a single chiral sulfur atom (eq 1).*



When the pure *R* and *S* enantiomers<sup>6</sup> of 1-cyclohexenyl tolyl sulfoxide (**1**, R = R' = L) were subjected to excess trichloroacetyl chloride (5 equiv) and zinc-copper couple in refluxing ether, high yields of the enantiomeric  $\gamma$ -butyrolactones **3** (R = R' = H, R' = Cl) were obtained. While the crystalline products<sup>7</sup> rotated plane polarized light to an equal extent in opposite directions, we sought independent evidence for their enantiomeric purity. An attempt to analyze the 360-MHz <sup>1</sup>H NMR spectra of the products in the

(1) Taken in part from: Perez, A. D. Ph.D. Thesis University of Michigan, Ann Arbor, 1984; paper presented in part at the 11th International Symposium on the Organic Chemistry of Sulfur, Lindau, West Germany, Sept 10, 1984.

(2) Tsuchihashi, G.; Mitamura, S.; Inoue, S.; Ogura, K. *Tetrahedron Lett.* **1973**, 323.

(3) For an up-to-date review, see: Posner, G. In "Asymmetric Synthesis"; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, Part A, Chapter 8, p 225.

(4) (a) Posner, G. H.; Hulce, M.; Mallamo, J. P.; Drexler, S. A.; Clardy, J. *J. Org. Chem.* **1981**, *46*, 5244. (b) Posner, G. H.; Mallamo, J. P.; Hulce, M.; Frye, L. L. *J. Am. Chem. Soc.* **1982**, *104*, 4180.

(5) Marino, J. P.; Neisser, M. *J. Am. Chem. Soc.* **1981**, *103*, 7687.

(6) Prepared from the Grignard of 1-chlorocyclohexene and the menthol *p*-toluenesulfonates according to the Anderson method. Anderson, K. K. *J. Org. Chem.* **1964**, *29*, 1953.

(7) The enantiomeric lactones **3a** possessed a mp 111-112 °C. All rotations were taken in acetone with *c*  $\approx$  2.09 g/100 mL.