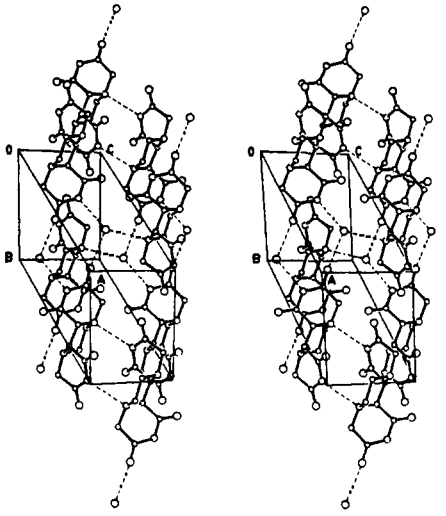

Figure 5. Stereoscopic representation of the molecular packing in the crystal of *trans*-**4**·H_2O.

speculate that one of the important stereochemical features for cytostatic action is an inter-ring separation of "proximal" oxygen atoms of about 4.5 Å; C6–C12 bond formation results in an interatomic O···O distance in *trans*-**4** compatible with that in *cis*-**3** and with activity, but in *cis*-**4** it results in a conformation in which the separation of "proximal" oxygens is constrained to be too short and therefore presumably incapable of interacting with some "receptor" system.

The crystal packing arrangements are quite different in the three crystal structures reported here. The most extensive system of hydrogen bonding occurs in *trans*-**4** monohydrate (Figure 5), in which the molecules are linked as dimers by a pair of N10–H···N1 hydrogen bonds, and the dimers are interconnected to other dimers through water molecules, each of which is a hydrogen donor to an oxygen and tetrahedral nitrogen atom and a hydrogen acceptor from N4–H. In the structure of *trans*-**4**·$(CH_3)_2SO$ solvate, the only hydrogen bonds are from N10–H to the $(CH_3)_2SO$ oxygen and a weak interaction between N4–H and N7 of another molecule. The molecular arrangement in *cis*-**4** consists of chains of molecules linked by two N–H···O bonds at each end, similar to the situation in the cis cyclopropane analogue of ICRF-159,[1] with only van der Waals interactions between chains.

Acknowledgment. We thank D. T. Witiak and B. K. Trivedi for supplying the title compounds. Financial support from the Medical Research Council of Canada and from a USPHS grant (CA15879) is gratefully acknowledged.

Registry No. *trans*-**4**·H_2O, 84924-33-4; *trans*-**4**·Me_2SO, 84894-19-9; *cis*-**4**, 84894-20-2.

Supplementary Material Available: A listing of observed and calculated structure factors, hydrogen atom coordinates, and heavy-atom anisotropic thermal parameters for all three structures (39 pages). Ordering information is given on any current masthead page.

Stereochemistry of the Sakurai Reaction. Additions to Cyclohexenones and Cycloheptenones

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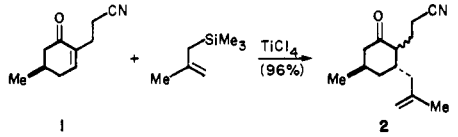
Abstract: The $TiCl_4$-mediated reactions of allyltrimethylsilane (Sakurai reaction) with cyclic enones **3–7** have been investigated. The stereochemistry of these reactions has been compared with the stereochemistry of the copper-catalyzed conjugate addition of *n*-propylmagnesium bromide with the same set of enones. It is shown that the major products formed in the Sakurai reactions are those favored on stereoelectronic grounds. In each case the copper-catalyzed Grignard addition affords less of the stereoelectronically preferred product, presumably as a result of steric hindrance to approach of the bulky cuprate cluster to the Lewis acid coordinated enone.

In our recent *Lycopodium* alkaloid synthesis we employed Sakurai's method for the conversion of cyanoenone **1** into compound **2**, in which the methallyl group has been introduced ex-



clusively trans to the methyl group at C-5.[1] This result represents a substantial improvement over the use of lithium dimethallylcuprate, which gives a mixture of products from which cyano ketone **2** can be isolated in only 66% yield. In addition, the allylsilane procedure is relatively simple compared with the lengthy and tedious procedures required for the preparation of allyllithium reagents.[2] Because of these desirable properties, we have carried out a systematic investigation of the stereochemistry of the Sakurai reaction with conformationally flexible α,β-unsaturated ketones. In this paper we report the results of additions to methylcyclohexenones **3**[3] and **4** and methylcycloheptenones **5–7**.[4]

Results

Allylsilane additions were carried out in the normal manner.[5,6] Reaction products were analyzed by ^{13}C NMR spectroscopy and,

(1) C. H. Heathcock, E. F. Kleinman, and E. S. Binkley, *J. Am. Chem. Soc.*, **104**, 1054 (1982).

(2) D. Seyferth and M. A. Werner, *J. Org. Chem.*, **26**, 4797 (1961). For conjugate additions of lithium diallylcuprate, see: H. O. House and W. F. Fischer, Jr., *ibid.*, **34**, 3615 (1969).

(3) G. Stork and R. L. Danheiser, *J. Org. Chem.*, **38**, 1775 (1973).

(4) C. H. Heathcock, T. C. Germroth, and S. L. Graham., *J. Org. Chem.*, **44**, 4481 (1979).

(5) A. Hosomi and H. Sakurai, *J. Am. Chem. Soc.*, **99**, 1673 (1977). For a review of the uses of allylsilanes in organic synthesis, see: H. Sakurai, *Pure Appl. Chem.*, **54**, 1 (1982).

(6) H. O. House, T. S. B. Sayer, and C. C. Yau, *J. Org. Chem.*, **43**, 2153 (1978).

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Scheme I

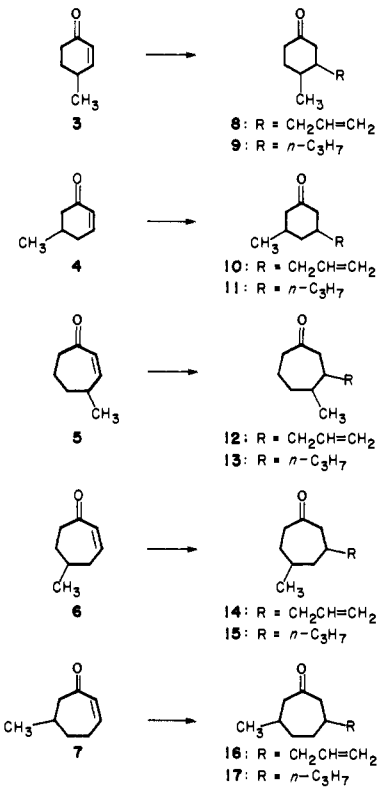


Table I. Conjugate Additions of Allyltrimethylsilane and *n*-Propylmagnesium Bromide to Enones **3–7**

	CH_2=$CHCH_2SiMe_3$, $TiCl_4$, −78 °C			*n*-C_3H_7MgBr, CuI, −20 °C		
enone	product	yield, %	trans:cis	product	yield, %	trans:cis
3	**8**	76	32:68	**9**	78	80:20
4	**10**	83	>98:2	**11**	81	93:7
5	**12**	71	35:65	**13**	65[a]	83:17[a]
6	**14**	76	>98:2	**15**	74	82:18
7	**16**	71	11:89	**17**	71	37:63

[a] Data given for conjugate addition of the di-*n*-propylcopper-boron trifluoride complex to **5**.[9]

in some cases, by gas chromatography. Stereochemical assignments were made by comparison of the ^{13}C NMR spectra of the hydrogenated allylsilane products with the spectra of the corresponding compounds obtained from the copper-catalyzed conjugate addition of *n*-propylmagnesium bromide to enones **3–7** (Scheme I). In most cases, both cis and trans diastereomeric products were obtained. Diastereomer ratios were determined by comparison of peak heights of ^{13}C NMR resonances of similar carbons in a pair of diastereomers. For those pairs of isomers that were also analyzed by GLC, the GLC-derived ratio was identical, within experimental error, with the ^{13}C NMR derived ratio. It is assumed that the major and minor isomers produced in the copper-catalyzed Grignard additions to enones **3–7** are the same as those produced in the di-*n*-alkyl cuprate additions to these enones.[4,7]

The stereochemical assignments for the cis and trans isomers of ketone **17** were supported by comparing the observed ^{13}C NMR resonances with calculated spectra.[4,8] The spectra were calculated by adding appropriate α, β, and γ shift corrections for changing a methyl group to a propyl group to the chemical shifts of the known isomers of 3,6-dimethylcycloheptanone.[4] Results are summarized in Table I.

(7) G. H. Posner, *Org. React.*, **19**, 1 (1972); see pp 18–22 and 32–40.
(8) J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, 1972.

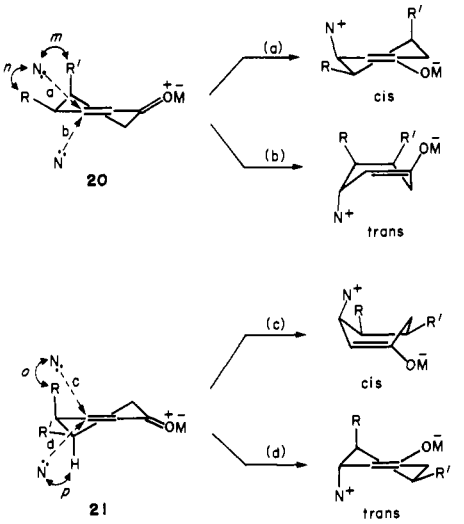
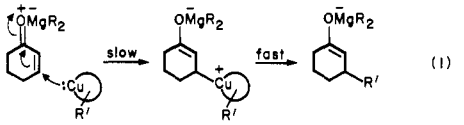


Figure 1. Stereoelectronic and steric factors for conjugate additions to Lewis acid complexes of 4-methylcyclohexenone (R = Me, R′ = H) and 5-methylcyclohexenone (R = H, R′ = Me).

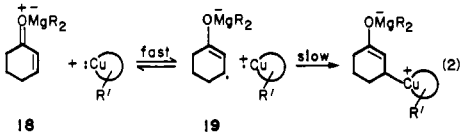
Discussion

Examination of Table I reveals several interesting trends. First, the stereoselectivity of the allylsilane additions is often higher than that observed with the copper-catalyzed Grignard additions (enones **4**, **6**, **7**).[10] Second, in two cases (enones **3** and **5**), the major isomer produced in the allylsilane addition is different from that resulting from the organocopper reaction. Finally, there is a striking parallel in the behavior of similarly substituted cyclohexenones and cycloheptenones (cf. enones **3** and **5**, **4** and **6**).

The results in Table I may be understood in terms of an interplay of stereoelectronic and steric hindrance effects. In the discussion that follows, we assume a mechanism for the copper-catalyzed Grignard reaction similar to that proposed by Krauss and Smith for the addition of lithium cuprates to enones.[11] It is assumed that the rate-limiting step in the reaction is nucleophilic addition of the copper of a cuprate cluster to the Lewis acid coordinated enone, and that the ensuing reductive elimination is rapid (eq 1). This mechanism is operationally identical with the



House mechanism, involving initial electron transfer from the cuprate cluster to the enone or the coordinated enone (eq 2),[12]



since the geometry of the resulting radical-anion **19** is expected to be virtually identical with that of the coordinated enone **18**. Thus, the rate-limiting collapse of the radical-anion–radical-cation pair should be subject to the same stereoelectronic and steric hindrance factors that would prevail in the nucleophilic addition summarized in eq 1. For the Sakurai reaction, it is assumed that

(9) (a) Y. Yamamoto and K. Maruyama, *J. Am. Chem. Soc.*, **100**, 3240 (1978); (b) C. M. Tice, Ph.D. Dissertation, University of California, Berkeley, 1981.
(10) It should be noted that stoichiometric homocuprate reagents often exhibit slightly greater stereoselectivity than the corresponding copper-catalyzed Grignard reactions.[7]
(11) S. R. Krauss and S. G. Smith, *J. Am. Chem. Soc.*, **103**, 141 (1981).
(12) (a) H. O. House, *Acc. Chem. Res.*, **9**, 59 (1976); (b) H. O. House and J. M. Wilkins, *J. Org. Chem.*, **43**, 2443 (1978); (c) R. A. J. Smith and D. J. Hannah, *Tetrahedron*, **35**, 1183 (1979).

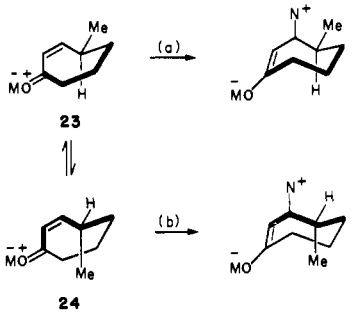
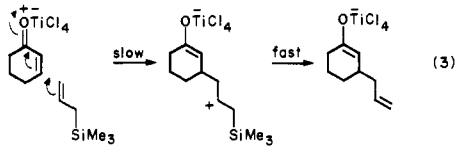


Figure 2. Nucleophilic additions to the Lewis acid complexes of 4-methylcycloheptenone.

the rate-limiting step is nucleophilic attack of the allylsilane double bond on the $TiCl_4$-coordinated enone (eq 3).[5,13]



Cyclohexenones **3** and **4** may each react from one of two half-chair conformations, designated as **20** and **21** in Figure 1. For the 4-methyl isomer, conformer **20** is more stable, while conformer **21** is preferred for the 5-methyl isomer. If maximum π-overlap is to be maintained throughout the course of the addition reaction, then conformations **20** and **21** may each be transformed into a chair or a boat adduct. It is reasonable to assume that the preferred reaction in each case might be the one that leads from the more stable reactant conformer to the more stable of its two stereoelectronically allowed adduct conformations. For 4-methylcyclohexenone (**3**) this would be path a, leading to the cis product. For 5-methylcyclohexenone (**4**), the stereoelectronically preferred reaction should be path d, leading to the trans isomer. However, steric hindrance of approach of the nucleophile to the enone double bond must also be taken into account. The principal steric factors are indicated *m*, *n*, *o*, and *p* in Figure 1. For 4-methylcyclohexenone interaction *n* hinders the stereoelectronically preferred reaction path a leading to the cis product. As a result, some reaction occurs by paths b and d, both of which give rise to trans product. Path c is disfavored on two accounts. First, it is unlikely on stereoelectronic grounds, since it leads from the less stable reactant conformer to a boat adduct. Second, interaction *o* appears to be even more serious than interaction *n*. It should also be noted that the steric hindrance factors *m*–*p* are expected to be more significant for the bulky cuprate cluster than for the monomeric allylsilane. Thus, the Sakurai reaction of enone **3** does yield mainly the stereoelectronically preferred product, although the cis:trans ratio is probably lower than would be expected in the absence of steric hindrance factors. For the copper catalyzed Grignard addition, steric hindrance predominates, and the trans isomer becomes the major product.

The foregoing analysis is consistent with the observation that cuprate additions to 3,4-dialkylcyclohexenones are exceedingly stereoselective, in the sense signified by path d in Figure 1.[14] For these compounds, conformation **21** is preferred over conformation **20** because of the $A^{1,2}$ strain that exists in the latter.[15] Thus, stereoelectronic and steric hindrance factors are cooperative. These factors are also apparent in allylsilane additions to 3,4-dialkylcyclohexenones. Sakurai has shown that the reaction of allyltrimethylsilane with $\Delta^{1,9}$-2-octalone (**22**) proceeds with exclusive

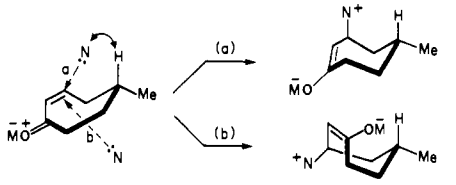


Figure 3. Nucleophilic additions to the Lewis acid complexes of 5-methylcycloheptenone.

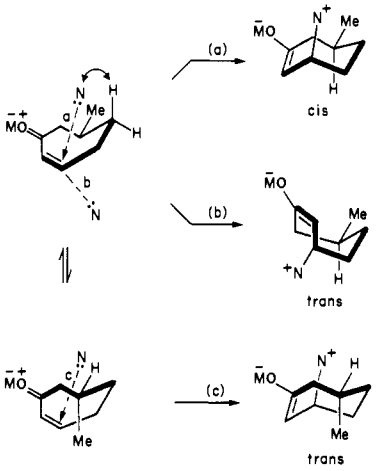
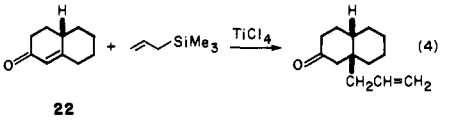


Figure 4. Nucleophilic additions to the Lewis acid complexes of 6-methylcycloheptenone.

Table II. Differences in Activation Energies for the Formation of Cis and Trans Products in the Addition of Allyltrimethylsilane and *n*-Propylmagnesium Bromide to Enones **3**–**7**

	CH_2=$CHCH_2SiMe_3$		*n*-C_3H_7MgBr		difference in $\Delta\Delta G^{\ddagger}$, kcal mol^{-1}
enone	trans:cis	$\Delta\Delta G^{\ddagger}$, kcal mol^{-1}	trans:cis	$\Delta\Delta G^{\ddagger}$, kcal mol^{-1}	
3	32:68	−0.29	80:20	+0.70	0.99
4	>98:2	>1.52	93:7	1.31	>0.21
5	35:65	−0.24	83:17	0.81	1.04
6	>98:2	>1.52	82:18	0.77	>0.75
7	11:89	−0.82	37:63	−0.27	0.55

production of the cis-fused decalone; i.e., addition occurs trans to the 4-alkyl substituent (eq 4).[5]



For 5-methylcyclohexenone (**4**), the stereoelectronically preferred reaction path d is not seriously hindered, and the only detectable product from the allylsilane addition is the trans isomer. Even the cuprate reaction provides 93% of the trans product. The 7% of cis product in this case may reflect interaction of the cuprate cluster with the axial hydrogen at C-5 (interaction *p*). In this case, there may be some reaction by path c, since path a appears to be seriously impeded by interaction *m*.

A priori conformational analysis is more difficult for cycloheptanes than for cyclohexanes, since there are more conformations that must be considered for the former compounds. However, the data presented in Table I suggest that the stereoelectronic and steric hindrance effects operating in enones **5** and **6** may be similar to those operating in cyclohexenones **3** and **4**. Thus, the major reaction paths for 4-methylcycloheptenone (**5**) may be those indicated in Figure 2. With the smaller reagent, the stereoelectronically preferred reaction path a leads to the cis isomer. However, the cuprate cluster experiences steric hindrance with the C-4 methyl group, and reaction also occurs through the less stable conformer **24**, leading to the trans isomer. For enone **6**,

(13) (a) R. Pardo, J.-P. Zahra, and M. Santelli, *Tetrahedron Lett.*, 4557 (1979); (b) T. K. Sakar and N. H. Andersen, *ibid.*, 3513 (1978).
(14) (a) F. E. Ziegler, G. R. Reid, W. L. Studt, and P. A. Wender, *J. Org. Chem.*, **42**, 1991 (1977); (b) P. M. Wege, R. D. Clark, and C. H. Heathcock, *ibid.*, **41**, 3144 (1976).
(15) (a) F. Johnson and S. K. Malhotra, *J. Am. Chem. Soc.*, **87**, 5492 (1965); (b) F. Johnson, *Chem. Rev.*, **68**, 375 (1968).

the principal reaction path for the allylsilane reaction is also postulated to be axial attack on the more stable chair conformation (Figure 3). With the more bulky cuprate cluster, the indicated interaction with the axial hydrogen at C-5 may force some reaction by path b, leading to the boat conformation of the cis isomer.

For 6-methylcycloheptenone (**7**), the major reaction path in both reactions is presumably axial attack on the chair conformation having the methyl group equatorial (path a in Figure 4). Again, however, there is steric hindrance from the axial hydrogen at C-5. Consequently, there is some trans product formed by paths b and c.

In summary, the present study suggests that stereoelectronic and steric hindrance factors can fully explain the stereoselectivity observed in the $TiCl_4$-mediated additions of allylsilanes and the CuI-promoted addition of Grignard reagents to cyclohexenones and cycloheptenones. In each case it appears that the allylsilane addition product is the stereoelectronically preferred one. In the cuprate additions there is a significant steric hindrance effect which reduces the amount of the stereoelectronically favored isomer. In energy terms, this steric hindrance effect appears to be on the order of 1 kcal mol^{-1} (Table II).

Experimental Section

General. Unless otherwise stated, materials were obtained from commercial suppliers and used without further purification. Tetrahydrofuran (THF) and methylene chloride were distilled from sodium/benzophenone and calcium hydride, respectively, immediately prior to use. Titanium tetrachloride was distilled from copper powder and stored under nitrogen. Cuprous iodide was purified as the dimethyl sulfide complex according to the procedure of House.[16] All reactions involving organometallic reagents were conducted under a nitrogen atmosphere. Upon workup, solvents were evaporated with a Büchi rotary evaporator, unless otherwise indicated. Boiling points are uncorrected. IR spectra were determined with a Perkin-Elmer Model 297 infrared recording spectrophotometer. ^1H NMR spectra were determined on the UCB-250, a super-conducting, FT instrument operating at 250 MHz. ^{13}C NMR spectra were measured at 62.89 MHz on the UCB-250. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane. Significant ^1H NMR data are tabulated in order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), number of protons, coupling constant(s) in hertz. ^{13}C NMR data are listed separately for each isomer; for those samples containing mixtures of diastereomers, the resonances for all carbons of the minor isomers were not always discernible. Mass spectra were obtained with an Atlas MS-12 mass spectrometer. Mass spectral data are tabulated as *m/e* (intensity as a percent of total ion current). Gas–liquid partition chromatography (GLC) was done with a Varian Aerograph 940 gas chromatograph. Elemental analyses were preformed by the Microanalytical Laboratory, operated by the College of Chemistry, University of California, Berkeley, Calif.

General Procedure for Allylsilane Conjugate Additions. 4-Methyl-3-(2-propenyl)cycloheptanone (12). A well-stirred[17] solution of 3.816 g (30.7 mmol) of enone **5** in 300 mL of dry methylene chloride was cooled to −78 °C. Titanium tetrachloride (4.00 mL, 6.90 g, 36.3 mmol) was added in one portion, giving rise to a deep red solution in which a yellow precipitate was evident. After 5 min, a solution of a 5.26 g (46.1 mmol) of allyltrimethylsilane in 10 mL of dry methylene chloride was added dropwise over a 45-min period. The dark purple mixture was stirred an additional 60 min, and 75 mL of water was then added over a 10-min period. The reaction mixture was allowed to warm to room temperature, during which time it became colorless. The mixture was partitioned between ether and brine. The ethereal layer was dried over Na_2SO_4 and the solvent was evaporated. Distillation of the residue through a short-path still afforded 3.63 g (71%) of a clear, colorless liquid, bp 57–63 °C (0.17 torr): IR (film) 1700, 1440, 990, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (d, 3, J = 7), 1.00 (d, 3, J = 7-minor), 2.03 (dd, 2, J = 7, 13), 5.00 (m, 2), 5.74 (m, 1); ^{13}C NMR ($CDCl_3$) major isomer δ 19.9, 20.8, 35.4, 37.6, 38.2, 41.3, 43.5, 45.2, 116.2, 136.5, 213.6; minor isomer δ 13.2, 20.5, 35.5, 38.0, 38.5, 43.2, 46.1, 116.7, 135.4, 213.9; mass spectrum (70 eV) *m/e* 167 (0.44) 166 (1.02), 151 (1.36), 125 (1.86), 108 (4.32), 81 (5.15), 55 (19.57). Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.30; H, 10.74.

The following compounds were prepared in a manner analogous to that described above.

(16) H. O. House, C. Y. Chu, J. M. Wilkins, and M. J. Umen, *J. Org. Chem.*, **40**, 1460 (1975).

(17) For larger scale preparations (employing 10 mmol or more of enone), use of a mechanical stirrer is recommended.

(3*RS*,5*RS*)-5-Methyl-3-(2-propenyl)cycloheptanone (14). The reaction was performed with 153 mg (1.23 mmol) of enone **6**, 0.165 mL (285 mg, 1.50 mmol) of titanium tetrachloride, and 225 mg (1.97 mmol) of allyltrimethylsilane. The crude product was purified by chromatography on silica gel (8% ether in hexanes) to afford 156 mg (76%) of **14**: IR (film) 1700, 1455, 990, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (d, 3, J = 7), 1.60 (m, 3), 1.80 (m, 1), 1.98 (m, 2), 2.04 (d, 2, J = 7), 2.33 (m, 2-minor), 2.40 (dt, 2, J = 5, 9), 2.60 (m, 2), 5.00 (d, 1, J = 4), 5.06 (s, 1), 5.76 (m, 1); ^{13}C NMR ($CDCl_3$) δ 20.6, 29.8, 30.3, 31.4, 39.9, 40.7, 42.3, 48.5, 116.5, 136.1, 213.7. Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.11; H, 10.78.

6-Methyl-3-(2-propenyl)cycloheptanone (16). The reaction was performed with 308 mg (2.48 mmol) of enone **7**, 0.35 mL (604 mg, 3.18 mmol) of titanium tetrachloride, and 430 mg (3.78 mmol) of allyltrimethylsilane. The crude product was purified by chromatography on silica gel (7% ether in hexanes) to afford 291 mg (71%) of **16**: IR (film) 1640, 1440, 990, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (d, 2, J = 7-minor), 0.95 (d, 2 J = 7), 1.63 (m, 3), 1.90 (m, 1), 2.03 (t, 2, J = 7), 2.23 (dd, 2, J = 9, 15), 2.62 (ddd, 2, J = 3, 7, 11), 4.99 (dd, 1, J = 1, 3), 5.00 (d, J = 1), 5.73 (m, 1); ^{13}C NMR ($CDCl_3$) major isomer δ 20.6, 29.0, 31.0, 34.1, 39.6, 48.8, 50.6, 116.2, 135.9, 212.1; minor isomer δ 23.4, 28.1, 31.4, 35.5, 41.8, 49.4, 51.6, 116.4, 135.6, 212.3. Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.15; H, 10.82.

4-Methyl-3-(2-propenyl)cyclohexanone (8). The reaction was performed with 3.515 g (31.91 mmol) of enone **3**, 4.25 mL (7.34 g, 38.7 mmol) of titanium tetrachloride, and 5.46 g (47.8 mmol) of allyltrimethylsilane. The crude product was purified by distillation through a short-path still to afford 3.69 g (76%) of a clear, colorless oil, bp 112–115 °C (3 torr): IR (film) 1710, 1440, 990, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 (d, 3, J = 7), 5.04 (m, 2), 5.71 (m, 1); ^{13}C NMR ($CDCl_3$) major isomer δ 13.0, 30.8, 31.2, 35.6, 37.7, 41.1, 43.2, 116.2, 135.9, 211.2; minor isomer δ 19.2, 28.3, 32.4, 35.0, 37.9, 40.6, 43.5, 116.9, 136.4, 211.3. Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.98; H, 10.47.

(3*RS*,5*SR*)-5-Methyl-3-(2-propenyl)cyclohexanone (10). The reaction was performed with 3.11 g (28.23 mmol) of enone **4**, 3.75 mL (6.47 g, 34.1 mmol) of titanium tetrachloride, and 4.85 g (42.5 mmol) of allyltrimethylsilane. The crude product was purified by distillation through a short-path still to afford 3.56 g (83%) of a clear, colorless liquid, bp 45–47 °C (0.25 torr): IR (film) 1710, 1225, 990, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (d, 3, J = 7), 1.60 (dd, 2, J = 7, 11), 2.02 (m, 4), 2.20 (ddd, J = 2, 7, 13), 2.36 (m, 2), 4.95 (dd, 1, J = 2, 5), 5.00 (s, 1), 5.67 (m, 1); ^{13}C NMR ($CDCl_3$) δ 20.5, 29.2, 34.1, 36.8, 39.1, 46.2, 48.5, 116.4, 135.7, 211.3. Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.67; H, 10.64.

General Procedure for Hydrogenations. 4-Methyl-3-propylcycloheptanone (13). Keto-olefin **12** (316 mg, 1.90 mmol) was dissolved in 25 mL of absolute ethanol and 50 mg of 5% palladium on carbon was added. The mixture was stirred under an atmosphere of hydrogen until the uptake of hydrogen had ceased. After removal of the catalyst by filtration through Celite, the solvent was evaporated to afford 300 mg (94%) of pure **13**: IR (film) 1700, 1455, cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (d, 3, J = 7), 0.89 (t, 3, J = 6), 0.99 (d, 3, J = 7-minor); ^{13}C NMR ($CDCl_3$) major isomer δ 13.6, 14.3, 20.2, 34.2, 35.1, 36.4, 38.1, 41.1, 43.3, 45.8, 213.6; minor isomer δ 13.8, 18.8, 34.8, 36.1, 37.8, 43.1, 45.5. Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.68; H, 11.89.

The following compounds were prepared in a manner analogous to that described above:

(3*RS*,5*RS*)-5-Methyl-3-propylcycloheptanone (15). The reaction was performed with 71.2 mg (0.428 mmol) of keto-olefin **14** and 20 mg of 5% palladium on carbon to afford 64 mg (89%) of pure **15**: IR (film) 1700, 1455 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (t, 3, J = 7), 0.93 (d, 3, J = 7); ^{13}C NMR ($CDCl_3$) δ 14.0, 20.2, 21.6, 30.2, 30.8, 31.6, 37.3, 41.2, 43.0, 48.9, 214.4. Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.83; H, 11.73.

6-Methyl-3-propylcycloheptanones (17). The reaction was performed with 134.3 mg (0.807 mmol) of keto-olefin **16** and 10 mg of PtO_2 to afford 122 mg (90%) of pure **17**: IR (film) 1700, 1455 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (t, 3, J = 7), 0.93 (d, 3, J = 7), 0.96 (d, 3, J = 7-minor), 2.58 (dt, 1, J = 3, 15); ^{13}C NMR ($CDCl_3$) major isomer δ 13.9, 20.0, 21.5, 29.6, 32.2, 34.0, 34.3, 37.2, 49.4, 51.1, 213.3; minor isomer δ 19.7, 23.9, 31.8, 35.7, 35.9, 38.2, 40.0, 50.2, 51.8, 213.5. Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.43; H, 11.81.

4-Methyl-3-propylcyclohexanone (9). The reaction was performed with 158 mg (1.04 mmol) of keto-olefin **8** and 10 mg of PtO_2 to obtain 146 mg (91%) of pure **9**: IR (film) 1715, 1460 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3, J = 7), 1.02 (d, 3, J = 7); ^{13}C NMR ($CDCl_3$) major isomer δ 14.0, 20.0, 31.2, 31.5, 32.6, 38.0, 41.2, 42.7, 43.9, 211.9; minor isomer δ 18.7, 34.1, 35.1, 35.9, 40.8, 45.6, 212.1. Anal. Calcd. for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.67; H, 11.58.

(3*RS*,5*SR*)-5-Methyl-3-propylcyclohexanone (11). The reaction was performed with 350 mg (2.30 mmol) of keto-olefin **10** and 50 mg of 10% palladium on carbon to afford 323 mg (91%) of pure **11**: IR (film) 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, 3, J = 7), 0.98 (d, 3, J = 7); ^{13}C NMR ($CDCl_3$) δ 13.8, 19.9, 20.6, 29.4, 34.1, 37.0, 37.3, 46.8, 48.7, 211.7. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.49; H, 11.54.

4-Methyl-3-propylcycloheptanone (13). To a well-stirred suspension of 763 mg (4.0 mmol) of purified copper(I) iodide in 5 mL of THF at 5 °C, 9.3 mL of 0.43 M *n*-propylmagnesium bromide (4.0 mmol) in THF was added dropwise over a 30-min period. The black mixture was stirred for 10 min at 5 °C and cooled to −70 °C; 0.49 mL (4.0 mmol) of boron trifluoride etherate was added, dropwise, over a 20-min period. The mixture was stirred for 20 min at −70 °C, and 239 mg (1.93 mmol) of enone **5** in 2 mL of dry THF was added dropwise over a 20-min period. The mixture was stirred for 2 h at −70 °C, allowed to warm to room temperature, and poured into a mixture of 100 mL of ether and 100 mL of a 4:1 mixture of saturated aqueous ammonium chloride solution and concentrated aqueous ammonia. The aqueous layer was separated and extracted with ether. The combined organic extracts were washed once each with 4:1 ammonia buffer and brine. After drying over $MgSO_4$, removal of solvent left 211 mg (65%) of crude product: ^1H NMR ($CDCl_3$) δ 0.87 (d, 3, J = 7-minor), 0.99 (d, 3, J = 7). ^{13}C NMR ($CDCl_3$): the resonances assigned to the major product correspond to those of the minor isomer from hydrogenation of **12**; the resonances of the minor product correspond to the major isomer from hydrogenation of **12**.

General Procedure for Copper-Catalyzed Grignard Reactions. 5-Methyl-3-propylcycloheptanone (15). To a well-stirred suspension of 64.0 mg (2.63 mmol) of magnesium turnings in 1 mL of dry THF at room temperature was added 5 drops of 1-bromopropane and a small crystal of iodine. After several minutes the violet color disappeared and the reaction was diluted with 2.5 mL of dry THF. The remaining 1-bromopropane [a total volume of 0.15 mL (203 mg, 1.65 mmol) of 1-bromopropane was added] was added dropwise over a 30-min period. After stirring for an additional 30 min, the mixture was cooled to −20 °C and 33 mg (0.17 mmol) of purified copper(I) iodide was added. After stirring for another 30-min period, 184 mg (1.48 mmol) of enone **6** in 1 mL of dry THF was added dropwise over a 20-min period. During this addition, the reaction became bright yellow in color. After stirring for 30 min, the reaction was allowed to warm to room temperature, during which time the mixture turned black and was subsequently poured into a well-stirred 4:1 mixture of saturated aqueous ammonium chloride solution and concentrated aqueous ammonia. The resulting mixture was extracted twice with ether. The combined ether extracts were washed once each with 4:1 ammonia buffer and brine before drying over Na_2SO_4. The solvent was evaporated to afford 240 mg of a pale yellow oil. The crude product was chromatographed on 10 g of silica gel (5% ether in hexanes) to afford 183 mg (74%) of a clear, colorless oil. ^{13}C NMR ($CDCl_3$): the resonances of the major isomer correspond to those of the hydrogenated allylsilane product 15; minor isomer δ 19.7, 24.1, 32.6, 35.1, 35.8, 40.2, 42.6, 45.7, 50.0.

The following compounds were prepared in a manner analogous to that described above.

6-Methyl-3-propylcycloheptanone (17). The reaction was performed with 347 mg (2.79 mmol) of enone **7**. The crude product was purified by chromatography on silica gel (4% ether in hexanes) to afford 332 mg (71%) of **17**. ^{13}C NMR ($CDCl_3$): the resonances observed for the major and minor isomers correspond to those obtained for the hydrogenated allylsilane product **17**.

4-Methyl-3-propylcyclohexanone (9). The reaction was performed with 3.643 g (33.07 mmol) of enone **3**. The crude product was purified by distillation using a short-path still to afford 3.957 g (78%) of a clear, colorless liquid, bp 42–46 °C (1.0 torr). ^{13}C NMR ($CDCl_3$): the resonances assigned to the major and minor products correspond to those of the minor and major isomers, respectively, obtained for the hydrogenated allylsilane product **9**.

5-Methyl-3-propylcyclohexanone (11). The reaction was performed with 2.861 g (25.97 mmol) of enone **4**. The crude product was purified by distillation using a short-path still to afford 3.27 g (81%) of a clear, colorless liquid, bp 83–85 °C (7.0 torr): ^1H NMR ($CDCl_3$) δ 0.98 (d, 3, J = 7), 1.02 (d, 3, J = 6-minor). ^{13}C NMR ($CDCl_3$): the resonances of the major isomer correspond to those of the hydrogenated allylsilane product **11** ; minor isomer δ 13.8, 33.6, 37.4, 47.0, 49.3, 210.9.

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Registry No. (±)-**3**, 79980-78-2; (±)-**4**, 54352-35-1; (±)-**5**, 83096-45-1; (±)-**6**, 84924-80-1; (±)-**7**, 84877-72-5; (±)-*cis*-**8**, 84877-73-6; (±)-*trans*-**8**, 84877-74-7; (±)-*cis*-**9**, 84877-75-8; (±)-*trans*-**9**, 84877-76-9; (±)-*trans*-**10**, 84877-77-0; (±)-*trans*-**11**, 84877-78-1; (±)-*cis*-**12**, 84877-79-2; (±)-*trans*-**12**, 84877-80-5; (±)-*cis*-**13**, 84877-81-6; (±)-*trans*-**13**, 84877-82-7; (±)-*trans*-**14**, 84877-83-8; (±)-*cis*-**15**, 84877-84-9; (±)-*trans*-**15**, 84877-85-0; (±)-*cis*-**16**, 84877-86-1; (±)-*trans*-**16**, 84877-87-2; (±)-*cis*-**17**, 84877-88-3; (±)-*trans*-**17**, 84877-89-4.