Intramolecular Cyclization of Allyl- and Propargylsilanes. The Regio- and Stereochemical Outcome of the Cyclization

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The syntheses of allyl- and propargylsilanes and their additions to enones and dienones are described. Propargylsilanes of type **1** undergo cyclization to spiro[4.5]decanes with $EtAlCl_2$ or $TiCl_4$ as the Lewis acid catalyst. Propargylsilanes of type **2** cyclize upon treatment with $EtAlCl_2$ to fused [4.3.0]nonanes. Allylsilanes of type **15** undergo regioselective 1,6-additions to dienones to form bicyclo[4.5.0]undecenones **21**, and propargylsilanes of type **14** cyclize regioselectively in 1,4 fashion (bicyclo[4.3.0]nonanones). Allylsilane **16** forms either a bicyclo-[4.6.0]dodecenone (with $TiCl_4$) or a 1:1 mixture of the latter compound and a bicyclo[4.4.0]decanone (with $EtAlCl_2$).

Introduction

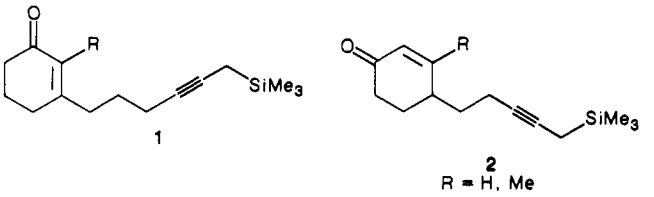
As part of a general study of Lewis acid catalyzed intramolecular reactions of allyl- and propargylsilanes, $EtAlCl_2$ was found to be a very useful catalyst for intramolecular Sakurai reactions forming stereoselectively a variety of spiro and fused bicyclo ketones.[1-5] In this account we describe syntheses of allyl- and propargylsilanes[6-9] and their cyclizations with enones and conjugated dienones.

Recent papers by Majetich and co-workers[10-17] have prompted us to submit a full account of our own investigations along these lines.

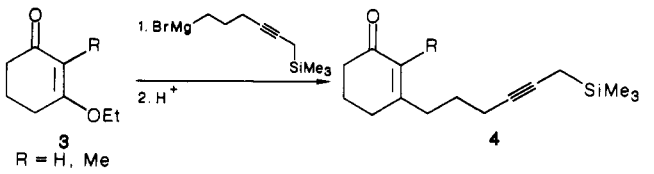
The construction of quaternary carbon centers remains as a fundamental test for synthetic methods in organic synthesis.[18] In particular, the syntheses of spirocyclic systems and fused bicyclo compounds with angular substituents are important testing grounds for such technologies.[19]

Furthermore, these results provide a new route to control the ring size in annulation reactions by the choice of the terminating group and the Lewis acid selected.

Scheme I



Scheme II



Results and Discussion

Preparation of Cyclization Substrates. In connection with these studies, we required an efficient entry to functionalized allyl- and propargylsilanes of the general structures **1** and **2** (Scheme I). As a result of Stork's early studies, vinylogous esters like 3-ethoxycyclohexenone[20] were deemed to be useful educts for constructing the desired starting materials.

Treatment of compounds **3** with the propargylsilane Grignard reagent followed by hydrolysis provided the precursors for the spiroannulation reactions (40–50% yield) (Scheme II).

Reaction of 3-ethoxycyclohexenones with lithium diisopropylamide (LDA) at −78 °C and subsequent alkylation with functionalized iodides[5,21] in the presence of 1.1 equiv of hexamethylphosphoric triamide (HMPT) [or 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU)] yielded the cyclization substrates for the annulation reactions.

As shown in Schemes III–V, compounds **5–8** can be used in a very flexible way for further transformations leading to various precursors for the construction of fused systems.

Cyclization Study. As previously reported in preliminary communications, compound **4a** reacted smoothly with 1.1 equiv of $EtAlCl_2$ in toluene at −78 °C to afford the desired spiro[4.5]decanone. Under the same conditions, compound **4b** reacted not at all. Even after 2 days

(1) Three independent updated reviews about allylsilane chemistry are in press [by Fleming and Dunogues, Majetich, and Schinzer (*Synthesis* **1988**, 263)].
(2) Schinzer, D. *Angew. Chem.* **1984**, *86*, 292; *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 308.
(3) Schinzer, D.; Sólyom, S.; Becker, M. *Tetrahedron Lett.* **1985**, *26*, 1831.
(4) Schinzer, D.; Steffen, J.; Sólyom, S. *J. Chem. Soc., Chem. Commun.* **1986**, 829.
(5) Schinzer, D.; Allagiannis, C.; Wichmann, S. *Tetrahedron*, "Symposia-in-Print", in press.
(6) Wilson, S. R.; Price, M. F. *J. Am. Chem. Soc.* **1982**, *104*, 1124.
(7) Denmark, S. E.; Weber, E. J. *Helv. Chim. Acta* **1983**, *66*, 1655.
(8) Despo, A. D.; Chiu, S. K.; Flood, T.; Peterson, P. E. *J. Am. Chem. Soc.* **1980**, *102*, 5122.
(9) Schmid, R.; Huesmann, P. C.; Johnson, W. S. *J. Am. Chem. Soc.* **1980**, *102*, 5123.
(10) Majetich, G.; Desmond, R.; Casares, A. M. *Tetrahedron Lett.* **1985**, *26*, 2747.
(11) Majetich, G.; Hull, K.; Desmond, R. *Tetrahedron Lett.* **1985**, *26*, 2751.
(12) Majetich, G.; Hull, K.; Defauw, J.; Shawe, T. *Tetrahedron Lett.* **1985**, *26*, 2755.
(13) Majetich, G.; Behnke, M.; Hull, K. *J. Org. Chem.* **1985**, *50*, 3615.
(14) Majetich, G.; Defauw, J.; Hull, K.; Shawe, T. *Tetrahedron Lett.* **1985**, *26*, 4711.
(15) Majetich, G.; Ringold, C. *Heterocycles* **1987**, *25*, 271.
(16) Majetich, G.; Hull, K. *Tetrahedron* **1987**, *43*, 5621.
(17) Majetich, G.; Defauw, J.; Ringold, C. *J. Org. Chem.* **1988**, *53*, 50.
(18) Martin, S. F. Tetrahedron Report No. 75, *Tetrahedron* **1980**, *36*, 419.
(19) Oppolzer, W.; Gorrichon, L.; Bird, T. G. C. *Helv. Chim. Acta.* **1981**, *64*, 186.
(20) Stork, G.; Danheiser, R. L. *J. Org. Chem.* **1973**, *38*, 1775.
(21) Hiemstra, H.; Klauer, W. J.; Speckamp, W. N. *J. Org. Chem.* **1984**, *49*, 1149.

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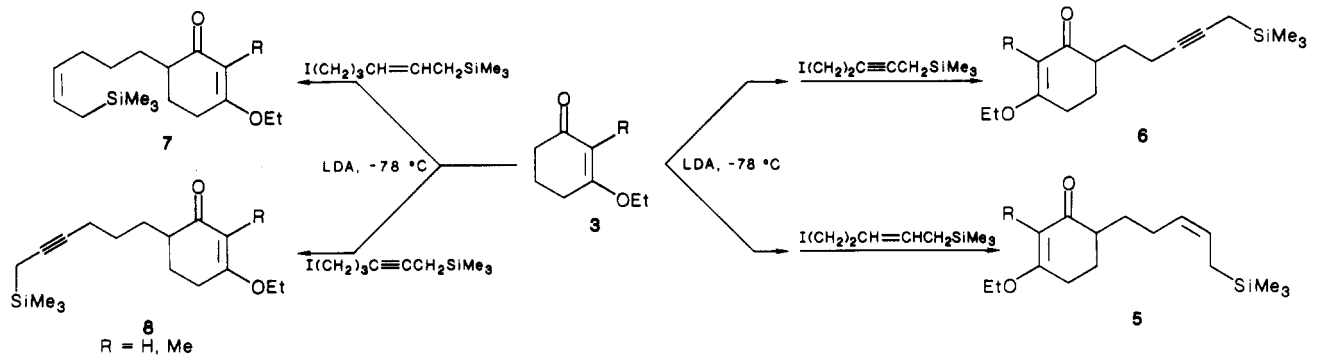
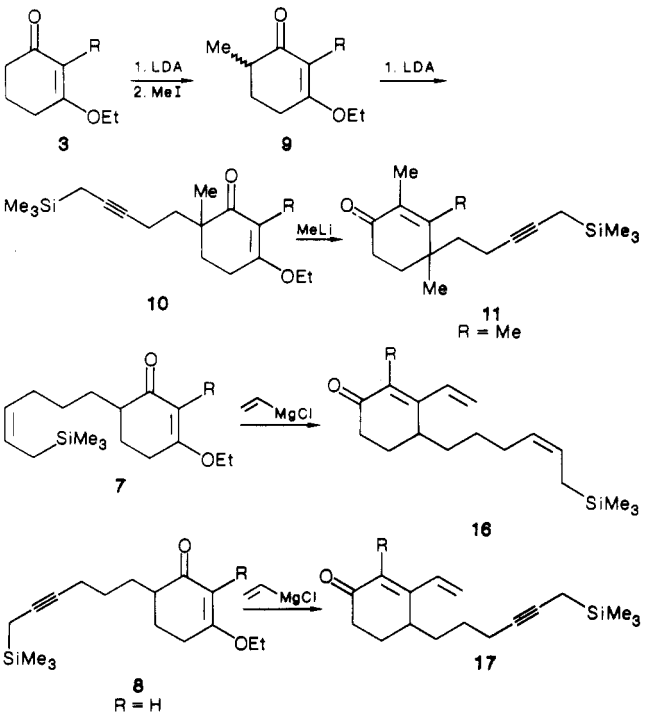
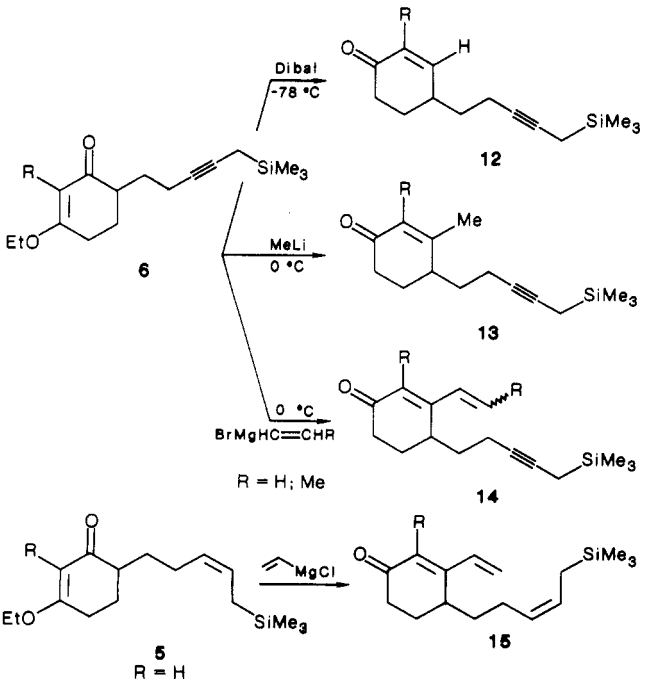
Scheme III



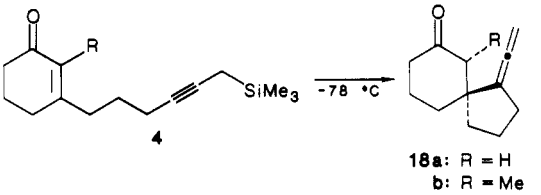
Scheme IV



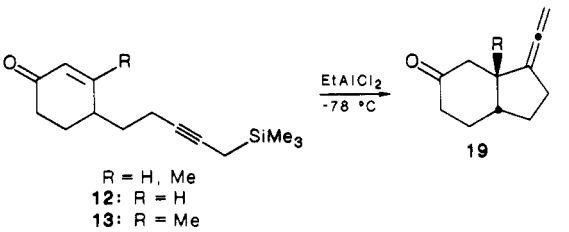
Scheme V



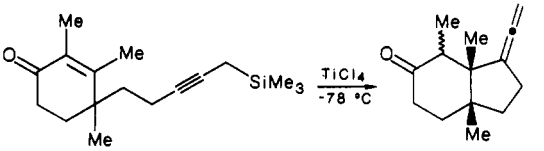
Scheme VI



Scheme VII



Scheme VIII



of stirring at room temperature, only starting material was recovered.

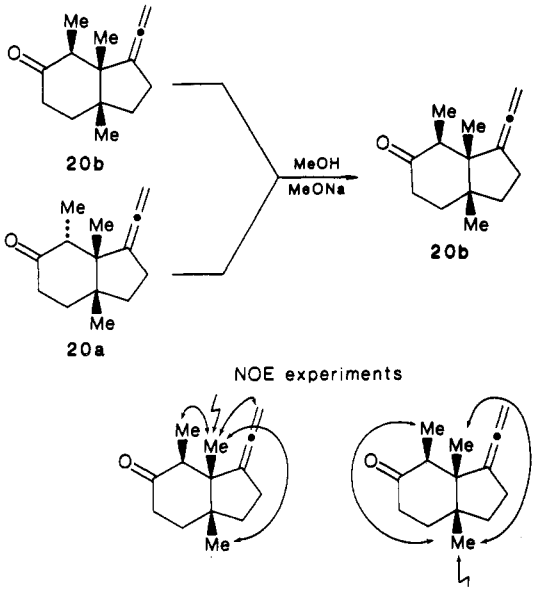
However, cyclization was brought about by using 1.1 equiv of $TiCl_4$ as the Lewis acid catalyst at −78 °C in methylene chloride. The latter cyclization reaction proceeded with remarkable stereocontrol, leading to a single isomer **18b**, which was obtained after quenching with water at −78 °C (Scheme VI).

Structural assignments were based on 400-MHz NOE difference spectra. The diastereomer shown is supported by the absence of a NOE between the methyl group and the terminal allene protons. In order to explain the observed stereoselectivity, one can postulate protonation at the least hindered face, and the reaction product observed should be the kinetically controlled one.

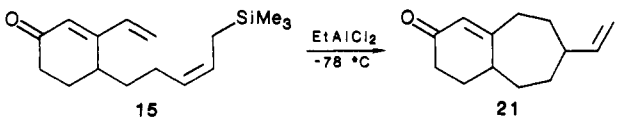
The cyclizations of compounds **12** and **13**, which bear an additional substituent in the 3-position, were carried out in toluene at −78 °C with $EtAlCl_2$ as the Lewis acid (Scheme VII). Even the construction of the quarternary center was carried out at −78 °C. In both cases we obtained single isomers of the expected cis-fused products.

In addition, we have examined the cyclization of **11**. Again, the reaction proceeded smoothly with 1.9 equiv of $TiCl_4$ at −78 °C forming the cis-fused hydrindanone **20** with two adjacent quaternary centers in 84% isolated yield

Scheme IX



Scheme X



Scheme XI

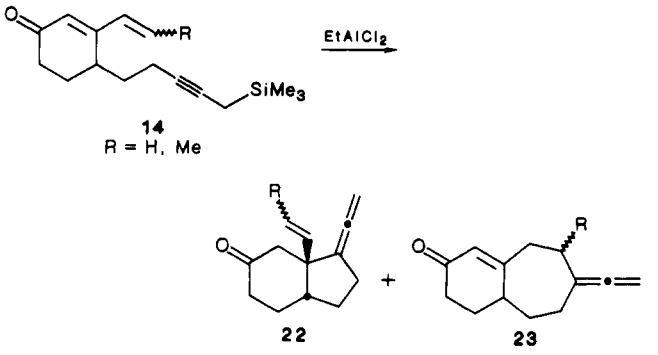


Table I. Conditions for the Conversion Ratio of the Isomers and Yields

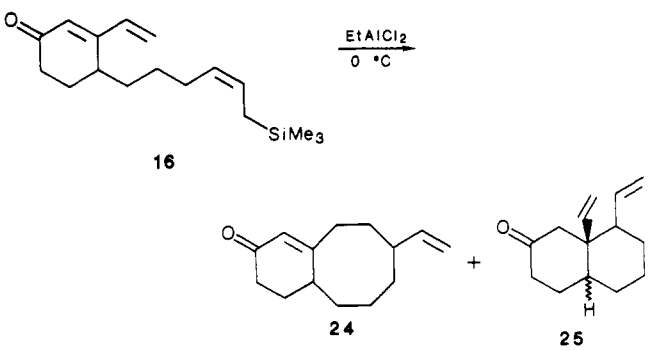
14	condtns	22:23	yield, %
a	PhMe, 0 °C	3:1	51
a	PhMe, −78 °C	10:1	88
b	PhMe, −78 °C	10:1	74

(Scheme VIII). The reaction mixture was quenched at −78 °C under kinetically controlled conditions, yielding a 2:1 mixture of diastereomers. These diastereomers can be separated with flash chromatography, and the structures were established by NOE difference spectra.

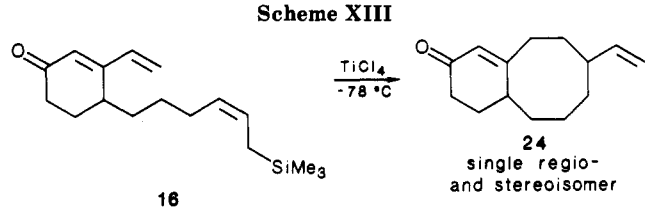
Compound **20** can be equilibrated by CH_3ONa/CH_3OH to form compound **20b** with three syn methyl groups in a row (supported by the NOEs shown in Scheme IX), which represents an interesting intermediate along the total synthesis of pinguisone.[22]

Finally, we have examined the addition of structurally identical allyl- and propargylsilanes **14**–**17** to conjugated dienones. Compound **15** cyclized only in a 1,6 fashion, leading to the bicyclo[4.5.0]undecenone **21** as a single regio- and stereoisomer (Scheme X). In contrast, the propargylsilane **14** *reversed* the regioselectivity, forming a 1,4-addition product as the major product (Scheme XI) (see Table I).

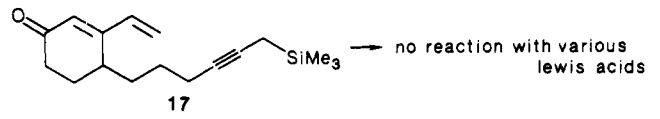
Scheme XII



Scheme XIII



Scheme XIV



The observed preference for obtaining the 1,4-addition products is probably influenced by the lower nucleophilicity of the propargylsilane terminator. Therefore, the formation of the five-membered ring reflects a reaction at the center with the highest charge density. On the other hand, the identical allylsilane shows the *opposite preference*, leading to the 1,6-addition product. This could be a result of the higher nucleophilicity of the allylsilane terminator. Now steric interactions become more important, and the molecule reacts at the less hindered part, forming a seven-membered ring.

These results shown an interesting change in ring-size selectivity between the allyl- and propargylsilane terminators and provide a route to controlled annulation. However, the one carbon homologated molecule **16** does not show the same cyclization behavior. With $EtAlCl_2$ as the Lewis acid, a 1:1 mixture of the 1,4- and 1,6-addition products[23] was obtained (Scheme XII). Exposure of the same substrate to $TiCl_4$ as the Lewis acid provided only the 1,6-addition product as a single regio- and stereoisomer, in 45% yield[24] (Scheme XIII). The structurally identical propargylsilane **17**, however, failed to cyclize under a variety of conditions, and instead, only starting material was recovered (Scheme XIV).

Conclusions

To summarize, we have shown that the Lewis acid mediated cyclizations of allyl- and propargylsilanes are a powerful tool to synthesize spiro and fused bicyclic compounds.

There are striking advantages over known annulation methods: (1) The annulation procedure allows stereose-

(22) Uyehara, T.; Kabasawa, Y.; Kato, T.; Furuta, T. *Tetrahedron Lett.* **1985**, *26*, 2343.

(23) The product mixture is a 4:1 mixture of diastereomers.

(24) The same effect was observed by Majetich and co-workers, private communication, 1986.

lective spirocyclizations at low temperatures. (2) The synthesis of adjacent quaternary centers proceeds under mild conditions. (3) The selected terminator governs the ring size and provides a route to controlled annulation. (4) The selected Lewis acid influences the regio- and stereochemical outcome of the cyclization. (5) The products obtained are useful precursors for a number of natural products and allow further functional-group manipulations.

Experimental Section

High-resolution mass spectra were obtained on a Finnigan MAT 312 spectrometer. IR spectra were recorded on a Perkin-Elmer 580 spectrometer. NMR spectra were taken on Bruker WH 90, WP 200, AM 300, and WH 400 spectrometers. Additions were carried out with a Braun Melsungen AG Unita syringe pump.

All reactions were run under inert gas (nitrogen), and pure products were obtained after flash chromatography using the solvent system ethyl acetate/petroleum ether (60–70 °C).

Grignard Reagent of 1-Bromo-6-(trimethylsilyl)-4-hexyne. To 1.51 g of Mg (62 mg-atom) activated by a trace of iodine in 15 mL of THF were added 8.20 g (35.15 mmol) of 1-bromo-6-(trimethylsilyl)-4-hexyne (in 80 mL of THF) with a syringe pump over 3 h. The mixture was refluxed for 2 h and then titrated to yield 28.8 mmol of Grignard solution.

3-[6-(Trimethylsilyl)-4-hexynyl]cyclohex-2-en-1-one (4a). To a solution of 1.57 g (11.23 mmol) of 3-ethoxycyclohexenone **3a** in 15 mL of THF were added 14.48 mL of the freshly prepared Grignard solution with a syringe pump over 15 min. The reaction mixture was stirred for 12 h at room temperature and was refluxed for an additional 1 h. The mixture was poured into 100 mL of saturate NH_4Cl solution at 0 °C and was stirred for 10 min. The resulting mixture was extracted three times with 80 mL of ether, and the combined organic layers were washed with 100 mL of brine and dried over $MgSO_4$. The solvent was removed, and the crude product was chromatographed (25% ethyl acetate/petroleum ether) to obtain 0.843 g (30%) of pure product **4a**: IR (film) 2959, 2215, 1670, 1250, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 0.1 (s, 9 H), 1.42 (t, J = 2.5 Hz, 2 H), 1.66 (m, 2 H), 1.93–2.49 (10 H), 5.88 (br s, 1 H) ppm; high-resolution mass spectrum calcd for $C_{15}H_{24}OSi$ 248.1596, found 248.1595.

3-[6-(Trimethylsilyl)-4-hexynyl]-2-methylcyclohex-2-en-1-one (4b). Reaction under the same conditions provided **4b** in 32.5% yield: IR (film) 2220, 1655, 1630, 1255, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 0.1 (s, 9 H), 1.43 (t, J = 2.5 Hz, 2 H), 1.49–2.0 (m, 4 H), 1.77 (br s, 3 H), 2.48 (m, 4 H) ppm; high-resolution mass spectrum calcd for $C_{16}H_{26}OSi$ 262.1753, found 262.1752.

General Procedure for Alkylations of 3-Ethoxycyclohexenones. 3-Ethoxy-6-[5-(trimethylsilyl)-3-pentenyl]-cyclohex-2-en-1-one (5a). To a solution of 3.5 mL (25 mmol) of diisopropylamine in 10 mL of THF at 0 °C was added 16.6 mL of a 1.5 M solution of *n*-butyllithium in hexanes. After 10 min, the solution was cooled to −78 °C and 3.5 g (25 mmol) of 3-ethoxycyclohexenone was added via a syringe pump over 30 min. After the mixture was stirred for 10 min at −78 °C, 8.7 mL (50 mmol) of HMPT was added in one portion. After 20 min of additional stirring, 6.7 g (25 mmol) of 1-iodo-5-(trimethylsilyl)-3-pentene was added over 2 min at −78 °C, and the mixture was allowed to warm to room temperature and was stirred overnight at this temperature. The reaction mixture was poured into 50 mL of a saturated solution of NH_4Cl and was extracted three times with 50 mL of ether. The combined organic layers were washed five times with 100 mL of water and 100 mL of brine and were dried over $MgSO_4$. The solvent was removed, and the crude product was chromatographed (10% ethyl acetate/petroleum ether) to yield 1.96 g (28%) of pure product: IR (film) 1655, 1605, 1250, 1190, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 0.08 (s, 9 H), 1.43 (t, J = 7 Hz, 3 H), 1.45–2.66 (11 H), 3.95 (q, J = 7 Hz, 2 H), 5.38 (s, m, 3 H) ppm; ^{13}C NMR ($CDCl_3$) 201.5, 176.5, 126.7, 102.1, 63.9, 44.6, 29.4, 27.8, 26.1, 24.4, 18.3, 14.0, −1.9 ppm; high-resolution mass spectrum calcd for $C_{16}H_{28}O_2Si$ 280.1858, found 280.1858.

3-Ethoxy-6-[5-(trimethylsilyl)-3-pentynyl]cyclohex-2-en-1-one (6a). Compound **6a** was obtained in 34% yield by using the general procedure: IR (film) 2160, 1650, 1600, 1245, 1190, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 0.077 (s, 9 H), 1.43 (t, J = 7 Hz, 3 H), 1.47 (t, J = 3 Hz, 2 H), 1.55–2.66 (9 H), 3.93 (q, J = 7 Hz, 2 H), 5.37 (s, 1 H) ppm; ^{13}C NMR ($CDCl_3$) 200.7, 176.3, 102.1, 77.9, 77.7, 63.9, 44.0, 29.2, 28.1, 26.2, 16.7, 13.9, 6.8, −2.3 ppm; high-resolution mass spectrum calcd for $C_{16}H_{26}O_2Si$ 278.1702, found 278.1700.

3-Ethoxy-6-[6-(trimethylsilyl)-4-hexenyl]cyclohex-2-en-1-one (7a). Reaction under the same conditions provided 3.16 g (34%) of pure **7a**: IR (film) 2960, 1645, 1610, 1385, 1200, 860 cm^{-1}; ^1H NMR ($CDCl_3$) −0.04 (s, 9 H), 1.32 (t, J = 7 Hz, 3 H), 1.39 (d, J = 10 Hz, 2 H), 1.17–2.20 (9 H), 2.38 (t, J = 6 Hz, 2 H), 3.85 (q, J = 7 Hz, 2 H), 5.26 (s, 1 H), 5.14–5.44 (m, 2 H) ppm; ^{13}C NMR ($CDCl_3$) 201.37 (s), 176.42 (s), 127.21 (d), 125.55 (d), 102.18 (d), 64.01 (t), 45.14 (d), 29.31 (t), 27.87 (t), 27.30 (t), 27.12 (t), 26.16 (t), 18.40 (t), 14.08 (q), −1.84 (q) ppm; high-resolution mass spectrum calcd for $C_{17}H_{30}O_2Si$ 294.2015, found 294.2015.

3-Ethoxy-6-[6-(trimethylsilyl)-4-hexynyl]cyclohex-2-en-1-one (8a). Compound **8a** was obtained in 28% yield by using the general procedure: IR (film) 2950, 2170, 1660, 1190, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 0.08 (s, 9 H), 1.356 (t, J = 7 Hz, 3 H), 1.41 (t, J = 3 Hz, 2 H), 1.42–2.25 (m, 9 H), 2.43 (t, J = 6 Hz, 2 H), 3.88 (q, J = 7 Hz, 2 H), 5.29 (s, 1 H) ppm; high-resolution mass spectrum calcd for $C_{17}H_{28}O_2Si$ 292.1858, found 292.1866.

2,6-Dimethyl-3-ethoxy-6-[5-(trimethylsilyl)-3-pentynyl]-cyclohex-2-en-1-one (10b). Compound **10b** was obtained in 40% yield by using the general procedure: IR (film) 2960, 2250, 1615, 1380, 1120, 910, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 0.03 (s, 9 H), 1.01 (s, 3 H), 1.265 (t, J = 7 Hz, 3 H), 1.33 (t, J = 3 Hz, 2 H), 1.56 (br s, 3 H), 1.6–2.2 (m, 6 H), 2.45 (br t, 2 H), 3.99 (q, J = 7 Hz, 2 H) ppm; high-resolution mass spectrum calcd for $C_{18}H_{30}O_2Si$ 306.2015, found 306.2002.

4-[5-(Trimethylsilyl)-3-pentynyl]cyclohex-2-en-1-one (12). To a solution of 200 mg (0.72 mmol) of **6a** in 10 mL of toluene was added at −78 °C 0.9 mL (1.08 mmol) of a 1.2 M solution of Dibal in toluene. The reaction mixture was stirred for 2 h at −78 °C and was quenched with 20 mL of a saturated solution of NH_4Cl, and the mixture was extracted twice with 30 mL of ether. The organic layer was washed with 20 mL of 1 N HCl and 50 mL of brine and was dried over $MgSO_4$. The solvent was removed, and the crude product was chromatographed (10% ethyl acetate/petroleum ether) to obtain 82 mg (49%) of pure product: IR (film) 2960, 2180, 1665, 1250, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 0.09 (s, 9 H), 1.44 (t, J = 2.7 Hz, 2 H), 1.5–1.95 (m, 4 H), 1.95–2.8 (m, 5 H), 5.97 (dd, J = 10, 2.5 Hz, 1 H), 6.86 (m, 1 H) ppm; high-resolution mass spectrum calcd for $C_{14}H_{22}OSi$ 234.1439, found 234.1439.

General Procedure for the Reaction of Vinylogous Esters with Grignard or Lithium Reagents. 3-Methyl-4-[5-(trimethylsilyl)-3-pentynyl]cyclohex-2-en-1-one (13). To a solution of 500 mg (1.79 mmol) of **6a** in 10 mL of THF was added at 0 °C 1.7 mL (2.04 mmol) of a 1.2 M solution of methyllithium in ether. After 30 min, the reaction mixture was poured into 50 mL of a saturated solution of NH_4Cl. The mixture was extracted three times with 50 mL of ether, and the combined organic layers were washed with 50 mL of brine and dried over $MgSO_4$. The solvent was removed, and the crude product was chromatographed (10% ethyl acetate/petroleum ether) to yield 331 mg (74%) of pure product: IR (film) 2960, 2180, 1665, 1250, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 0.07 (s, 9 H), 1.41 (d, J = 2.7 Hz, 2 H), 1.5–1.9 (m, 4 H), 1.94 (s, 3 H), 2.0–2.6 (m, 6 H), 5.79 (s, 1 H) ppm; high-resolution mass spectrum calcd for $C_{15}H_{24}OSi$ 248.1596, found 248.1595.

2,3,4-Trimethyl-4-[5-(trimethylsilyl)-3-pentynyl]cyclohex-2-en-1-one (11b). Compound **11b** was obtained in 85% yields by using the general procedure: IR (film) 2970, 2160, 1660, 1615, 1260, 860 cm^{-1}; ^1H NMR ($CDCl_3$) 0.03 (s, 9 H), 1.07 (s, 3 H), 1.32 (t, J = 3 Hz, 2 H), 1.4–2.4 (6 H), 1.625 (d, J = 0.5 Hz, 3 H), 1.725 (d, J = 0.5 Hz, 3 H) ppm; high-resolution mass spectrum calcd for $C_{17}H_{28}OSi$ 276.1909, found 276.1901.

3-Ethenyl-4-[5-(trimethylsilyl)-3-pentynyl]cyclohex-2-en-1-one (14a). Compound **14a** was obtained in 85% yield by using the general procedure: IR (film) 2960, 2180, 1665, 1250, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 0.07 (s, 9 H), 1.43 (t, J = 2.7 Hz, 2 H), 1.5–1.85 (m, 5 H), 5.46 (d, J = 10 Hz, 1 H), 5.81 (d, J = 17 Hz, 1 H), 5.86 (s, 1 H), 6.35 (dd, J = 10, 17 Hz, 1 H) ppm; high-resolution mass spectrum calcd for $C_{16}H_{24}OSi$ 260.1596, found 260.1595.

3-Propenyl-4-[5-(trimethylsilyl)-3-pentynyl]cyclohex-2-en-1-one (14b). Compound **14b** was obtained in 82% yield by

using the general procedure: IR (film) 2960, 2220, 1670, 1570, 1250, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 0.04 (s, 9 H), 1.37 (d, J = 2.7 Hz, 2 H), 1.5–1.7 (m, 5 H), 1.77 (d, J = 5 Hz, 3 H), 5.85 (m, 3 H) ppm; high-resolution mass spectrum calcd for $C_{17}H_{26}OSi$ 274.1752, found 274.1751.

3-Ethenyl-4-[5-(trimethylsilyl)-3-pentenyl]cyclohex-2-en-1-one (15a). Compound **15a** was obtained in 80% yield by using the general procedure: IR (film) 2980, 1670, 1625, 1585, 1250, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 1.35–1.85 (m, 5 H), 1.9–2.5 (m, 6 H), 5.0–5.65 (m, 2 H), 5.45 (d, J = 10.5 Hz, 1 H), 5.68 (d, J = 17.5 Hz, 1 H), 5.86 (s, 1 H) ppm; ^{13}C NMR ($CDCl_3$) 199.65 (s), 161.06 (s), 147.23 (d), 136.98 (d), 130.38 (d), 127.18 (d), 120.61 (t), 54.37 (d), 46.38 (t), 32.96 (t), 32.03 (t), 31.23 (t), 25.17 (t), 0.16 (q) ppm; high-resolution mass spectrum calcd for $C_{16}H_{26}OSi$ 262.1753, found 262.1752.

3-Ethenyl-4-[6-(trimethylsilyl)-4-hexenyl]cyclohex-2-en-1-one. (16). Compound **16** (2.47 g) was obtained in 85% yield by using the general procedure: IR (film) 2960, 1665, 1250, 860 cm^{-1}; ^1H NMR ($CDCl_3$) –0.02 (s, 9 H), 1.11–1.67 (m, 6 H), 1.81–2.17 (m, 4 H), 2.30–2.74 (m, 3 H), 5.03–5.50 (m, 2 H), 5.43 (d, J = 10.5 Hz, 1 H), 5.64 (d, J = 17 Hz, 1 H), 6.37 (dd, J = 17, 10.5 Hz, 1 H), 5.83 (s, 1 H) ppm; high-resolution mass spectrum calcd for $C_{17}H_{28}OSi$ 276.1909, found 276.1914.

3-Ethenyl-4-[6-(trimethylsilyl)-4-hexynyl]cyclohex-2-en-1-one (17). Compound **17** was obtained in 54% yield by using the general procedure: IR (film) 2950, 2170, 1670, 1620, 1580, 1250, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 0.07 (s, 9 H), 1.425 (t, J = 3 Hz, 2 H), 1.45–1.85 (m, 5 H), 2.0–2.8 (m, 6 H), 5.49 (d, J = 11 Hz, 1 H), 5.72 (d, J = 18 Hz, 1 H), 5.88 (s, 1 H), 6.40 (dd, J = 18, 11 Hz, 1 H) ppm; high-resolution mass spectrum calcd for $C_{17}H_{26}OSi$ 274.1752, found 274.1751.

Cyclization Study. 1-Vinylidenespiro[4.5]decan-7-one (18a). To a stirred solution of 104 mg (0.41 mmol) of **4a** in 10 mL of toluene was added at –78 °C 0.12 mL (0.44 mmol) of a solution of $EtAlCl_2$ in hexanes (50%). After being stirred for 2 h at –78 °C, the reaction mixture was quenched with 5 mL of water. The mixture was extracted three times with 10 mL of toluene, washed with 20 mL of saturated solution of $NaHCO_3$ and 50 mL of brine, and dried over $MgSO_4$. The solvent was removed, and the crude product was chromatographed (40% ethyl acetate/petroleum ether) to obtain 45 mg (62%) of pure product: IR (film) 1950, 1700, 1260, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 1.3–2.6 (14 H), 4.80 (t, J = 4.46 Hz, 2 H, irradiation at 2.45 ppm showed a singlet at 4.80 ppm) ppm; ^{13}C NMR ($CDCl_3$) 211.0 (s), 202.36 (s), 110.84 (s), 78.56 (t), 52.36 (t), 49.22 (s), 40.99 (t), 38.85 (t), 37.68 (t), 30.34 (t), 23.64 (t), 22.92 (t); high-resolution mass spectrum calcd for $C_{12}H_{16}O$ 176.1201, found 176.1199.

(5*RS*,6*RS*)-6-Methyl-1-vinylidenespiro[4.5]decan-7-one (18b). To a stirred solution of 210 mg (0.8 mmol) of **4b** in 12 mL of CH_2Cl_2 at –78 °C was added 0.09 mL (0.84 mmol) of $TiCl_4$, and the mixture was stirred for 3 h at that temperature. The reaction mixture was quenched at –78 °C with 10 mL of water, extracted three times with 30 mL of CH_2Cl_2, washed with 50 mL of brine, and dried over $MgSO_4$. The solvent was removed, and the crude product was chromatographed (10% ethyl acetate/petroleum ether) to yield 70 mg (46%) of pure product: IR (film) 1950, 1700, 1260, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 1.06 (d, J = 7 Hz, 3 H), 1.38–2.6 (13 H), 4.69 (t, J = 3.5 Hz, 2 H) ppm; ^{13}C NMR ($CDCl_3$) 212.38 (s), 203.67 (s), 105.74 (s), 78.02 (t), 52.38 (d), 51.91 (s), 39.90 (t), 39.66 (t), 35.71 (t), 31.91 (t), 23.55 (t), 21.88 (t), 10.67 (q); high-resolution mass spectrum calcd for $C_{13}H_{18}O$ 190.1357, found 190.1367.

General Procedure for Annulation Reactions with $EtAlCl_2$ as the Lewis Acid Catalyst. (1*RS*,6*RS*)-9-Vinylidenebicyclo[4.3.0]nonan-3-one (19a). To a stirred solution of 76 mg (0.32 mmol) of **12** in 10 mL of toluene at –78 °C was added 0.1 mL (0.4 mmol) of a solution of $EtAlCl_2$ (in hexanes, 50%). The mixture was stirred for 2 h at –78 °C and was quenched with 10 mL of a saturated solution of $NaHCO_3$. The reaction mixture was extracted three times with 30 mL of ether, washed with brine, and dried over $MgSO_4$. The solvent was removed, and the crude product was chromatographed (10% ethyl acetate/petroleum ether) to obtain 26 mg (50.2%) of pure product: IR (film) 2940, 1960, 1715, 1450, 1250, 850, 730, 695 cm^{-1}; ^1H NMR ($CDCl_3$) 1.05–2.1 (m, 6 H), 2.1–2.7 (m, 6 H), 4.73 (m, 2 H) ppm; ^{13}C NMR ($CDCl_3$) 211.4, 130.8, 128.8, 105.2, 42.9, 40.8, 38.1, 30.1, 28.1, 27.3 ppm; high-resolution mass spectrum calcd for $C_{11}H_{14}O$ 162.1044, found 162.1044.

(1*RS*,6*RS*)-1-Methyl-9-vinylidenebicyclo[4.3.0]nonan-3-one (19b). Reaction under the same conditions provided 204 mg (87%) of pure **19b**: IR (film) 2930, 1965, 1720, 1460, 850, 735, 700 cm^{-1}; ^1H NMR ($CDCl_3$) 1.08 (d, J = 1.5 Hz, W coupling, 3 H), 1.5–2.9 (11 H), 4.74 (t, J = 4.5 Hz, 2 H) ppm; ^{13}C NMR ($CDCl_3$) 210.9, 201.6, 110.7, 78.4, 49.0, 48.0, 45.0, 37.9, 28.3, 27.6, 27.1 ppm; high-resolution mass spectrum calcd for $C_{12}H_{16}O$ 176.1201, found 176.1200.

9-Ethenylbicyclo[4.5.0]undec-1-en-3-one (21). Reaction under the same conditions provided compound **21** in 60% yield: IR (film) 2940, 1670, 1615, 870 cm^{-1}; ^1H NMR ($CDCl_3$) 1.2 (m, 2 H), 1.5–2.0 (m, 6 H), 2.1 (m, 1 H), 2.2–2.5 (m, 5 H), 4.86 (dddd, 1 H), 4.92 (dddd, 1 H), 5.69 (dddd, 1 H), 5.86 (d, 1 H) ppm; ^{13}C NMR ($CDCl_3$) 199.0 (s), 171.0 (s), 143.0 (d), 127.0 (d), 112.0 (t), 45.0(d), 39.5 (d), 37.3 (t), 35.5 (t), 34.7 (t), 33.0 (t), 30.5 (t), 30.0 (t) ppm; high-resolution mass spectrum calcd for $C_{13}H_{18}O$ 190.1358, found 190.1358.

(1*RS*,6*RS*)-1-Ethenyl-9-vinylidenebicyclo[4.3.0]nonan-3-one (22a) and (6*RS*)-9-Vinylidenebicyclo[4.5.0]undec-1-en-3-one (23a). Reaction under the same conditions provided 228 mg (80%) of pure **22a** and 23 mg (8%) of pure **23a**. **22a**: IR (film) 2920, 1955, 1720, 1670, 1455, 1250, 850, 730 cm^{-1}; ^1H NMR ($CDCl_3$) 1.1–2.65 (11 H), 4.73 (t, J = 4.73 Hz, 2 H), 5.0 (dd, J = 17, 1.2 Hz, 1 H), 5.01 (dd, J = 10, 1.2 Hz, 1 H), 5.7 (dd, J = 10, 17 Hz, 1 H) ppm; ^{13}C NMR ($CDCl_3$) 210.1, 203.2, 143.6, 113.5 107.3, 78.5, 54.8, 46.2, 43.8, 38.6, 28.2, 27.7, 27.2 ppm; high-resolution mass spectrum calcd for $C_{13}H_{16}O$ 188.1201, found 188.1201. **23a**: IR (film) 2920, 1955, 1720, 1670, 1455, 1250, 850, 730 cm^{-1}; ^1H NMR ($CDCl_3$) 1.5–2.7 (13 H), 4.51 (d, J = 2 Hz, 1 H), 4.53 (d, J = 2 Hz, 1 H), 5.80 (s, 1 H) ppm; ^{13}C NMR ($CDCl_3$) 206.2, 199.9, 169.9, 126.8, 101.4, 73.1, 39.5, 35.5, 32.5, 31.6, 31.4, 30.6 ppm high-resolution mass spectrum calcd for $C_{13}H_{16}O$ 188.1201, found 188.1202.

Reaction under the same conditions (except at 0 °C) provided 97 mg (37%) of pure **22a** and 31 mg (12%) of pure **23a**.

(1*RS*,6*RS*)-1-Propenyl-9-vinylidenebicyclo[4.3.0]nonan-3-one (22b) and 10-Methyl-9-vinylidenebicyclo[4.5.0]undec-1-en-3-one (23b). Reaction under the same conditions provided 202 mg (68%) of pure **22b** and 18 mg (6%) of pure **23b**. **22b**: IR (film) 2950, 1960, 1720, 1670, 1250, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 1.5–2.6 (11 H), 1.64 (d, J = 5 Hz, 3 H), 4.72 (t, J = 4 Hz, 1 H), 5.33 (m, 1 H) ppm; ^{13}C NMR ($CDCl_3$ 212.0, 205.3, 138.0, 129.0, 80.5, 55.5, 49.1, 47.6, 41.2, 39.5, 29.8, 29.7, 29.3 ppm; high-resolution mass spectrum calcd for $C_{14}H_{18}O$ 202.1357, found 202.1357. **23b**: IR (film) 2950, 1960, 1720, 1250, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 1.05 (d, J = 6.5 Hz, 3 H), 1.5–2.8 (12 H), 4.60 (m, 2 H), 5.76 (s, 1 H); ^{13}C NMR ($CDCl_3$) 199.3 (s), 197.6 (s), 167.8 (s), 127.4 (d), 106.7 (s), 75.2 (t), 44.5 (t), 39.2 (d), 35.3 (t), 33.5 (d), 33.3 (t), 31.6 (t), 30.8 (t), 20.4 (q) ppm; high-resolution mass spectrum calcd for $C_{14}H_{18}O$ 202.1357, found 202.1357.

1,10-Diethenylbicyclo[4.4.0]decan-3-one (25). Compound **24** and compound **25** were obtained as a 1:1 mixture in 40% yield by using the general procedure. **25**: IR (film) 2940, 1710, 1620, 1110, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 1.04–2.56 (14 H), 4.78–5.23 (m, 3 H), 5.51–5.92 (m, 2 H), 6.11 (dd, J = 11, 7 Hz, 1 H) ppm; high-resolution mass spectrum calcd for $C_{14}H_{20}O$ 204.1514, found 204.1515.

General Procedure for Annulation Reactions with $TiCl_4$ as the Lewis Acid Catalyst. 1,2,6-Trimethyl-9-vinylidenebicyclo[4.3.0]nonan-3-one (20). to a solution of 6.99 g (25.31 mmol) of **10b** in 150 mL of CH_2Cl_2 was added at –78 °C 5.1 mL (44.4 mmol) of $TiCl_4$, and the reaction mixture was stirred for 3 h at –78 °C. The mixture was quenched at –78 °C with 100 mL of water and extracted three times with 50 mL of CH_2Cl_2, and the organic layer was washed with 150 mL of brine and dried over $MgSO_4$. The solvent was removed, and the crude product was chromatographed (3% ethyl acetate/petroleum ether) to yield 4.32 g (84%) of pure product as a 2:1 (**20a**/**20b**) mixture of diastereomers: IR (film) 2960, 1955, 1460, 1175, 1095, 1065, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 0.72 (s, 3 H), 0.87 (s, 3 H), 0.89 (d, J = 7 Hz, 3 H), 1.10 (s, 6 H), 1.16 (d, J = 7 Hz, 3 H), 1.35–2.50 (9 H), 4.62 (dt, J = 4.5, 2 Hz, 2 H), 4.74 (m, 2 H) ppm; ^{13}C NMR ($CDCl_3$) 212.20 (s), 211.63 (s), 203.64 (s), 202.90 (s), 109.48 (s), 107.16 (s), 77.47 (2 t), 56.15 (s), 53.99 (s), 49.11 (d), 48.31 (d), 44.75 (s), 44.70 (s), 37.93 (t), 37.74 (t), 35.91 (t), 35.76 (t), 33.81 (t), 32.92 (t), 26.52

(t), 25.38 (t), 25.14 (q), 22.62 (q), 20.02 (q), 13.05 (q), 8.92 (q), 8.35 (q) ppm; high-resolution mass spectrum calcd for $C_{14}H_{20}O$ 204.1514, found 204.1509.

10-Ethenylbicyclo[6.4.0]dodec-1-en-3-one (24). Compound **24** was obtained in 45% yield by using the general procedure: IR (film) 2940, 1660, 1615, 1260, 850 cm^{-1}; ^1H NMR ($CDCl_3$) 1.15–2.6 (16 H), 4.85 (m, 2 H), 5.75 (m, 1 H), 5.89 (s, 1 H) ppm; ^{13}C NMR ($CDCl_3$) 212.96 (s), 199.20 (s), 143.99 (d), 126.69 (d), 111.90 (t), 42.31 (d), 38.20 (d), 35.99 (t), 34.15 (t), 33.37 (t), 30.60 (t), 30.21 (t), 28.99 (t), 24.42 (t) ppm; high-resolution mass spectrum calcd for $C_{14}H_{20}O$ 204.1514, found 204.1515.

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Registry No. **3a**, 5323-87-5; **3b**, 20643-20-3; **4a**, 110477-25-3; **4b**, 105222-80-8; **5a**, 115142-35-3; **6a**, 115142-36-4; **7a**, 115142-38-6; **8a**, 115142-39-7; **9**, 72535-08-1; **10b**, 115142-40-0; **11b**, 115142-41-1; **12**, 115142-42-2; **13**, 115142-43-3; **14a**, 115142-44-4; **14b**, 115142-45-5; **15a**, 115142-46-6; **16**, 115142-47-7; **17**, 115142-48-8; **18a**, 115142-49-9; **18b**, 115142-50-2; **19a**, 115142-51-3; **19b**, 115142-52-4; **20a**, 115223-79-5; **20b**, 115223-80-8; **21**, 105222-84-2; **22a**, 115142-53-5; **22b**, 115142-55-7; **23a**, 115142-54-6; **23b**, 105222-88-6; **24**, 115142-56-8; **25**, 115142-57-9; $Br(CH_2)_3C{\equiv}CCH_2SiMe_3$, 112129-48-3; $BrMg(CH_2)_3C{\equiv}CCHzSiMe_3$, 105222-94-4; $I(CH_2)_2CH{=}CHCH_2SiMe_3$, 105222-91-1; $I(CH_2)_2C{=}CCH_2SiMe_3$, 88996-00-3; $I(CH_2)_3CH{=}CHCH_2SiMe_3$, 115142-37-5; $I(CH_2)_3C{\equiv}CCH_2SiMe_3$, 88996-02-5; $BrMgCH{=}CH_2$, 1826-67-1; $BrMgCH{=}CHCH_3$, 14092-04-7; $CH_2{=}CHMgCl$, 3536-96-7; $EtAlCl_2$, 563-43-9; $TiCl_4$, 7550-45-0.

Enolization of 2-Decalones

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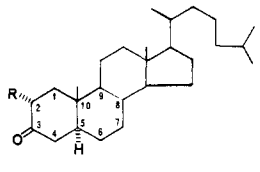
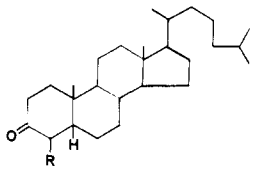
It is well-known that under thermodynamic conditions 5α-3-keto steroids such as 3-cholestanone enolize predominantly toward C-2, while the 5β-isomers enolize toward C-4. It has been tacitly assumed that 2-decalones, bicyclic analogues of the steroids, show similar selectivity. In a systematic investigation of the direction of enolization of 2-decalones, 11 bicyclic ketones plus two representative steroids have been converted to the corresponding trimethylsilyl enol ethers under thermodynamic conditions. The classical generalizations have been found to be valid for *trans*-2-decalones and steroidally locked *cis*-2-decalones with an angular methyl group. Nonsteroidally locked *cis*-2-decalones with an angular methyl enolize in a direction opposite to that predicted. Without an angular methyl, all three types of 2-decalones enolize in the predicted manner, but with attenuated regioselectivity. Molecular-mechanics calculations have been carried out for the olefins corresponding to decalone enols. With the exception of the nonsteroidal cis compounds with an angular methyl, the calculations agree well with the experimental data.

It has been known for many years that bromination, under acidic conditions of 5α-3-keto steroids such as 3-cholestanone (**1**) affords predominantly the 2-bromo 3-ketone **2**, while 5β-3-keto steroids (e.g., coprostanone, **3**) give 4-bromo 3-ketones **4**.[1] These observations have



1 R = H
2 R = Br



3 R = H
4 R = Br

usually been explained in terms of the relative stabilities of the enol precursors, intermediates in the bromination of ketones, and have been related to the stabilities of the corresponding olefins which have served as models for the enols.[1f,2]

On the basis of vector-analysis calculations[3] and subsequent semiquantitative empirical torsional analysis,[4] again using olefins as models, these observations have been extended to the bicyclic analogues of the steroids, the 2-decalones. More refined calculations for the cis olefins were carried out by using Hill calculations[5] and molecular mechanics.[6] These empirical or semiempirical analyses have consistently indicated that the decalones should enolize in the same regioselective sense as steroidal ketones which possess similar stereochemistry about the A–B ring fusion.

However, in contrast to the two steroid models **1** and **3**, the 2-decalones can be divided into six structural classes, two of which have trans ring fusions, and four cis. The *trans*-decalones are locked in a conformation similar to that of cholestanone (**1**) and may have or lack an angular substituent.[7] In contrast to the 5β-steroids **3**, which are

(1) (a) Djerassi, C.; Scholz, C. R. *J. Am. Chem. Soc.* **1948**, *70*, 417. (b) Corey, E. J. *J. Am. Chem. Soc.* **1953**, *75*, 2301, 3297, 4382. (c) Fieser, L. F.; Dominguez, X. A. *J. Am. Chem. Soc.* **1953**, *75*, 1704. (d) Butenandt, A.; Wolf, A. *Chem. Ber.* **1935**, *68*, 2091. (e) Fieser, L. F.; Ettore, R. *J. Am. Chem. Soc.* **1953**, *75*, 3513. (f) Fieser, L. F.; Fieser, M. *Steroids*; Reinhold: New York, 1959; pp 37–41, 276–279 and references therein.

(2) (a) Villotti, R.; Ringold, H. J.; Djerassi, C. *J. Am. Chem. Soc.* **1960**, *82*, 5693 and earlier papers in this series. (b) Taylor presents an argument specific to 5β-steroids: Taylor, D. A. H. *Chem. Ind. (London)* **1954**, 250. (c) Dreiding, A. S. *Chem. Ind. (London)* **1954**, 1419.

(3) Corey, E. J.; Sneen, R. A. *J. Am. Chem. Soc.* **1955**, *77*, 2505.

(4) (a) Velluz, L.; Valls, J.; Nomine, G. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 181. (b) Bucourt, R.; Hainaut, D. *Bull. Soc. Chim. Fr.* **1965**, 1366.

(5) Liston, A. J. *J. Org. Chem.* **1966**, *31*, 2105.

(6) Allinger, N. L.; Hirsch, J. A.; Miller, M. A.; Tyminski, I. J. *J. Am. Chem. Soc.* **1968**, *90*, 5773.

0022-3263/88/1953-3828$01.50/0