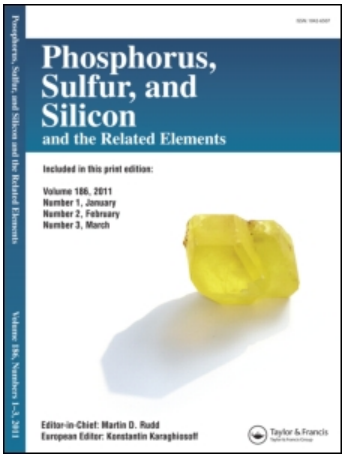

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REGIOSELECTIVITY OF RADICAL CYCLIZATION OF UNSATURATED ORGANOSILICON THIOLS

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REGIOSELECTIVITY OF RADICAL CYCLIZATION OF UNSATURATED ORGANOSILICON THIOLS

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Regiochemistry of radical cyclizations of isomeric dimethylsila-substituted 5-hexene-1-thiols (**1** and **2**) and 6-heptene-1-thiols (**5** and **6**) has been studied. It has been found that the ring closure of alkenylthiyl radicals having a vinyl group at silicon is a reversible and non-selective process. Preferred cyclization mode is determined by chain length of alkenethiol. By contrast, whatever the length of thiol chain, intramolecular cyclization of thiyl radicals generated from thiols **2** and **6** involving an allyl group at silicon proceeds irreversibly and as endo-mode exclusively. These differences in regioselectivity support the importance of stabilizing effect of the β-silyl group on the radical centre of cyclic intermediate.

Key words: Unsaturated organosilicon thiols, radical cyclization, medium-sized thiasilacyloalkanes.

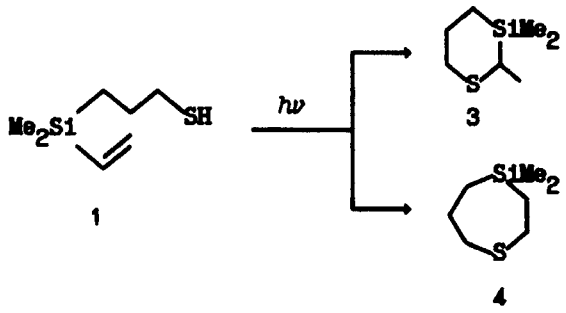
INTRODUCTION

Free-radical cyclization of unsaturated compounds has proved to be an efficient approach to the synthesis of heterocyclic compounds.[1–3] One of the most carefully studied reaction is the ring closure of ω-alkenyl radicals $CH_2{=}CH(CH_2)_nX^{\cdot}$ (X = CH_2) and related heteroatom-containing species (X = O or N). Regioselectivity of these homolytic ring closures is generally controlled by steric and stereoelectronic factors (Baldwin-Beckwith rules).[4–6]

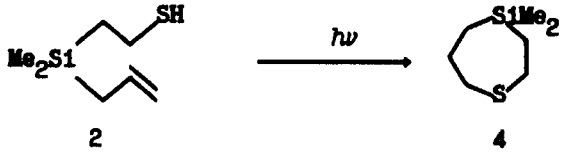
However exceptions from Baldwin-Beckwith rules arise for species in which the radical centre is located on a second row element.[7–8] In this case structural factors such as bond lengths and configurations at the radical centre can also affect cyclization mode. Thus, because of a longer C—S bond (relative to C—C bond) alkenylthiyl radicals generally show lower ring closure regioselectivity compared to alkenyl radicals.[7]

Previously we have reported that regioselectivity of photochemical intramolecular cyclization of isomeric dimethylsila-substituted 5-hexene-1-thiols (**1** and **2**) is highly dependent on the position of the double bond relative to silicon.[9] Ring closure involving a vinyl group at silicon results in a mixture of six-membered **3** and seven-membered **4** cyclic products (Equation 1) whereas only 7-endo-attack occurs via an allyl group at silicon leading to **4** (Equation 2).

To prove the generality of this trend we now extend the reaction to longer homologous thiols, namely isomeric dimethylsila-substituted 6-heptene-1-thiols **5** and **6**.



(1)



(2)

RESULTS AND DISCUSSION

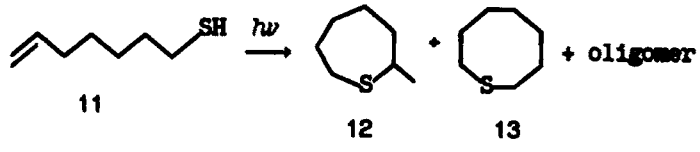
The routes chosen for the synthesis of the starting thiols **5–6** are outlined in Schemes I and II.

Tetrahydrofuran is readily cleaved by trimethylsilyl bromide generated *in situ* by reaction of trimethylsilyl chloride with lithium bromide in the presence of *n*-tetra-butylammonium bromide to give 4-bromo-1-trimethylsiloxy-butane **7** in high yield (Scheme I). The reaction of **7** with magnesium in ether followed by treatment with dimethylvinylchlorosilane afforded the alcohol **8** in 50% yield. This alcohol was converted to the tosylate **9** by treatment with *p*-toluenesulfonyl chloride and pyridine. Heating of crude **9** with thiourea in DMF followed by alkaline hydrolysis of the isothiuronium salt **10** gave the thiol **5** in 53% yield.

Thiol **6** was similarly obtained from the corresponding isothiuronium salt readily prepared by treatment of dimethyl (3-chloropropyl) allylsilane with thiourea in DMF in the presence of *n*-Bu_4NI (Scheme II).

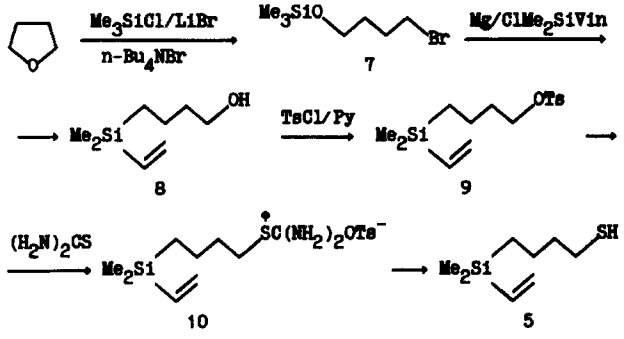
As far as we know, 7-exo versus 8-endo free-radical cyclization of unsaturated thiols has not been reported.[7] Therefore we initially examined the behavior of 6-heptene-1-thiol **11** prepared by photochemical addition of thiolacetic acid to 1,6-heptadiene followed by hydrolysis of thioacetate with ammonia in ethanol (Scheme III).

Being irradiated in hexane solution at 45°C, the thiol **11** mainly undergoes intermolecular addition resulting in oligomeric compounds (65% yield).

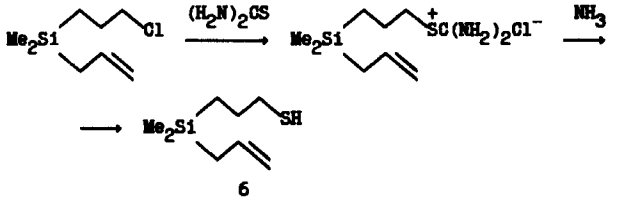


(3)

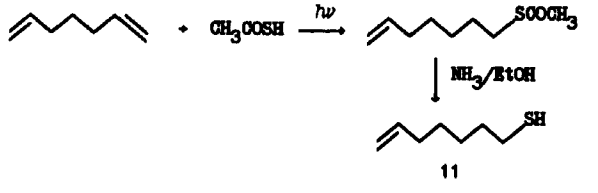
The volatile fraction showed the presence of two major components (GLC). Elemental analysis confirmed that the two compounds were isomeric with one



SCHEME I



SCHEME II

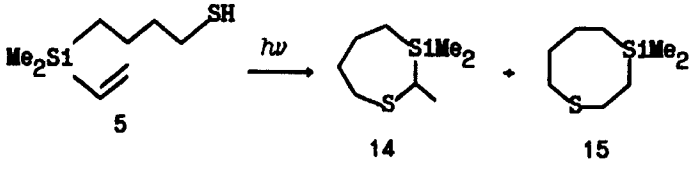


SCHEME III

another and also with the thiol **11**. This mixture displays a strong infrared band at 1350 cm^{-1} as expected for 2-methylthiacycloalkanes.[10] On the basis of these data the compound with shorter retention time was assigned exo-structure **12**. The seven-line ^{13}C spectrum of pure **13** was assigned by analogy with the data previously reported for unsubstituted thiacycloalkanes.[11]

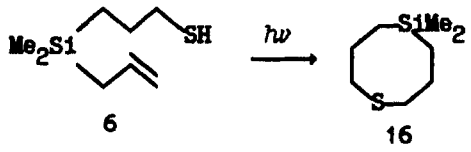
Thus, cyclization of the thiol **11** proceeds in two competing ways as exo- and endo-mode.

Photochemical ring closure of the thiol **5** also results in a mixture of seven-membered **14** and eight-membered **15** heterocycles, the latter being predominant (**14:15** = 1:4). Although we were unable to separate these compounds structural assignment of **14** and **15** was made on the basis of ^1H NMR spectra and mass spectrometry.



(4)

Unlike the latter reaction, cyclization of the thiol **6** provides only the heterocycle **16** arising from 8-endo-attack.



6 **16** (5)

Thus, it appears that relative position of the double bond and silicon plays an important role in determining the cyclization regiochemistry of unsaturated organosilicon thiols.

In order to account for these results, one should test the possibility of reversible ring closure of alkenylthiyl radicals generated from thiols **1–2** and **5–6**. As known, the cyclization of thiyl radicals $H_2C{=}CHCH_2XCH_2CH_2S^{\cdot}$ (X = CH_2, S, O) is reversible owing to which the ratio of exo:endo products strongly depends on the thiol concentration and reaction temperature. An increase in the concentration of thiol favors 7-endo-cyclization.[12-13]

We studied the effect of increasing the concentration of thiol **1** on the reaction regiochemistry (Equation 1). To our surprise, the exo:endo ratio increases markedly with increasing the concentration of **1** (Table I). The heterocycle **4** is formed in trace amounts at a high (7 M) thiol concentration.

A similar effect was also observed in the cyclization of thiol **5** (Equation 4). The **14:15** ratio increases from 1:4 to 1:2.3 with a five-fold increase in the thiol concentration.

These results clearly indicate that the initial ring closure of thiyl radicals having a vinyl group at silicon is reversible.

Under these conditions, radicals **IIa** and **IIIa** are in equilibrium with each other via the open radical **Ia** (Scheme IV). The ratio of products depends on the **IIa:IIIa** ratio (equilibrium constant) and the relative rates of hydrogen transfer (k_3 and k_4). The increasing extent of competition between exo- and endo-reactions at higher concentration of thiol may be due to both a decrease in recyclization rate k_{-1} of exo-cyclic radical **IIa**, and enhance of the hydrogen transfer rate k_3.

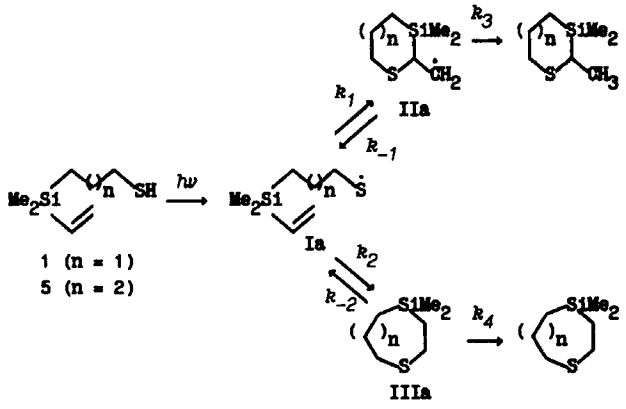
As for reactions (Equations 2 and 5), the selective formation of the endo-isomers **4** and **16** suggests irreversibility of the cyclization of radicals generated from thiols **2** and **6**. In the two cases the three-fold increase in the thiol concentration does not change the regiochemistry of ring closure. It was also noted that the cyclization mode of the thiol **6** is not affected by lowering or increasing the reaction temperature.[14-15] These results support the proposed irreversible intramolecular addition of thiyl radicals via an allyl group at silicon (Scheme V).

We think that the main reason for the highly preferred formation of endo-cyclic

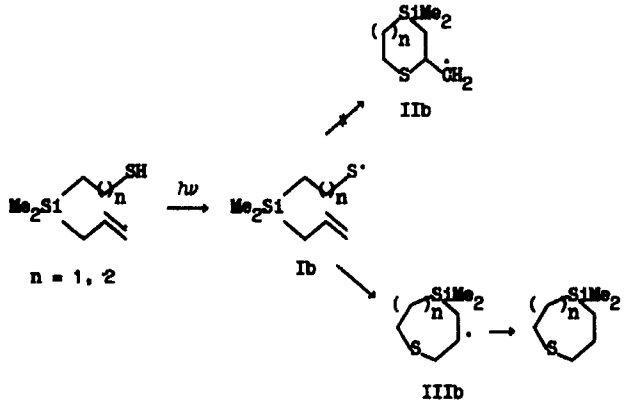
TABLE I

Exo:endo ratio as a function of thiol **1** concentration

Concentration, M	0.07	0.08	0.35	0.70	7.00
3:4 ratio	1.72	1.91	2.70	4.55	39.00



SCHEME IV



SCHEME V

products from thiols **2** and **6** is stabilization of the transition state by the β-silyl group due to hyperconjugation between the molecular orbital of the σ—Si—C bond and the single occupied orbital of the radical center. It is obvious that the stabilization of incipient cyclic radical **IIIb** (n = 0) resulting in seven-membered heterocycle **4** overrides the entropic and stereoelectronic factors. In such a system exo-attack would be disfavored due to relative inability of the silyl group to stabilize a transient γ-carbon-centered radical **IIb**.

Finally, the results obtained in the free radical cyclization of thiols **1** and **6** can also be rationalized in similar manner. The reverse step (Scheme IV) can be slowed down by radical stabilizing β-silyl group. The lower recyclization rate k_{-1} of β-silyl exo-cyclic radical **IIa** (compared with k_{-2} of α-silyl radical **IIIa**) which is still slowed down with increasing the thiol concentration may be responsible for the noted variations in the regiochemistry of reactions (Equations 2 and 5).

EXPERIMENTAL

^1H and ^{13}C spectra were recorded on a Jeol FX 90Q spectrometer using tetramethylsilane as internal standard. Infrared spectra were taken with an UR-20 spectrometer. Mass spectra were recorded with

a LKB-2091 GC-MS mass spectrometer equipped with a 25 m capillary column packed with SE-30. Analytical gas chromatography (GLC) was carried out on a LCHM-8MD instrument with a 2.0 m × 3 mm column packed with 10% Lukopren G-1000 on Chromaton N-AW-HMDS.

Solvents (diethyl ether, tetrahydrofuran, hexane) were dried and distilled from sodium metal or lithium aluminum hydride (under argon) immediately before use. Hygroscopic lithium bromide was dried *in vacuo* at 100°C. Compounds **1–4**, **16** were described elsewhere.[9,15,16] All reactions were carried out under nitrogen or argon atmosphere using oven-dried glassware. Photolyses were done by means of a DRT-400 mercury lamp. Yields of cyclic products were determined by GLC using peak areas.

5,5-Dimethyl-5-sila-6-heptene-thiol-1 (**5**). THF (43.50 g, 0.60 mol) was added dropwise to a mixture of trimethylsilyl chloride (49.00 g, 0.45 mol), lithium bromide (39.29 g, 0.45 mol) and *n*-Bu_4NBr (0.49 g, 0.013 mol). The mixture was stirred at reflux for 6 h until temperature reached 92°C. The precipitate of salts was removed by filtration. Vacuum distillation of filtrate gave 82.16 g (81%) of 4-bromo-1-trimethylsiloxybutane **7**, b.p. 80–81°C at 12 Torr, n_D^{20} 1.4450. Lit.[17]: b.p. 82–84°C at 12 Torr, n_D^{20} 1.4483.

A solution of dimethylvinylchlorosilane (10.86 g, 0.09 mol) in ether (15 mL) was added to a Grignard reagent, prepared from **7** (26.30 g, 0.117 mol) and magnesium turnings (2.40 g, 0.10 mol) in dry ether (100 mL). The reaction mixture was heated at reflux for 15 h. A saturated aqueous solution of NH_4Cl was added to the reaction mixture, the aqueous layer was separated and extracted with ether. The combined ether layers were dried ($MgSO_4$) and distilled to give 5,5-dimethyl-5-sila-6-hepten-1-ol **8** (9.47 g, 52%), b.p. 80°C at 9 Torr, n_D^{20} 1.4505. Found: C 60.57, H 11.63, Si 17.43. $C_8H_{18}SiO$. Calc.: C 60.69, H 11.46, Si 17.74. ^1H NMR ($CDCl_3$, δ): 0.06 (s, 6H, Me_2Si), 0.56 (m, 2H, $SiCH_2$), 1.50 (m, 4H, CCH_2CH_2C), 3.55 (m, 2H, CH_2O), 5.86 (m, 3H, $CH{=}CH_2$).

Alcohol **8** (9.47 g, 0.06 mol) was added to a solution of *p*-toluenesulfonyl chloride (28.00 g, 0.089 mol) in dry pyridine (35 mL) at -20°C. The mixture was stirred at -20°C for 2 h, and the resulting solution was kept in a refrigerator for 16 h. The mixture was then poured over ice and water. The organic layer was separated, acidified with 10% HCl, and washed with 10% K_2CO_3. Agueous layer was extracted with chloroform (100 mL). The combined organic layers were dried (Na_2SO_4), the solvent was removed at room temperature and under reduced pressure to give 9.38 g (53%) of crude 1-tosyloxy-5,5-dimethyl-5-sila-6-heptene **9** as a yellow oil. Analytically pure sample of **9** was obtained by column chromatography on silica gel (hexane/iso-propanol, 99:1). Found: C 57.52, H 7.90, Si 8.38, S 10.40. $C_{15}H_{24}SiSO$. Calcd: C 57.52, H 7.74, Si 8.99, S 10.26. ^1H NMR ($CDCl_3$, δ): 0.05 (s, 6H, Me_2Si), 0.43 (m, 2H, $SiCH_2$), 1.57 (m, 4H, CCH_2CH_2C), 2.42 (s, 3H, $CH_3C_6H_4$), 4.01 (t, 2H, CH_2O), 5.87 (m, 3H, $CH{=}CH_2$), 7.32-7.72 (dd, 4H, C_6H_4).

A mixture of crude tosylate **9** (8.88 g, 0.028 mol), thiourea (3.53 g, 0.046 mol), NaI (0.84 g, 0.006 mol) in DMF (37 mL) was stirred at 90°C for 18 h to give a solution of crude isothiuronium salt **10**. Then dry amonia was passed into the reaction mixture for 3 h. A saturated aqueous ammonium chloride solution was added, the reaction mixture was acidified to pH 7 with 5% HCl. Water layer was extracted with pentane, the organic layers was dried ($MgSO_4$). After removal of solvent at room temperature and under reduced pressure the product was distilled to give 2.65 g (53%) of **5**, b.p. 68–78°C at 12 Torr, $n_D^{22.5}$ 1.4748. Found: C55.04, H 10.30, $C_8H_{18}SiS$. Calc.: C 55.10, H 10.41. IR (neat, cm^{-1}): 1690 (C=C), 2580 (SH).

4,4-Dimethyl-4-sila-6-heptene-1-thiol (**6**). A mixture of dimethyl (3-chloropropyl) allylsilane (8.84 g, 0.05 mol), thiourea (3.90 g, 0.052 mol) and Bu_4NI (0.088 g, 0.20 mmol) in DMF (10 mL) was stirred at 90°C for 20 h and then worked up as described for **10**. Distillation gave 2.44 g (43%) of **6**, b.p. 50–52°C at 3 Torr, n_D^{20} 1.4790. The physical and spectral data of **6** were identical with those of an authentical sample.[15]

6-Heptene-1-thiol (**11**). A mixture of 1,6-heptadiene (3.84 g, 0.039 mol) and thiolacetic acid (3.04 g, 0.039 mol) was stirred and irradiated at 55°C for 1.5 h. Distillation afforded 2.97 g (46%) of 6-heptenyl thioacetate, b.p. 113–115°C at 20 Torr, n_D^{27} 1.4739. Found: S 18.16, $C_9H_{16}SO$. Calc.: S 18.60. A dry ammonia was passed through the solution of thioacetate (2.97 g, 0.017 mol) in ethanol (6 mL) for 1.5 h. The reaction mixture was washed with 10% ammonium chloride, water, extracted with pentane, dried ($MgSO_4$) and concentrated under reduced pressure (200 Torr). Distillation gave thiol **11** (1.18 g, 50%), b.p. 40–43°C at 7 Torr, n_D^{21} 1.4680. Found: C 63.89, H 10.87, S 24.71. $C_7H_{14}S$. Calc.: C 64.62, H 10.77, S 24.62. ^1H NMR ($CDCl_3$, δ): 1.39–1.40 [(m, 7H, $(CH_2)_3$, SH], 2.03 (m, 2H, $=CCH_2$), 2.48 (m, 2H, CH_2S), 5.02(m, 2H, $CH_2{=}$), 5.80 (qt, H, $=CH$). IR (neat, cm^{-1}): 1630 (C=C), 2540 (SH).

General procedure for radical cyclization. 0.1 M solution of thiol in hexane was placed in a flame-dried quartz flask, flushed with argon for 20–30 min and irradiated with a DRT lamp at 45°C for 2–9 h. The solvent was evaporated under reduced pressure. The residue contained unreacted thiol (10–20%) and cyclic products (GLC). The products were isolated by vacuum distillation of the residue as described for the individual experiments.

Cyclization of thiol **1** was carried out as described.[9] The effect of initial concentration of **1** on the **3:4** ratio was studied for the solution concentration shown in Table I.

Cyclization of thiol **11** (1.18 g, 0.014 mol) in 90 mL of hexane was carried out as described above. Vacuum distillation gave a fraction (0.17 g), b.p. 44–60°C at 2 Torr. GLC, IR and NMR analysis indicated a mixture of **12** and **13** in a ratio of 1.2:1. An analytical sample of **12** was prepared by repeated distillation. ^{13}C NMR ($CDCl_3$, δ): 33.66 (C^2 or C^8), 31.94 (C^3 or C^7), 28.52 (C^4 or C^6), 27.94 (C^5).

Cyclization of thiol **5** (0.74 g, 0.004 mol) in 37 mL of hexane was carried out as described above. Irradiation time was 9 h. Distillation yielded 0.07 g (10%) of a 1:4 mixture of 2,3,3-trimethyl-1-thia-3-silacycloheptane **14** and dimethyl-1-thia-4-silacyclooctane **15** (by GC-MS and ^1H NMR). **14.** ^1H NMR ($CDCl_3$, δ): 0.05 (s, 6H, Me_2Si), 0.91 (m, 2H, CH_2Si), 1.16 (m, 2H, $SiCH_2C$), 1.23 (s, 1H, CH), 1.72 (m, 2H, CCH_2C), 2.56 (m, 2H, CH_2S); mass spectrum, m/e: 174 (M^+, 69), 159 (M—CH_3, 100), 131 (M—CH_3—C_2H_4, 75). **15.** ^1H NMR ($CDCl_3$, δ): 0.06 (s, 6H, Me_2Si), 0.52 (m, 2H, CH_2Si), 0.84 [m, 4H, $Si(CH_2)_2S$], 1.60 [m, 4H, $C(CH_2)_2C$], 2.50 (m, 4H, CH_2CH_2S); mass spectrum, m/e: 174 (M^+, 2), 159 (M—CH_3, 1), 131 (M—CH_3—C_2H_4, 100), 97 (M—CH_3—C_4H_8, 13).

Cyclization of thiol **6** was carried out as described above. 2.18 g (41%) of 5,5-dimethyl-1-thia-5-silacyclooctane **16** was obtained from thiol **6** (2.90 g, 0.017 mol) in hexane (150 mL). **16.** B.p. 76–78°C at 2 Torr, n^{20} 1.4932. ^1H NMR ($CDCl_3$, δ): 0.01 (s, 6H, Me_2Si), 0.61 (m, 2H, CH_2Si), 1.75 (m, 2H, CCH_2C), 2.46 (m, 2H, CH_2S). The physical and spectral data of **6** were identical with those of an authentical sample.[14,15]

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REFERENCES

1. M. Ramaiah, *Tetrahedron*, **43,** 3541 (1987).
2. D. P. Curran, *Synthesis*, 417 (1988).
3. C. Thebtaranonth, *Tetrahedron*, **46,** 1385 (1990).
4. A. L. Beckwith, *Tetrahedron*, **37,** 3073 (1981).
5. A. L. Beckwith and C. H. Schiesser, *Tetrahedron*, **41,** 3925 (1985).
6. D. C. Spellmeyer and K. N. Houk, *J. Org. Chem.*, **52,** 959 (1987).
7. J.-M. Surzur, in "Reactive Intermediates," edited by R. A. Abramovich, Plenum, New York, 1982, Vol. 2, pp. 121–295.
8. J. W. Wilt, *Tetrahedron*, **41,** 3979 (1985).
9. S. V. Kirpichenko, L. L. Tolstikova, E. N. Suslova and M. G. Voronkov, *Tetrahedron Lett.*, **34,** 3889 (1993).
10. N. J. Leonard and J. Figueras, *J. Am. Chem. Soc.*, **74,** 917 (1952).
11. K. Nagasawa and A. Yoneta, *Chem. Pharm. Bull.*, **33,** 5048 (1985).
12. J.-M. Surzur, M. P. Crozet and C. Dupuy, *Tetrahedron Lett.*, 2025 (1971).
13. M. P. Crozet, J.-M. Surzur and C. Dupuy, *Tetrahedron Lett.*, 2031 (1971).
14. K. E. Koenig, R. A. Felix and W. P. Weber, *J. Org. Chem.*, **39,** 1539 (1974).
15. M. G. Voronkov, S. V. Kirpichenko, E. N. Suslova, V. V. Keiko and A. I. Albanov, *Zh. Obshch. Khim.*, **53,** 2404 (1983).
16. M. G. Voronkov, S. V. Kirpichenko, E. N. Suslova and L. L. Tolstikova, *Zh. Obshch. Khim.*, **60,** 2630 (1990).
17. H. R. Kricheldorf, G. Morber and W. Regel, *Synthesis*, 383 (1981).