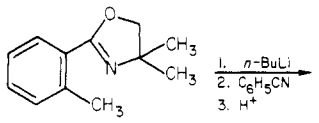
Table I. Structures, Yields, and Physical Data for Isoquinolinones 3[a]

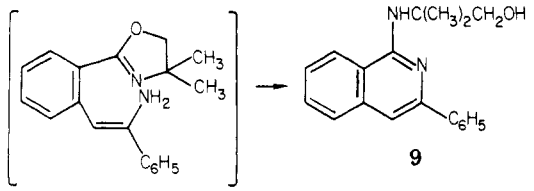
entry	R	compd	% yield	mp, °C	solvent	lit. mp (°C) or formula
1	$(CH_3)_2CH$	3a	42	188-190	C_2H_5OH	186-188[b]
2	$(CH_3)_3C$	3b	48	187-188	CH_3OH/H_2O	187.5-189.0[c]
3	Ph	3c	87	198-199	C_2H_5OH	199.5-200.0[d]
4		3d	66	179-180	C_2H_5OH/H_2O	180-181.5[e]
5		3e[f]	60	212-213	$(CH_3)_2CHOH$	$C_{16}H_{10}F_3NO$
6		3f[f]	58	213-214	$(CH_3)_2CHOH/(CH_3)_2NCHO$	$C_{13}H_9NOS$

[a] All reactions were carried out as described in the Experimental Section. [b] Reference 3a. [c] Reference 4b. [d] Gabriel, S. *Chem. Ber.* **1885**, *18*, 3470. [e] Dave, V.; Warhoff, E. *Synth Commun.* **1974**, *4*, 17. [f] Satisfactory analytical values for C, H, and N were obtained.

7[10] with *n*-butyllithium and reaction with benzonitrile, only isoquinoline **9** was obtained.[11] No intermediate enamino



7



8 9

oxazoline **8** was detected. Thus ring closure of these general types of intermediates to isoquinoline structures is highly favorable.[12]

Experimental Section

General Methods. IR spectra were recorded on a Nicolet MX-1 FT spectrophotometer. ^1H NMR spectra were recorded at 90 MHz on a Perkin-Elmer R32 spectrometer. Data are reported in the following manner: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, spt = septet, br = broadened, and m = unresolved multiplet), integration, coupling constant. ^{13}C NMR spectra were recorded on a Varian FT-80A spectrometer at 22.5 MHz by using an internal deuterium lock. Data are reported as follows: $\{^1H\}$ ^{13}C chemical shifts and multiplicity as obtained from the coupled spectra (s = singlet, d = doublet, t = triplet, q = quartet). Melting points were determined by using a Thomas-Hoover capillary apparatus and are both uncorrected and uncalibrated. Starting amide **1** was either purchased from Aldrich Chemical Co., Milwaukee, WI, or prepared according to literature procedures.[5] The tetrahydrofuran (THF) solvent used in all the metalation reactions was distilled under nitrogen from sodium benzophenone ketyl immediately prior to use.

General Preparative Procedure for Isoquinolinones 3. Under nitrogen and with cooling (ice–salt bath) was slowly added 96 mL (0.23 mol) of *n*-butyllithium (2.4 M in *n*-hexane) via syringe to a stirred solution of 14.9 g (0.100 mol) of amide **1** in 200 mL of THF. The addition rate was maintained so that the reaction temperature never exceeded 20 °C. After the addition was complete (ca. 30 min), the orange-red solution was stirred at 0 °C for 1 h and then cooled to −50 °C (dry-ice/2-propanol). A solution of 0.125 mol of the appropriate organic nitrile in 50 mL of THF was quickly added, the cooling bath removed, and the resulting mixture allowed to warm to room temperature. Saturated aqueous ammonium chloride solution (50 mL) was then carefully added via pipet. Occasionally during this operation rapid gas evolution occurred. The resulting phases were separated, and the organic portion was washed with water (50 mL) and saturated sodium chloride solution (50 mL) and then dried over anhydrous magnesium sulfate. After filtration, the solvent was removed in vacuo to afford the crude isoquinolinones as pale yellow to dark solids which were subsequently recrystallized. Yields, melting points, and recrystallization solvents for the above experiments are listed in Table I. See the paragraph at the end of the paper about supplementary material. 3-(2-Methylethyl)-1(2*H*)-isoquinolinone (**3a**) for an example was isolated as a colorless solid: IR (KBr) 1648, 1608, 1555, 1478, 1384, 1349, 1257, 822, 754 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 1.25 (d, 6, J = 6.9 Hz), 2.81 (spt, 1, J = 6.9 Hz), 6.34 (s, 1), 7.55 (m, 3), 8.17 (d, 1, J = 7.5 Hz), 11.16 (br s, 1) ppm; ^{13}C NMR (Me_2SO-d_6), 162.6 (s), 148.2 (s), 138.3 (s), 132.1 (d), 126.5 (d), 125.9 (d), 125.4 (d), 124.5 (s), 99.4 (d), 31.1 (d), 21.2 (q) ppm.

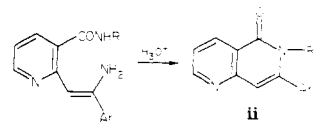
Acknowledgment. We express appreciation to Messrs. C. M. Combs and J. G. Schmidt or their assistance in obtaining spectral data and to Mr. C. I. Kennedy for microanalyses.

Supplementary Material Available: Full spectral data (IR and ^1H and ^{13}C NMR) for compounds **3b–f** (1 page). Ordering information is given on any current masthead page.

(10) Gschwend, H. W.; Hamdan, A. *J. Org. Chem.* **1975**, *40*, 2008.

(11) 2,2-Dimethyl-2-[(3-phenyl-1-isoquinolinyl)amino]ethanol (**9**) was isolated as a colorless solid: mp 158–160 °C (CH_3OH); IR (KBr) 3350, 1577, 1567, 1544, 1454, 1427, 1073, 1065, 769, 697 cm^{-1}; ^1H NMR (Me_2SO-d_6) 8.21 (m, 3), 7.50 (m, 7), 6.46 (br s, 1), 5.41 (t, 1, J = 5.8 Hz), 3.82 (d, 2, J = 5.8 Hz), 1.65 (s, 6) ppm; ^{13}C NMR (Me_2SO-d_6) 154.7 (s), 147.8 (s), 140.0 (s), 137.6 (s), 129.8 (d), 128.6 (d), 128.0 (d), 127.3 (d), 126.3 (d), 125.5 (d), 123.2 (d), 117.9 (s), 105.7 (d), 68.9 (t), 55.4 (s), 23.8 (q) ppm.

(12) A recent report by Swiss chemists claims analogous enamino nicotinamides i are isolable compounds and require acid hydrolysis to complete cyclization to the corresponding 6,7-disubstituted naphthyridin-5(6*H*)-ones ii (Damon, R. E.; Nadelson, J., United Kingdom Patent Application GB 2 054 593, 1981).



i ii

Concerning the Formation, Reduction, and Conformations of β-(Trimethylsilyl)- and β-(Trimethylstannyl)cyclohexanones

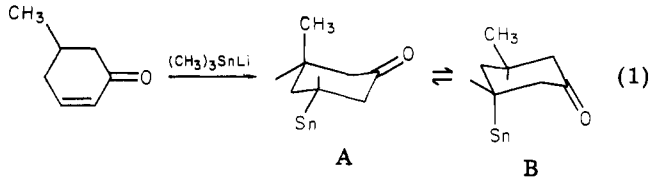
Geoffrey Wickham, Henry A. Olszowy, and William Kitching*

Department of Chemistry, University of Queensland, Brisbane 4067, Australia

Received November 3, 1981

There has been considerable interest in the addition of (trimethylsilyl)- and (trimethylstannyl)alkalis to α,β-unsaturated ketones; with cyclohexenones, (kinetic) 1,4-addition and exclusive axial approach are regarded as

characteristic features of silylation, whereas stannylation involves a facile equilibration of the kinetic 1,2-addition product.[1-5] Hudec[6] reported that the Cu(I)-promoted addition of $(CH_3)_3SnLi$ to 5-methylcyclohex-2-en-1-one, afforded, after preparative TLC, only that epimer of 3-methyl-5-(trimethylstannyl)cyclohexan-1-one resulting from axial 1,4-addition. Hudec further argued, on the basis of ^{13}C chemical shifts, that the predominant, if not the only important, conformation of the ketone was A (eq 1).



(1)

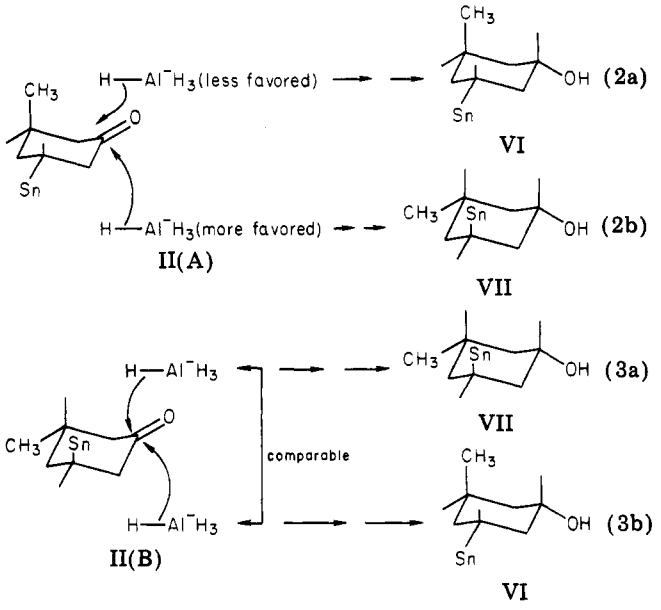
Unless a stabilizing through-bond interaction between an equatorially oriented β-carbon–tin bond and the carbonyl π system was operating,[6] we would have anticipated a substantial if not predominant population of B.[7] Still examined the addition of both $(CH_3)_3SiLi$ and R_3SnLi (R = methyl, *n*-butyl) to various cyclohex-2-en-1-ones and reported overall 1,4-addition (no Cu(I) needed, THF or ether–HMPA solvent) via axial approach of the reagent.[1-3] More recently, Ager et al.[8] described the reaction of (dimethylphenylsilyl)lithium (mixed with Cu(I)) with enones, esters, and aldehydes and certain functionalizations of the silanes. In the case of methyl 5-oxocyclohex-3-ene-1-carboxylate, the product stereochemistry was that expected for axial attack by the silyl–copper reagent.

In this note we report that while the additions of $(CH_3)_3SiLi$ (HMPA) and $(CH_3)_3SnLi$ (THF) to 5-methylcyclohex-2-en-1-one are regiospecific (1,4), there are significant leakages from stereospecific axial approach. We provide a useful description of the conformational situation in some of these ketones and the stereochemistry of $LiAlH_4$ reduction, as well as listings of ^{13}C, ^{119}Sn, and ^{29}Si chemical shifts.

Addition of $(CH_3)_3SnLi$ (THF solution) to cyclohex-2-en-one and 5-methylcyclohex-2-en-1-one proceeded in a 1,4 fashion overall (without Cu(I) promotion) as reported previously.[2,6] However, axial approach in the 5-methyl case was not exclusive, as on the basis of ^{13}C and ^{119}Sn NMR examination, ca. 18% of the cis isomer (III) was formed (Chart I and Table I). The stereochemistries of the various cyclohexanes listed in Table I and Chart I are defined unambiguously on the basis of ^{13}C and ^{1}H chemical shifts and vicinal ^{13}C–^{119}Sn couplings, which show a sensitive dependence on dihedral angle.[9]

Vicinal ^{119}Sn–^{13}C coupling in I and III (to C_5) was measured to be 68.4 and 72 Hz, respectively, values appropriate for an equatorially disposed $Sn(CH_3)_3$.[10] Hence for conformation A of II a value for $^3J_{^{119}Sn-^{13}C}$ (to C_3) of ca. 70 Hz would be anticipated, but it is actually much lower, viz., 46.2 Hz. This value is consistent with a conformational ratio A/B of ca. 60:40, indeed indicative of a stabilizing interaction in A, for otherwise on the basis of conformational A values for CH_3 (1.74 kcal/mol) and $Sn(CH_3)_3$ (1.0 kcal/mol)[10] B would be expected to predominate. (The chemical shift of C–CH_3 (20.08 ppm) also indicates a substantial population of A, but notice (Table I) the C–CH_3 shift of 19.14 ppm in the corresponding silyl ketone (XI), for which the conformation analogous to A is more dominant, as expected for the "larger"[11] $(CH_3)_3Si$ group. The magnitude of $^3J_{^{119}Sn-^{13}C}$ to C_3 (46.2 Hz) could be consistent also with a pseudoequatorial tin group in a stable half-chair conformation, but the vicinal ^1H–^1H couplings do not suggest distortions from the "normal" chair conformations, and examinations of many cyclohexanes bearing both methyl and metalloid groups have not required postulation of other than chair conformations.

Reduction[12] of I provided predominantly alcohol IV (^1H, ^{13}C, ^{119}Sn NMR) resulting from axial hydride approach. Similarly III yielded mainly VIII with some IX. However reduction of conformationally inhomogeneous *trans*-II is far less specific, affording ca. 1:3 VI and VII. If the transition state for reduction by $LiAlH_4$ has largely ketone character, axial hydride attack is favored, unless there are large groups at C_3 or C_5, as is the case here.[13] The situation is summarized in eq 2 and 3. Available data[13] would

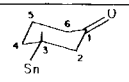
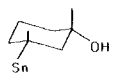
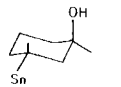
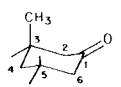
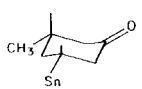
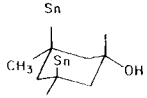
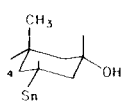
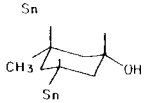
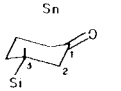
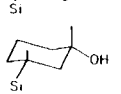
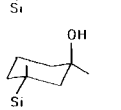
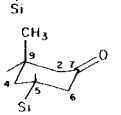
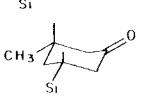
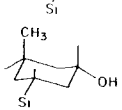


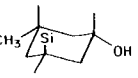
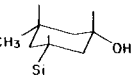
indicate that reduction of conformer A of II would provide more VII than VI, and considering that an axial CH_3 at C_3 or C_5 leads to a ca. 60:40 equatorial:axial approach[13] in other cyclohexanones, the smaller[7] *axial*-$Sn(CH_3)_3$ in conformer B of II would make an axial:equatorial hydride approach about equally likely and may even favor the former. Thus reduction of B would probably lead to a predominance of VII as well.

$(CH_3)_3SiLi$ (generated from $(CH_3)_6Si_2$ and CH_3Li in HMPA–THF)[1] reacts readily at −78 °C with 5-methylcyclohex-2-en-1-one to provide the conjugate addition product exclusively.[14] ^{13}C and ^{29}Si NMR examinations

(1) Still, W. C. *J. Org. Chem.* **1976**, *41*, 3063.
(2) Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4836.
(3) Still, W. C.; Mitra, A. *Tetrahedron Lett.* **1978**, 2659.
(4) Fleming, I.; Goldhill, J. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1493.
(5) Ager, D.; Fleming, I. *J. Chem. Soc., Chem. Commun.* **1978**, 177.
(6) Hudec, J. *J. Chem. Soc., Perkin Trans 1* **1975**, 1020.
(7) This conclusion is suggested by the relative A values (in cyclohexane) of CH_3 (1.74 kcal/mol) and $Sn(CH_3)_3$ (1.0 kcal/mol).
(8) Ager, D. J.; Fleming, I.; Patel, S. K. *J. Chem. Soc., Perkin Trans 1* **1981**, 2520.
(9) Doddrell, D.; Burfitt, I.; Kitching, W.; Bullpitt, M.; Lee, C.; Mynott, R. J.; Considine, J. L.; Kuivila, H. G.; Sarma, R. H. *J. Am. Chem. Soc.* **1974**, *96*, 1640.
(10) (a) Kitching, W.; Doddrell, D.; Grutzner, J. B. *J. Organomet. Chem.* **1976**, *107*, C5. (b) Kitching, W.; Olszowy, H.; Waugh, J. A. Doddrell, D. *J. Org. Chem.* **1978**, *43*, 898. (c) Kitching, W.; Olszowy, H. A.; Harvey, K. *J. Org. Chem.* **1982**, *47*, 1893.
(11) The A value of $Si(CH_3)_3$ has been determined to be 2.5–2.6 kcal/mol (Kitching, W.; Olszowy, H. A.; Drew, G. H.; Adcock, W., accepted for publication.
(12) Reductions were conducted with 1 mol equiv of lithium aluminum hydride in ether at 0 °C, followed by a standard workup and Kugelrohr distillation.
(13) For a recent summary of the position regarding stereochemistry and mechanism of ketone reduction by hydride reagents see: Wigfield, D. C. *Tetrahedron* **1979**, *35*, 449.

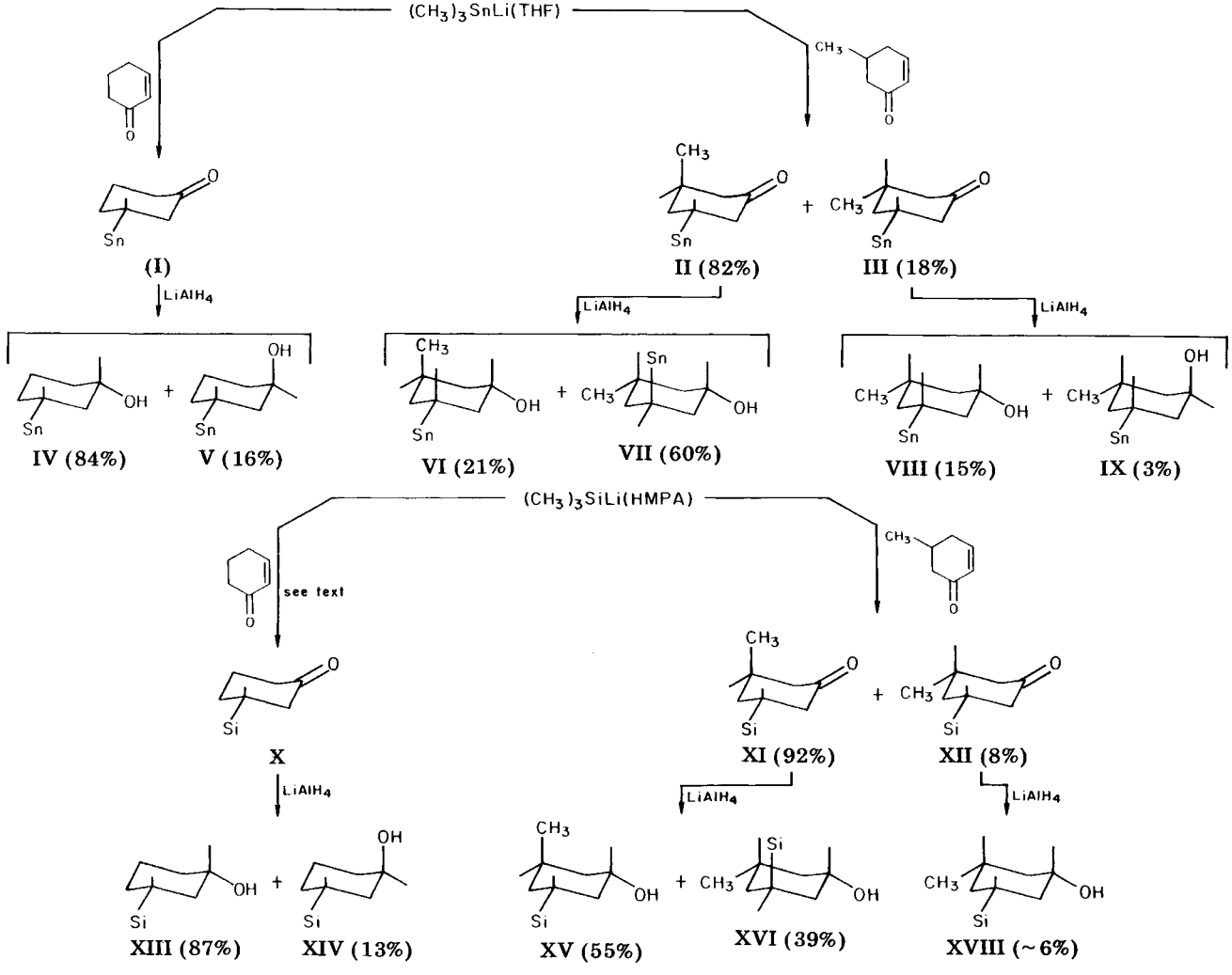
Table I. NMR Characteristics[a] of β-Metallocyclohexanones and Reduction Products

compound	^{13}C 1	2	3	4	5	6	other	^{119}Sn or ^{29}Si
I 	212.21 (58.6)	45.69 (14.7)	25.11 (369)	29.32 (13.7)	30.8 (68.4)	42.07	−11.7 (320.3)	+6.53
IV 	72.03 (78.7)	39.96 (14.6)	22.17 (395.5)	29.58 (15)	27.29 (74.4)	36.04 (6.7)	−11.92 (311.9)	+0.59
V 	67.76 (~38)	37.94 (nl)	19.93 (nl)	29.89 (nl)	23.02 (nl)	34.06	−11.09 (nl)	+2.35
II 	211.93 (41)	49.02	34.24 (46.2)	36.05 (12.8)	20.63 (369)	45.23 (11)	20.08, −11.08 (318)	+9.82
III 	212.0 (nl)	50.21	40.49 (72)	38.34 (15)	23.59 (367)	44.72 (8)	22.23, −11.79 (321)	+7.69
VII 	69.76 (14.6)	44.71	31.04 (~14)	39.20* (12)	23.58 (385)	38.03* (10)	22.34, −9.44 (304)	+2.84
VI 	67.28 (~66)	41.52 (6)	29.07 (58)	33.84 (nl)	16.81 (nl)	35.60 (14.7)	18.90, −11.36 (nl)	+3.96
VIII 	71.83 (~81)	44.59	38.3 (~68?)	39.33* (nl)	21.29 (nl)	39.52* (nl)	22.07, −11.92 (nl)	+1.26
X 	212.76	42.31	25.93	27.96	29.88	41.87	−3.79	+3.58
XIII 	72.00	36.46	24.41	26.66	25.99	36.05	−3.62	+2.81
XIV 	66.09	33.53	18.41	25.02	21.19	32.92	−2.39	+3.50
XI 	212.87	48.22	31.89*	32.68*	21.39	41.93	19.14, −3.62	+4.52
XII 	212.46	50.03	37.72	34.64	26.61	41.46	22.48, −3.82	+3.70
XV[b] 	67.23	41.37	29.14	31.45	18.34*	35.82*	17.83*, −3.66	+3.65

XVI[b] 	68.5	43.64	29.09	34.53*	21.29	36.86*	22.41, −1.20	+3.65
XVII 	71.81	44.57	33.14	34.75*	23.63	35.9*	22.29 (nl)	+2.84

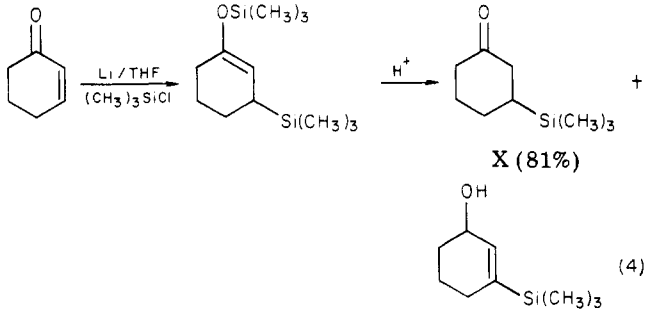
[a] Shifts to lower field are positive; asterisked signals could be interchanged; nl = not located. ^{117,119}Sn satellites are not observable about certain low-intensity signals, and $^{2}J_{^{119}Sn-^{13}C}$ is frequently difficult to resolve from the main signal. Values in parentheses are ^{119}Sn–^{13}C coupling constants (hertz). See Experimental Section for description of spectral procedures. [b] The asterisked signals assigned to C_6 in XV and C_4, C_6, in XVI may be interchanged.

Chart I



(Table I) confirm predominant, but not exclusive, axial attack on the enone, with the products being *trans*-3-methyl-5-(trimethylsilyl)cyclohexan-1-one (XI) (92%) and the corresponding cis isomer XII (8%). Still[1] reported the formation of one isomer only (from axial approach) in the reaction of 3,5-dimethylcyclohex-2-en-1-one, but careful ^{13}C NMR examination of this product and others[8] may confirm stereo leakage.

3-(Trimethylsilyl)cyclohexan-1-one was obtained by reaction of cyclohex-2-en-1-one with lithium and trimethylchlorosilane in THF, followed by acidic hydrolysis of the silyl enol ether.[15] A significant and previously unreported byproduct was also formed. On the basis of ^1H, ^{13}C, and ^{29}Si NMR behavior, this was formulated as the isomeric vinyl–silane[16] XVIII (eq 4), which was unaffected by reduction.

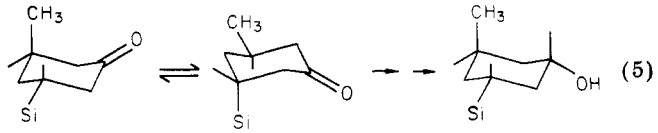


X (81%)

(4)

XVIII (19%)

Reduction of X to yield mainly XIII is unexceptional, as is the XII → XVII conversion. (A very minor proportion (~1%) of axial alcohol corresponding to XVII may have escaped detection). There is, however, an interesting variation in that reduction of XI yields mainly XV, with ~1.4:1 XV:XVI, which may be compared with the corresponding ratio (VI:VII) of 1:3 in the tin case. Whereas reduction of the conformers of II and XI with equatorial metalloid groups (A and C, eq 5) would be anticipated to



C D XV (5)

produce a similar slight excess of VII (over VI) and XVI (over XV), reduction of the alternative conformers with axial-metallo groups (B and D) would show divergent behavior. The larger effective size of $Si(CH_3)_3$[11] (compared with $Sn(CH_3)_3$ and even CH_3 itself) could enforce almost complete equatorial approach as shown in eq 5, producing XV. However, ^{13}C and ^1H NMR examination demonstrate quite conclusively that D is a very minor component (at best) in the C ⇄ D conformational equilibrium,[17] and thus the overall predominance of XV over XVI in the reduction of XI suggests reduction proceeds chiefly through conformer D (despite its low population). This situation requires reduced reactivity of the carbonyl group in C, perhaps partly a result of specific equatorial β-silyl interaction with the carbonyl. Reduction of XI by sodium borohydride–2-propanol was very similar to $LiAlH_4$ reduction, a similarity reported for reduction of 3,3,5-trimethylcyclohexan-1-one.[13] This is not inconsistent with the idea that the transition states for these reductions differ,[13] as a late transition state for $NaBH_4$ reduction would presumably involve axial approach to conformer C to avoid 1,3-CH_3–O interaction with product development.

We may conclude that (i) additions of $(CH_3)_3SnLi$ and $(CH_3)_3SiLi$ to 5-methylcyclohex-2-en-one proceed regio- but not stereospecifically, (ii) *trans*-3-methyl-5-(trimethylstannyl)cyclohexan-1-one is conformationally quite inhomogeneous, and (iii) a contributory reason for the slight dominance at 35 °C of the conformer with an equatorial $Sn(CH_3)_3$ may be associated with a stabilizing β-stannylcarbonyl interaction, with a stereoelectronic requirement of an equatorial carbon–tin bond, as suggested by Hudec,[6] and (iv) the stereochemistry of reduction of the *trans*-3-methyl-5-(trimethylstannyl)- (and silyl-) cyclohexan-1-ones is regulated not only by the different steric requirements of $Sn(CH_3)_3$ and $Si(CH_3)_3$ but also apparently by conformer reactivity.

Experimental Section

Synthesis of Compounds. Stannylation of Cyclohex-2-en-1-one. (Trimethylstannyl)lithium was prepared from trimethyltin chloride (5.99 g, 30 mmol) and excess lithium (150 mmol) in tetrahydrofuran (~20 mL) at 0 °C under N_2. To this filtered and stirred solution (N_2, 0 °C) was added dropwise a solution of cyclohex-2-en-1-one (2.4 g, 25 mmol) in tetrahydrofuran (~7 mL). Stirring was continued for 4 h at room temperature after the initial exothermic reaction had subsided. Standard workup with aqueous ammonium chloride, ether extraction, drying, etc., provided crude 3-(trimethylstannyl)cyclohexan-1-one (I), 6.1 g (94%). Distillation (55 °C (2 mmHg)) provided pure material.

Anal. Calcd for $C_9H_{18}OSn$: C, 41.38; H, 6.90. Found: C, 41.17; H, 7.00. ^1H NMR δ 0.09 ($Sn(CH_3)_3$, $J_{^{119}Sn-^1H}$ = 52 Hz), 1.5–2.7 (ring protons).

3-Methyl-5-(trimethylstannyl)cyclohexan-1-one (II, III) was obtained from a similar stannylation of 5-methylcyclohex-2-en-one, in 80% crude yield. Distillation (99 °C (2 mmHg)) provided pure material.

Anal. Calcd for $C_{10}H_{20}OSn$: C, 43.64; H, 7.27. Found: C, 44.17; H, 7.44. ^1H NMR: δ 0.07 ($Sn(CH_3)_3$, $J_{^{119}Sn-^1H}$ = 51 Hz), 1.00 (CH_3, d, J = 6.5 Hz), 1.6–2.7 (ring protons).

Silylation of Cyclohex-2-en-1-one. Two procedures were employed for the preparation of 3-(trimethylsilyl)cyclohexan-1-one (X). Careful duplication of the reported procedure[1] for trimethylsilylation of cyclohex-2-en-1-one with $(CH_3)_3SiLi$ failed to provide the reported high yields of X, and we resorted to direct silylation as described below.[15]

Lithium slivers (0.80 g; 115.3 mmol) and chlorotrimethylsilane (14.2 g, 130.6 mmol) were added to tetrahydrofuran (78 mL) maintained at 0 °C under N_2. Cyclohex-2-en-1-one (5.0 g, 52.1 mmol) was added dropwise over an hour and the temperature kept below 10 °C. The mixture was stirred at room temperature for an additional 2 h, and excess lithium and salts were filtered off. Solvent and excess chlorotrimethylsilane were removed by distillation. Hydrolysis of this crude silyl enol ether by the method of Dunogues[15] (i.e., concentrated hydrochloric acid, 1:1 ether:methanol) produced a complex mixture, apparently consisting of the desired 3-(trimethylsilyl)cyclohexan-1-one (X), the isomeric vinyl silane XVIII, and isomeric acetals. (e.g. $CH_3OCR_1R_2OSi(CH_3)_3$?). Complete hydrolysis was achieved by dissolving the oil in tetrahydrofuran (25 mL), followed by the addition of aqueous HCl (10%, 25mL). The mixture was stirred (0.5 h), poured into water, and extracted (ether). Ether was removed from the dried extract, and the residual oil was distilled (80 °C (11 mmHg)) to provide a mixture of X and XVIII (2.59 g, 29%).

(14) In our hands, reactions of $(CH_3)_3SiLi$ with enones according to the published procedure[1] have provided poor yields. This encouraged our preparation of X by the Li/$(CH_3)_3SiCl$ route; see Experimental Section.

(15) Dunogues, J.; Ekouya, A.; Calas, R.; Duffaut, N. *J. Organomet. Chem.* **1975**, *87*, 151–167.

(16) The ^1H NMR had signals at δ 5.95 (1 H, >C=CH) and δ 4.47 (1 H, C*H*OH), while ^{13}C signals were observed at −2.48, 19.20, 26.28, 34.42, 56.00, 134.68, and 143.78 ppm. The ^{29}Si shift was −4.52 ppm (relative to Me_4Si), which may be compared with −6.24 ppm for the vinylsilane, 1-(trimethylsilyl)-4-methylcyclohex-1-ene, or −6.8 for vinyltriemthylsilane itself.

(17) The 300-MHz ^1H spectrum of XI (as well as the ^{13}C NMR spectrum) confirmed the overwhelming predominance of conformation C. In particular the $CHSi(CH_3)_3$ signal was a clear triplet of triplets (J = 11.9, 4.2 Hz), appropriate for an axial orientation.

Anal. Calcd for $C_9H_{18}OSi$: C, 63.49; H, 10.67. Found: C, 62.16; H, 10.27. ^1H NMR δ –0.26 ($Si(CH_3)_3$, X), –0.20 ($Si(CH_3)_3$, XVIII), 0.54–2.38 (ring protons), 4.47 (>C*H*OH, XVIII), 5.95 (>C=CCH), XVIII).

3-Methyl-5-(trimethylsilyl)cyclohexan-1-one was obtained in low yield by faithful repetition in all particulars of the reported procedure,[1] and on one occasion none of the desired product was obtained. Still[1] did not silylate 5-methylcyclohex-2-en-1-one (with $(CH_3)_3SiLi$), but he did report no conjugate addition to isophorone. The reasons for these differences have not been established, but the $(CH_3)_3SiLiCu^I$ reagent appears to have certain advantages.[8]

3-Methyl-5-(trimethylsilyl)cyclohexan-1-one (XI and XII) was distilled (92 °C (8 mmHg)).

Anal. Calcd for $C_{10}H_{20}OSi$: C, 65.17; H, 10.95. Found: C, 65.18; H, 11.05. ^1H NMR δ –0.12 ($Si(CH_3)_3$, XI), 0.84 (CH_3, d, J = 7 Hz), 0.94–2.52 (ring protons).

Reductions of Stannyl- and Silylcyclohexanones. Reductions with lithium aluminum hydride (ether, 0 °C) and sodium borohydride (2-propanol solvent) were conducted in the normal way to provide the cyclohexanols in high yields (>90%). These alcohols were examined by ^1H, ^{13}C, ^{119}Sn, and ^{29}Si NMR to provide isomer percentages reported in the text.

3-(Trimethylstannyl)cyclohexanol (IV, V): bp 83 °C (2 mmHg). Anal. Calcd for $C_9H_{20}OSn$: C, 41.07; H, 7.60. Found: C, 41.28; H, 7.75. ^1H NMR δ 0.04 ($Sn(CH_3)_3$, $J_{^{119}Sn-^1H}$ = 51 Hz), 3.4 (CHOH, IV (85%), $w_{1/2}$ = 20 Hz), 3.8 (CHOH, V (15%), $w_{1/2}$ = 12 Hz).

3-Methyl-5-(trimethylstannyl)cyclohexanol (VI–IX): bp 72–74 °C (1 mmHg). Anal. Calcd for $C_{10}H_{22}OSn$: C, 43.22; H, 7.94. Found: C, 43.66; H, 8.09. ^1H NMR δ 0.07 (major), –0.03 ($J_{^{119}Sn-^1H}$ = 49 Hz, $Sn(CH_3)_3$), overlapping CHOH signals from 3.3–3.9 with $w_{1/2}$ characteristic of axial protons.

3-(Trimethylsilyl)cyclohexanol (XIII, XIV): bp 85 °C (2 mmHg) (Kugelrohr). Anal. Calcd for $C_9H_{20}OSi$: C, 62.74; H, 11.71. Found: C, 61.13; H, 10.88. ^1H NMR δ –0.22 ($Si(CH_3)_3$, XIII), –0.12 ($Si(CH_3)_3$, XIV, XVIII), 0.19–2.11 (ring protons), 3.39 (C*H*OH, XIII), 3.91 (C*H*OH, XIV), 4.47 (C*H*OH, XVIII), 5.59 (CH=C<, XVIII).

3-Methyl-5-(trimethylsilyl)cyclohexanol (XV, XVI, XVII): bp 123 °C (8 mmHg) (Kugelrohr). Anal. Calcd for $C_{10}H_{22}OSi$: C, 64.47; H, 11.91. Found: C, 64.62; H, 11.92. ^1H NMR δ –0.24 ($Si(CH_3)_3$, XV), –0.18 ($Si(CH_3)_3$, XVI), 0.78 (CH_3, d, J = 6 Hz, XVI), 0.81 (CH_3, d, J = 7.5 Hz, XV), 0.61–2.16 (ring protons), 3.58 (C*H*OH). The >CHOH region (ca. δ 3.6) is consistent only with axial hydrogens. The more intense CCH_3 doublet is at lower field (δ 0.81), whereas the more intense $Si(CH_3)_3$ signal is at higher field (δ –0.24) with the other observable $Si(CH_3)_3$ signal at δ –0.18. (Ratio ca. 1.4:1). The relative positions of the CCH_3 and $Si(CH_3)_3$ signals for XV and XVI are appropriate for the indicated stereochemistries and conformations. The dominance of XV over XVI (Chart I) is shown in the ^{13}C spectrum by the positions of the CCH_3 and $Si(CH_3)_3$ resonances: both should be to higher field for those of XV than for those of XVI. Signals ascribable to XVII (~6%) were not identified in the ^1H spectrum.

NMR Spectra. ^{13}C NMR spectra were obtained at 25.05 MHz (JEOL FX-100) for $CDCl_3$ solutions, and chemical shifts are referenced to the center peak of the $CDCl_3$ triplet at 77.00 ppm. ^{119}Sn and ^{29}Si NMR spectra were recorded at 37.08 and 19.79 MHz, respectively (JEOL FX-100). The ^{29}Si spectra were obtained by a polarization transfer technique (INEPT) as described by Doddrell et al.[18] The ^{119}Sn and ^{29}Si chemical shifts are relative to internal $(CH_3)_4Sn$ and $(CH_3)_4Si$, respectively, and positive shifts are to lower field. ^1H NMR spectra were recorded for $CDCl_3$ solutions at 100 MHz (JEOL PS-100) and 300 MHz (Bruker CXP-300) with $CHCl_3$ (7.24 ppm) as internal reference.

Acknowledgment. This research was funded in part by the Australian Research Grants Committee.

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Registry No. I, 63831-50-5; II, 82569-82-2; III, 82569-83-3; IV, 82521-58-2; V, 82521-59-3; VI, 82521-60-6; VII, 82570-82-9; VIII, 82569-84-4; IX, 82570-83-0; X, 7531-60-4; XI, 82521-61-7; XII, 82521-62-8; XIII, 7452-98-4; XIV, 7452-99-5; XV, 82521-63-9; XVI, 82569-85-5; XVII, 82569-86-6; XVIII, 82521-64-0; $(CH_3)_3SnLi$, 17946-71-3; $(CH_3)_3SiLi$, 18000-27-6; 2-cyclohexen-1-one, 930-68-7; 5-methyl-2-cyclohexen-1-one, 7214-50-8; 3-(trimethylsilyl)-1-[trimethylsilyl)oxy]-1-cyclohexene, 55942-21-7.

Syntheses of the Stereoisomers of the Sex Pheromones of the Southern Corn Rootworm and Lesser Tea Tortrix

Philip E. Sonnet

Insect Attractants, Behavior, and Basic Biology Research Laboratory, ARS, USDA, Gainesville, Florida 32604

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Assignments of stereostructure and precise composition of insect sex pheromones are often necessarily made by physiological evaluation of candidate synthetics.[1] Generally the amount of isolate available for structure assignment is less than 0.1 mg, and for chiral materials the difficulty in configuration assignment is often compounded by asymmetric centers remotely situated from spectrally useful functionality. Although the stereoisomers of a pheromonal enantiomer frequently act only as diluents in bioassays of racemic mixtures, the enantiomer of the Japanese beetle sex pheromone inhibits male response to the active stereoisomer at the 1% level.[2] In addition, at least one case is known of an insect sex pheromone that is a nonracemic mixture of stereoisomers on the basis of identification of the natural ratio directly.[3] Despite dramatic accomplishments in asymmetric synthesis by induction of asymmetry[4] and the often clever means by which these have been applied in the cause of insect chemistry, ultimate purification of either key intermediates or final products must be achieved by some form of kinetic resolution in order to obtain unambiquous biological data. We report here the synthesis of the stereoisomers of two insect sex pheromones from readily available 10-undecenoic acid. The key steps involved a facile purification of crystalline diastereomeric amides followed by N-hydroxyethylation of the amides as a ploy to render the purified amides susceptible to mild acid hydrolysis.

Stereochemically undefined structures have been assigned to the sex pheromones of the southern corn rootworm, *Diabrotica undecimpunctata* howardi Barber,[5] and the lesser tea tortrix, *Adoxophyes* spp.[6] The structure assigned the pheromone of the former insect (a beetle) is 10-methyl-2-tridecanone (1, Scheme I). The latter insect, a moth, employs a pheromone blend containing 10-methyl-1-dodecanol acetate (2) as a minor component.

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