

TRIMETHYLSTANNYL LITHIUM MEDIATED SYNTHESIS OF 2-, 3- AND 4-TRIMETHYLSTANNYL CYCLOHEXANOLS

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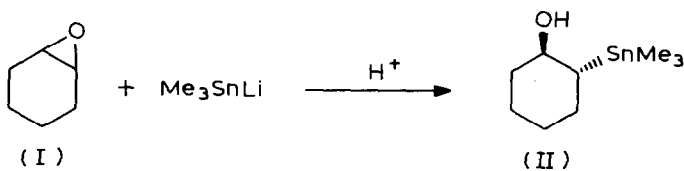
Summary

The use of trimethylstanyllithium for the preparation of 2-, 3- and 4- trimethylstannylcyclohexanols is described. The stereochemistries of these products are discussed on the basis of the ^1H , ^{13}C , and ^{119}Sn NMR data.

Various types of functional organostannanes have been much used in the recent years in synthesis, and in this context the stereochemical outcome of the reactions used in their preparation appears to be crucial [1,2]. As a part of our interest in developing new synthetic procedures based on organostannanes [3], we report here the synthesis and the stereochemical features of regioisomeric trimethylstannylcyclohexanols.

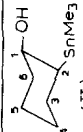
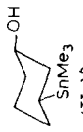
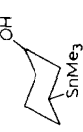



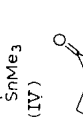
2-Trimethylstannylcyclohexanol (II) was prepared through the ring opening reaction of 7-oxabicyclo[4.1.0]heptane (I) with trimethylstanyllithium which takes place at -78°C (see Scheme 1).

The reaction is stereoselective, affording compound II in the *trans* conformation, as proved by the proton resonance at 0.04 ppm for the Me_3Sn group as well as by the ^{13}C and ^{119}Sn data (see Table 1); the *trans* diequatorial arrangement of the vicinal

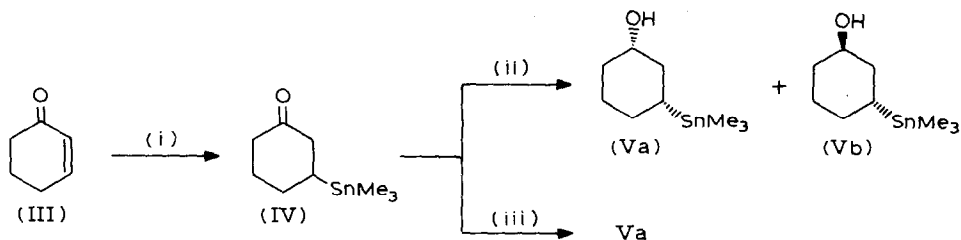


SCHEME 1

TABLE I. NMR DATA ^a FOR β, γ- AND δ-TRIMETHYLSNANYLCYCLOHEXANOLS AND CYCLOHEXANONES

Compound	δ(¹³ C)						δ(¹ H) SnMe ₃	δ(¹¹⁹ Sn) Sn	
	C ¹	C ²	C ³	C ⁴	C ⁵	C ⁶			Me
 (II)	72.40 (25)	35.30 (400)	28.99 (16)	27.19 (60)	25.30 (-)	38.09 (46)	-10.79 (302)	0.05	-2.35
 (Va) ^b	72.05 (80)	40.05 (17)	22.17 (400)	29.80 (20)	27.25 (71)	36.10 (10)	-11.90 (310)	0.04	0.59
 (Vb) ^b	67.70 (40)	37.90 (-)	20.10 (-)	29.00 (-)	23.10 (-)	34.06	-11.00 (-)	0.02	2.35
 (VIIIa) ^b	70.54	37.79 (66)	28.98 (9)	23.34 (268)	C ⁵ = C ³	C ⁶ = C ²	-12.01 (295)	-0.05	1.20
 (VIIIb) ^b	68.27	34.93 (-)	26.17 (12)	24.82 (-)	C ⁵ = C ³	C ⁶ = C ²	-11.99 (290)	-0.01	-1.84
 (IV)	210.20 (59)	45.70 (15)	25.06 (400)	29.30 (14)	30.76 (70)	42.10	-11.70 (320)	0.11	6.53
 (IX)	212.82	45.78 (63)	33.46 (-)	24.97 (243)	C ⁵ = C ³	C ⁶ = C ²	-9.93 (264)	0.03	3.50
(Vb) ^c	67.71 (39)	37.89 (91)	20.08 (375)	29.01 (12)	23.00 (45)	34.01 (16)	-11.06 (295)	0.02	2.27
(VIIIb) ^c	68.25	35.00 (57)	26.18 (12)	24.86 (128)	C ⁵ = C ³	C ⁶ = C ²	-11.98 (290)	0.00	-1.80

^a Positive shift values denote shifts to lower fields; values in parentheses are ¹³C-¹¹⁹Sn coupling constants (Hz). See experimental section for description of spectral procedure. ^b Values obtained from spectra of mixtures of conformers. ^c Values obtained from spectra of isomerically pure compounds.



SCHEME 2. (i) Me_3SnLi , H^+ ; (ii) LiAlH_4 ; (iii) LiSiAm_3BH .

substituents was supported by the $^3J(^{13}\text{C}-^{119}\text{Sn})$ values of 48 and 60 Hz, consistent with a "normal chair" conformation of the ring [4].

This approach could not be extended to the synthesis of 3-trimethylstannylcyclohexanol (V) owing to the unavailability of 6-oxabicyclo[3.3.1]heptane (X) [5], but 1,4-addition of the stannyl lithium to cyclohexen-2-one (III) led to the target alcohol as a mixture of isomers Va and Vb in a ratio of ca. 38/62 as indicated by GLC. Compounds Va and Vb were previously reported by Kitching [6] but only Vb, the predominant species, was fully characterised.

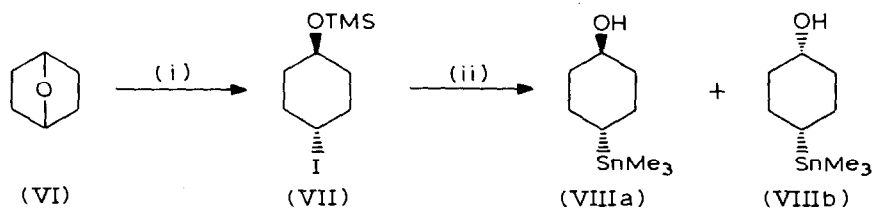


(X)

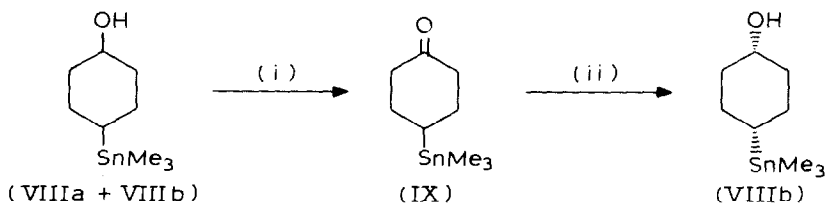
Reduction of IV with lithium triisiamylborohydride gave Va with a GLC purity as high as 98%, permitting complete NMR characterisation of that isomer (see Table 1). It was also possible to assign definitely the signals of Vb in the spectra of the mixture produced by LiAlH_4 reduction of IV.

4-Trimethylstannylcyclohexanol (VIII) was prepared starting from the cyclic ether 7-oxabicyclo [2.2.1]heptane (VI). The unreactivity of this ether towards trimethylstannyl lithium was overcome by using trimethylsilyloxy silane (TMSI) to generate *trans*-4-iodotrimethylsilyloxycyclohexane (VII): nucleophilic substitution of the halogen by the stannyl anion gave alcohols VIIIa and VIIIb, in 59%/41% ratio (GLC), with the organometallic substituent in the equatorial position as revealed out by the ^1H NMR data (see Table 1).

The lack of stereoselectivity in the reaction of VII with trimethylstannyl lithium may be related to the availability of several mechanistic pathways in the displacement of iodine, as has been demonstrated for the reactions of bromides with stannyl lithium reagents [7].



SCHEME 3. (i) TMSI; (ii) Me_3SnLi .



SCHEME 4. (i) Jones reagent; (ii) LiSiAm_3BH .

It was possible to isolate compound VII and then treat it with the lithium reagent, but such isolation was unnecessary and the one-pot process gave good yields of products derived from the starting ether (VI).

Conformationally pure VIIIb (up to 98% by GLC) was obtained by using the sequence shown in Scheme 4 involving oxidation of the isomeric mixture to the ketone IX followed by lithium trisiamylborohydride reduction.

The availability of the NMR spectrum of pure VIIIb allowed unambiguous assignment of the spectral data for VIIIa present in the previously described mixture.

Experimental

GLC-mass spectrometric analyses were carried out with a Hewlett-Packard HP5790 GC-HP5970 MS system, equipped with a HP dimethyl-silicone fluid high performance 25 m capillary column. ^1H NMR spectra were recorded on a Perkin-Elmer R32 instrument (90 MHz), in CDCl_3 as solvent; δ values are given in ppm from Me_4Si as internal standard; ^{13}C and ^{119}Sn NMR spectra were recorded on a Varian FT 80A spectrometer with noise decoupling in ca. 0.1 M CDCl_3 solutions: $\delta(^{13}\text{C})$ values are quoted in ppm from Me_4Si as internal standard, and $\delta(^{119}\text{Sn})$ in ppm from Me_4Sn as external reference THF was distilled over Na and LiAlH_4 , and all reactions were carried out under dry nitrogen.

2-Trimethylstannylcyclohexanol (II)

To a solution of Me_3SnLi prepared as described by Tamborski [8] from trimethylstannyl chloride (10.8 g, 55.3 mmol) and lithium shot (3.84 g, 550 mmol), in THF (25 ml), I (5.43 g, 55.3 mmol) was added slowly at 0°C . The mixture was maintained for 3 h at room temperature and methanol (5 ml) was then added. After a further 1 h stirring at room temperature, Et_2O (100 ml) was added and the mixture was washed twice with saturated aqueous NH_4Cl . The ethereal layer was separated, dried over Na_2SO_4 and the solvent was evaporated off. Fractional distillation of the residue gave II (11.7 g, 81%), b.p. $62\text{--}64^\circ\text{C}$ (0.045 mmHg). ν_{max} 3350, 2920, 1450, 1110, 760 cm^{-1} . δ : 0.05 (9H,s, Me_3Sn), 1.0–2.1 (1OH, br, cyclohexane ring and OH), 3.5 (1H,m,CH-O). MS m/z : 244($M^+ - 18$), 165, 135. Found: C, 40.98; H, 7.58. $\text{C}_9\text{H}_{20}\text{OSn}$ calcd.: C, 41.07; H, 7.60%.

cis-3-Trimethylstannylcyclohexanol (Va)

3-Trimethylstannylcyclohexanone (3 g, 11.5 mmol), made as described by Kitching [6], was added slowly to an ethereal solution of lithium trisiamylborohydride (12 ml of a 1 M solution) at -50°C . After 3 h at this temperature, the mixture was

warmed to room temperature and water (5 ml) and ethanol (5 ml) added, followed by hydrogen peroxide (5 ml of a 30% solution) and NaOH (5 ml of a 6 M solution). After 15 min stirring and addition of more Et₂O, the upper layer was separated, washed with water and dried over Na₂SO₄, and the solvent was evaporated off. The residue was fractional distilled to give Va (2.6 g, 86%), b.p. 60–61°C (0.08 mmHg). ν_{\max} 3460, 2960, 1110, 760 cm⁻¹, δ : 0.01 (9H,s,Me₃Sn), 0.9–2.0 (1OH, br, cyclohexane and OH), 3.8 (1H, m, CH-O). MS m/z 247($M^+ - 15$), 231, 165. Found: C, 41.00; H, 7.54. C₉H₂₀OSn calcd.: C, 41.07; H, 7.60%.

4-Iodotrimethylsiloxycyclohexane (VII)

A mixture of 7-oxabicyclo[2.2.1]heptane (VI) (6.0 g, 61.2 mmol) and TMSI (12.25 g, 61.2 mmol) in chloroform (30 ml, free from ethanol) was stirred for 3 h. The solvent was evaporated off, and the residue fractionally distilled to give (VII) as a clear oil, which became yellow on standing in the light (15.2 g, 91%). b.p. 82–83°C (0.3 mmHg). ν_{\max} 2960, 1460, 1250, 860 cm⁻¹. δ 0.08 (9H,s,Me₃Si), 1.1–2.3 (9H, br, cyclohexane), 3.7 (1H,m, CH-O), 4.2 (1H,m,CH-I). MS m/z 298 (M^+), 283, 171, 73. Found: C, 36.00; H, 6.31. C₉H₁₉IOSi calcd.: C, 36.24; H, 6.38%.

4-Trimethylstannylcyclohexanols (VIIIa and VIIIb)

To a solution of Me₃SnLi prepared from trimethylstannyl chloride (3.31 g, 16.7 mmol) and lithium shot (1.14 g, 167 mmol) in THF (10 ml), VII (5 g, 16.7 mmol) was added at 0°C. The mixture was warmed to room temperature then stirred for 10 h, and subsequently treated with aqueous HCl (10 ml of a 2 N solution). Et₂O (150 ml) was added, and the organic layer was separated, washed with NaHCO₃ (50 ml of a sat. solution) then water, and dried over Na₂SO₄. The solvent was evaporated off, and the residue fractionally distilled to give VIIIa–VIIIb as a mixture of isomers. B.p. 89–91°C (0.4 mmHg). ν_{\max} 3340, 2980, 1460, 1120, 780 cm⁻¹. δ -0.05 (9H,s,Me₃Sn, VIIIa), -0.05–0.01 (9H,Me₃Sn,VIIIb), 1.0–2.0 (1OH,br, cyclohexane and OH), 3.5 (1H,m,CH-O,VIIIa), 3.8(1H,m,CH-O,VIIIb). MS, m/z (VIIIa): 247 ($M^+ - 15$),231,135; (VIIIb): 247, 221, 133. Found: C, 41.02; H, 7.61. C₉H₂₀OSn calcd.: C, 41.07; H, 7.60%.

4-Trimethylstannylcyclohexanone (IX)

To a solution of VIIIa–VIIIb (1 g, 3.8 mmol) in acetone (5 ml), the Jones reagent prepared from chromium trioxide (0.4 g, 4 mmol), H₂SO₄ conc. (0.3 ml) and H₂O (1.2 ml) was added slowly at 0–5°C. After 2 h at this temperature, ethanol (1 ml) was added, and the mixture diluted with Et₂O (25 ml). The dark green precipitate was filtered off and the organic layer washed with aqueous NaHCO₃ (10 ml). The upper layer was separated, and dried over Na₂SO₄, and the solvent was evaporated off. Fractional distillation of the residue gave IX (0.88 g, 89%). B.p. 80–82°C (0.6 mmHg). ν_{\max} 2920, 1713, 1110, 760 cm⁻¹. δ 0.03 (9H,s,Me₃Sn), 1.0–2.5 (9H,br,cyclohexane). MS m/z : 260(M^+), 165, 134. Found: C, 41.43; H, 6.93. C₉H₁₈OSn calcd.: C, 41.38; H, 6.90%.

Reduction of IX to VIIIb

The procedure described for Va gave VIIIb (0.76 g, 85%); b.p. 88–89°C (0.4 mmHg). Found: C, 41.05; H, 7.61. C₉H₂₀OSn calcd.: C, 41.07; H, 7.60%.

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