

Synthesis of C,Sn-Chiral Triorganotin Halides via C-Chiral Arylcopper and Arylgoldlithium Intermediates. Crystal and Molecular Structure of One {2-[1-(S)-(Dimethylamino)ethyl]phenyl}methylphenyltin Bromide Diastereomer

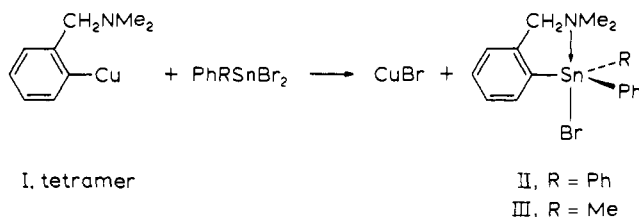
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Abstract: The crystal and molecular structure and absolute configuration of 2-[1-(S)-Me₂NCH(Me)]C₆H₄SnMePhBr, which is the first example of a diastereomerically pure chiral triorganotin halide, are determined by a single-crystal x-ray diffraction study. Crystals are orthorhombic, space group *P*2₁2₁2₁ with *Z* = 4 in a unit cell of dimensions *a* = 9.370 (4), *b* = 13.361 (3), and *c* = 14.283 (4) Å. The final *R* value is 0.048 for 2784 reflections. The tin atom has a distorted trigonal bipyramidal geometry with the C,N-bonded Me₂NCH(Me)C₆H₄ group spanning one equatorial (C) and one axial (N) site. The Ph and Me groups reside in the two equatorial positions resulting in an (*S*)_{Sn} configuration at the tin atom (cf. Figure 1). The configuration at Sn was unambiguously determined by using anomalous diffraction effects which likewise resulted in an independent check of the configuration at the α-C atom (*S* configuration). The (*S*)_C(*S*)_{Sn} diastereomer (mp 119–123 °C) was separated by preferential crystallization from a 40/60 molar equilibrium mixture of the (*S*)_C(*S*)_{Sn} and (*S*)_C(*R*)_{Sn} diastereomers, respectively. The latter mixture was obtained by the reaction of MePhSnBr₂ with the C-chiral arylcopper and arylgoldlithium intermediates {2-[1-(*S*)-Me₂NCH(Me)]C₆H₄]_nM (M = Cu, *n* = 1, or M = AuLi, *n* = 2). Slow epimerization of the (*S*)_C(*S*)_{Sn} diastereomer, which involves inversion of configuration at the tin atom, takes place in solution. On the basis of the dynamic NMR resonance patterns and the geometric constraints of the five-membered chelate ring [Me₂NCH(Me)C₆H₄Sn: C–Sn–N 75.2°] it is concluded that epimerization proceeds in a hexacoordinate intermediate (transition state) formed by association of two diastereomers.

Introduction

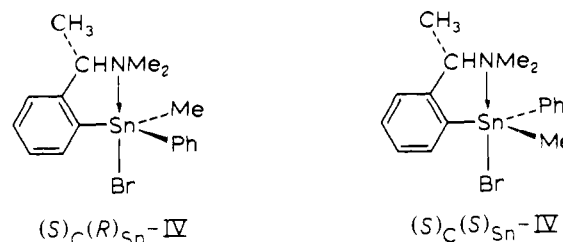
Recently, we reported the isolation and characterization of the first examples of chiral, pentacoordinate, triorganotin halides in which the center of chirality is the tin atom.^{2a} These compounds have become accessible as a result of our earlier finding^{2b} that, different from the reaction of aryllithium compounds, reaction of arylcopper compounds with diorganotin dihalides invariably results in the selective formation of triorganotin halides, i.e.



An x-ray investigation of prochiral II (R = Ph) showed that the tin atom is pentacoordinate as a result of intramolecular Sn–N coordination.³ An NMR spectroscopic investigation of chiral III (R = Me) revealed that also in solution Sn–N coordination takes place and that inversion of configuration about tin does not occur on the NMR time scale (up to 123 °C).^{2a} This high configurational stability about tin in III has been ascribed to the fact that complex formation with external Lewis bases, believed to be the first step in the stereoisomerization process of triorganotin halides, cannot compete with intramolecular Sn–N coordination.

Because the possibility cannot be excluded that in these compounds slow stereoisomerization processes take place, which thus are undetectable by NMR techniques, we have now synthesized {2-[1-(*S*)-(dimethylamino)ethyl]phenyl}methylphenyltin bromide (IV).

This compound has, in addition to the two possible configurations about tin in a trigonal bipyramidal array, a second center of chirality [CH(CH₃)NMe₂] of which the configuration cannot invert. Accordingly, starting from either the *S* or the *R* enantiomer of 1-(*N,N*-dimethylamino)ethylbenzene (V) the formation of two diastereomers can be anticipated, e.g., starting from (*S*)-V,



These compounds in principle allow the detection of stereoisomerization processes (epimerization) at tin, even when these processes are very slow on the NMR time scale, because the diastereomers (*S*)_C(*R*)_{Sn}-IV⁴ and (*S*)_C(*S*)_{Sn}-IV⁴ have different spectra.

In this paper we will report (1) the synthesis and characterization of these C,Sn-diastereomeric triorganotin halides, (2) the resolution of one of these diastereomers, (3) the molecular geometry and absolute configuration of the resolved diastereomer, and (4) a mechanistic interpretation of stereoisomerization processes at chiral tin centers.

Experimental Section

General Remarks. The reactions were carried out under dry oxygen-free nitrogen. Solvents were purified, dried, and distilled under nitrogen before use.

IR spectra were recorded on a Perkin-Elmer 577 grating IR spectrometer. ¹H NMR spectra were recorded on a Varian Associates

Table I. Absolute Configuration Determination

A. Effects of Anomalous Dispersion on the Agreement for the Accepted Configuration (S) _C (S) _{Sn} [Model (1)] and for the (R) _C (R) _{Sn} Configuration [Model (2)]				
	Model (1)		Model (2)	
R_F	0.048		0.058	
R_{wF}	0.052		0.065	

B. Some Friedel-Related Pairs of Reflections ^a				
hkl	$F_c(hkl)$	$F_c(\bar{h}\bar{k}\bar{l})$	$I_0(hkl)$	$I_0(\bar{h}\bar{k}\bar{l})$
238	20.8	<22.0	47 (3)	<55 (3)
354	87.0	<90.4	835 (17)	<978 (21)
361	43.2	>40.5	216 (5)	>195 (5)
412	89.8	<90.6	1280 (24)	<1366 (24)
511	103.3	>100.3	1408 (25)	>1233 (23)
723	60.1	<61.9	322 (8)	<347 (8)
8 4 11	34.3	<35.8	50 (3)	<55 (3)

^a The intensities are on a relative scale. The $\sigma(I)$'s are given in parentheses.

HA-100 NMR spectrometer. The spectra and molecular weight data were obtained by Mrs. T. van Montfort-Volp, Mrs. G. M. Bijlsma-Kreuger, and J. W. Marsman.

Elemental analyses were carried out in the Analytical Department of the TNO Institute.

Synthesis of 1-(S)-(Dimethylamino)ethylbenzene [(S)-V]. A mixture of α -(S)-methylbenzylamine (24 g, 161 mmol), 42 mL of 88% formic acid, and 35 mL of 36% formaldehyde (excess) was refluxed for 1.5 h.⁷ After the evolution of CO₂ had ceased, 12 mL of concentrated hydrochloric acid was added. The acidic layer was separated, washed with ether (3 × 25 mL), and subsequently made alkaline with an aqueous solution of potassium hydroxide (50%). The resulting mixture was extracted with ether (3 × 25 mL). The ethereal layers were dried over Na₂SO₄, filtered, and then concentrated yielding (S)-V as a colorless oil: bp 80–82 °C (0.2 mm); 75% yield; $[\alpha]_D^{25} +48.6^\circ$.

Synthesis of [1-(S)-(Dimethylamino)ethyl]phenyllithium [(S)-VI]. A solution of [1-(S)-(dimethylamino)ethyl]benzene [(S)-V, 7.15 mmol] and butyllithium (7.15 mmol) in ether (20 mL) was stirred for 24 h. The resulting yellow solution was added at 4 °C to 5 mL of D₂O. The ether layer was dried over Na₂SO₄, filtered, and then concentrated, yielding ortho-deuterated (quantitatively according to NMR) 1-(S)-(dimethylamino)ethylbenzene in quantitative yield: IR ν C–D 2258 w and 2262 cm⁻¹ sh;⁸ NMR (CCl₄) δ 2.10 (s, NMe₂, 6 H), 3.12 (q, α -H, 1 H), 1.28 (d, α -CH₃, 3 H), 7.18 (aromatic H, 4 H).

Synthesis of [1-(S)-(Dimethylamino)ethyl]phenylcopper [(S)-VII]. Solid CuBr (27 mmol) was added at –20 °C to a solution of Ar*Li [(S)-VI, 27 mmol] in ether (100 mL). The resulting mixture was stirred at –20 °C for 1 h and then for 2 h at ambient temperature. The greenish colored precipitate was filtered off and extracted with ether until a test on LiBr (with AgNO₃) was negative. The resulting solid was recrystallized from a large volume of ether affording yellow, crystalline (S)-VII which was washed with pentane and dried in vacuo: yield 37%; mol wt (cryoscopic in benzene) found, 853 (calcd for Ar*₄Cu₄, 847). Anal. Calcd for C₁₀H₁₄NCu: C, 56.72; H, 6.66; N, 6.61; Cu, 30.00. Found: C, 56.0; H, 6.5; N, 6.4; Cu, 29.5. Mp 200–210 °C dec (10 °C/min); NMR (toluene-*d*₈) δ 1.87 (s, NMe₂, 6 H), 3.20 (q, α -H, 1 H), 0.95 (d, α -CH₃, 3 H), 8.55 (m, H₆, $J_{5,6} = 7$, $J_{4,6} = 1.5$ Hz, 1 H), 6.81 (m, H₃, 1 H), 7.0–7.3 (m, H_{4,5}, 2 H).

Synthesis of Bis[1-(S)-(Dimethylamino)ethyl]phenylgoldlithium Dimer [(S)-VIII]. Solid AuBr·PPh₃ (10 mmol) was added at 0 °C to a solution of Ar*Li [(S)-VI, 20 mmol] in ether (100 mL). Initially a brown-yellow colored solution is obtained from which after 0.5 h a white, crystalline solid precipitated. The resulting mixture was stirred at 0 °C for 2 h and then filtered. The solid was washed with ether (2 × 20 mL) and pentane (2 × 10 mL) and dried in vacuo: mol wt (cryometry in benzene) 950 (calcd for dimer, 1000); mp 140 °C dec; yield 40%; NMR (benzene-*d*₆) δ 1.75 (s, NMe₂, 6 H), 4.83 (q, α -H, 1 H), 0.86 (d, α -CH₃, $J = 7$ Hz, 3 H), 8.60 (d of d, H₆, 1 H), 7.42 (t of d, H₄, 1 H), 7.0–7.2 (H_{3,5}, 2 H).

Synthesis of [2-[1-(S)-(Dimethylamino)ethyl]phenyl]methylphenyltin Bromide (IV). Via Ar*Li [(S)-VI] with MePhSnBr₂. A solution of

Ar*Li [(S)-VI, 19.1 mmol] in ether (50 mL) was added in 1 h to a solution of methylphenyltin dibromide in ether (100 mL). The yellow reaction mixture was stirred for 1 h and then concentrated. The resulting oily residue was extracted with benzene (removal of LiBr). Concentration of the benzene filtrate afforded a yellow oil which according to NMR spectroscopy consisted of a mixture of at least five organotin products.

Via Ar*Cu [(S)-VII] with MePhSnBr₂. A solution of Ar*Cu [(S)-VII, 9.5 mmol] in benzene (60 mL) was added to a solution of MePhSnBr₂ (9.5 mmol) in benzene (100 mL). The resulting colorless solution which contained a white precipitate was stirred for an additional 1 h and was then filtered (quantitative amount of CuBr). The benzene filtrate was concentrated affording (S)-IV as a viscous oil. This oil was dissolved in 10 mL of ether. Addition of pentane (100 mL) yielded a white precipitate which was filtered off and then dried in vacuo (96% yield). NMR spectroscopy indicated this solid to be a 40/60 mixture of two diastereomers of (S)-IV (see Table III), mp 47–65 °C.

Isolation of the (S)_C(S)_{Sn} Diastereomer of IV. The 40/60 mixture (1 g) was dissolved in 10 mL of ether. To this solution 10 mL of pentane was distilled in about 24 h. The resulting crystals were collected by filtration, washed with pentane, and then dried in air: mp 119–123 °C; mp of the solidified melt 50–60 °C. Anal. Calcd for C₁₇H₂₂NSnBr: C, 46.52; H, 5.05; Br, 18.20; N, 3.19; Sn, 27.04. Found: C, 46.5; H, 4.9; Br, 18.0; N, 3.2; Sn, 26.9. Mol wt (osmometry in benzene) found, 441; calcd, 439.

Isolation of the (R)_C(R)_{Sn} Diastereomer of IV. Following the same procedure but now starting from 2-[1-(R)-(dimethylamino)ethyl]phenylcopper afforded white crystals melting at 121–123 °C.

Via Ar*₂AuLi Dimer [(S)-VIII] with MePhSnBr₂. Solid methylphenyltin dibromide (0.08 mmol) was added to a solution of (S)-VIII (0.08 mmol) in toluene-*d*₈ (0.4 mL). NMR spectroscopy revealed that in addition to 2-[1-(S)-(dimethylamino)ethyl]phenylgold [(S)-IX] (the respective NMR patterns for the gold compounds will be presented and discussed in a forthcoming paper¹⁶) the two diastereomers of IV were present in solution in a 40/60 molar ratio (NMR, see Table III) whereas the spectrum of the starting goldlithium dimer [(S)-VIII] was essentially absent.

Structure Determination and Refinement. Crystals of the pure diastereomer of (S)-IV are orthorhombic; space group P2₁2₁2₁; $Z = 4$. Cell dimensions were measured on a Nonius CAD 4 automatic diffractometer (Zr-filtered Mo K α radiation; $\lambda = 0.7107$ Å) and are $a = 9.370$ (4), $b = 13.361$ (3), and $c = 14.283$ (4) Å; $V = 1788$ Å³; $d_x = 1.631$ g cm⁻³; μ (Mo K α) = 39.7 cm⁻¹; crystal dimensions are 0.1 × 0.2 × 0.7 mm. Intensities were collected on the same equipment in the $\omega/2\theta$ scan mode. The applied scan angle was 0.45 + 1.18 tan θ . Two sets of equivalent reflections which form Bijvoet pairs were measured up to $\theta = 25^\circ$. Of the 3289 reflections 2784 had $I > 2.5\sigma(I)$ and only these were used for structure determination and refinement. The data were corrected for the Lp factor, but not for absorption.

The positions of tin and bromine were determined from the Patterson synthesis. All nonhydrogen atoms were located from subsequent Fourier syntheses. In view of the scope of this study no attempts have been made to determine the hydrogen positions. The structure was refined by block-diagonal least squares varying positional and anisotropic thermal parameters. Thirteen reflections, apparently suffering from extinction, were omitted from the refinement.

In case anomalous diffraction effects are neglected discrimination between the (S)_C(S)_{Sn} and (R)_C(R)_{Sn} configuration is not possible. However, by using this effect unambiguous determination of the absolute configuration is possible. Application of this method for the present compound leads unambiguously to a (S)_C(S)_{Sn} configuration; see Table I. This observed (S)_C configuration is in agreement with the S configuration at α -C in the starting (S)-1-(dimethylamino)ethylbenzene. In fact the x-ray analysis gives an independent check that the starting amine used had the S configuration at α -C. The final R_F index corresponding to the (S)_C(S)_{Sn} configuration amounts to 0.048 ($R_{wF} = 0.052$) with $w^{-1} = \sigma^2(F)$.

Scattering factors are those of Cromer and Mann.¹⁰ Anomalous dispersion corrections used for Sn are $f' = -0.81$, $f'' = 1.73$, and for Br $f' = -0.21$ and $f'' = 2.68$.¹¹ Final parameters are listed in Table II.

The final difference Fourier synthesis showed no significant features except in the neighborhood of the heavy atoms.

Most of the crystallographic calculations were carried out with an extended version of the X RAY system.¹²

Table II. Atomic Parameters^a

Atom	<i>x/a</i>	<i>y/b</i>	<i>z/c</i>	<i>U</i> ₁₁	<i>U</i> ₂₂	<i>U</i> ₃₃	<i>U</i> ₁₂	<i>U</i> ₁₃	<i>U</i> ₂₃
Sn	62 431 (6)	107 937 (4)	47 514 (4)	4.47 (2)	4.57 (3)	3.51 (3)	-0.47 (4)	0.11 (3)	0.05 (3)
Br	3786 (1)	11 042 (1)	3817 (1)	6.6 (1)	7.6 (1)	7.2 (1)	0.2 (1)	-2.9 (1)	-0.3 (1)
N	8585 (7)	10 292 (6)	5403 (5)	4.2 (4)	6.7 (5)	5.0 (5)	-0.6 (4)	0.8 (4)	-0.3 (4)
C(1)	6490 (8)	9246 (7)	4350 (6)	4.9 (5)	4.8 (5)	4.8 (5)	-1.1 (5)	0.8 (4)	0.7 (5)
C(2)	5660 (10)	8784 (7)	3656 (6)	7.4 (6)	6.0 (6)	2.3 (5)	-1.9 (5)	1.4 (4)	-1.1 (5)
C(3)	5898 (10)	7781 (8)	3442 (6)	7.8 (7)	7.2 (7)	5.1 (6)	-1.3 (6)	2.7 (5)	-0.4 (6)
C(4)	6976 (12)	7217 (9)	3925 (8)	9.9 (8)	8.0 (8)	7.8 (8)	-3.4 (7)	3.9 (7)	-1.9 (7)
C(5)	7789 (11)	7705 (8)	4627 (7)	7.5 (7)	5.8 (7)	7.7 (8)	-0.1 (5)	3.6 (6)	0.1 (7)
C(6)	7565 (9)	8713 (7)	4819 (7)	5.2 (5)	5.5 (6)	6.1 (6)	0.1 (4)	2.3 (5)	0.9 (6)
C(7)	8444 (9)	9200 (8)	5619 (6)	6.4 (6)	5.8 (6)	5.3 (5)	1.3 (5)	-0.1 (4)	0.7 (5)
C(8)	7758 (12)	8985 (9)	6584 (7)	9.3 (7)	9.5 (10)	4.2 (6)	0.3 (7)	1.3 (6)	1.5 (7)
C(9)	9086 (9)	10 887 (9)	6216 (7)	6.0 (6)	9.4 (8)	6.2 (6)	0.3 (6)	-2.6 (5)	-3.8 (7)
C(10)	9667 (10)	10 392 (9)	4589 (8)	5.5 (6)	9.1 (8)	8.1 (8)	0.0 (6)	2.4 (6)	-0.8 (7)
C(11)	7203 (11)	12 093 (8)	4108 (6)	7.9 (7)	5.5 (7)	4.8 (6)	-1.8 (6)	1.2 (5)	2.4 (5)
C(12)	5308 (8)	11 056 (7)	6086 (6)	3.6 (4)	5.8 (6)	3.8 (5)	0.3 (4)	0.8 (4)	0.4 (5)
C(13)	5714 (9)	11 865 (8)	6607 (6)	5.3 (6)	8.2 (8)	4.1 (6)	1.8 (5)	-1.9 (4)	-1.9 (6)
C(14)	5006 (12)	11 999 (10)	7553 (8)	6.9 (6)	11.7 (10)	6.2 (7)	3.8 (7)	-1.5 (5)	-1.4 (8)
C(15)	3975 (13)	11 356 (10)	7834 (7)	9.0 (8)	13.0 (10)	6.2 (7)	4.4 (8)	1.3 (7)	1.5 (7)
C(16)	3575 (12)	10 579 (10)	7285 (8)	9.0 (8)	12.7 (11)	10.4 (9)	4.0 (9)	5.3 (8)	6.0 (9)
C(17)	4242 (10)	10 410 (9)	6349 (7)	7.3 (7)	9.1 (9)	6.2 (7)	-0.4 (6)	2.6 (5)	1.4 (7)

^a The positional parameters are $\times 10^4$ (for Sn $\times 10^5$). The thermal parameters are in the form $T = \exp(-2\pi^2/100 \sum_i \sum_j U_{ij} h_i h_j a_i^* a_j^*)$.

Table III. NMR Spectroscopic Data for the Equilibrium Mixture of (S)_C(S)_{Sn} and (S)_C(R)_{Sn}^a

Solvent	Temp, °C	δ , ppm ^b						
		NMe ₂	α -Me	α -H	Sn-Me	H ₆	H ₃	Arom H
C ₆ D ₆ ^c	Ambient	1.36 (br)	0.71 (0.72)	3.08	0.91, <i>J</i> (SnCH) = 65 Hz	8.95 m	6.86 m	7.0-7.8
	0	1.34, 2 s, $\Delta\nu$ 41 Hz (1.30, 2 s, $\Delta\nu$ 11 Hz)	2 d, <i>J</i> = 6 Hz	2 q	(0.99, <i>J</i> (SnCH) = 67 Hz) (0.99)	<i>J</i> (SnCCCH) = 72 Hz		
CDCl ₃ ^d	Ambient	2.04, 2 s, $\Delta\nu$ 64 Hz	1.25 (1.33)	3.62	1.10, <i>J</i> (SnCH) = 65.5/63.0 Hz	8.49 m		7.0-7.8
		(2.01, 2 s, $\Delta\nu$ 23 Hz)	2 d, <i>J</i> = 7 Hz	(3.77)	(1.16, <i>J</i> (SnCH) = 68.0/65.0 Hz)	<i>J</i> (SnCCCH) = 73 Hz		
Pyridine- <i>d</i> ₅	Ambient	1.82 (br)	1.08 (1.10)	3.56 (br)	1.18, <i>J</i> (SnCH) = 66 Hz	8.88 m		7.0-7.8
			2 d, <i>J</i> = 7 Hz	2 q	(1.22; <i>J</i> (SnCH) = 67.5 Hz)	<i>J</i> (SnCCCH) = 72 Hz		

^a Value between parentheses. ^b Me₄Si internal; aliphatic part of the resonance pattern has been recorded at 250 Hz sweep width on a 100-MHz NMR spectrometer. ^c Coalescence temperature T_{coal} about 28 °C; essentially the same spectra were obtained in toluene-*d*₈. ^d T_{coal} about 40 °C.

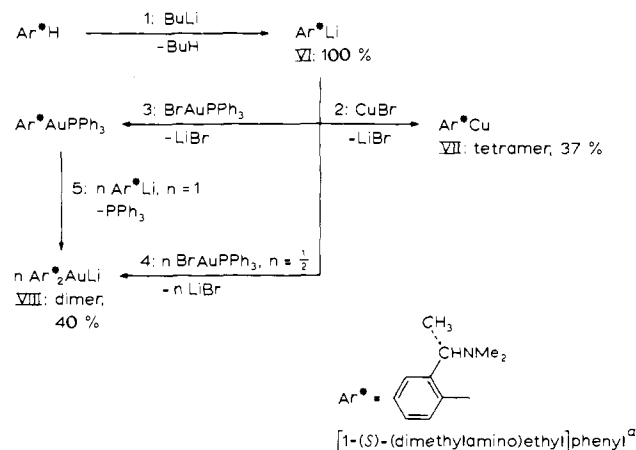
Results

Synthesis and Properties. For the preparation of [2-{1-[(S) or (R)]-(dimethylamino)ethyl}phenyl]methylphenyltin bromide (IV) the reactions of methylphenyltin dibromide with 2-{1-[(S) or (R)]-(dimethylamino)ethyl}phenyllithium [(S)- or (R)-VI], -copper¹³ [(S)- or (R)-VII], and -goldlithium [(S)- or (R)-VIII], respectively were studied. All reactions were carried out starting from either the *S* or the *R* enantiomer of the benzylamino ligand. The discussion of the hitherto unreported arylating reagents VII and VIII, which both belong to a novel class of C-chiral arylmetal IB cluster compounds,¹⁵ will be restricted to synthetic details necessary for a successful synthesis of IV.

The aryllithium derivative VI, which is a white, stable solid, is formed in almost quantitative yield in the 1/1 reaction of the chiral amine with butyllithium in ether (cf. Scheme I, eq 1).

Interaction of VI with cuprous bromide, according to the directions^{8,17a} given for the synthesis of related 2-[(dimethylamino)methyl]phenylcopper tetramer,^{17b} affords a green-colored reaction mixture from which the organocopper (Scheme I, eq 2; VII is a tetramer in benzene) is isolated as a yellow, crystalline solid in 37% yield. Reaction of the organo-

Scheme I. Synthesis of the Arylating Reagents



^a Similar results are obtained by using the (R)_C-enantiomer

lithium compound with either 2-{1-[(S) or (R)]-(dimethylamino)ethyl}phenyl(triphenylphosphino)gold(I) (eq 3 and 5; cf. ref 18) or bromo(triphenylphosphino)gold (I) (eq 4; cf. ref

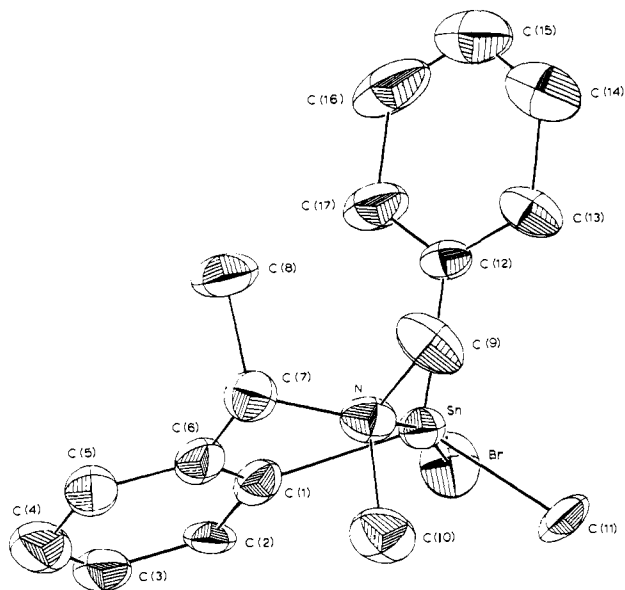
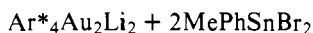
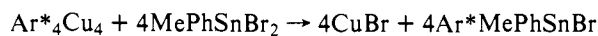


Figure 1. Molecular geometry of $(S)_C(S)Sn-IV$ (vibrational ellipsoids scaled to include 40% probability).

18) afforded reaction mixtures from which the pure goldlithium (aurate) VIII was isolated in about 40% yield.

The 1/1 reactions of methylphenyltin bromide with the pure arylcopper as well as with the arylgoldlithium derivative afforded a white solid which was isolated in 96% yield. Isolation of the quantitative amounts of $CuBr$ from the $MePhSnBr_2/Ar^*Cu$ reaction as well as both the organogold derivative 2-[1-(*S*) [or (*R*)]-(dimethylamino)ethyl]phenylgold dimer [(*S*)-IX]¹⁶ and $LiBr$ from the $Ar^*AuLi/MePhSnBr_2$ reaction confirmed that quantitative aryl transfer from the arylmetal 1B derivative to the organotin moiety had occurred.



Surprisingly, the 1/1 reaction of the organolithium compound VI with $MePhSnBr_2$, in which VI was added to the $MePhSnBr_2$ solution (cf. ref 2), resulted in a mixture of products from which IV could not be isolated. This result contrasts with the successful synthesis of 2-[(dimethylamino)methyl]phenylmethylphenyltin bromide in 90% yield via the organolithium route.^{2a}

The white solid, which was isolated from the arylmetal 1B/ $MePhSnBr_2$ reactions, melted between 47 and 65 °C. NMR spectroscopy revealed that the solid consists of a mixture of two diastereomers of IV (see Table II). The fact that the molar ratio of both diastereomers is different from 1 (the $(S)_C(R)Sn$ diastereomer is present in excess, see Molecular Geometry) enables the assignment of each resonance to a distinct diastereomer.

Both diastereomers are assigned a trigonal bipyramidal structure having the amino and bromine ligands in axial positions.² This can be concluded from the great similarity between the aromatic resonance patterns of III^{2a} and IV. The H_6 proton ($H[C(2)]$) is shifted by almost 2 ppm to lower field as compared with the free benzylamine, whereas the proton ortho to the $CH(Me)NMe_2$ ligand is slightly shifted upfield. The $J(Sn-C-C-H_6)$ is solvent independent (72 Hz) and its value is of the same order of magnitude as was found for the penta-coordinate compounds II and III ($\approx 72-74$ Hz).² The 100-MHz NMR spectra reveal only one resonance pattern for H_6 whereas a different chemical shift value for this proton in the respective diastereomers is expected. This difference obviously

Table IV. Bond Distances (Å) with Standard Deviations in Parentheses

Sn-Br	2.683 (1)	N-C(7)	1.50 (1)
Sn-N	2.476 (7)	N-C(9)	1.48 (1)
Sn-C(1)	2.158 (9)	N-C(10)	1.55 (1)
Sn-C(11)	2.160 (10)		
Sn-C(12)	2.127 (8)	C(7)-C(6)	1.55 (1)
		C(7)-C(8)	1.55 (1)
C(1)-C(2)	1.40 (1)	C(12)-C(13)	1.37 (1)
C(2)-C(3)	1.39 (1)	C(13)-C(14)	1.52 (1)
C(3)-C(4)	1.44 (2)	C(14)-C(15)	1.35 (2)
C(4)-C(5)	1.42 (2)	C(15)-C(16)	1.35 (2)
C(5)-C(6)	1.39 (1)	C(16)-C(17)	1.49 (2)
C(6)-C(1)	1.40 (1)	C(17)-C(12)	1.37 (1)

is very small, which most probably is caused by the fact that in both diastereomers H_6 experiences largely the asymmetry in the equatorial plane which is either *S* or *R*. The observation below 30 °C of two sets of two singlets with different $\Delta\nu$ for the NMe protons, which coalesce above 30 °C into two singlets, confirms the occurrence of Sn-N coordination in both diastereomers.^{2a} The $J(Sn-CH_3)$ values of about 67 Hz (vide infra) are in the range for penta-coordinate triorganotin species.¹⁹

The two diastereomers have different $J(Sn-CH_3)$ values as is expected for spin-spin coupling in two different, unique molecules.

One of the diastereomers [obtained from (*S*)-V] could be isolated by a procedure involving slow saturation of a concentrated ether solution of the mixture of the two diastereomers with pentane. The crystalline material obtained via this procedure had a melting point of 119–123 °C. Dissolution of these crystals at -70 °C and recording the NMR spectra at this temperature revealed that only one diastereomer [(*S*) $_C(S)Sn-IV$, see Molecular Geometry] had crystallized because only one resonance pattern was observed. Upon increasing the temperature the resonance pattern of the other diastereomer appeared at 0 °C indicating the occurrence of slow epimerization. Finally, an equilibrium mixture [40/60 molar ratio $(S)_C(S)Sn/(S)_C(R)Sn$] was again reached. Also in the melt epimerization takes place. This was confirmed by an NMR spectrum of a solution of the pure diastereomer after melting.

Osmometric molecular weight determinations of the crystalline material showed that the diastereomers exist as monomers in benzene.

Molecular Geometry. The molecular structure along with the adopted numbering scheme are shown in an ORTEP drawing,²⁰ Figure 1. Bond distances and angles are given in Tables IV and V. The crystal structure consists of discrete monomeric 2-[1-(*S*)-(dimethylamino)ethyl]phenylmethylphenyltin bromide units having the Br and N atoms in axial positions of a trigonal bipyramidal arrangement. Table VI, in which significant structural features of the present diastereomer are compared with those of earlier reported II,³ illustrates that both structures are closely related.

The rotational arrangement of the phenyl group C(12)-C(17) is given by its angle of 29° with the plane through C(1), C(11), C(12), and Sn.

The configuration of C(7) is unambiguously assigned to the *S* configuration, which is in accord with the configuration in the starting benzylamine [(*S*) $_C$]. Accordingly the configuration at the tin atom is (*S*) $_Sn$ (cf. Experimental Section).

No significant nonbonding intermolecular contacts (excluding hydrogen, cf. Experimental Section) were found.

Discussion

Molecular Geometry of (*S*) $_C(S)Sn-IV$. The (*S*) $_C(S)Sn$ diastereomer of IV is the first example of a diastereomerically pure chiral triorganotin halide of which the absolute config-

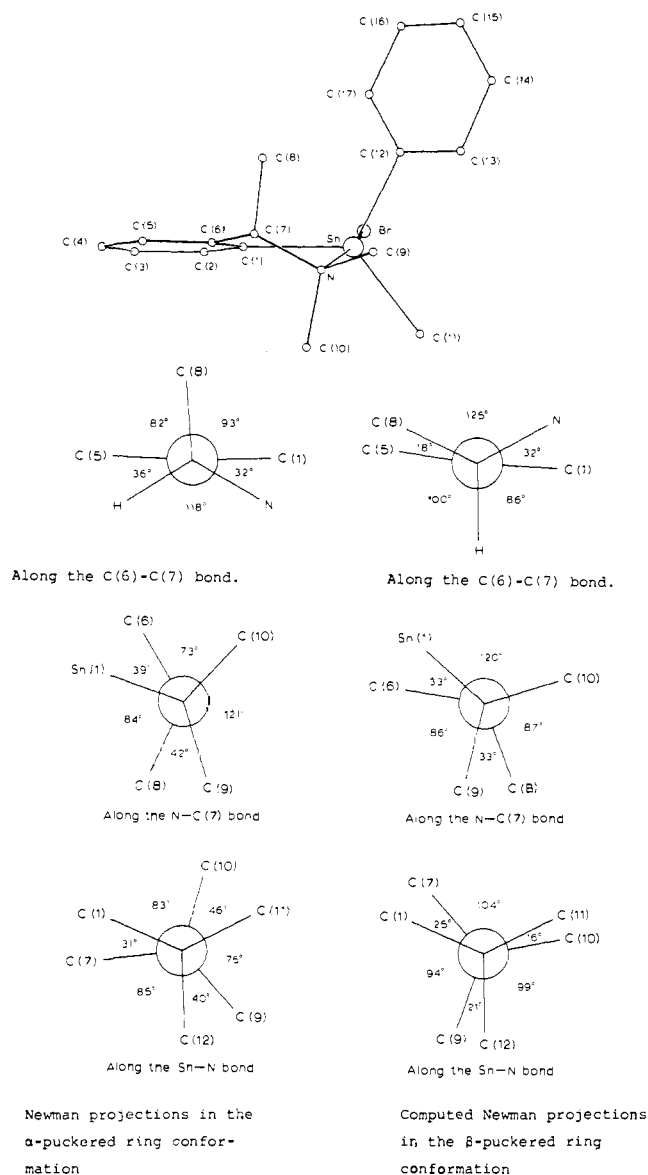


Figure 2.

uration has been established. The structural features of this compound provide insight concerning the factors which determine the stereochemistry about tin in pentacoordinate triorganotin species.

In both II and IV the N-Sn-C angles in the five-membered chelate ring are 75.2°. It is noteworthy that in Cp₂(2-Me₂NCH₂C₆H₄)₂Ti²¹ and Cp₂(2-Me₂NCH₂C₆H₄)Ti^{22a} the corresponding N-Ti-C angles are 73.4 and 73°,^{22b} respectively, indicating that the bite of the bidentate benzylamino ligand has a rather constant value.²³ Also in ionic {2,6-(Me₂NCH₂)₂C₆H₃}Me₂Sn⁺Br⁻, the structure of which recently has been elucidated, the N-Sn-C angles in the two five-membered chelate rings are about 75°.²⁶

The five-membered chelate ring is puckered at the CNSn part both in II and in IV. The two ring conformers of II have equal stability. However, this is not the case for the two ring conformations of IV as can be concluded from a series of Newman projections along the respective axes in the chelate ring of the (S)_C(S)_{Sn} diastereomer; see Figure 2. Comparison of these projections shows that the respective dihedral angles between vicinal groups, and thus the repulsive forces between these groups, alter on going from the α to the β conformer (see Figure 3). For example, the C(7)-C(6) projection shows two conformers which markedly differ; see Figure 2. In the α

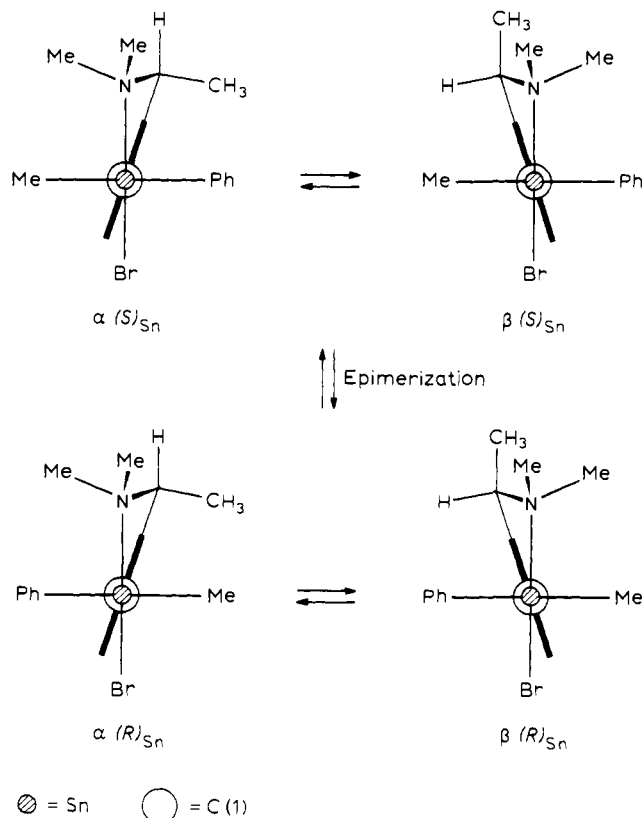


Figure 3. Projections along the Sn-C(1) axis showing the different ring conformations in connection with the stereochemistry around tin in the equatorial plane [*S* configuration at C(7)].

Table V. Bond Angles (deg) with Standard Deviations in Parentheses

Br-Sn-N	168.9 (2)	C(7)-N-C(9)	112.8 (7)
Br-Sn-C(1)	94.5 (2)	C(7)-N-C(10)	107.3 (7)
Br-Sn-C(11)	92.6 (3)	C(7)-N-Sn	105.3 (5)
Br-Sn-C(12)	94.1 (2)	C(9)-N-C(10)	109.5 (7)
N-Sn-C(1)	75.2 (3)	C(9)-N-Sn	115.4 (5)
N-Sn-C(11)	90.5 (3)	C(10)-N-Sn	106.0 (5)
N-Sn-C(12)	94.2 (3)	C(1)-C(2)-C(3)	119.3 (8)
		C(2)-C(3)-C(4)	120.8 (9)
C(1)-Sn-C(11)	127.8 (3)	C(3)-C(4)-C(5)	118.4 (10)
C(1)-Sn-C(12)	116.1 (3)	C(4)-C(5)-C(6)	120.3 (9)
C(11)-Sn-C(12)	114.8 (4)	C(5)-C(6)-C(1)	120.4 (9)
		C(6)-C(1)-C(2)	120.8 (8)
Sn-C(1)-C(2)	123.3 (6)		
Sn-C(1)-C(6)	115.9 (6)	C(12)-C(13)-C(14)	117.2 (9)
Sn-C(12)-C(13)	120.2 (6)	C(13)-C(14)-C(15)	120.1 (11)
Sn-C(12)-C(17)	116.2 (7)	C(14)-C(15)-C(16)	120.8 (11)
		C(15)-C(16)-C(17)	121.2 (11)
C(1)-C(6)-C(7)	121.3 (8)	C(16)-C(17)-C(12)	117.0 (10)
C(6)-C(7)-C(8)	111.0 (8)	C(17)-C(12)-C(13)	123.5 (8)
C(6)-C(7)-N	107.7 (7)		
C(8)-C(7)-N	113.7 (8)		

conformation steric repulsion between the [C(5)]-H atom and the [C(7)]-CH₃ group will be minimal whereas in the β conformation the [C(7)]-CH₃ group is almost in the plane of the phenyl ring C(1)-C(6). These results argue for a higher stability for the α conformation.

Figure 3 shows that preference of the five-membered chelate ring for the α conformation has consequences for the Δν values of the diastereotopic^{27a} N-CH₃ protons in both diastereomers because the ring conformation (α or β) determines which N-CH₃ group experiences the anisotropy of the Sn-C₆H₅ group (compare the Sn-CH₃ values for both diastereomers at

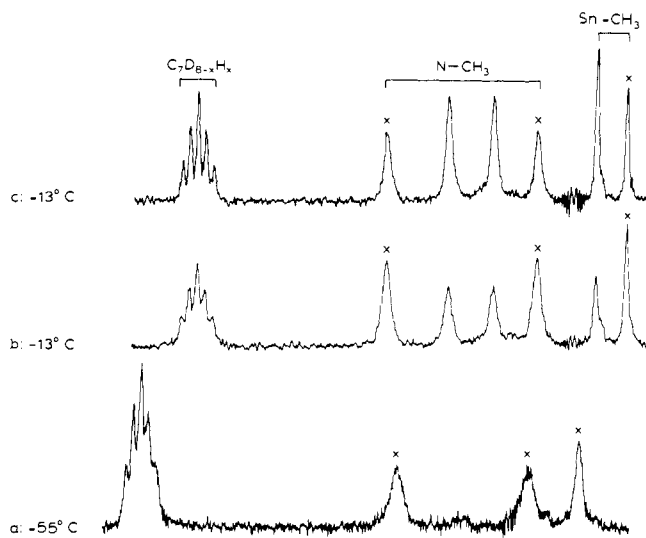


Figure 4. NMR spectra of saturated solutions of IV in toluene- d_8 showing the epimerization process: (a) pure $(S)_C(S)_{Sn}$; (b) spectrum at -13°C (after 0.5 h); (c) spectrum of the equilibrium mixture at -13°C (after 1.5 h).

low temperature, Table III). However, variable temperature NMR experiments have shown that the two conformations cannot be frozen out. The existence of two distinct ring conformers in solution was established by low-temperature NMR spectroscopy in the case of (5-MeO-8-Me $_2$ NCH $_2$ naphthyl)-MePhSnBr.^{2a,16} This compound contains a six-membered chelate ring in which puckering is likewise concentrated in the SnN(Me $_2$)CH $_2$ part of the ring.¹⁶

When pentane was slowly distilled into a 40/60 [(S) $_C$ -(S) $_{Sn}$]/(S) $_C$ (R) $_{Sn}$] equilibrium mixture of IV in diethyl ether preferential crystallization of the (S) $_C$ (S) $_{Sn}$ diastereomer occurred. Obviously, the less abundant diastereomer is the less soluble one. This preferential crystallization represents an example of an asymmetric transformation because ultimately the whole sample of (S) $_C$ -IV could be crystallized from the solution as the (S) $_C$ (S) $_{Sn}$ diastereomer. The marked stereoselectivity of this process is most probably a result of the formation of a more stable crystal structure in the case of the (S) $_C$ (S) $_{Sn}$ diastereomer which has both the α -Me and the phenyl(-Sn) group at the same side of the plane bisecting the C(12)SnCH $_3$ angle.

The Epimerization Process. The fact that only the (S) $_C$ (S) $_{Sn}$ diastereomer is obtained from the 40/60 equilibrium mixture implies that during the crystallization process epimerization involving inversion of configuration at the tin center from the (R) $_{Sn}$ into the (S) $_{Sn}$ conformation occurs thus maintaining the equilibrium in the supernatant solution. From this it is obvious that solutions of the separated diastereomer (S) $_C$ (S) $_{Sn}$ -IV are not stable and will undergo epimerization to give the 40/60 equilibrium mixture. This is exactly what can be concluded from the dynamic NMR spectra of separated (S) $_C$ (S) $_{Sn}$ -IV in toluene- d_8 (Figure 4).

At -55°C exclusively the resonance pattern due to the (S) $_C$ (S) $_{Sn}$ diastereomer is observed. When the temperature is raised to -13°C epimerization involving inversion of configuration at the tin atom occurs as illustrated in spectrum b which shows the two diastereomers to be present in 66/34 [(S) $_C$ (S) $_{Sn}$]/(S) $_C$ (R) $_{Sn}$] molar ratio. Equilibrium is reached at a 40/60 molar ratio of both diastereomers (Figure 4c). The rate of the epimerization process has not been determined because of the limited solubility of the compound at low temperature.²⁸ However, some interesting qualitative conclusions about the epimerization process, and more generally about inversion processes involving chiral tin centers, can be drawn from the dynamic NMR patterns.

Table VI. Comparison of Main Structural Features of the (S) $_C$ (S) $_{Sn}$ Diastereomer 2-Me $_2$ NCH(CH $_3$)C $_6$ H $_4$ SnMePhBr (IV) and 2-Me $_2$ NCH $_2$ C $_6$ H $_4$ SnPh $_2$ Br (II)

	IV	II ³
N-Sn-Br	169°	171°
Planarity of the SnC $_3$ unit ^a		
Σ C-Sn-C	358.7°	357.7°
Br-Sn-C	94.5°	96.2°
Br-Sn-C	94.1°	96.3°
Br-Sn-C	92.6°	92.7°
N-Sn	2.476 Å	2.511 Å
Br-Sn	2.683 Å	2.630 Å
Bite of ligand		
C-Sn-N	75.2°	75.3°
C-N-Sn	105.3°	101.1°
Angle between 1,2-disubstituted Ph ring and "mirror plane" through MePhSnBr or Ph $_2$ SnBr	14.7°	12.5°

^a Sn atom in IV is displaced by 0.11 Å from the plane through the equatorial C atoms on the side of the Br atom.

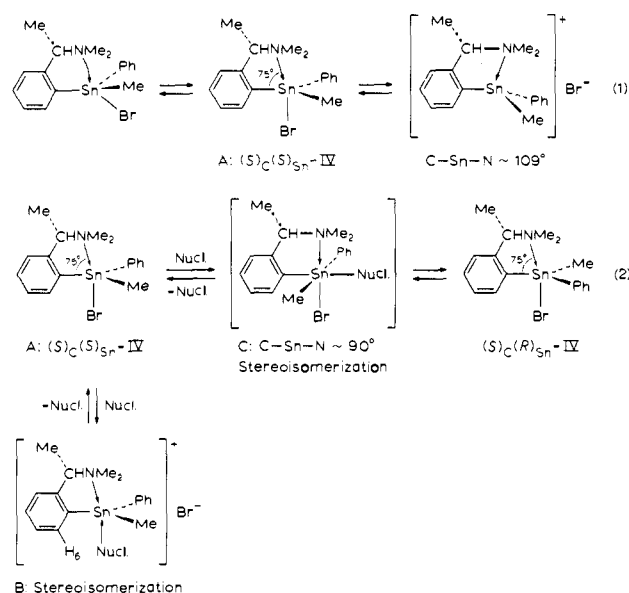
The NMR spectra shown in Figures 4a-c clearly show that in IV epimerization, i.e., inversion of configuration at the tin atom, takes place already at -13°C . Spectrum c shows that Sn-N dissociation in the pentacoordinate conformer is slow on the NMR time scale at -13°C . This is concluded from the presence of two N-CH $_3$ singlets for each diastereomer which points to diastereotopic N-CH $_3$ groups. Rate-determining Sn-N dissociation would lead to coalescence of the two CH $_3$ singlets into one singlet as a result of a process involving pyramidal inversion at nitrogen, which is blocked in the coordinated situation, with concomitant 180° rotation about the CH(CH $_3$)-N bond and re-formation of the Sn-N bond.^{27b}

Nevertheless, inversion of configuration at tin in the pentacoordinate conformer occurs as can be inferred from the occurrence of the epimerization process at -13°C . In our recent dynamic NMR study of 2-Me $_2$ NCH $_2$ C $_6$ H $_4$ SnMePhBr (III) the conclusion was reached that inversion of configuration at tin cannot take place in the pentacoordinate conformer, i.e., in the conformer with inert Sn-N coordination.^{2a,16} In III the prochiral CH $_2$ group is present as a probe for the detection of dissymmetry at tin by NMR spectroscopy. The fact that a sharp AB pattern was observed for the CH $_2$ protons at temperatures below the coalescence temperature for the NMe $_2$ resonances excluded the occurrence of stereoisomerization in the pentacoordinate conformer, e.g., by Berry pseudorotation processes. Such processes²⁹ are energetically unfavorable for various reasons: (1) the site preference of the N and Br atoms for axial positions³⁰ and (2) the constraints of the five-membered chelate ring. The bite of the benzylamino ligand at 75.2° dictates an axial-equatorial spanning of the bidentate ligand which in an ideal TBP array amounts to 90°. Any pseudorotation process would require passing through configurations containing the Br and N atoms in the equatorial plane as well as opening of the CSnN angle in the transition state to values higher than 90°. This would represent a high barrier for activation.

An inversion process at tin in IV which overcomes the above-mentioned steric constraint involves extension of the coordination sphere about tin to six by attack of an external nucleophile (Scheme II, eq 2). In a hexanuclear intermediate the angles at tin are about 90° and, as a consequence, the energy barrier for stereoisomerization will be lowered considerably.

Although hexacoordinate triorganotin complexes are not

Scheme II



usually observed,³¹ we have recently shown that hexacoordinate intermediates play a decisive role in stereoisomerization processes at tin in chiral triorganotin halides.^{2d} The limiting NMR spectrum of $[2-(Me_2NCH_2)C_6H_4]_2SnMeBr$ ($-50^\circ C$), which contains two intramolecular Me_2NCH_2 ligands, shows that the tin atom is pentacoordinate. At higher temperatures stereoisomerization processes take place which involve hexacoordinate intermediates as can be inferred from the resonance patterns of the prochiral CH_2 grouping.

Corriu³² and Cartledge³³ have observed that racemization of chiral triorganotin halides proceeds by a process which is second order in nucleophile. Later on Gielen and Mokhtar-Jamai observed that racemization of chiral triorganotin halides is likewise second order in nucleophile.³⁴ In the proposed mechanisms the actual stereoisomerization takes place either in a hexacoordinate intermediate formed by successive attack of two molecules of the nucleophile or in a pentacoordinate triorganotin cation formed by displacement of the halide ion by the second nucleophile. Various arguments have been put forward which are in favor of either the hexacoordinate or the pentacoordinate cation intermediate. The present study can contribute to a further discussion of these mechanisms.

The intramolecular coordination of the $CH(R)NMe_2$ ligand to tin can be envisaged as the first step of the proposed mechanisms. In our case an attack of the internal nucleophile (see Scheme II, eq 1) stops at the stage of the trigonal bipyramid because the pentacoordinate tin conformer represents the stable situation. Continuation of this process beyond the TBP configuration involving Sn-Br dissociation would require opening of the C-Sn-N angles from 75° to formally 109° . This is unlikely in view of the geometric constraints of the chelate ring and accordingly no Sn-Br bond dissociation occurs.

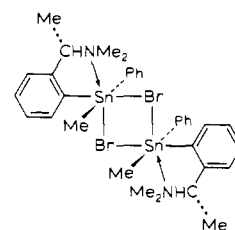
In the next step the stereoisomerization takes place (see Scheme II) either in a pentacoordinate triorganotin cation of type B or in a hexacoordinate intermediate of type C. The formation of a cation B seems unlikely in the case of this type of triorganotin halides because of the presence of H_6 (i.e., $H[C(2)]$) in the area where the axial ligand resides. This represents a high degree of steric crowding in a cation of type B irrespective of whether the CH_3 , the Ph, or the second nucleophile occupies the axial position. The location of H_6 , which

in $2-Me_2NCH_2C_6H_4SnPh_2Br$ amounts to a $H_6 \cdots Br$ non-bonding distance of 2.80 \AA ,³⁵ is dictated by the equatorial-

axial spanning of the benzylamine ligand. Furthermore, we

have shown that in the case of $2-Me_2NCH_2C_6H_4SnMePhBr$ (III) external ligands such as pyridine, which readily cause inversion of configuration in other chiral triorganotin halides,³²⁻³⁴ do not interact with the tin atom as can be concluded from the observation of anisochronous ($\Delta\delta \sim 10 \text{ Hz}$, 270-MHz proton spectrum) and thus diastereotopic CH_2N protons of solutions of III in pyridine- d_5 at room temperature.^{2a} Finally, any pseudorotation process in a pentacoordinate triorganotin cation would represent a high-energy route for exactly the same reasons already pointed out for the pentacoordinate triorganotin bromide III.

The alternative to this route involves the formation of the hexacoordinate intermediate C in which stereoisomerization then takes place (vide supra). Intermediate C is reached by either equatorial or facial attack of nucleophile on the pentacoordinate compound A. The stereoisomerization process is catalytic in nucleophile, i.e., the presence of only traces of nucleophiles in solutions of IV is required to cause its epimerization. In principle, a second molecule of IV may act as the external nucleophile with formation of an intermediate of type D. An intermediate of this type was earlier preferred by



Intermediate D; e.g. dimer formed by association of two molecules $(S)_C(S)_{Sn}$ -IV.

Corriu et al.³² in explaining the Cl/F exchange between halosilanes to that of heterolytic fission of the SiF bond.

The fact that racemization of III was not observed^{2a} (AB pattern for NCH_2 - still present at $123^\circ C$) confirms that inversion of configuration at tin has a very low frequency with respect to the NMR time scale. The present study shows unambiguously that a proper choice of intramolecular ligands allows the isolation of optically pure chiral triorganotin halides in the solid.

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Supplementary Material Available: A listing of structure factor amplitudes (20 pages). Ordering information is given on any current masthead page.

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Electron Transfer Reactions of Trifluoroacetylated Horse Heart Cytochrome *c*

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Abstract: Rate parameters have been determined for the reactions of fully trifluoroacetylated (19 lysine residues) horse heart cytochrome *c* with the reductant Fe(EDTA)²⁻ and the oxidants Co(phen)₃³⁺ and Fe(CN)₆³⁻. Respective second-order rate constants and activation parameters obtained for the reduction of trifluoroacetylated (TFA) ferricytochrome *c* by Fe(EDTA)²⁻ and the oxidation of TFA ferrocycytochrome *c* by Co(phen)₃³⁺ are $(5.1 \pm 0.3) \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$; $\Delta H^\ddagger = 3.9 \pm 0.5 \text{ kcal/mol}$, $\Delta S^\ddagger = -28 \pm 3 \text{ cal/mol-deg}$ and $(1.67 \pm 0.05) \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$; $\Delta H^\ddagger = 10.5 \pm 1.0 \text{ kcal/mol}$, $\Delta S^\ddagger = -3.9 \pm 0.3 \text{ cal/mol-deg}$ (25.0 °C, $\mu = 0.1 \text{ M}$, pH 7.0 (phosphate)). Rate constants found for the oxidation of TFA and native cytochromes by Fe(CN)₆³⁻ under the same conditions are $(1.20 \pm 0.06) \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ (25.4 °C) and $(2.3 \pm 0.2) \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$ (25.4 °C), respectively. Ionic strength dependences of rate constants for TFA cytochrome *c* electron transfer reactions were fit using equations from transition state and Marcus theories, treating the protein charge as a variable. Electrostatics-corrected apparent TFA cytochrome *c* self-exchange electron transfer rate constants based on Fe(EDTA)²⁻ and Co(phen)₃³⁺ cross reactions are in good agreement with those obtained previously for the native protein.

Introduction

The study of the reactions of electron transfer proteins with inorganic reagents has recently been an area of active research. We have presented a method, based on the Marcus theory of outer sphere electron transfer, for quantitatively extracting several of the contributions to the energetics of these reactions from available kinetic data.²⁻⁴ In view of the wealth of structural and rate data available for horse heart cytochrome *c*,² we have paid particular attention to its electron transfer

reactions in our work. Compensation for electrostatic interactions between the reactants is an important consideration in the analysis of redox reactivity trends for cytochrome *c* within the framework of Marcus theory.^{2,3} The availability of the fully trifluoroacetylated derivative of horse heart cytochrome *c* has now allowed us to test the analytical method developed to estimate Coulombic contributions to the activation free energies for reactions of the metalloprotein with oxidants and reductants. Rate parameters are reported in this