Pure & Appl. Chem., Vol.52, pp.657-667.
Pergamon Press Ltd. 1980. Printed in Great Britain.

0033-4545/80/0301-0657$02.00/0

STEREOSELECTIVE SUBSTITUTION REACTIONS AT THE METAL ATOM OF OPTICALLY ACTIVE ORGANOTIN COMPOUNDS.

Marcel GIELEN

Vrije Universiteit Brussel, T.W. - AOSC, Pleinlaan 2, B-1050 Brussels - Belgium
and
Université Libre de Bruxelles, Collectif de Chimie Organique Physique.

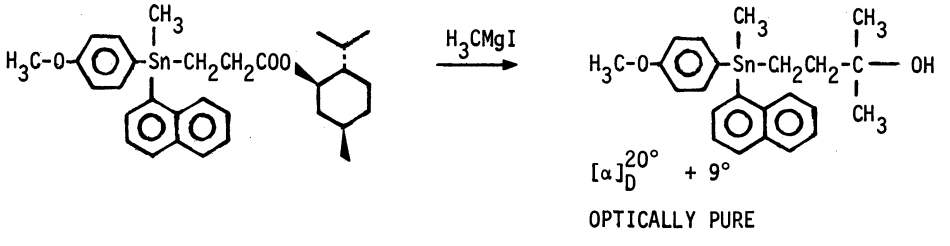
Abstract Besides the classical resolution of enantiomeric tetraorganotin compounds, which is a quite long and tedious route to optically active molecules, the use of chiral reagents provides a very simple way to synthesize optically active triorganotin compounds like triorganotin hydrides for instance. Their optical stability is sufficient to transform them stereoselectively into other optically stable organotin compounds like tetraorganotins, hexaorganoditins or into optically unstable triorganotin halides. The optically stability of triorganostannyl transition metal complexes is such that it is realistic to undertake the synthesis of optically active tin-transition metal compounds in order to study the stereochemistry of substitution compounds at their tin atom.

INTRODUCTION

I would like to compare two sentences taken from papers of pionneers in the field of chiral organotin compounds. Peddle and Redl wrote in 1970:
"Thus while it should be possible to resolve an optically active organotin compound with four carbon-tin bonds, it seems unlikely that such a compound would be very useful in investigating the stereochemistry of substitution at tin" (1).
Three years later, Folli, Iarossi and Taddei made a comment to this affirmation :
"As pointed out previously, it should be possible to resolve optically active organotin compounds with four carbon-tin bonds, since they seem to have a high stereochemical stability. In any event, we believe that their importance in investigating the stereochemistry of substitution at tin might be more important than is generally thought, if this optical activity is obtained through a reaction which enables one to investigate the stability of the asymmetric tin atom" (2).

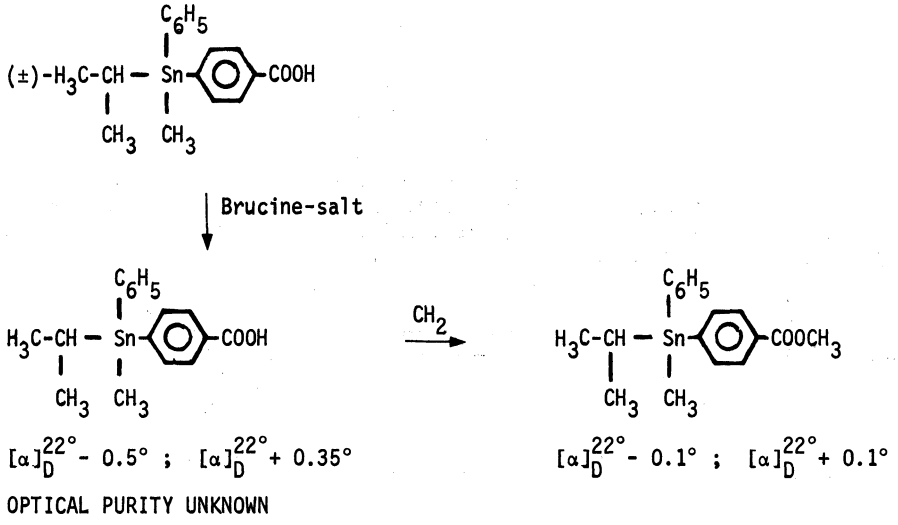
OPTICALLY ACTIVE TETRAORGANOTIN COMPOUNDS

In fact, an optically active tetraorganotin compound had been prepared in our laboratories two years before Folli, Iarossi and Taddei's paper and had been obtained in optically pure form : the diastereomeric menthyl esters of 3-(p-anisylmethylnaphthylstannyl)propionic acid could be separated by recrystallization and the one obtained in pure form reacted with methylmagnesium iodide to give the corresponding tertiary alcohol (see scheme I), containing only one asymmetric atom, the tin atom (3)



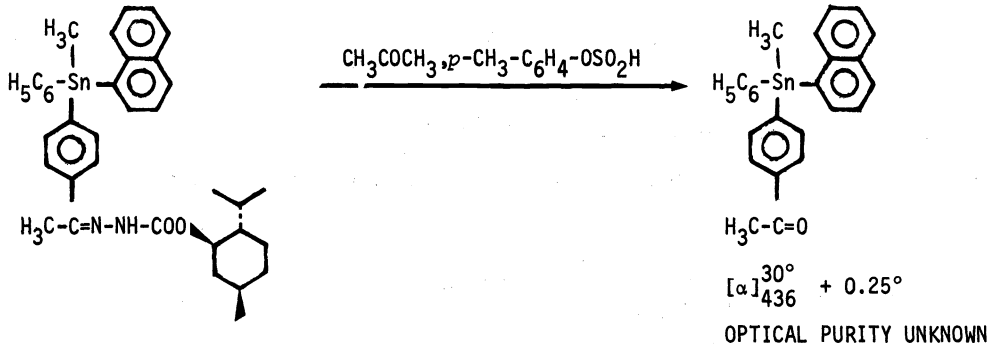
Scheme 1. Synthesis of optically pure (+)-3-(p-anisylmethylnaphthylstannyl)-1,1-dimethyl-1-propanol from one of the diastereomers of the menthyl esters of 3-(p-anisylmethylnaphthylstannyl)propionic acid.

An analogous ways has been used four years later by Lequan (4) to prepare enantiomeric methyl esters of an optically active p-triorganostannylbenzoic acid of unknown optical purity (the NMR spectra of their diastereomeric brucine salts being identical). Furthermore, two of the substituents of these optically active compounds are a phenyl and a p-substituted phenyl ; this is probably also responsible for the very low optical rotations he obtained (see scheme 2).



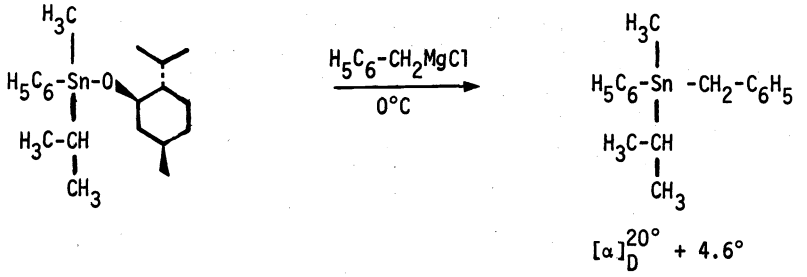
Scheme 2. Synthesis of optically active (+) and (-) p-(i-propylmethylphenylstannyl)benzoic acids and of their methyl esters.

A similar optically active p-triorganostannyl acetophenone of unknown optical purity was also prepared and is also characterized by a low optical rotation (see scheme 3).



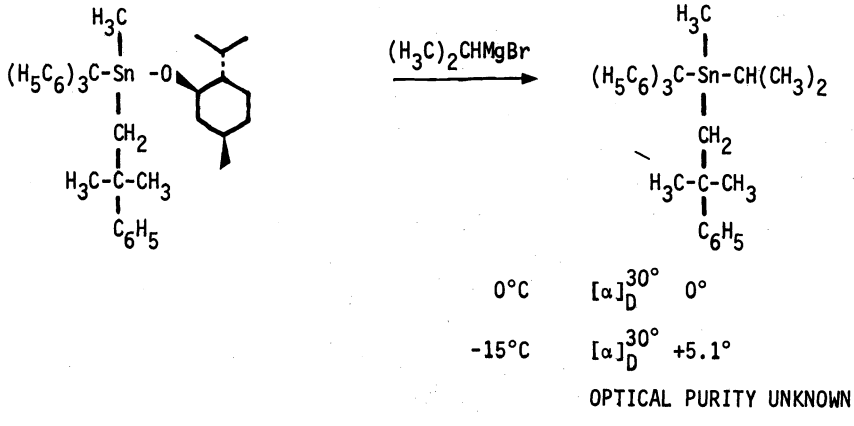
Scheme 3. Synthesis of optically active (+)-p-(methyl-1-naphthylphenylstannyl) acetophenone.

Besides these syntheses based on the separation of diastereomeric organotin compounds followed by the cleavage of the auxiliary chiral group (without cleavage of any of the carbon-tin bonds, which is sometimes very difficult to achieve (5)), there remains the possibility of the replacement of the chiral leaving group of an optically unstable triorganotin compound (a menthoxide for instance) by a more nucleophilic species (like a Grignard reagent) ; this type of approach has been described by Folli, Iarossi and Taddei (2) :
they prepared optically active (+)-benzyl-i-propylmethylphenyltin of unknown optical purity by reacting i-propylmethylphenyltin menthoxide with benzylmagnesium chloride (see scheme 4).



Scheme 4. Synthesis of optically active (+)-benzyl-i-propylmethylphenyltin of unknown optical purity.

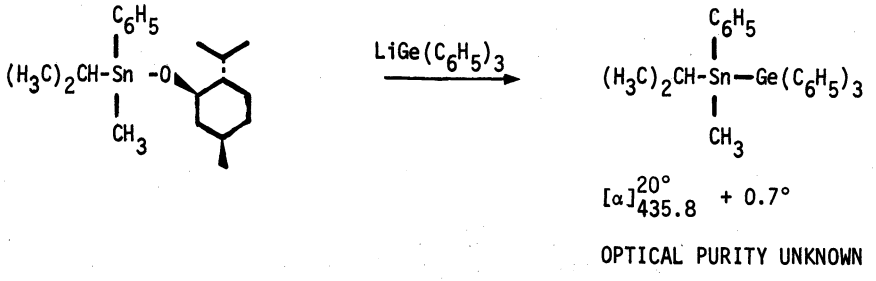
It may be mentioned that the optical yield of the analogous reaction between methylneophyltrityltin menthoxide and isopropylmagnesium bromide is influenced by the temperature : at -15°C, (+)-i-propylmethylneophyltrityltin is obtained whereas, at 0°C, the optically inactive tetraorganotin compound is formed (6) (see scheme 5).



Scheme 5. Influence of the temperature on the optical yield of the replacement of a menthoxide ligand by an isopropyl group.

OTHER OPTICALLY ACTIVE ORGANOTIN COMPOUNDS

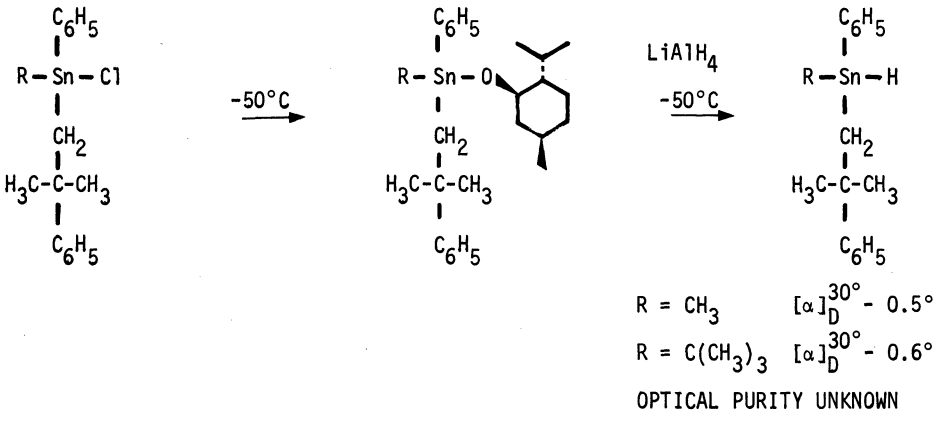
Triphenylgermyl lithium has also been used to displace the menthoxide from tin (7) (see scheme 6).



Scheme 6. Synthesis of the first example of an optically active triorganostannylgermane.

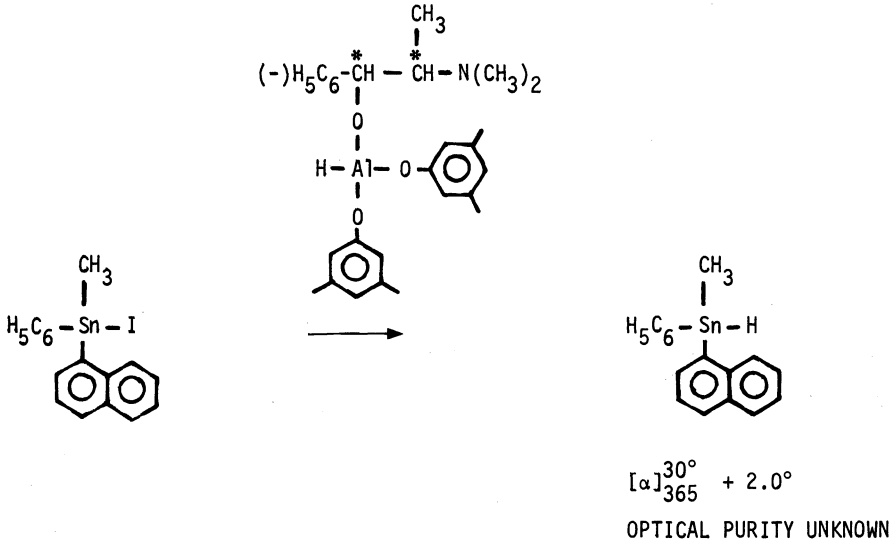
The optical rotation of the chiral triphenylgermyltriorganotin compound obtained stays unchanged for weeks even in the presence of nucleophiles (vide infra). This shows that hexaorganotin-germanium compounds are optically stable.

The menthoxide ion can also be displaced from tin by a hydride ion (8) (see scheme 7).

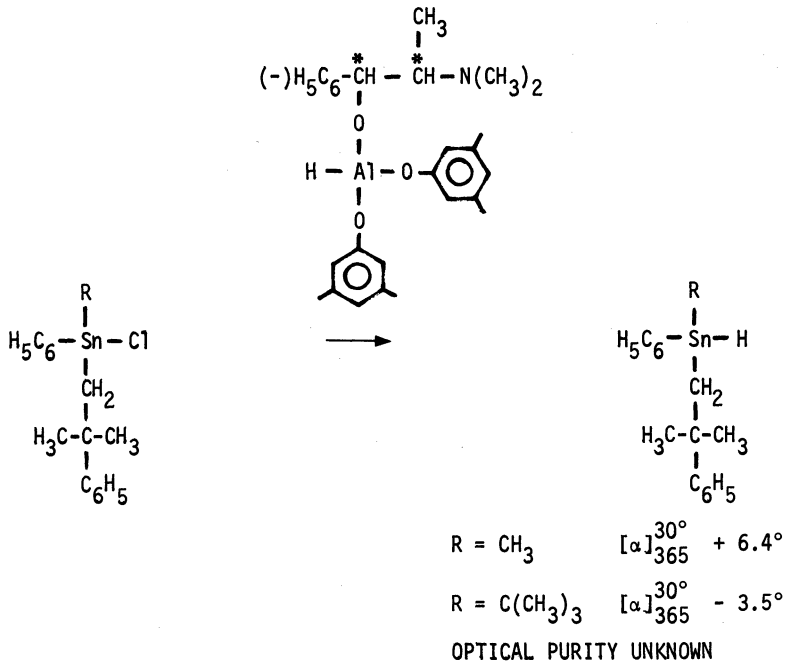


Scheme 7. Synthesis of the first example of an optically active triorganotin hydride.

Chiral triorganotin hydrides have however been obtained with much better optical yields by the reaction of a triorganotin halide with a chiral reducing agent (see schemes 8 and 9).



Scheme 8. Synthesis of optically active (+)-methyl-1-naphthylphenyltin hydride (9).



Scheme 9. Synthesis of optically active (-)-t-butyl or (+)-methylneophylphenyltin hydride (10).

OPTICAL STABILITY OF CHIRAL TRIORGANOTIN HYDRIDES

Methylneophylphenyltin hydride is optically stable, as shown in fig. 1.

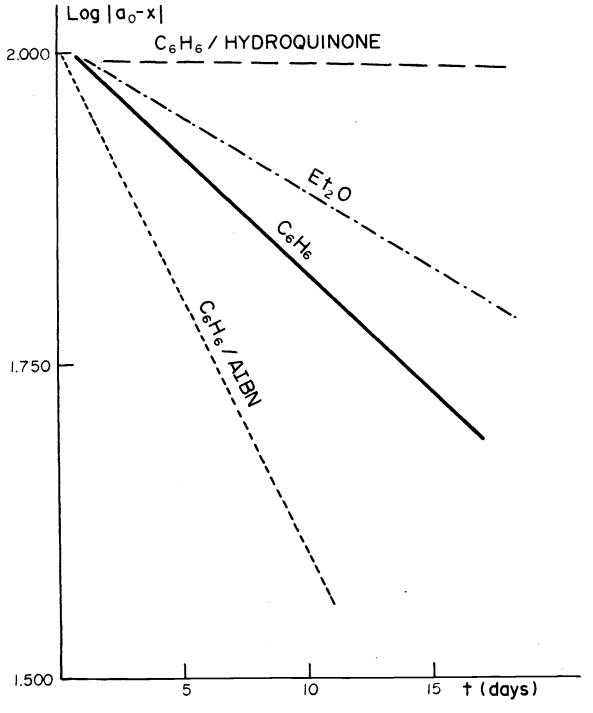
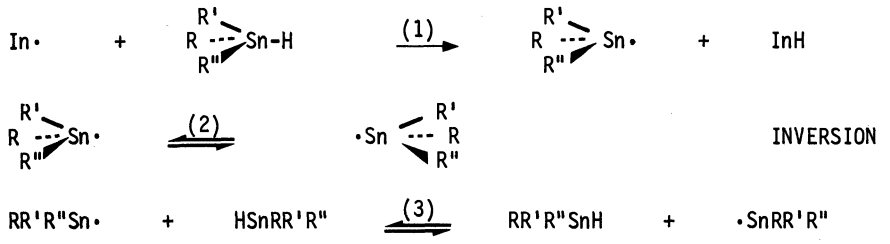


Fig. 1. Optical stability of methylneophylphenyltin hydride.

In the presence of hydroquinone, it can be kept for weeks with an unchanged optical rotation. In the presence of AIBN, it racemizes in about twelve days at room temperature. A radical mechanism accounts for these observations (9) (see scheme 10).



Scheme 10. Radical mechanism for the racemization of triorganotin hydrides.

In the presence of polar solvents, it also racemizes even in the presence of hydroquinone (see table 1).

TABLE 1. Influence of polar solvents on the racemization of methylneophylphenyltin hydride.

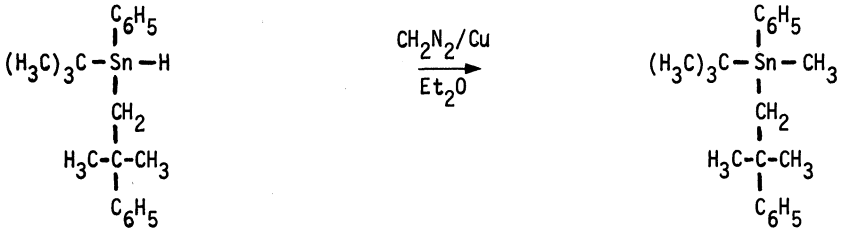
Solvent	Contact time (h) at 23°C	% Racemization
(±) $PhCHMeNH_2$	2	0
CH_3CN	1	0
DMSO	1	51
CH_3OD	< 1	100
CH_3OD + 2 mole % hydroquinone	< 1	100

After the contact time, more than 90% of the initial amount of the triorganotin hydride could be recovered.

A mechanism analogous to the one explaining the optical unstability of triorganotin chlorides can be proposed here *(vide infra)*.

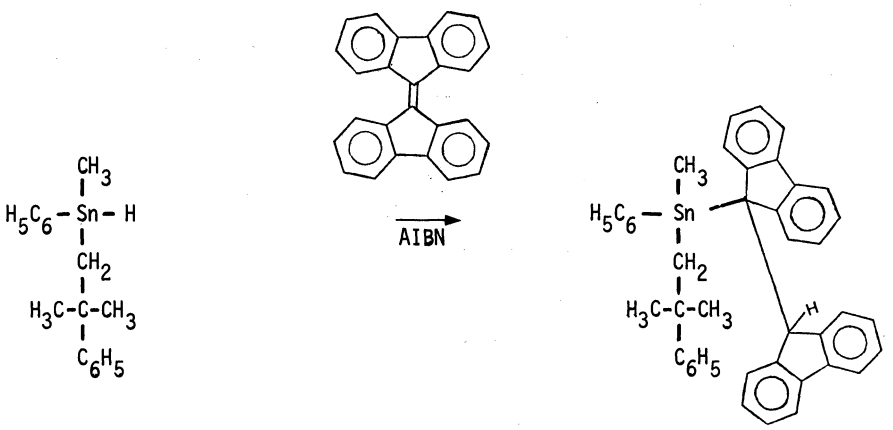
STEREOSELECTIVE SUBSTITUTION REACTIONS AT CHIRAL TRIORGANOTIN HYDRIDES

Triorganotin hydrides are well known as key intermediates in organotin chemistry. They can be transformed into tetraorganotin compounds either by reacting with diazomethane (11) (see scheme 11).



Scheme 11. The first example of a stereoselective substitution reaction at tin.

or by reacting with unsaturated compounds like bifluorenylidene in the presence of AIBN (11) (see scheme 12).



$[\alpha]_D^{30°}$ + 1.8°

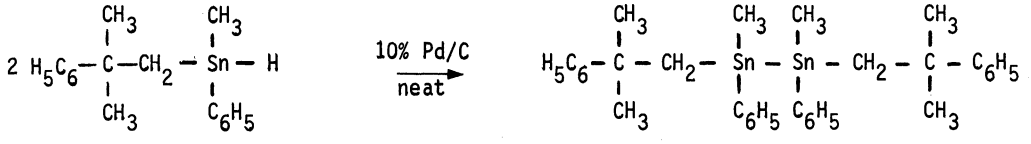
OPTICAL PURITY UNKNOWN

$[\alpha]_D^{30°}$ + 0.8°

OPTICAL PURITY UNKNOWN

Scheme 12. Stereoselective addition of methylneophylphenyltin hydride to bifluorenylidene.

The fact that the first one is stereoselective is not surprising, because this substitution reaction at tin can be visualised as an insertion between tin and hydrogen. The fact that the second one is stereoselective is rather interesting because this type of reaction is known to proceed via the triorganostannyl radical, which must therefore be trapped by the double bond more rapidly than it racemizes (see scheme 10).
Triorganotin hydrides can also be converted stereoselectively into hexaorganoditin compounds (12) (see scheme 13).



Scheme 13. The first example of an optically active hexaorganoditin compound.

The reaction between triorganotin hydrides and carbon tetrachloride, which is known since a long time (13), also proceeds stereoselectively, yielding a triorganotin chloride which racemizes (see fig. 2).

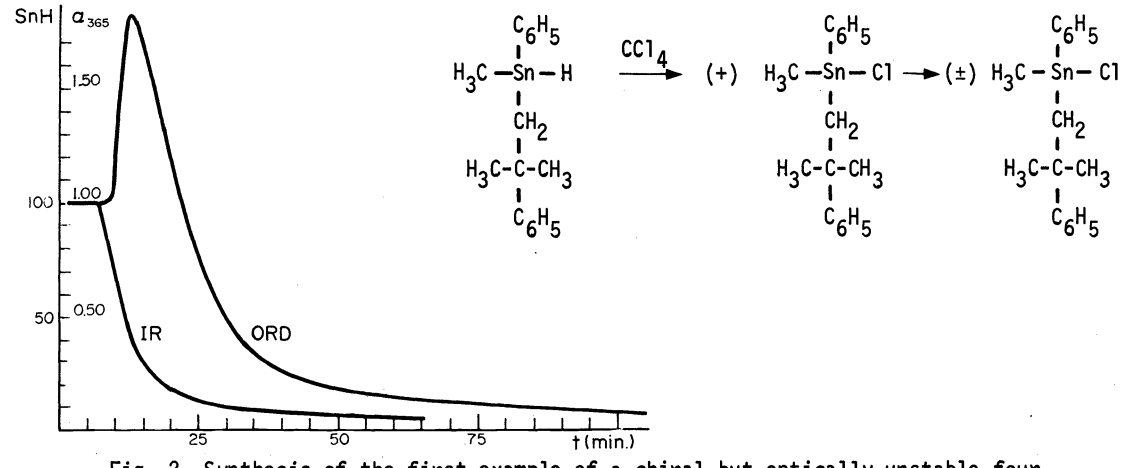
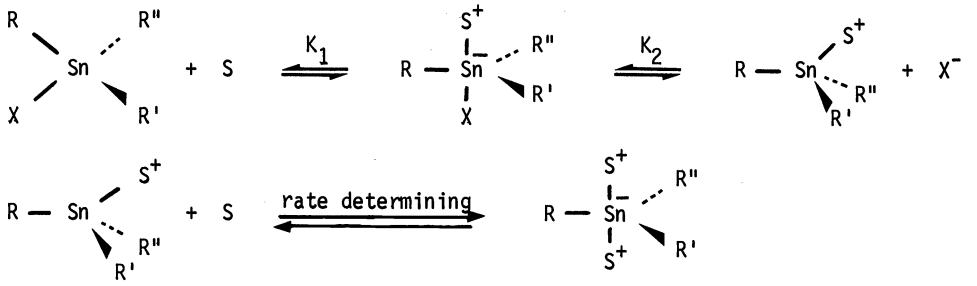


Fig. 2. Synthesis of the first example of a chiral but optically unstable four-coordinate triorganotin chloride (14).

The nice synthesis of a diastereomerically pure chiral five-coordinate triorganotin bromide by van Koten, Jastzebski, Noltes, Pontenagel, Kroon and Spek (15) may be mentioned here.

THE OPTICAL UNSTABILITY OF TRIORGANOTIN HALIDES

A possible mechanism for the optical unstability of triorganotin halides catalyzed by nucleophiles (16), compatible with the fact that the rate of racemization is second-order with respect to the nucleophile S, is given in scheme 14.



Scheme 14. Possible mechanism for the optical unstability of the triorganotin halides catalyzed by nucleophile S.

It consists of
a) a nucleophilic attack of S at tin, yielding a five-coordinate intermediate
b) a nucleophilic loss of $X^{(-)}$, yielding a four-coordinate species
c) a rate-determining attack of S at tin, yielding an achiral five-coordinate complex.
The addition of the nucleophile S at tin should be favoured by anything which increases the electrophilicity of the tin atom, for instance by a *p*-CF_3 substituent replacing a H atom of a phenyl ring.
The coalescence of the diastereotopic neophylic methyl signals of methylneophyl(p-trifluoromethylphenyl)tin chloride is observed at 60 MHz in the presence of 0.02 M of pyridine (see fig. 3) whereas the coalescence of the diastereotopic neophylic methyl signals of methylneophylphenyltin chloride is observed at 60 MHz in the presence of 0.1 M of pyridine.
This strongly suggests that the addition of the nucleophile at tin (step a) or c)) is indeed the determining factor.

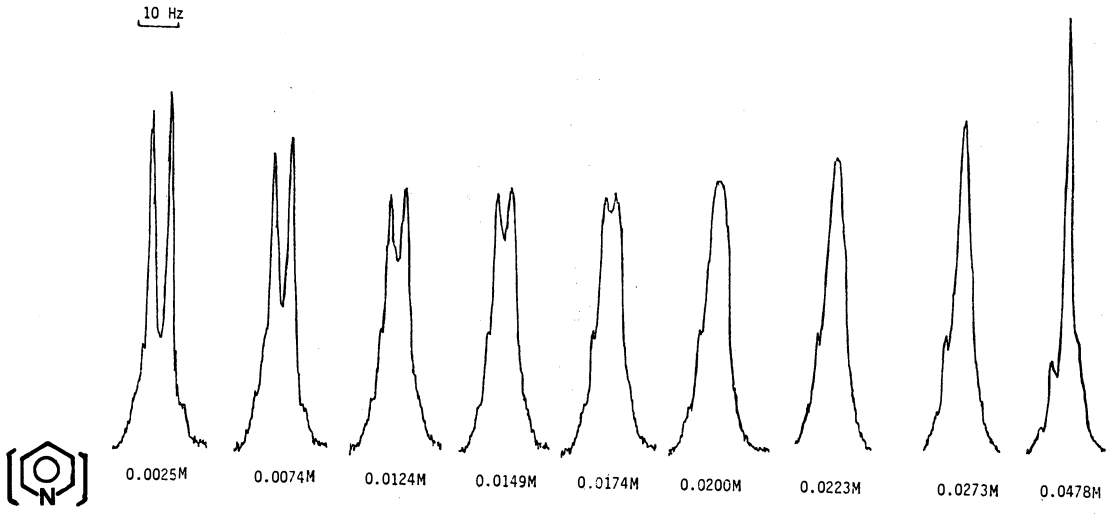


Fig. 3. Coalescence of the diastereotopic neophylic methyl signals of methylneophyl(*p*-trifluoromethylphenyl)tin chloride.

THE OPTICAL STABILITY OF TRIORGANOSTANNYL-TRANSITION METAL COMPLEXES

Triorganostannyl-iron, -manganese and -cobalt complexes are configurationally stable. This has been shown on methylphenyl(2-phenylpropyl)stannyl transition metal complexes $[C_6H_5(CH_3)\overset{*}{C}H\text{-}CH_2](CH_3)(C_6H_5)\overset{*}{Sn}\text{-}M(CO)_nL$, with $M(CO)_nL$ being respectively $Fe(CO)_2C_5H_5$, $Mn(CO)_5$, $Mn(CO)_4PPh_3$ and $Co(CO)_3PPh_3$ (19).The two asymetrically tetrahedrally substituted atoms of these compounds allow them to exist as four stereoisomers = an erythro and a threo pair of enantiomers, which give together two anisochronous ^1H_3C-Sn signals (see fig. 4).

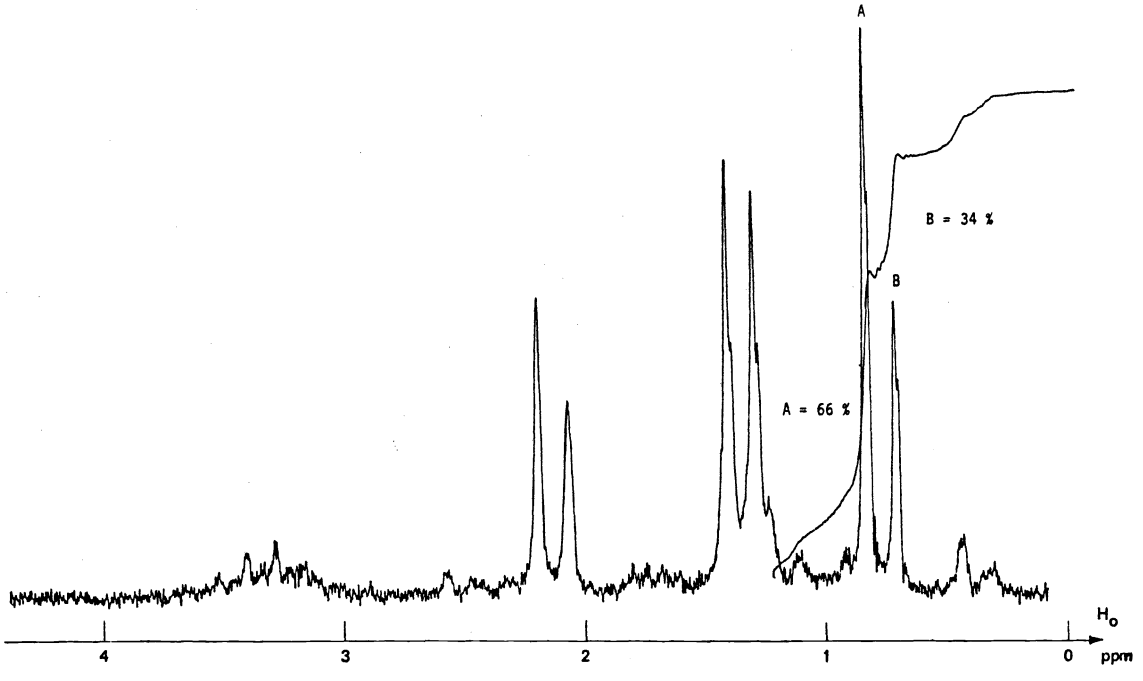


Fig. 4. 60 MHz ^1H spectrum of the aliphatic part of a mixture of methylphenyl(2-phenylpropyl)stannyltriphenylphosphinetricarbonylcobalt.
The ^1H_3C-Sn signal absorbing at higher field is named B, the other one, A.
The diastereomeric ratio A/B (erythro/threo or threo/erythro) can be determined by integrating the corresponding signals.

The threo and erythro racemic mixtures can sometimes be enriched in either A or B. The evolutions of the diastereomeric ratios A/B of these enriched threo or erythro mixtures in fuction of time give a quantitative evaluation of their configurational stability at tin, carbon being configurationally stable. So, the compositions of two different diastereomeric mixtures (A/B = 45/55 and A/B = 60/40) of methylphenyl(2-phenylpropyl)stannylcyclopentadienyldicarbonyl iron, remain unchanged for weeks *in pyridine*. This shows that triorganostannyliron complexes are configurationally stable at tin for very long periods. On the contrary, two different diastereomeric mixtures (A/B = 40/60 and A/B = 50/50) of methylphenyl(2-phenylpropyl)stannylpentacarbonylmanganese remain unchanged for long periods *in non-nucleophilic solvents*, but the addition of small quantities of pyridine or of DMSO causes an epimerization by which these two fractions are both transformed in a few hours into an equilibrium mixture (A/B = 48/52). This shows that triorganostannylpentacarbonylmanganese compounds are much less configurationally stable than analogous triorganostannylcyclopentadienyldicarbonyliron compounds. The presence of a more electron donating triphenylphosphine ligand on the manganese atom increases the configurational stability at tin.
Whereas the iron and manganese complexes described above were obtained as oily products, methylphenyl(2-phenylpropyl)stannyltricarbonyl(triphenylphosphine)cobalt is a crystalline solid which can be enriched in one of the two diastereoisomers by fractional crystallization. After twenty recrystallizations, it could be obtained as almost pure A. Its composition does not change after melting under nitrogen (105°C), but the addition of pyridine causes a slow epimerization which is being studied kinetically.

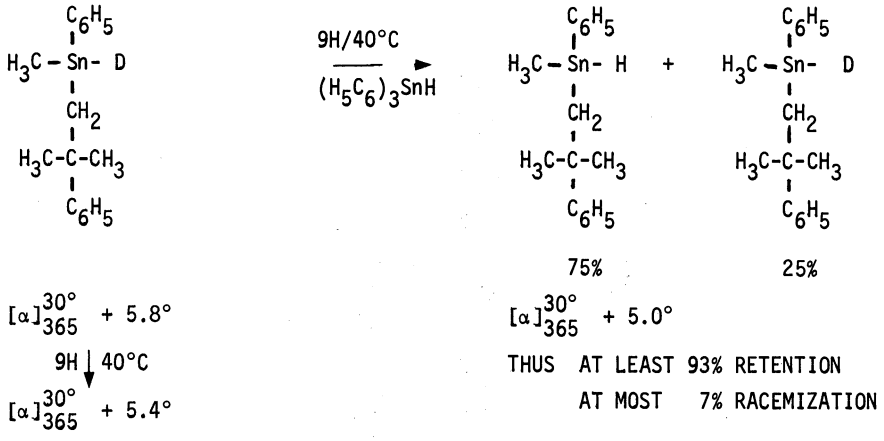
We have shown that the nucleophilicity sequence is

$$Cp(CO)_2Fe^{(-)} \gg Ph_3P(CO)_4Mn^{(-)} > Ph_3P(CO)_3Co^{(-)} \gg (CO)_5Mn^{(-)}$$

by studying the composition of reaction mixtures of ions $L'(CO)_mM'^{(-)}$ with $L(CO)_nM\text{-}SnPh_2Me$ (19). From these results, it appears that the configurational stability of triorganostannyl-transition metal complexes is higher when the nucleophilicity of the corresponding metallate ion is high. The configurational stability of these diastereoisomers is such that it is realistic to undertake the synthesis of optically active tin-transition metal compounds in order to study the stereochemistry of the above discussed substitution reactions.

A STEREOSPECIFIC SUBSTITUTION REACTION AT TIN PROCEEDING WITH RETENTION OF CONFIGURATION

Sofar, owing to the fact that the optical purity of the triorganotin hydrides is not known yet, only the stereoselectivity of some substitution reactions could be checked. However, there is a substitution reaction for which the stereochemistry can be determined even without knowing the optical purity of the starting material. This is shown in scheme 15.



Scheme 15. An almost stereospecific H/D exchange proceeding with retention of configuration.

When chiral methylneophylphenyltin deuteride is left for nine hours at 40°C, its optical rotation is lowered by 7%. When a mixture of triphenyltin hydride and of chiral methylneophylphenyltin deuteride is left for 9 hours at 40°C, the optical rotation is lowered by 14% and 75% of the initial amount of chiral triorganotin deuteride has been transformed into the corresponding hydride. Assuming that the optical rotation of methylneophylphenyltin deuteride is approximately equal to that of methylneophylphenyltin hydride, this shows that the H/D exchange proceeds with at least 93% retention and at most 7% racemization (9).

CONCLUSION

Whereas the stereochemistry of substitution reactions at silicon and at germanium atoms have been the object of many experimental studies, the stereochemistry at tin had non yet been examined. The reason for this is simply the fact that no chiral organotin compounds were available. Besides the classical resolution of enantiomeric tetraorganotin compounds, which is a quite long and difficult route to optically active molecules, the use of chiral reagents provides a very simple way to synthesize optically active triorganotin hydrides for instance. Their optical stability allows the study of the stereochemistry of reactions transforming them in other optically stable organotin compounds. A very promising field seems to be the study of the substitution reactions leading to and starting from triorganostannyl-transition metal complexes (19), which is now under study.

Acknowledgements

It is a pleasure to thank our coworkers for their important contribution to an exciting field : dynamic organometallic stereochemistry. Dr. Hassan Mokhtar-Jamaï prepared the first optically pure chiral tetraorganotin compound. In that respect he can be considered as a pionneer in this field. He also proposed a mechanism for the optical unstability of triorganotin halides.
Dr. Serge Simon continued Dr. Jamaï's work, prepared another optically active tetraorganotin compound and synthesized the first example of a chiral triorganostannyltriphenylgermane.

The contribution of Dr. Yves Tondeur is really very fundamental : he prepared the first example of a stereoselective reaction at tin, he synthesized the first example of a chiral hexaorganoditin compound, he showed that methylneophylphenyltin chloride is much more optically stable than what was thought before and he found the first example of an almost stereospecific H/D exchange at tin proceeding with retention of configuration.
Mr. Michel Van de Steen is studying the stereoselectivity at tin of substitution reactions at tetraorganotin compounds.
Mr. Ivan Vanden Eynde is doing an excellent job in preparing optically active triorganostannyl-transition metal complexes and is studying the stereochemistry of the formation and of the cleavage of the tin-iron, tin-cobalt and tin-manganese bonds.
We are also indebted to all the students and post-doctoral fellows for their experimental and intellectual contributions to this research.
We thank the "Fonds voor Kollektief en Fundamenteel Onderzoek" (F.K.F.O.), the "Nationaal Fonds voor Wetenschappelijk Onderzoek - Fonds National de la Recherche Scientifique" (N.F.W.O. - F.N.R.S.), the "Instituut ter aanmoediging van het Wetenschappelijk Onderzoek in Nijverheid en Landbouw - Institut pour l'encouragement de la Recherche Scientifique dans l'Industrie et l'Agriculture" (I.W.O.N.L. - I.R.S.I.A.) and the "Nationale Raad voor Wetenschapsbeleid" for their financial support.
The usual fine secretarial assistance of Mrs. G. Vandendaele-Joris is also acknowledged.

REFERENCES

1. G.J.D. Peddle and G. Redl, J.Am.Chem.Soc. 92, 365 (1970)
2. U. Folli, D. Iarossi and F. Taddei, JCS Perkin II, (1973), 638
3. H. Mokhtar-Jamaï, C. Dehouck, S. Boué and M. Gielen, Proceed. 5th Int.Conf.Organometal. Chem. Moscow, 1, 523 (1971) ; 2, 359 (1971) ; H. Mokhtar-Jamaï and M. Gielen, Bull.Soc.Chim.France 9B, 32 (1972) ; M. Gielen and H. Mokhtar-Jamaï, Annals N.Y. Acad. Sci. 239, 208 (1974) ; M. Gielen and H. Mokhtar-Jamaï, Bull.Soc.Chim.Belg. 84, 197 (1975)
4. M. Lequan and F. Meganem, J.Organometal.Chem. 94, C1 (1975)
5. M. Lequan, F. Meganem and Y. Besace, J.Organometal.Chem. 113, C13 (1976)
6. M. Gielen, Annual Reports Inorg.Gen.Synth. (1976), 337
7. M. Gielen and S. Simon, Bull.Soc.Chim.Belg. 86, 589 (1977)
8. M. Gielen, S. Simon, Y. Tondeur, M. Van de Steen, C. Hoogzand and I. Vanden Eynde, Israel J.Chem. 15, 74 (1977)
9. M. Gielen and Y. Tondeur, J.Organometal.Chem. 169, 265 (1979)
10. M. Gielen and Y. Tondeur, J.Organometal.Chem. 127, C75 (1977)
11. M. Gielen and Y. Tondeur, J.Organometal.Chem. 128, C25 (1977)
12. M. Gielen and Y. Tondeur, JCS Chem.Comm. (1978), 81
13. G.J.M. van der Kerk, J.G. Noltes and J.G.A. Luijten, J.Appl.Chem. 7, 356 (1957) ; J.G. Noltes and G.J.M. van der Kerk, Chem. & Ind. (1959), 294 ; E.J. Kupchik and R.E. Connolly, J.Org.Chem. 26, 4747 (1961) ; D.H. Lorenz and E.I. Becker, J.Org.Chem. 27, 3370 (1962) ; H.G. Kuivila and L.W. Menapace, J.Am.Chem.Soc. 86, 3047 (1964)
14. M. Gielen and Y. Tondeur, Nouv.J.Chim. 2, 117 (1978) ; see also ref. (18)
15. G. van Koten, J.T.B.H. Jastrzebski, J.G. Noltes, W.M.G.F. Pontenagel, J. Kroon and A.L. Spek, J.Am.Chem.Soc. 100, 5021 (1978)
16. M. Gielen and H. Mokhtar-Jamaï, J.Organometal.Chem. 129, 325 (1977)
17. M. Gielen and H. Mokhtar-Jamaï, J.Organometal.Chem. 91, C33 (1975)
18. M. Gielen and H. Mokhtar-Jamaï, Bull.Soc.Chim.Belg. 84, 1037 (1975)
19. M. Gielen and I. Vanden Eynde, Israel J.Chem., in press