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Synthesis and structure of a chiral bicyclic stannylated phosphoric triamide

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Abstract

Bicyclic chiral phosphoric triamide **1** reacts after lithiation and addition with several electrophiles in a highly regio- and diastereoselective fashion. The stannylated product **2** can be recrystallised to a single diastereomer. Its X-ray analysis is the first solid state structure determination of a chiral hexamethylphosphoric triamide analogue.

Keywords: Phosphoric triamide; Chiral stannane; Crystal structure; Asymmetric synthesis; Lithium

1. Introduction

Electrophilic addition to lithio-organic compounds, which contain a chiral auxiliary, is an important method for the creation of new stereocentres. We have combined the derivatisation of activated phosphoric triamides, introduced by Savignac et al. [1], with the use of *trans*-1,2-cyclohexanediamine as a chiral auxiliary [2,3] (Scheme 1).

Chiral α-stannylated amines or esters have frequently been used in asymmetric synthesis in a transmetalation and electrophilic addition sequence [4–6]. Despite this fact, X-ray structures of compounds possessing a stannane in an α-position to a chiral amine are rare [7,8]. This is surprising, because such α-aminocarbanion equivalents represent important intermediates.

During the reaction of lithiated **1** with Me_3SnCl we obtained **2**, which could be recrystallised to diastereomeric purity [9]. In this paper we present the synthesis and X-ray structure analysis of the first chiral bicyclic stannylated phosphoric triamide **2**. A comparison of its structure with related chiral amino stannanes, phosphoric triamides, and phosphonamides which contain the *trans*-1,2-cyclohexanediamine motif is drawn. A rationale for the stereochemical outcome of the reactions of lithiated **1** is given.

2. Results and discussion

2.1. Synthesis and experimental data for 2

Lithiation and electrophilic addition to bicyclic chiral phosphoric triamide **1** leads diastereoselectively to the products derivatised α to the nitrogen [9].

After treatment of racemic lithiated **1** in THF with trimethylstannylchloride, a mixture of two diastereomeric products was obtained in 39% yield [9]. The diastereomeric ratio was determined by ^{31}P-NMR spectroscopy as 89:11. Diastereomerically pure **2** was accessible after recrystallisation from ethyl acetate and hexane in 25% yield (rel. to starting material **1**) (Scheme 2).

$R_f = 0.66$ (10% EtOH/EtOAc). ^{1}H-NMR (300 MHz, $CDCl_3$, rel. to TMS signal): δ 0.03 (s, $^2J_{Sn,H} = 50.9$ Hz and 53.2 Hz, 9H), 1.14–1.36 (m, 8H), 1.80–2.01 (m, 8H), 2.36–2.65 (m, 11H), 4.09 (d, $^2J_{Sn,H} = 56.5$ and 73.1 Hz, $^3J_{P,H} = 8.2$ Hz, 1H), 7.11–7.28 (m, 5H).

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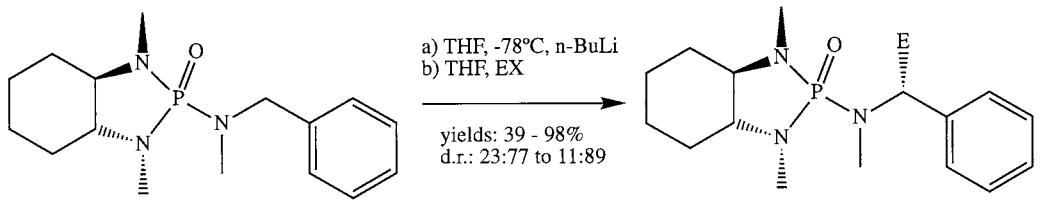


Scheme 1.

^{13}C-NMR (75 MHz, $CDCl_3$, $CDCl_3$ as internal standard): δ −6.24 (d, $^1J_{Sn,C}$ = 348 Hz, $Sn(CH_3)_3$), 24.3 (d, $^4J_{P,C}$ = 6.5 Hz, CH_2), 28.0 (d, $^2J_{P,C}$ = 4.1 Hz, NCH_3), 28.3 (d, $^3J_{P,C}$ = 10.4 Hz, CH_2), 28.7 (d, $^2J_{P,C}$ = 7.9 Hz, CH_2), 29.1 (d, $^2J_{P,C}$ = 2.0 Hz, NCH_3), 35.5 (d, $^2J_{P,C}$ = 7.1 Hz), 57.6 (d, $^2J_{P,C}$ = 6.6 Hz, *C*H(Sn(CH$_3$)$_3$)C$_6$H$_5$), 63.5 (d, $^2J_{P,C}$ = 8.5 Hz, CH*C*HN), 64.8 (d, $^2J_{P,C}$ = 9.5 Hz, CH*C*HN), 124.8 (d, $J_{Sn,C}$ = 11.2 Hz, arom. C), 126.2 (d, $J_{Sn,C}$ = 21.8 Hz, arom. C), 128.1 (d, $J_{Sn,C}$ = 8.7 Hz, arom. C) and 145.5 (d, $^3J_{P,C}$ = 4.2 Hz, *ipso* C).

^{31}P-NMR (121 MHz, $CDCl_3$, $(C_6H_5O)_3PO$ = −18.0 ppm as external standard): δ 31.7 (s, $^3J_{Sn,P}$ = 36.2 Hz).

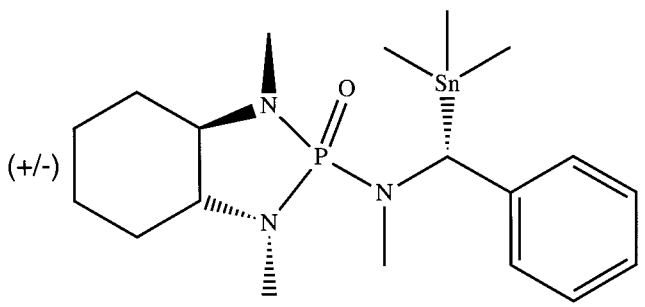
MS (EI, 70 eV): m/z (%) = 471 (13) [M^+], 456 (56) [$(M-CH_3)^+$], 306 (92) [$(M-Sn(CH_3)_3)^+$], 187 (100) [$(M-CH_3NCH(Sn(CH_3)_3)C_6H_5)^+$].

Elemental analysis: $C_{19}H_{34}N_3OPSn$ (470.17). Calc.: C 48.54, H 7.29, N 8.94. Found: C 48.52, H 7.31, N 8.87.

2.2. Crystal structure of **2**

In order to examine the stereochemical course of the reaction we determined the relative configuration and the geometry of **2** by X-ray structure analysis.

The two methyl groups at the endocyclic nitrogen atoms are in equatorial positions and *trans* to one another. The five-membered ring is of a envelope type with the fold along C(15) and N(2). This geometry has also been reported in two phosphonamides [10], but was found to depend upon the substituent in the *exo* chain β to the phosphorus atom [11]. The five-membered ring is *trans*-fused to the cyclohexane ring. The oxygen atom is holding the axial, the group connected to the exocyclic nitrogen atom the equatorial position in the five-membered ring.



Scheme 2.

The newly built stereogenic centre C(4) has the same relative configuration as at the two carbon atoms C(10) and C(15) of the cyclohexanediamine motif (like configuration) (Fig. 1).

The bond length from the exocyclic nitrogen atom N(1) to the benzylic carbon C(4) (1.459 (5) Å) does not vary significantly from those of the other nitrogen carbon bonds (1.440 (6)–1.467 (5) Å).

The tin atom has a distorted tetrahedral coordination geometry (see Table 1) with C–Sn–C angles varying from 99.4(2) to 118.6(2)° as found in the related structures [7,8]. The phosphorus atom also has a distorted tetrahedral arrangement (see Table 1), the smallest angle being part of the five-membered ring. One of the endocyclic nitrogen atoms N(3) and the exocyclic nitrogen N(1) have a hybridisation close to sp^2 (sum of the angles: 358.4 and 353.8°). The remaining endocyclic nitrogen N(2) shows a pronounced pyramidalisation (sum of the angles, 343.4°).

The oxygen atom and the methyl group of the exocyclic nitrogen atom are in an almost perfect planar *trans* conformation (O(1)–P(1)–N(1)–C(1), 1.9°).

2.3. Explanation of the diastereoselectivity

As a simple model we suggest the electrophilic attack on lithiated **1** as the stereodeterminating step. The methyl group at the exocyclic nitrogen and the phenyl ring prevent an attack of the electrophile from the lower side of the molecule (see Fig. 2). Therefore, the

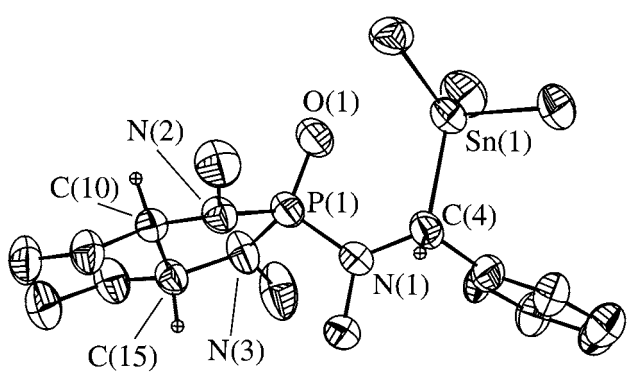


Fig. 1. ORTEP plot of **2**. (Ellipsoids show 50% probability. For clarity, hydrogens are omitted except for those at the stereogenic centres. Only one of the disordered phenyl rings is depicted. See Section 2.4.)

Table 1
Selected bond lengths (Å) and angles (°) for **2**

Sn(1)–C(4)	2.205(4)	C(4)–Sn(1)–C(5)	118.6(2)
Sn(1)–C(5)	2.129(5)	C(4)–Sn(1)–C(6)	112.6(2)
Sn(1)–C(6)	2.121(5)	C(5)–Sn(1)–C(6)	116.8(2)
Sn(1)–C(7)	2.187(4)	C(4)–Sn(1)–C(7)	99.4(2)
P(1)–N(1)	1.655(3)	C(5)–Sn(1)–C(7)	101.4(2)
P(1)–N(2)	1.674(3)	C(6)–Sn(1)–C(7)	104.3(2)
P(1)–N(3)	1.650(3)	N(1)–P(1)–N(2)	109.0(2)
P(1)–O(1)	1.468(3)	N(1)–P(1)–N(3)	110.9(2)
N(1)–C(4)	1.459(5)	N(2)–P(1)–N(3)	94.2(2)
		N(1)–P(1)–O(1)	108.1(2)
		N(2)–P(1)–O(1)	117.1(2)
		N(3)–P(1)–O(1)	116.9(2)

electrophile has to approach from the upper part where complexation of the axial oxygen may also take place. The upwards oriented methyl group at the endocyclic nitrogen N(2) now shields the unlike side, leading to the diastereoselectivity.

This model also explains the selectivities previously found with other electrophiles [9].

2.4. Crystallographic experimental details

The essential X-ray structure analysis data of **2** are listed in Table 2.

Data collection has been carried out using an Enraf–Nonius CAD4 diffractometer equipped with a Mo–K_α fine focus sealed tube and with a graphite monochromator. Absorption correction was carried out using ψ scans (minimum and maximum transmission: 0.95/1.00). The structure was solved by direct methods using the program SIR92 [12]. Anisotropic least squares full matrix refinement was carried out on all non-hydrogen atoms using the program CRYSTALS [13]. The high thermal displacement ellipsoids of the phenyl group suggested a disorder. The atom positions were split and refined applying appropriate restraints (50% occupancy for each set of atoms). Hydrogen atoms are in calculated positions. Chebychev polynomial weights [14] have been used to complete the refinement. Scattering factors have been taken from the International Tables, Vol. IV, Table 2.2B. The fractional coordinates have been deposited at the Cambridge Crystallographic Data Center.

Table 2
Crystal data and parameters of data collection for **2**

Formula	$C_{19}H_{34}N_3OPSn$
Formula weight	470.16
Crystal system	Monoclinic
Space group	$C2/c$
a (Å)	24.251(2)
b (Å)	6.5857(4)
c (Å)	28.322(2)
β (°)	92.324(6)
V (Å^3)	4519.5(5)
Z	8
$F(000)$	1936
D_{calc} (g cm^{-3})	1.38
μ (mm^{-1})	1.21
Crystal size (mm)	$0.24 \times 0.25 \times 0.64$
Temperature (K)	293
Radiation	Mo–K_α ($\lambda = 0.71069$ Å)
Scan type	$\omega/2 \times \theta$
θ max. (°)	30.44
Intensity decay	23.17%
Reflections measured	6393
Independent reflections	5902
Reflections in refinement	4161
Number of variables	281
Final R	0.0614
Final Rw	0.0410
Last max./min. in difference map	1.17/−1.26 (near the tin atom)

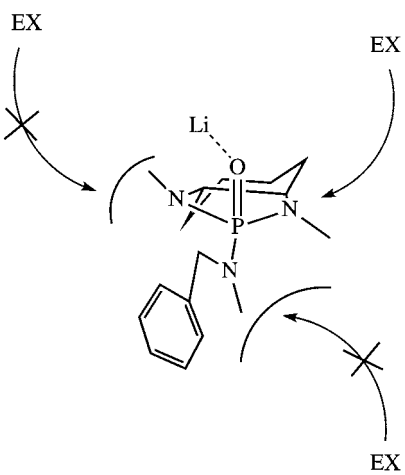


Fig. 2. Model for the electrophilic attack to lithiated **1**.

Acknowledgements

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