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Influence of the *rac–meso* isomerization of seven-membered cyclic bisphosphines on the predominant formation of chelate complexes

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ABSTRACT

The seven-membered cyclic bisphosphines **3**–**5** were synthesized by a Mannich-like condensation reaction of 1,2-bis(phenylphosphino)ethane, formaldehyde and primary amines (*tert*-butylamine, 1,1-(diphenyl) methylamine, (2*R*)-tetrahydro-2-furanylmethylamine) as a mixture of R_PR_P/S_PS_P (*rac*, **3a**–**5a**) and R_PS_P (*meso*, **3b**–**5b**) stereoisomers. The structures of the *rac* stereoisomers **3a**–**5a** were investigated by X-ray crystal structure analyses. The *RR*/*SS* to *RS* isomerization of **3**–**5** and oxidation processes of **4** in solution were studied. Platinum(II) P,P-chelate complexes are formed exclusively from *rac*/*meso* mixtures of **3**–**5**.

1. Introduction

Chelating phosphine ligands are an excellent tool to obtain metal complexes with tailor-made properties and have been widely used in several fields such as water-soluble and asymmetric metal complexes [1,2]. In the last three decades, the facile and effective synthesis of various medium-sized cyclic bisphosphines [3,4,7], macrocyclic tetrakisphosphines [5] and cyclophanes [6] based on the Mannich-like condensation reaction of primary or secondary phosphines, formaldehyde and primary or secondary amines has been developed. P,P-chelating bisphosphines with pendant amino groups, in particular cyclic aminomethylphosphines, have received increasing attention due to the remarkable catalytic properties of their complexes in the electrochemical production of dihydrogen [7]. Thus, nickel and cobalt complexes containing bisphosphine ligands with amine bases in the second coordination sphere exhibit much higher catalytic rates and lower overpotentials for H_2 production than analogous compounds lacking these groups. An extremely high turnover frequency ($>100{,}000\ s^{-1}$) for H_2 production was observed for a nickel complex of 1-aza-3,6-diphosphacycloheptanes [7b,d]; 1-aza-3,6-diphosphacycloheptanes were obtained as a mixture of *meso* and *rac* diastereomers by a Mannich-like condensation reaction of secondary bisphosphines, formaldehyde and primary amines [4a–c,7b]. Due to steric reasons, only the *meso* isomers can form P,P-chelate complexes with transition metals [4b,7a], while the *rac* isomers give oligomeric complexes which are inactive in hydrogen production processes [4a–c]. It was shown that the nature of the primary amine controls the stereoselectivity of the reaction. Thus, amines with branched alkyl substituents (methyl- or ethylbenzylamines) favored the formation of the *meso* diastereomers, whereas benzyl-, 2-phenylethyl- or pyridylamine led to the preferred formation of the *rac* isomer [4a–c]. In solution isomerization of *meso* to *rac* isomers was observed [4b].

The present work is devoted to the synthesis of novel 1-aza-3,6-diphosphacycloheptanes with various primary amines which are structurally similar to α-methylbenzylamine (*tert*-butylamine, 1,1-(diphenyl)methylamine, (2*R*)-tetrahydro-2-furanylmethylamine) to study the factors influencing the stereochemistry of the condensation and isomerization reaction. 1,1-(Diphenyl)methylamine and *tert*-butylamine were chosen as sterically hindered amines with different electron–donor properties, and the enantiopure (2*R*)-tetrahydro-2-furanylmethylamine was selected to investigate the influence of a more distal chiral center, as enantiopure amines were already observed to cause a chiral induction at the phosphorus atoms of the heterocycles [4b].

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2. Results and discussion

2.1. Synthesis

Condensation of an equimolar mixture of *RR*/*SS*-(*rac*) and *RS*-(*meso*) 1,2-bis[(hydroxymethyl)phenylphosphino]ethane (**2**) [4] with primary amines, namely, *tert*-butylamine, 1,1-(diphenyl) methylamine or (2*R*)-tetrahydro-2-furanylmethylamine, in ethanol led to formation of the air-stable crystalline products **3**–**5** (Scheme 1) which are soluble in benzene, chloroform, acetone and DMF.

The structure elucidation of these compounds was based on ^{31}P, ^{1}H NMR spectroscopy, mass spectrometry and elemental analysis.

In the ^{31}P{H} NMR spectra of reaction mixtures of **3** and **4**, two signals of approximately equal intensity (−21.8 and −27.5 ppm for **3**; −37.5 and −38.5 ppm for **4**) were observed confirming the formation of two isomers with R_PR_P/S_PS_P (**3a** and **4a**) or R_PS_P (**3b** and **4b**) configuration of the phosphorus atoms. ^{31}P NMR spectra of the reaction mixture of **5** showed three groups of signals (ratio 0.6:0.8:1.0) indicating the formation of the expected mixture of isomers: $R_PR_PR_C$ (**5a**$_{(\boldsymbol{R})}$), $S_PS_PR_C$ (**5a**$_{(\boldsymbol{S})}$) and $R_PS_PR_C$ (**5b**). The nonequivalence of the two phosphorus atoms in **5b** results in two doublets (AB system) at −35.6 and −36.0 ppm ($^{3}J_{PP}$ = 61.4 Hz) as was also observed for chiral *RS* isomers of 1-aza-3,6-diphosphacycloheptanes [4b]. The remaining two singlets at −36.5 and −37.3 ppm belong to **5a**$_{(\boldsymbol{R})}$ and **5a**$_{(\boldsymbol{S})}$. The approximately equal intensity of signals of different isomers in reaction mixtures of **3**–**5** indicates the low selectivity of the reaction. Only the *rac* isomers **3a**, **4a** or **5a**$_{(\boldsymbol{S})}$ could be obtained in pure crystalline form; **3a** and **5a**$_{(\boldsymbol{S})}$ crystallized spontaneously from the reaction mixture after prolonged heating at 60–70 °C in ethanol for 3 h and subsequent cooling, whereas **4a** was obtained by fractional crystallization from the crude mixture of isomers in ethanol/acetonitrile. After isolation of the crystalline *rac* isomers, the filtrates contained *meso* and *rac* isomers in approximately equal ratio indicating a fast isomerization of *meso* to *rac* isomers (R_PS_P to R_PR_P/S_PS_P) [4]. All attempts of isolating of pure *meso* isomers were unsuccessful possibly due to their higher solubility. The successful isolation of **3a**, **4a** or **5a**$_{(\boldsymbol{R})}$ allowed the assignment of the signals of the other stereoisomers in the NMR spectra by subtracting the signals of pure **3a**, **4a** or **5a**$_{(\boldsymbol{R})}$ from the NMR spectra of the diastereomers.

The ^{1}H NMR spectra of **3**–**5** showed the signals of the cyclic methylene protons in the range of 2.69–3.91 ppm as two groups of multiplets for each isomer, with the protons of the *meso* isomer appearing at higher field [4]. The protons of the P–CH$_2$–CH$_2$–P fragments showed patterns similar to those of 1-aza-3,6-diphosphacycloheptanes [4]. For **4**, an especially large difference of the chemical shifts was observed for the methine protons of the diphenylmethyl fragments which were registered at 5.58 and 4.97 ppm for the *meso* and *rac* isomer, respectively.

These results indicate that the Mannich-like condensation reaction of 1,2-bis(phenylphospino)ethane, formaldehyde and *tert*-butylamine, diphenylmethylamine and (2*R*)-tetrahydro-2-furanylmethylamine is nonselective and both isomers (*meso* and *rac*) of 1-aza-3,6-diphosphacycloheptane are formed.

2.2. X-ray crystallography

One isomer of compounds **3**–**5** could be obtained by fractionally crystallization. X-ray structure analysis unambiguously established the *rac* isomers (the $S_PS_PR_C$ isomer **5a**$_{(\boldsymbol{S})}$ in the case of **5**) (Figs. 1–3), as well as the typical “twist-chair” conformation of the seven-membered ring as was also observed for the *rac* isomers of N-aryl-1-aza-3,6-diphosphacycloheptanes [4]. Crystals of **3a** and **4a** are true racemates. There are three independent molecules present in the asymmetric unit of **4a** with R_PR_P or S_PS_P configurations (Fig. 2, and Figs. S.1, S.2 in the Supporting Information). However, the overall ratio of R_PR_P or S_PS_P enantiomers in the crystal is 1:1.

The endocyclic nitrogen atom is in a trigonal pyramidal environment (sums of bond angles are 333.77°, 342.04°, 337.39° for **3a**, **4a** and **5a**$_{(\boldsymbol{S})}$, respectively). The phenyl groups on the phosphorus atom are in pseudo-equatorial positions, and the pseudo-axial lone pairs of electrons on phosphorus are pointing toward opposite sides of the ring. The furan ring of **5a**$_{(\boldsymbol{S})}$ has a puckered “twist” conformation in which three carbon atoms are coplanar.

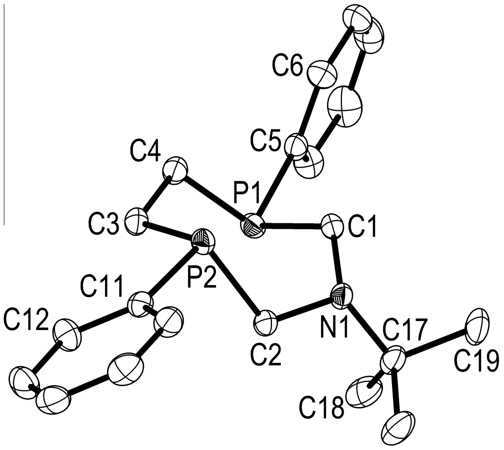
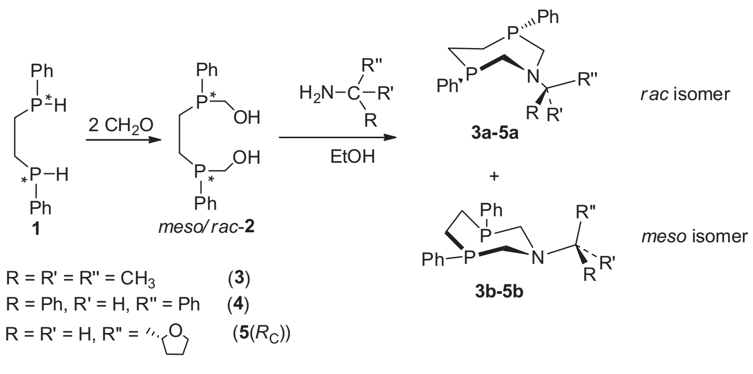


Fig. 1. Molecular structure of **3a**. Hydrogen atoms are omitted for clarity. Thermal ellipsoids are drawn at the 50% level of probability.



Scheme 1. Synthesis of seven-membered cyclic bisphosphines **3**–**5**.