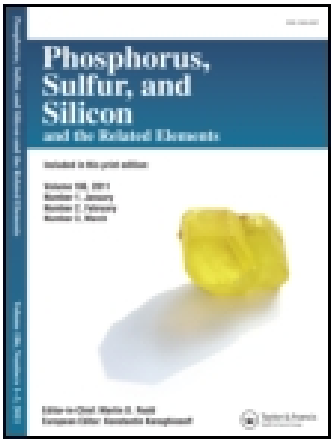

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AMBIDENT REACTIVITY OF P=CH−N−HETEROCYCLES: LITHIATION AND SUBSTITUTION SITES

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Abstract *Benzofused 1H-1,3-azaphospholes are lithiated at the N-atom by tBuLi but phosphinylation takes place at either the N- or the P-atom. Smaller chlorophosphines react at nitrogen, bulkier react at phosphorus. Substituents at C2 promote the latter mode. N-Substituted 2H-1,3-benzazaphospholes undergo CH-metalation or addition at the P=C bond, depending on the conditions, and allow access to 2-functionally substituted benzazaphospholes or their 2,3-dihydro derivatives, new σ^2P,X or σ^3P,X hybrid ligands (X=O,P).*

Keywords Ambident reactivity; hybrid ligands; lithiation; phosphinylation; phosphenes; phosphorus heterocycles

INTRODUCTION

Lithium 1,3-azaphospholides[1] are cyclodelocalized five-membered anions that are electronically related to cyclopentadienides,[2] but the structure and reactivity, studied in particular with the easily accessible benzazaphospholides **1**[3,4] or 2-lithiobenzazaphospholes **2**,[5] are modified and controlled by the heteroatoms. Lithiation of non- or benzo-anellated 1*H*-1,3-azaphospholes and arsenic analogues was achieved with LDA,[1a,3] but later *t*BuLi was preferred[4,5] to avoid the formation of diisopropylamine, which may interfere in consecutive substitution reactions with electrophiles. It was found that the bulky *t*BuLi in polar solvents at low temperature favors NH− or (for N-alkyl or N-aryl derivatives) 2-CH-lithiation to addition at the P=C bond of benzazaphospholes, yielding the lithium reagent **1** or **2**, respectively (Scheme 1). Recent work showed that bulky N-substituents hinder CH-lithiation at the 2-position and cause competing addition at the P=C bond. Polar systems such as tetrahydrofuran (THF)/KO*t*Bu were found to favor 2-CH lithiation and to suppress

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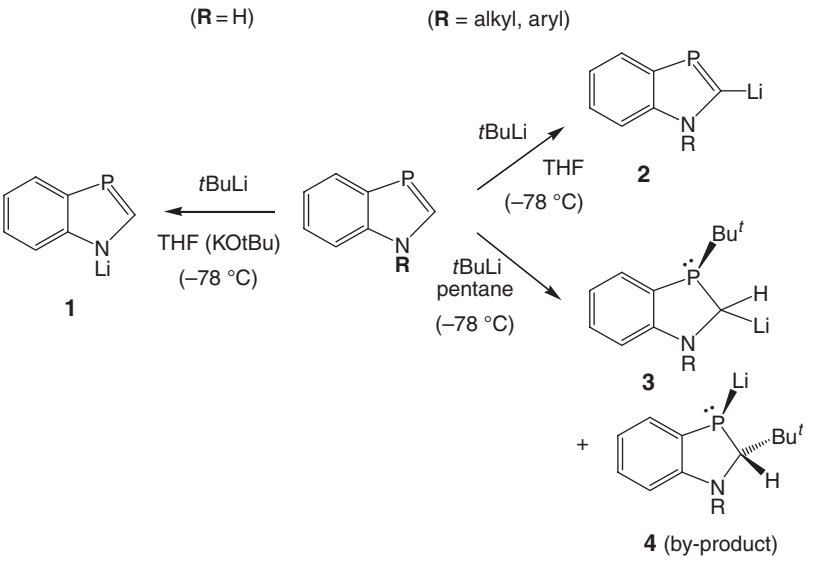
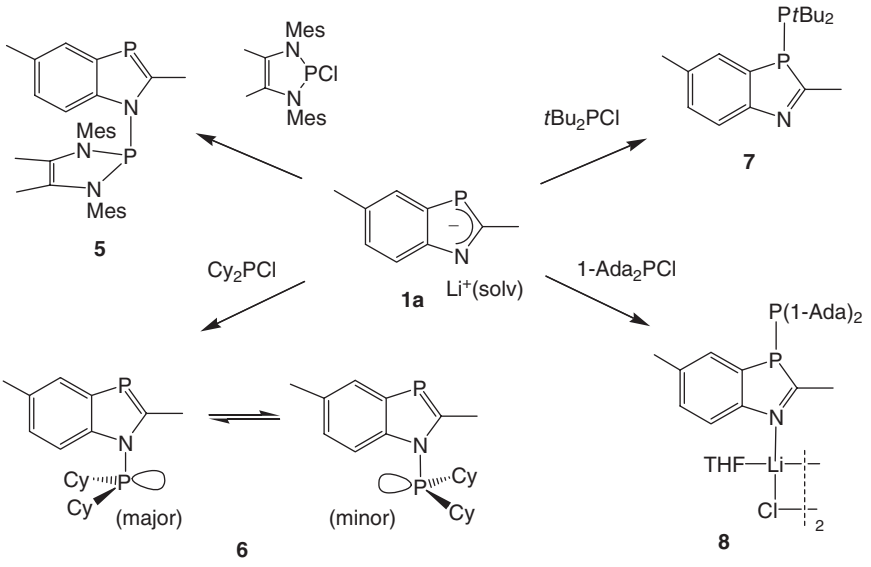


Scheme 1 Lithiation of benzazaphospholes by *t*BuLi at N, C2, and P.

addition completely in the case of *N*-neopentyl groups, whereas less polar solvents such as diethyl ether and in particular nonpolar solvents such as hexane were found to support the addition. The "normal" addition product **3** with *tert*-butyl attached at phosphorus is strongly preferred, but for *N*-neopentyl substitution small amounts of the "inverse" addition product **4** were also detected. For the bulkier *N*-adamantyl group inverse addition is sterically prevented and only normal addition is observed (in hexane).[5a,b]

PHOSPHINYLATION OF AMBIDENT BENZAZAPHOSPHOLIDE 1

In the THF solvate of lithium 2,5-dimethyl-1,3-benzazaphospholide **1a** the metal is bonded to nitrogen but substitution reactions with alkyl halides, pivaloyl chloride, or cyclopentadienylcarbonyl transition metal halides ($CpW(CO)_3Cl$, $CpFe(CO)_2Cl$) occur at phosphorus. Chlorotrimethylsilane undergoes N- or P-substitution, depending on the 2-substituent.[4] Phosphinylation of benzazaphospholides had not been studied in the earlier investigations. However, it was of interest with respect to the relative stabilities of N- and P-substituted isomers and in view of the unusual properties of the P-P bonded 2-phospholyl-1,3,2-diazaphospholes.[6] The latter display bond lengthening and increased P-P bond ionicity, implying a diazaphospholium phospholide resonance structure, and possess high reactivity for insertion reactions into polar single and multiple bonds.[7] The reaction of **1a** with 2-chloro-1,3-dimesityl-1,3,2-diazaphosphole leads, however, to the N-substitution product **5**. The same is observed in the reaction with chlorodicyclohexyl phosphine to **6**, whereas chloro-di-*tert*-butyl and chlorodiadamantyl phosphine react at phosphorus, yielding diphosphines **7** and **8** (Scheme 2). Quantum chemical calculations show that N-phosphinylation for 2-unsubstituted benzazaphospholes is generally preferred.[8] The aromaticity is maintained for N-substituted benzazaphospholes.[9] However, substituents in the 2-position, even when small (methyl), favor P-substitution in the case of bulkier phosphino groups by steric reasons. Thus, the formation of aromatic N-(**5**,**6**) or nonaromatic P-substituted phosphinobenzazaphospholes (**7**,**8**) depends on the size of the substituents in 2-position and at the



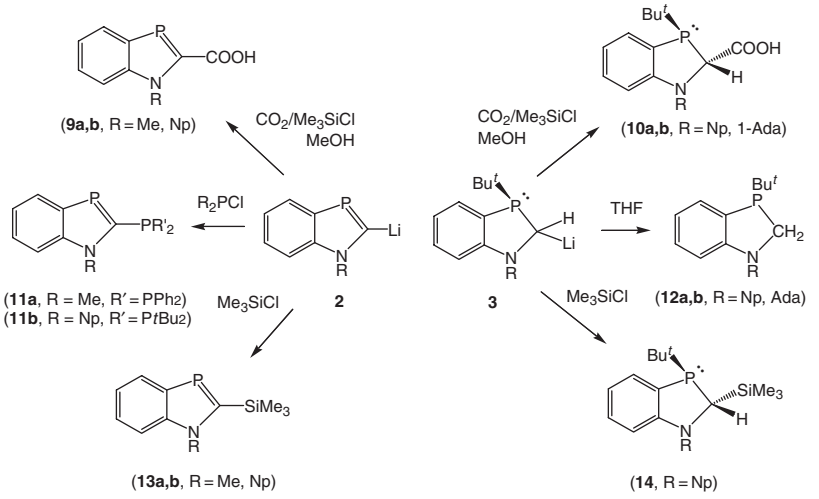
Scheme 2 Ambident reactivity in the phosphinylation of lithium dimethyl-1,3-benzazaphospholide **1a**.

phosphino group. The barrier for rotation around the N-P bond is quite high for **6**, which displays sharp signals for two rotamers at 25°C in the NMR spectra, confirmed by the respective cross peaks in a 2D-EXSY spectrum. The two phosphorus resonances of the diphosphines are broadened and indicate flexible molecules in solution. VT-NMR studies of **7** revealed two dynamic processes, low-temperature inversion at ring phosphorus ($\Delta H^{\#} = 22$ kJ/mol, $\Delta S^{\#} = 2$ J/(K mol)) and very low-temperature rotation of the tBu$_2$P group.[8]

REACTIVITY OF 2-LITHIO-(DIHYDRO)-1,3-BENZAZAPHOSPHOLES 2 AND 3

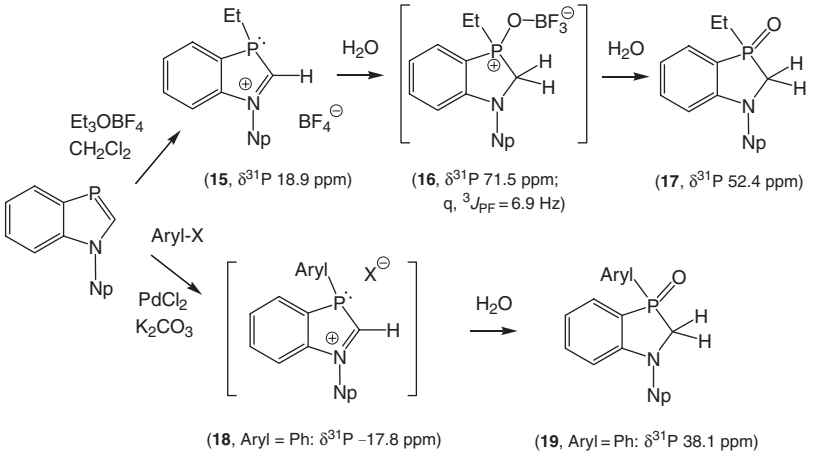
2-Lithio-1,3-benzazaphospholes are relatively stable and could be crystallized for **2a** (R = Me) as Li(THF)$_2$-solvates.[5c] 2-Lithio-3-*tert*-butyl-dihydro-1,3-benzazaphospholes **3** are highly reactive cyclic α-phosphino, α-amino sp^{3}C-lithium reagents that rapidly deprotonate THF, and slowly deprotonate diethyl ether, but use of hexane allows substitution reactions with electrophiles to give functionally substituted dihydrobenzazaphospholes; for example, with CO_2 the corresponding heterocyclic α-phosphinocarboxylic acids. Like **1**, the lithium reagents **2** and **3** possess each two nucleophilic sites, at carbon and phosphorus, but electrophiles show a strong preference for reaction at carbon, as is typical for α-lithiated phosphines. The introduction of functional groups such as COOH or R$_2$P in **9–12** or of SiMe$_3$ groups in **13** and **14** illustrates the variety of new σ^2P and σ^3P hybrid ligands accessible in this way, whereas the formation of **12** in THF shows limitations in the case of **3** by rapid solvent deprotonation (Scheme 3).[10]

For RLi **2**, reactions at phosphorus would result in cyclic phosphino-aminocarbenes (PNHC) which, because of the threefold coordinated P-atom, would be incapable of cyclodelocalization and be much less stable than the isomeric, aromatically stabilized benzazaphospholes. Therefore, apart from the much lower nucleophilicity at σ^2P, *C*-substitution by electrophiles is also favored thermodynamically. However, because of the π-donor



Scheme 3 Reactivity of **2** and **3** to some electrophiles.

properties of nitrogen, P-alkylation and even catalytic P-arylation are possible for non-metalated benzazaphospholes and distinguishes these π-excess P=C aromatics from phosphinines.[11] The handling of the benzazaphospholium salts **15** and particularly **18** proved difficult because they are extremely sensitive to hydrolysis and furnish P,N-disubstituted benzazaphospholine-*P*-oxides **17** and **19**, respectively, with any trace of moisture (Scheme 4). The nature of the phosphine oxides is confirmed by conclusive multinuclear NMR data and by crystal structure analyses for **19** (aryl = 2-thienyl and 2-dimethylamino-5-methylphenyl). Attempts to detect PNHC by 2-CH deprotonation or trapping have failed so far.



Scheme 4 P-Alkylation and arylation of benzazaphospholes.

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