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A persistent P,N-heterocyclic carbene^w

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Abstract

Conjugate acids of cyclic (amino)(phosphino)carbenes (P-NHCs) have been prepared, and several different processes have been observed during their deprotonation, which include the formation of a metastable P-NHC, an azomethine ylide, and a bicyclic phosphirane.

Following the discovery of a distillable (phosphino)(silyl)carbene in 1988,¹ a variety of stable acyclic and cyclic carbenes have been prepared.² With the exception of bis(amino) cyclopropenylidenes,³ all these carbenes feature at least one amino or phosphino group directly bonded to the electron-deficient center. Surprisingly, although cyclic diaminocarbenes (NHCs) I,⁴ cyclic diphosphinocarbenes (PHCs) II,⁵ and acyclic (amino)(phosphino)carbenes III have been isolated,⁶ cyclic carbenes of type IV have eluded the synthetic skills of investigators (Fig. 1). Cyclic carbenes have found numerous applications as ligands for transitionmetal based catalysts,^{7,8} as catalysts on their own rights,⁹ and as initiators for polymerization.¹⁰ In contrast, most acyclic carbenes are poor ligands or give fragile complexes with transition metals,¹¹ probably because of large carbene bond angles (120–153°).^{12,13} The only notable exceptions are the (amino)(phosphino)carbenes III, which allow for different coordination modes.¹⁴ Here we report our efforts towards the synthesis of cyclic (amino)-(phosphino) carbenes (P-NHCs), which should feature the advantages of cyclic carbene systems, and the different coordination modes already described for their acyclic analogues.

We have recently shown that conjugate acids of cyclic bis(amino)carbenes (NHC,H⁺s), (amino)(thio)carbenes and (alkyl)(amino)carbenes can be readily prepared by the addition of a compound featuring two leaving groups to 1,3-diaza-allyl-, 1,3-azathio-allyl and 1-aza-allyl anions, respectively.¹⁵ By analogy, phosphoramidates 1,¹⁶ prepared by deprotonation of the corresponding phosphoramidines with butyl-lithium in diethyl ether, appeared to be potential starting materials for the desired P-NHC precursors. Indeed, when the lithium phosphoramidate 1a was treated with an excess (4–6 eq.) of 1,3-dibromopropane in Et₂O, the P-substituted phosphoramidine 2a was obtained as a light yellow oil in 90% yield (Scheme 1). A THF solution of 2a was then heated at 40 °C for 18 h, and after workup, the cyclic salt 3a was isolated as a white powder in 85% yield. The down field ¹H (d, 8.3 ppm, J_{PH} = 6.9 Hz) and ¹³C NMR signals (d, 178.4 ppm, J_{PC} = 2.9 Hz) confirmed the iminium structure of 3a. All attempts to deprotonate 3a with a variety of strong bases (LDA, LiTMP, etc.) led to the cyclic alkene 4a, which was isolated in 75% yield. Interestingly monitoring the deprotonation reaction in THF at 60 °C, by multinuclear NMR spectroscopy, showed the disappearance of the starting material 3a, and the clean formation of a new product, tentatively

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identified as the cyclic azomethine ylide 5a,¹⁷ instead of the desired P-NHC. Indeed, the ¹³C NMR spectrum shows two CH signals at 89.7 (d, J_{PC} = 26.9 Hz) and 103.8 ppm (s), and no signal at low field as expected for a carbene. Note, that the formation of a transient azomethine ylide has already been postulated in the deprotonation of (amino)(aryl)carbenes.¹⁸ Warming up the solution to room temperature afforded again the alkene 4a, which probably results from the intermolecular deprotonation of the carbon at the β-position of N by the negatively charged azomethine ylide carbon.

These results suggest that the electropositivity of phosphorus decreased the acidity of the iminium proton of 3a, and favored the deprotonation at the α⁰ position of nitrogen. Therefore, we first chose to protect this position by a methyl substituent. However, deprotonation of iminium 3b yielded again the corresponding alkene 4b.

It is well recognized that bulky substituents decrease the inversion barrier at phosphorus, but also at nitrogen.¹⁹ Consequently, the lone pair of the nitrogen becomes parallel with the vacant orbital of the adjacent electron-deficient species, which allows for maximum donation. This should result in an increase acidity of the iminium proton and stability of the ensuing carbene. Therefore, we replaced the mesityl group of 3b by a 2,6-diisopropylphenyl group (Dipp). In order to expedite the synthesis, lithium phosphoramidinate 1c was reacted with 1,3-dibromobutane in THF at 70 °C (Scheme 2).

However, two products were isolated from the reaction, the expected salt 3c along with derivative 3c⁰ (40/60 ratio) in which the methyl group is in α-position of the phosphorus atom. Both compounds have been characterized by X-ray diffractions studies, and the molecular structure of 3c is shown in Fig. 2. The C1–N bond distance [1.302(6) Å] is typical for an NC double bond, and the C1–P bond length [1.761(5) Å] is halfway between those expected for single and double bonds, and significantly longer than in PHC,H⁺s (1.69–1.72 Å). Since the phosphorus center is much more pyramidalized (sum of angles: 3301) than in PHC,H⁺s (348–3541), one can conclude that the nitrogen and phosphorus lone pairs strongly and poorly interacts, respectively, with the cationic carbon center. The non-selectivity leading to 3c,c⁰ can be avoided by using diethyl ether as the solvent for the coupling reaction of 1c with 1,3-dibromobutane. Then, heating a THF solution of 2c at 50 °C for 48 h afforded 3c in 89% isolated yield.

We first used LiTMP in Et₂O at 78 °C to deprotonate salt 3c. After the solution was warmed to room temperature, and after workup, the cyclic alkene 4c was isolated as a yellow solid in 76% yield (Scheme 3). In marked contrast, when LDA was added to a THF solution of 3c at 78 °C, the reaction mixture stirred at 30 °C for 30 min and then warmed to room temperature, bicyclic phosphirane 6c was obtained in 84% yield, as a 70 : 30 mixture of diastereomers. The three-membered ring structure was apparent from the high field ³¹P NMR signals (151 and 175 ppm),²⁰ and unambiguously confirmed by a single-crystal X-ray diffraction study of the major isomer. Note that compared to 3c and 3c⁰, the phosphorous atom in 6c is highly pyramidalized (sum of the angles ~2441), but this is usual for phosphiranes.²⁰ The formation of 6c implies that the deprotonation occurs at the CH₂-group in α⁰-position of the phosphorous atom of 3c, and this surprisingly result has not yet been explained.

Monitoring the previous reaction by ³¹P NMR spectroscopy, we observed a small signal at 32.8 ppm, which was replaced after a few hours at room temperature by a signal at 68.4 ppm. Therefore, we carried out the deprotonation reaction of 3c with LDA under various experimental conditions. The best results were obtained, when the reaction mixture was kept for only 2 min at 78 °C, and rapidly warmed up to room temperature. In this case the ³¹P NMR spectrum showed mainly the signal at 32.8 ppm (>90%). Importantly, in the ¹³C NMR spectrum there was a doublet at very low field (314.5 ppm, J_{PC} = 122 Hz) in the range expected for the

carbene carbon of the desired P-NHC 7c, the acyclic (amino)(phosphino)carbenes III appearing between 320 and 348 ppm ($J_{PC} = 22\text{--}101$ Hz).⁶

Note that the carbene carbon chemical shift for 7c is much further downfield shifted than those observed for both NHCs I (205–245 ppm)² and PHCs II (184 ppm),⁵ but comparable with those for cyclic (alkyl)(amino)carbenes (304–320 ppm).²¹ This implies that the phosphorus center plays the role of a spectator substituent, as observed in the acyclic version III. All attempts to obtain single crystals of carbene 7c failed. After two days at 30 °C, compound 8c resulting from the carbene insertion into the CH bond of a tert-butyl group was obtained quantitatively, and characterized by an X-ray diffraction study (Fig. 3).

These results as a whole are very surprising. In contrast to the imidazolidinium salts (NHC, H⁺s), the conjugate acids of P-NHCs can undergo deprotonation at the iminium carbon, but also in position α^0 of the nitrogen and phosphorus centers. The kinetic instability of the P-NHC 7c contrasts with the high stability of NHCs I, PHCs II, and even acyclic (amino)-(phosphino)carbenes III, and this is not yet understood. In the hope of isolating cyclic (amino)-(phosphino)carbenes, the synthesis of an unsaturated five-membered ring version is under active investigation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Fig. 1.

Fig. 2. Molecular structure of compound 3c in the solid state (hydrogen atoms, except this for C1 are omitted for clarity; ellipsoids are drawn at 50% probability).

Fig. 3.
Molecular structure of derivative 8c in the solid state (hydrogen atoms are omitted for clarity; ellipsoids are drawn at 50% probability).

Scheme 1.

Reagents and conditions: (i) 1,3-dibromopropane, Et_2O , R.T., 14 h; (ii) for **2a**: THF, 40 °C, 18 h; for **2b**: THF, 70 °C, 6 h; (iii) LDA, THF, 78 °C, 1 h; (iv) LiHMDS, THF, 78 °C; (v) THF, R.T., 1 h.

Scheme 2.

Reagents and conditions: (i) 1,3-dibromobutane, R.T., 14 h; (ii) THF, 50 °C, 48 h; (iii) THF, 70 °C, 72 h.

Scheme 3.