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A Novel Preparation of Chlorophospholenium Chlorides and their Application in the Synthesis of Phospholene Boranes

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ABSTRACT

A novel preparation of 1-chloro-3-methyl-3-phospholenium chlorides was developed by reacting 1-substituted-3-methyl-3-phospholene 1-oxides with oxalyl chloride. The obtained cyclic chlorophosphonium salts were reacted with $LiBH_4$ to afford the corresponding 1-substituted-3-methyl-3-phospholene boranes. The latter protocol involves a silane-free deoxygenation, and borane complex formation. In one instance, a 2-phospholene borane and the corresponding *P*-oxide were synthesized *via* rearrangement of the double bond in the cyclic chlorophosphonium salt. This double bond migration was investigated by quantum chemical calculations.

Amongst 5-membered *P*-heterocycles, 3-phospholene 1-oxides are of special importance as potential starting materials for the synthesis of 6-, 7- and bridged 8-membered *P*-heterocycles.[1-4] Racemic and optically active aryl- and alkyl-phospholene oxides can also be converted, after deoxygenation, to 3-phospholene-platinum(II) complexes characterized as PtL_2Cl_2 (where L is the phospholene moiety) which can be used as catalysts in the hydroformylation of styrene.[5-11]

The conversion of cyclic and acyclic tertiary phosphine oxides to the corresponding phosphines is an area of current focus. The need for regeneration of triphenylphosphine from triphenylphosphine oxide, formed as the by-product in the Wittig-, Mitsunobu- or Appel reactions also underlies the importance for deoxygenation of the P=O functional group. The development of catalytic versions of the Wittig- or Mitsunobu reactions, whose methods involve *in situ* reduction of the phosphine oxides, has become a hot topic in organophosphorus chemistry.[12-17] Catalytic Appel reactions were also described involving the transformation of a phosphine oxide to a halogenophosphonium salt in the catalytic cycle using oxalyl chloride or bromide.[18]

The classical deoxygenation of the P=O functional group can be accomplished with a wide range of silane or hydride reagents. Considering the corresponding cyclic phosphine oxides, mainly silanes [*e.g.* Cl_3SiH (with or without a tertiary amine), and $PhSiH_3$] are used for the preparation of the corresponding cyclic phosphines.[8,11,13,19,20] Recently, the more user-friendly (inexpensive and non-corrosive) tetramethyldisiloxane, polymethylhydrosiloxane and other silane derivatives were also found to be suitable for the deoxygenation of acyclic and cyclic phosphine oxides.[21-23]

Once the phosphines are formed, they can be easily converted to the corresponding transition metal- or borane complexes. The phosphine-boranes may be regarded as precursors for phosphines, as the corresponding phosphines can be regenerated from them by heating with secondary amines (*e.g.* diethylamine) in an aromatic solvent.[24,25] The practical synthesis of phosphine-boranes involves reaction of the phosphine with a borane source (*e.g.* $Me_2S{\cdot}BH_3$ or $BH_3{\cdot}THF$).[11,26] Imamoto and co-workers reported the synthesis of phosphine-boranes *via* reaction of the corresponding phosphine oxides with $LiAlH_4$-$CeCl_3$-$NaBH_4$.[24,27] Keglevich and co-workers reported a one-pot synthesis of cyclic phosphine-boranes. The reaction of bridged phosphine oxides (*e.g.* 7-phosphanorbornane 7-oxides with considerable ring strain) with borane-dimethylsulfide led to the corresponding *P*-boranes.[28-30] Recently, Gilheany and co-workers reported a novel protocol for phosphine-boranes allowing access to mainly acyclic derivatives. The phosphine oxides or phosphine sulfides were reacted with oxalyl-chloride, and the formed chlorophosphonium

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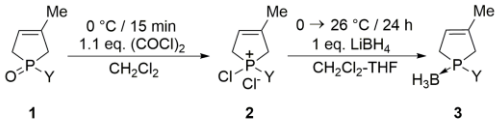
salts were treated with $NaBH_4$ or $LiBH_4$ to afford the corresponding phosphine-boranes.[31,32] Their methods were successfully extended to the preparation of aminophosphine-boranes from the corresponding aminophosphine oxides.[33] In these syntheses, the key intermediates were the corresponding chlorophosphonium salts, which have been known in the literature for several decades.[34] However, the novel application of these reactive intermediates has received more attention in recent years.[16,18,35,36]

The corresponding chlorophosphonium salts are also challenging species within the sphere of *P*-heterocycles. However, their preparation involves using the McCormack cycloaddition reaction, and the chlorophospholenium salts are key intermediates in the synthesis of phospholene derivatives.[37-40] The corresponding chlorophospholenium chloride was also prepared by reacting 1-phenyl-3-methyl-phosphole with dry hydrochloric acid.[41]

In contrast, the novel preparation and utilization of cyclic chlorophospholenium salts as reactive intermediates is a rather unexplored field. Herein, we report the novel synthesis of 1-chloro-3-methyl-3-phospholenium chloride derivatives, and their utilization in further syntheses.

Our first aim was to find an alternative route for the preparation of chloro-3-phospholenium salts (**2**) instead of the classical McCormack cycloaddition reaction. Gilheany and co-workers showed in a few examples, that their method for the preparation of chlorophosphonium salts was also applicable to the synthesis of cyclic derivatives.[31,33,42] Inspired by these results, the
1-substituted-3-methyl-3-phospholene 1-oxides (**1**) were reacted with oxalyl chloride at 0 °C (Scheme 1). The reaction was monitored by ^{31}P NMR spectroscopy which revealed that chloro-3-phospholenium salts (**2**) were immediately formed with 100% conversion. The ^{31}P NMR shifts of the cyclic chlorophosphonium salts (**2**) were in the range of δ_P 74.3–96.5 for the aryl derivatives, and in the range of δ_P 114.2–120.2 for the alkyl derivatives, which was in accordance with the chemical shift of δ_P 98.8 for 1-chloro-3-methyl-1-phenyl-3-phospholenium chloride (**2a**), the only reported ^{31}P NMR shift in this class of compounds.[41] It is noteworthy that the ^{31}P NMR chemical shift (δ_P 74.3) of the 2-methylphenyl substituted derivative (**2b**) was somewhat lower than the other aryl-phospholenium salts (**2a**, **2c** and **2d**) (δ_P 89.4–96.5) (ESI). This observation may be attributed to the methyl group in the *ortho*-position which changes the hybridization at phosphorus and hence the chemical shift. Despite the fact that a few of these cyclic chlorophosphonium salts (**2a**, **c-e**) have been described, they were not fully characterized.[41] This is obviously a consequence of the sensitivity of the chlorophosphonium salts to moisture. In order to isolate the corresponding chloro-3-phospholenium salts (**2**) from the reaction mixture, the solvent and the excess oxalyl chloride were evaporated under reduced pressure at 0 °C, before the chloro-3-phospholenium salts (**2**) were characterized by ^{31}P, ^{1}H and ^{13}C NMR spectroscopy.

In order to demonstrate the synthetic value of the prepared chloro-3-phospholenium salts (**2**), we wished to use them as reactive intermediates in reductions and borane-complex formation reactions. In the literature, only one example can be found for the reduction of phenyl-chloro-3-phospholenium salt (**2a**) to the corresponding P(III)-derivative by applying $LiAlH_4$ or magnesium as the reducing agent.[43] Based on the method published by Gilheany and co-workers, we thought that the chloro-3-phospholenium salts (**2**) could also be reduced by borohydrides (*e.g.* $LiBH_4$ or $NaBH_4$). The chloro-3-phospholenium salts (**2**) were prepared by reaction of the corresponding 1-substituted-3-methyl-3-phospholene 1-oxide (**1**) with oxalyl chloride. Subsequent treatment of a dichloromethane solution of the chloro-3-phospholenium salts (**2**) with $LiBH_4$ (1 equiv.) in THF at 0 °C, and stirring for 24 h furnished the corresponding 1-substituted-3-methyl-3-phospholene boranes (**3**) in 58–85% yield (Scheme 1). It is worth noting, that when more than 1 equivalent of $LiBH_4$ was used, the excess reagent caused a side-reaction involving saturation of the heterocyclic ring double bond. The slow and dropwise addition of the $LiBH_4$ solution at low temperature was helpful to ensure maximum selectivity.



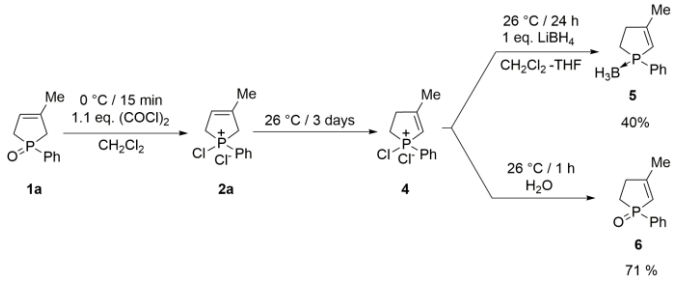
Y	Ph (**a**)	2-MeC$_6$H$_4$ (**b**)	4-MeC$_6$H$_4$ (**c**)	1-Napht (**d**)	Et (**e**)	Pr (**f**)	^{n}Bu (**g**)	^{i}Bu (**h**)	^{i}Pent (**i**)
Yield (%)[a]	85	80	80	83	75	58	80	79	76

[a] Yield based on **1**.

Scheme 1. General procedure for the preparation of 1-substituted 3-methyl-3-phosphlene-boranes (**3**) by the reduction of chloro-3-phospholenium salt intermediate **2**.

It is known, that the double bond of chloro-3-phospholenium salts may rearrange to give the thermodynamically more stable chloro-2-phospholenium salts.[38,41,44] Therefore, we wished to make use of this isomerization reaction to explore a novel route for the preparation of 2-phospholene boranes and oxides.

1-Phenyl-3-methyl-3-phospholene 1-oxide (**1a**) was chosen as the model compound, which was reacted with oxalyl chloride as described above. After reagent addition, the reaction mixture was stirred at 26 °C for 3 days to allow time for the formation of the thermodynamically more stable 1-chloro-3-methyl-1-phenyl-2-phospholenium salt (**4**). The cyclic chlorophosphonium salt (**4**) was then reacted with a THF solution of $LiBH_4$ to afford 1-phenyl-3-methyl-2-phospholene-borane (**5**) in 40% yield. In a separate reaction, 1-chloro-3-methyl-1-phenyl-3-phospholenium salt (**4**) was hydrolyzed to give 1-phenyl-3-methyl-2-phosphlene 1-oxide (**6**) in 71% yield (Scheme 2).



Scheme 2. Preparation of 1-phenyl-3-methyl-2-phospholene borane (**5**) and 1-phenyl-3-methyl-2-phospholene-oxide (**6**) by the derivatization of 1-chloro-3-methyl-1-phenyl-2-phospholenium salt (**4**).

The isomerization of **2a** to **4** upon extending the reaction time during the conversion of **1a** to **2a** can be explained by means of the olefinicity concept.[45] The olefinicity percentage (OL%) expresses the conjugation degree of an olefinic double-bond; a higher percentage, means a stronger conjugation, as shown in several publications.[46-49] Scheme 3 summarises the calculated olefinicity percentage values for compounds **1a**, **2a**, **4** and **6** [according to the B3LYP/6-31G(d,p)//PCM(THF) level of

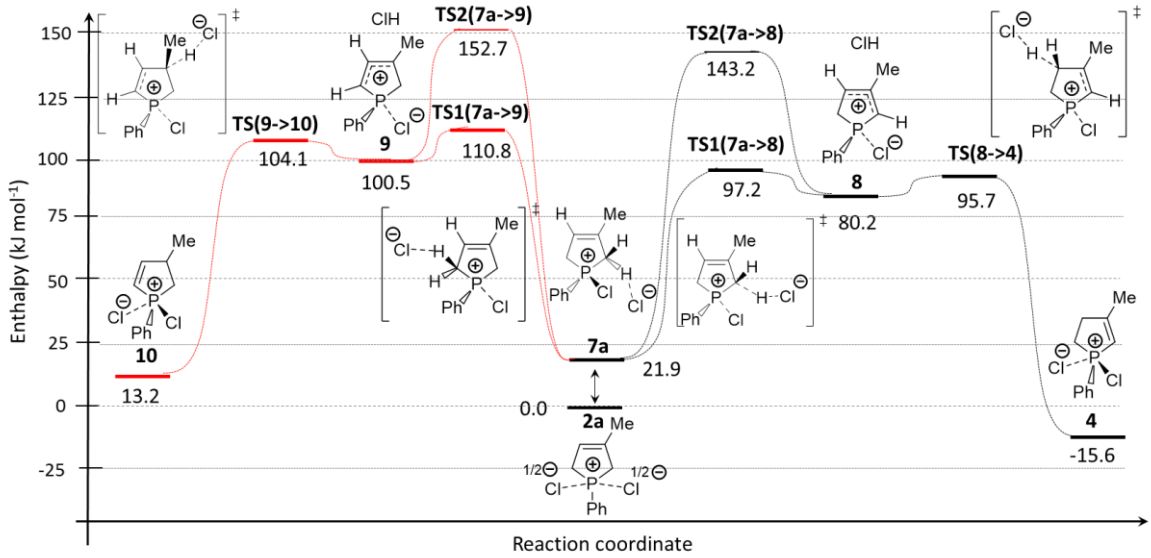
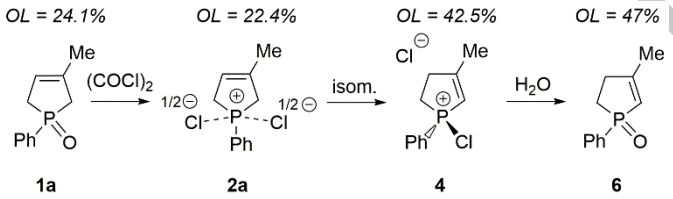


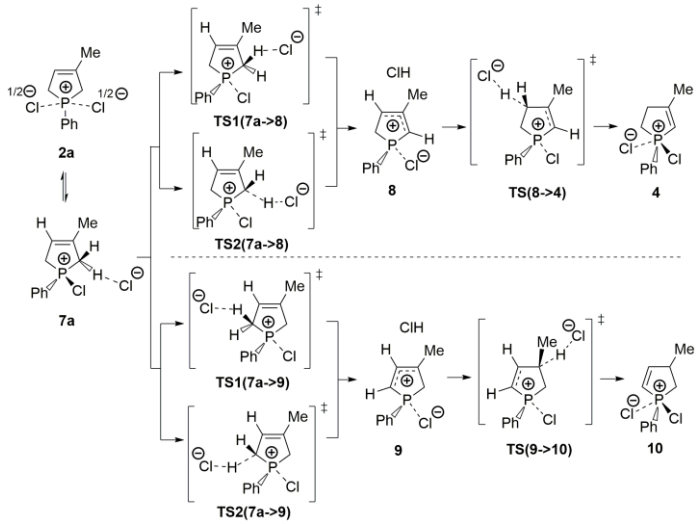
Figure 1. Computed enthalpy diagram for the transformation of **2a** → **4** at the B3LYP/6-31G(d,p)//PCM(THF) level of theory.

theory]. The olefinicity percentage values are undoubtedly higher (≥45%) for the 2-phospholene isomers (**4** and **6**), while the corresponding values are ≤ 25% for 3-phospholene derivatives **1a** and **2a**. The increase in the olefinicity percentage during the **2a**→**4** transformation refers to the stronger conjugation between the P atom and the double-bond of **4** and **6**, resulting in a resonance energy change of 22.5 kJ mol^{-1}, thus providing a thermodynamic driving force for the double-bond rearrangement.



Scheme 3. Olefinicity change in the course of the 4-step process **1a**→**2a**→**4**→**6**.

Investigating different possibilities for the mechanisms, the most probable route together with the corresponding energetic profile are represented in Scheme 4 and Figure 1.



Scheme 4. Possible reaction mechanism for the transformation of **2a** to expected product **4** and to possible side-product **10**.

In this multistep process, one can propose a preequilibrium between the neutral quasi pentavalent **2a** and the ionic salt **7a**. This equilibrium shows a significant solvent dependence. Aprotic solvents prefer the formation of **2a,** and the dissociation of the neutral form is an endothermic process. However, in protic solvents, the dissociated form **7a** predominates over the neutral form **2a**. In the next step, a proton is eliminated by the assistance of the Cl anion, eventually resulting in neutral intermediates. Theoretically, the proton elimination may involve four hydrogen atoms involving four transition states; two H atoms from C2 [**TS1(7a→8)**, **TS2(7a→8)**], as well as two H atoms from C5 [**TS1(7a→9)**, **TS2(7a→9)**], leading to high energy intermediates **8** and **9**. It is noteworthy, that the elimination is *ca*. 40 kJ mol^{-1} more favorable from the anti-position of the P–Cl bond. This enthalpy difference is the consequence of repulsion between the two Cl ions on the same side. As expected, the proton elimination is *ca*. 10 kJ mol^{-1} more favorable from the C2 position due to the electron donating methyl group at position C3 in intermediate **8**. In the second elementary step, HCl is added to the phospholene ring, exhibiting somewhat lower activation enthalpies for these transition states [*e.g.* **TS(8→4)**]. Overall, the 97.2 kJ mol^{-1} activation enthalpy represents a "moderate transition state", which allows a slow reaction rate at room temperature.

In summary, a novel method was developed for the preparation of a series of 1-chloro-3-methyl-3-phospholenium chlorides (**2**) by the reaction of the corresponding 1-substituted-3-methyl-3-phospholene oxide (**1**) with oxalyl chloride. The cyclic chlorophosphonium salts (**2**) reacts readily with $LiBH_4$ to furnish the corresponding 3-methyl-3-phospholene boranes (**3**). In this manner, deoxygenation and borane complex formation were accomplished in a one-pot reaction without using silanes. In one instance, the corresponding 3-phospholenium salt (**2a**) was allowed to rearrange to the thermodynamically more stable 2-phospholenium salt (**4**), which was then converted to the corresponding 2-phospholene borane and *P*-oxide (**5** and **6**, respectively). Isomerization of the phenyl-3-phospholenium salt (**2a**) was also elucidated by quantum chemical calculations, which allowed a possible reaction mechanism for double bond migration in the given phospholenium salt (**2a**) to be proposed.

Acknowledgments

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Supplementary Material

Supplementary data (characterization data for compounds **2**, **3**, **5** and **6**; and the details of the quantum chemical calculations) associated with this article can be found, in the online version, at http:

Graphical Abstract

A Novel Preparation of Chloro-phospholenium Chlorides and their Application in the Synthesis of Phospholene Boranes

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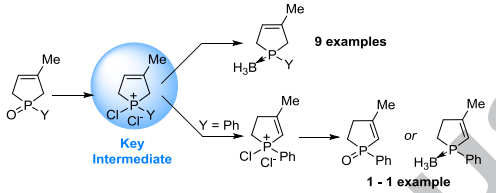

Research Highlights

- A novel preparation of cyclic chloro-3-phospholenium salts was described.
- The chloro-3-phospholenium salts were converted to borane complexes using $LiBH_4$.
- A silane-free, one-pot preparation of 3-phosholene boranes was elaborated.
- Synthetic utility of isomerization of a chlorophospholenium salt was demonstrated.
- The mechanism was calculated for the isomerization of a chlorophospholenium salt.