Atomic Carbon Sources

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An Isolable Mixed P,S-Bis(ylide) as an Asymmetric Carbon Atom Source[**]

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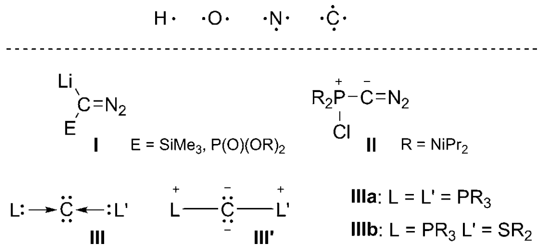
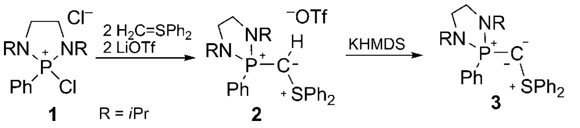
The transformation of molecules by introduction of atomic elements is one of the most fundamental reactions in chemistry. Indeed, the reactions of atomic hydrogen (reduction, hydrogenation) and oxygen (oxidation, epoxidation) are exceedingly important in organic synthesis, and numerous reagents and catalysts for this purpose are available. In marked contrast, the manipulation of atomic elements with a higher valence number, such as nitrogen and carbon, remains a more difficult task.

Although several C1 sources have been intensely investigated, only a few atomic carbon synthetic equivalents, such as unsaturated diazo derivatives **I**[1] and **II**,[2] have been described. It is also possible to generate genuine atomic carbon by the carbon arc method.[3] However, such a species is so reactive that it requires the use of sophisticated apparatus and careful control of the reaction conditions. To reduce the reactivity and allow easier laboratory handling, atomic carbon can be stabilized by two donating ligands. These complexes can be represented either as divalent carbon(0) complexes (**III**) or bis(ylide)s (**III′**).[4] To date, several stable carbon(0) complexes have been synthesized, and investigations into the electronic and geometric properties associated with their coordination chemistry have been reported.[5,6] Surprisingly, their chemical properties as an atomic carbon source have received very little attention, with the exception of carbodiphosphoranes (CDPs) **IIIa**.[7] CDPs are known to react with two equivalents of ketone, leading to the formation of cumulenes as a result of a double-Wittig reaction. We have recently described the synthesis of the first persistent mixed P,S-bis(ylide) of type **IIIb**.[8] In contrast to the symmetrical CDPs **IIIa**, bis(ylide) **IIIb** features two different ylide functions (phosphonium[9] and sulfonium[10]), each of which have significantly different chemical behavior.[11] Therefore, it is expected that this type of unsymmetrical bis(ylide) **IIIb** behaves as a source of atomic carbon with a masked asymmetric dicarbene character. Herein we present the synthesis of a stable and isolable P,S-bis(ylide) **3** and its reactivity as an asymmetric atomic carbon source.



P,S-bis(ylide) derivative **3** was synthesized from the corresponding carbon-atom-protonated cationic salts **2**, which are readily obtained by the reaction of chlorinated phosphonium salts **1** with two equivalents of diphenylsulfonium ylide (Scheme 1). Deprotonation of **2** using potassium hexamethyldisilazane (KHMDS) results in the clean formation of P,S-bis(ylide) **3**, which was successfully isolated as pale yellow crystals in good yield (72 %). In the ^{31}P NMR spectrum, derivative **3** displays a signal shifted to higher field ($\delta = 39.6$ ppm) compared to **2** ($\delta = 49.2$ ppm). The central carbon appears as a doublet at $\delta = 16.6$ ppm ($^{1}J_{PC} = 22$ Hz) in the ^{13}C NMR spectrum.



Scheme 1. Synthesis of P,S-bis(ylide) **3**. KHMDS = potassium hexamethyldisilazane.

The structures of both **2** and **3**[12] were confirmed by X-ray crystallography (Figure 1). Interestingly, the angle at the central carbon decreases significantly from the salt **2** (116.6°) to the bis(ylide) **3** (109.8°). This observation is in contrast to the trend in CDPs **IIIa**, in which the angle tends to become

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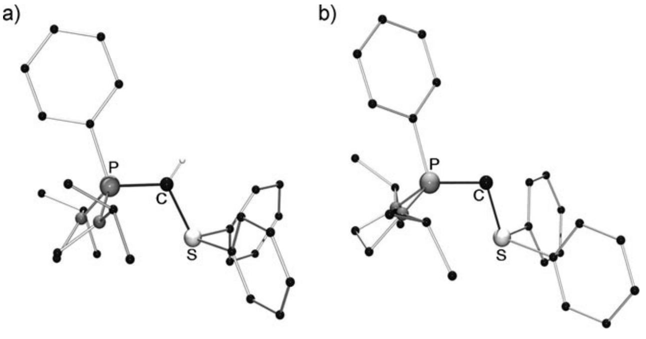
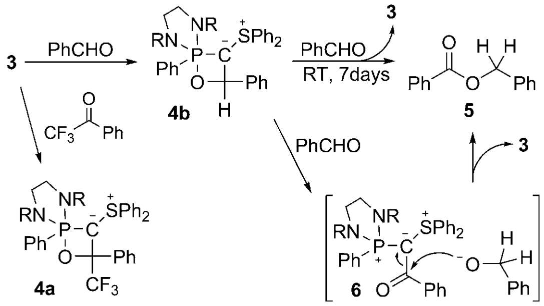


Figure 1. Molecular structures of a) **2** and b) **3**. Hydrogen atoms (except for that on C of **2**) and the triflate anion (of **2**) are omitted for clarity. Selected bond lengths [Å] and angles [°]: **2**: C–P 1.690(4), S–C 1.687(3); S-C-P 116.6(2). **3**: P–C 1.667(3), S–C 1.684(3); P-C-S 109.78(17).

larger (121–180°) upon deprotonation.[13] In fact, the P-C-S fragment is so strongly bent that it nearly matches that of the highly strained five-membered cyclic CDP (105°).[14] The P–C bond of **3** (1.667 Å) is slightly shorter compared to the precursor **2** (1.690 Å), but is longer than those of CDPs (1.549–1.635 Å).[15] In contrast, the C–S bond length remains almost unchanged ($\Delta_{C-S} = 0.003$ Å).

To gain more insight into the electronic structure of the molecule, DFT calculations were performed on **3**. The geometry optimization at the M05-2X/6-31+G(d,p) level closely reproduced the X-ray structure (P–C 1.671 Å, C–S 1.692 Å; P-C-S 110.7°; Figure 1).[16] The Wiberg bond index for C1–S (1.214) is lower than for P–C1 (1.415). The electronic structure has been analyzed by means of the natural bond orbital (NBO) method, which localizes a C1 lone pair nearly in the P-C-S plane ($n\sigma_C$), forming a dihedral angle of about 160° with the sulfur lone pair, and an out-of-plane lone pair $n\pi_C$. The geometry of the molecule allows stabilization of both carbon lone pairs through interactions with σ^*(S–C4,5), σ^*(P–C3), and σ^*(P–N) orbitals as determined by second-order perturbation analysis of donor–acceptor interactions in the NBO basis. In particular, $n\sigma_C$ interacts with σ^*(P–N1) (16.7 kcal mol^{-1}) whereas $n\pi_C$ interacts with σ^*(S–C5) (31.4 kcal mol^{-1}), σ^*(P–N2) (28.5 kcal mol^{-1}), and σ^*(P–N1) (20.8 kcal mol^{-1}), indicating the much less stabilized $n\sigma_C$ by the ylidic interaction with adjacent substituents compared with $n\pi_C$. Meanwhile, the $n\sigma_C$ has a significantly enhanced s character (42.5 %), indicating its hybridization close to sp. In contrast, the out-of-plane lone pair $n\pi_C$ has a 100 % p character. These results demonstrate that the $n\sigma_C$ is efficiently stabilized by the strongly bent structure rather than by the ylidic interactions. Indeed, the energy difference between the bent and the linear structures was also calculated ($\Delta E_{P-C-S(110°-180°)}$: ca. 10 kcal mol^{-1}) and found to be much larger than those for CDPs **IIIa** ($\Delta E_{P-C-P(136°-180°)}$: 0.3–3.0 kcal mol^{-1}).[5b]

The next logical step was to compare and contrast the reactivity of bis(ylide) **3** and CDPs especially Wittig-type reactions. The bis(ylide) **3** reacts with carbonyl compounds exclusively on the phosphonium ylide side. Indeed, the reaction of **3** with trifluoroacetophenone cleanly forms oxaphosphetane **4a**, as indicated by the ^{31}P NMR signal, which appears at high field ($\delta = -33.0$ ppm), which is typical for pentacoordinate phosphoranes.[17] In the ^{13}C NMR spectrum, the ylidic carbon of **4a** appears at 41.0 ppm as a doublet with a large coupling constant of 176.7 Hz. It is interesting to note that the sulfonium ylide function remains intact even in the presence of excess ketone. Like oxaphosphetanes derived from CDPs **IIIa**,[18] compound **4a** shows high thermal stability. In fact, its decomposition, associated with the elimination of the phosphine oxide, requires thermal activation (3 h at 160 °C). Owing to the harsh conditions, the reaction is not selective and a complicated mixture of unidentified products was formed, although only one peak corresponding to the phosphine oxide ($\delta = 24.5$ ppm) in the ^{31}P NMR spectrum was observed. In contrast, the oxaphosphetane **4b**, obtained from **3** and benzaldehyde, is more reactive. It slowly reacts with another equivalent of aldehyde to give benzyl benzoate **5**, and regenerate bis(ylide) **3**. This catalytic hydroacylation reaction probably proceeds via a hydride transfer from the electron-rich oxaphosphetane **4b** to benzaldehyde, leading to the transient ion pair **6**. Subsequent nucleophilic attack of the anion gives rise to the benzyl benzoate **5**, and regeneration of bis(ylide) **3** (Scheme 2). Similar hydroacylation reactions catalyzed by N-heterocyclic carbenes (NHC) have already been described.[19] This catalytic hydroacylation reaction is probably the reason that no Wittig reactions between CDPs **IIIa** and aldehydes have been reported.[20]



Scheme 2. Synthesis of oxaphosphetanes **4a**,**b** and the reaction of **4b** with benzaldehyde.

In the solid-state structure of oxaphosphetane **4a** (Figure 2), the pentacoordinate phosphorane has oxygen and nitrogen atoms at the apical position. The most striking features are the short P–C1 (1.758 Å) and elongated P–O bonds (1.837 Å) compared with those of classical oxaphosphetanes **7** derived from phosphonium ylides (P–C 1.820 Å, P–O 1.745 Å).[21] The alteration of bond lengths in **4** relative to **7** is certainly caused by the additional negative charge on the carbon atom in **4**, which is delocalized towards the phosphorane center (**4′** in Scheme 3). As a consequence, the P–C bond is strengthened, and the P–O bond is weakened, which could explain the increased reluctance of **4** to undergo a Wittig-type reaction as for **7**.[7]

Taking into account the electronic features of **4a**, we considered the use of a Lewis acid catalyst to accelerate the Wittig reaction. Indeed, the formation of adduct **8** by

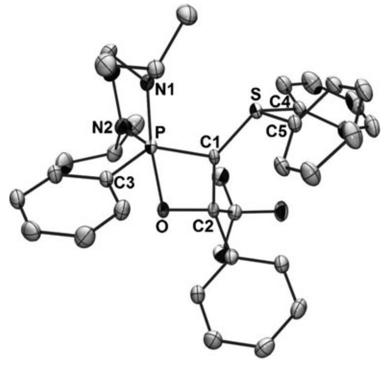
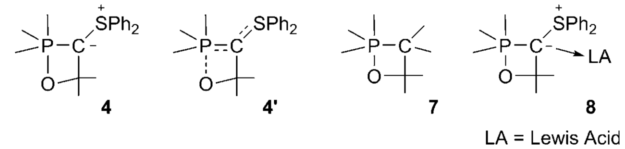
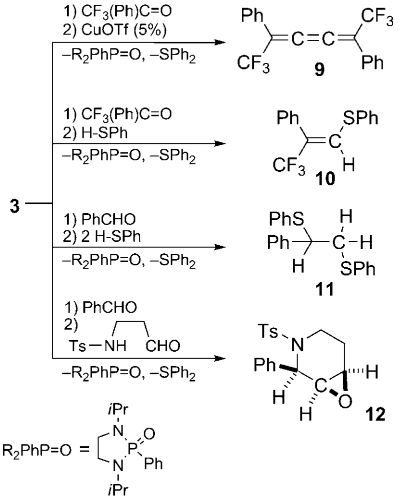


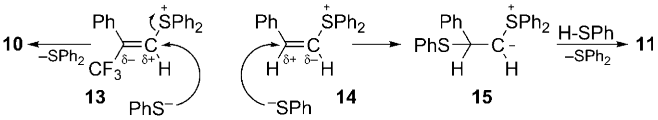
Figure 2. Molecular structure of **4a**. Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: P–C1 1.758(2), S–C1 1.669(2), C1–C2 1.527(3), P–O 1.8372(14), C2–O 1.415(2), S-C1-P 124.98(11), P-C1-C2 95.74(13), C1-C2-O 94.15(14), C1-P-O 73.65(8), C2-O-P 96.43(11), S-C1-C2 137.61(15).



Scheme 3. Representation of oxaphosphetanes **4**, **4′**, **7**, and **8**.



Scheme 4. Reactions of P,S-bis(ylide) **3**.



Scheme 5. Reactivity of transient vinylsulfonium species **13** and **14**.

complexation of the remaining lone pair on the central carbon atom should destabilize the system (Scheme 3). Therefore, the reaction of bis(ylide) **3** with trifluoroacetophenone was performed in the presence of a catalytic amount of copper(I) triflate (5%). The reaction proceeds smoothly at room temperature with elimination of phosphine oxide and diphenylsulfide, and involves both ylide functions of **4a**. The formation of allene **9** can be rationalized by dimerization of a transient vinylidene.[22] Probably, after the first Wittig reaction, the resulting unsaturated sulfonium ylide decomposes into the corresponding vinylidene carbene, catalyzed by copper(I)[23,24] (Scheme 4).

The Wittig reaction can also be triggered by weak acid species, such as thiophenol. The reaction goes to completion almost immediately upon the addition of thiophenol (1 equiv) to **4a** at room temerpature, and quantitatively affords the vinyl phenyl sulfide **10** as a result of the formal insertion of the vinylidene carbene into the S–H bond (Scheme 4). Furthermore, this efficient triggering system can also be applied in the case of benzaldehyde. However, in contrast to the previous case, the reaction consumes two equivalents of thiophenol to give the α,β-disulfide **11**. The different reaction patterns observed between trifluoroacetophenone and benzaldehyde can be rationalized by the inverted polarization of the vinylsulfonium intermediate **13** owing to the presence of the strong electron-withdrawing trifluoromethyl substituent (Scheme 5). Therefore, in the case of **13**, the thiolate nucleophilic attack occurs at the α carbon, affording **10**, whilst vinylsulfonium **14** undergoes the nucleophilic attack at the β carbon. This reaction leads to the corresponding sulfonium ylide **15** which reacts with another equivalent of thiophenol to give the bis(adduct) **11**.

Of particular interest, bis(ylide) **3** reacts with benzaldehyde (1 equiv) and *N*-tosyl-γ-amino-aldehyde (1 equiv) diastereoselectively, affording the *cis*-fused bicyclic epoxide **12** (Scheme 4). This result is in good agreement with the transient formation of a sulfonium ylide, which undergoes an intramolecular epoxidation reaction.[25] This is, to the best of our knowledge, the first reaction of bis(ylide)s as an atomic carbon source, thus allowing the formation of a stereogenic quaternary carbon center.

In summary, we have successfully synthesized and characterized a stable mixed P,S-bis(ylide), which can be involved in Wittig-type reactions with carbonyl derivatives. Interestingly, Lewis acids efficiently promote the decomposition of the transiently formed oxaphosphetanes, and this cumulenic bis(ylide) can be used in multicomponent reactions. Clearly, P,S-bis(ylide) **3** behaves as an unsymmetrical atomic carbon source, allowing a direct creation of quaternary carbon centers. Given the wide variety of known ligands, the results shown here should be a major breakthrough, thereby allowing the preparation of a large variety of carbon(0) complexes as asymmetric single atomic dicarbene sources with tunable properties simply by changing the combination of ligands.

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