

= Persistent carbene =

A persistent carbene ( also known as stable carbene ) is a type of carbene demonstrating particular stability . The best known examples and by far largest subgroup are the N heterocyclic carbenes ( NHC ) ( sometimes called Arduengo carbenes ) , for example diaminocarbenes with the general formula  $(R_2N)_2C:$  , where the ' R 's are typically alkyl and aryl groups . The groups can be linked to give heterocyclic carbenes , such as those derived from imidazole , imidazoline , thiazole or triazole .

Traditionally carbenes are viewed as so reactive that were only studied indirectly , e.g. by trapping reactions . This situation has changed dramatically with the emergence of persistent carbenes . Although they are fairly reactive substances , i.e. , undergoing dimerization , many can be isolated as pure substances .

Persistent carbenes can exist in the singlet or the triplet states with the singlet state carbenes being more stable . The relative stability of these compounds is only partly due to steric hindrance by bulky groups . Some singlet carbenes are thermodynamically stable in the absence of moisture and ( in most cases ) oxygen , and can be isolated and indefinitely stored . Others are not thermodynamically stable and will dimerise slowly over days . The less stable triplet state carbenes have half lives measured in seconds , and therefore can be observed but not stored .

= = History = =

= = = Early evidence = = =

In 1957 , Ronald Breslow proposed that a relatively stable nucleophilic carbene , a thiazol 2-ylidene derivative , was involved in the catalytic cycle of vitamin B1 ( thiamine ) that yields furoin from furfural . In this cycle , the vitamin 's thiazolium ring exchanges a hydrogen atom ( attached to carbon 2 of the ring ) for a furfural residue . In deuterated water , the C2 proton was found to rapidly exchange for a deuteron in a statistical equilibrium .

This exchange was proposed to proceed via intermediacy of a thiazol 2-ylidene . In 2012 the isolation of the so called Breslow intermediate was reported .

In 1960 , Wanzlick and co workers conjectured that carbenes derived from dihydroimidazol 2-ylidene were produced by vacuum pyrolysis of the corresponding 2-trichloromethyl dihydroimidazole compounds with the loss of chloroform . They conjectured that the carbene existed in equilibrium with its dimer , a tetraaminoethylene derivative , the so called Wanzlick equilibrium . This conjecture was challenged by Lemal and co workers in 1964 , who presented evidence that the dimer did not dissociate ; and by Winberg in 1965 . However , subsequent experiments by Denk , Herrmann and others have confirmed this equilibrium , albeit in specific circumstances .

= = = Isolation of persistent carbenes = = =

In 1970 , Wanzlick 's group generated imidazol 2-ylidene carbenes by the deprotonation of an imidazolium salt . Wanzlick as well as Hoffmann , proposed that these imidazole based carbenes should be more stable than their 4,5-dihydro analogues , due to Hückel type aromaticity . Wanzlick did not however isolate any imidazol 2-ylidene , but their coordination compounds with mercury and isothiocyanate :

In 1988 , Bertrand and others isolated phosphinocarbene . These species can be represented as either a 3-phosphinocarbene or 5-phosphaacetylene :

These compounds were called " push pull carbenes " in reference to the contrasting electron affinities of the phosphorus and silicon atoms . They exhibit both carbenic and alkynic reactivity . An X-ray structure of this molecule has not been obtained and at the time of publication some doubt remained as to their exact carbenic nature .

In 1991, a stable, isolated, and crystalline diaminocarbene, which can be represented as a carbene or a nitrogen carbon ylide, was obtained by Arduengo and co-workers, by deprotonation of an imidazolium chloride with a strong base:

This carbene, the forerunner of a large family of carbenes with the imidazol-2-ylidene core, was found to be indefinitely stable at room temperature (in the absence of oxygen and moisture), and melted at 240–241 °C without decomposition. Another interesting chemical property of this ylidic compound was a characteristic resonance in the <sup>13</sup>C NMR spectrum at 211 ppm for the carbenic atom. The X-ray structure revealed longer N–C bond lengths in the ring of the carbene than in the parent imidazolium compound, indicating that there was very little double bond character to these bonds.

The first air-stable ylidic carbene, a chlorinated member of the imidazol-2-ylidene family, was obtained in 1997.

In 2000, Bertrand obtained additional carbenes of the phosphanyl type, including (phosphanyl) (trifluoromethyl) carbene, stable in solution at -30 °C and a moderately stable (amino) (aryl) carbene with only one heteroatom adjacent to the carbenic atom.

== Factors affecting stability of heteroatom-stabilized carbenes ==

The stability of Arduengo carbenes was initially attributed to the bulky N-adamantyl substituents, which prevents the carbene from dimerising due to steric hindrance. However, Arduengo's group later obtained an imidazol-2-ylidene in which the N-adamantyl groups were replaced with methyl groups, showing that steric hindrance was not the predominant stabilising factor. Instead imidazole-2-ylidenes are thermodynamically stable.

It had been also conjectured that the double bond between carbons 4 and 5 of the imidazolium ring backbone, which gave aromatic character to that system, was important for the carbene's stability. This conjecture was disproved in 1995 by Arduengo's group, who obtained a derivative of dihydroimidazol-2-ylidene, lacking the double bond. The thermodynamical stability in this compound, and the role of steric protection in preventing dimerisation, has been a topic of some dispute.

The first acyclic persistent carbene was reported in 1996, thus showing that a cyclic backbone was not necessary for their stability. Unlike the cyclic derivatives, the acyclic carbenes are flexible with respect to rotation of the bonds to the carbenic atom. By measuring the barrier to rotation of these bonds, the extent of their double bond character could be measured, and the ylidic nature of this carbene could be determined. Like the cyclic diaminocarbenes, unhindered variants tend to dimerise.

Until 1997, all stable carbenes were stabilized by two nitrogen centers bound to the carbenic atom. This pattern was broken in 1997–1998 with the synthesis of a thiazol-2-ylidene derivative by Arduengo's group and an aminothiocarbene and an aminooxycarbene. In these stable compounds, the carbenic atom lies between a nitrogen atom and either a sulfur or oxygen atom:

However, these carbenes are not thermodynamically stable as decomposition and dimerisation have been observed for unhindered examples.

A more radical development was the synthesis in 2006 of bis(diisopropylamino) cyclopropenylidene by Bertrand's group. In this compound, which is stable at room temperature, the carbene atom is connected to two carbon atoms, in a three-member ring that retains the aromaticity and geometry of the cyclopropenylidene ring. This example demonstrated that the presence of heteroatoms next to the carbene is not necessary for stability, either.

== Classes of stable carbenes ==

The following are examples of the classes of stable carbenes isolated to date:

== Imidazol-2-ylidenes ==

The first stable carbenes to be isolated were based on an imidazole ring, with the hydrogen in carbon 2 of the ring (between the two nitrogen atoms) removed, and other hydrogens replaced by various groups. These imidazol-2-ylidenes are still the most stable and the most well studied and understood family of persistent carbenes.

A considerable range of imidazol-2-ylidenes have been synthesised, including those in which the 1,3-positions have been functionalised with alkyl, aryl, alkyloxy, alkylamino, alkylphosphino and even chiral substituents:

In particular, substitution of two chlorine atoms for the two hydrogens at ring positions 4 and 5 yielded the first air-stable carbene. Its extra stability probably results from the electron-withdrawing effect of the chlorine substituents, which reduce the electron density on the carbon atom bearing the lone pair, via induction through the sigma backbone.

Molecules containing two and even three imidazol-2-ylidene groups have also been synthesised.

Imidazole-based carbenes are thermodynamically stable and generally have diagnostic  $^{13}\text{C}$  NMR chemical shift values between 210–230 ppm for the carbenic carbon. Typically, X-ray structures of these molecules show N–C–N bond angles of 101–102°.

== Triazol-5-ylidenes ==

Another family of persistent carbenes are based on the 1,2,4-triazole ring, with the unfilled orbitals in carbon 5 of this ring. The triazol-5-ylidenes pictured below were first prepared by Enders and co-workers by vacuum pyrolysis through loss of methanol from 2-methoxytriazoles. Only a limited range of these molecules have been reported, with the triphenyl substituted molecule being commercially available.

Triazole-based carbenes are thermodynamically stable and have diagnostic  $^{13}\text{C}$  NMR chemical shift values between 210–220 ppm for the carbenic carbon. The X-ray structure of the triphenyl substituted carbene above shows an N–C–N bond angle of ca. 101°. The 5-methoxytriazole precursor to this carbene was made by the treatment of a triazolium salt with sodium methoxide, which attacks as a nucleophile. This may indicate that these carbenes are less aromatic than imidazol-2-ylidenes, as the imidazolium precursors do not react with nucleophiles due to the resultant loss of aromaticity.

== Other diaminocarbenes ==

Carbenes that formally derive from imidazol-2-ylidenes by substitution of sulfur, oxygen, or other chalcogens for both nitrogen atoms are expected to be unstable, as they have the potential to dissociate into an alkyne ( $\text{R}_1\text{C}\equiv\text{CR}_2$ ) and a carbon dichalcogenide ( $\text{X}_1=\text{C}=\text{X}_2$ ). The two families above can be seen as special cases of a broader class of compounds which have a carbenic atom bridging two nitrogen atoms. A range of such diaminocarbenes have been prepared principally by Roger Alder's research group. In some of these compounds, the N–C–N unit is a member of a 5 or 6 membered non-aromatic ring, including a bicyclic example. In other examples, the adjacent nitrogens are connected only through the carbenic atom, and may or may not be part of separate rings.

Unlike the aromatic imidazol-2-ylidenes or triazol-5-ylidenes, these carbenes appear not to be thermodynamically stable, as shown by the dimerisation of some unhindered cyclic and acyclic examples. Studies suggest that these carbenes dimerise via acid catalysed dimerisation (as in the Wanzlick equilibrium).

Diaminocarbenes have diagnostic  $^{13}\text{C}$  NMR chemical shift values between 230–270 ppm for the carbenic atom. The X-ray structure of dihydroimidazole-2-ylidene shows a N–C–N bond angle of ca. 106°, whilst the angle of the acyclic carbene is 121°, both greater than those seen for imidazol-2-ylidenes.

=== Heteroamino carbenes ===

There exist several variants of the stable carbenes above where one of the nitrogen atoms adjacent to the carbene center ( the 2 nitrogens ) has been replaced by an alternative heteroatom , such as oxygen , sulfur , or phosphorus . :

In particular , the formal substitution of sulfur for one of the nitrogens in imidazole would yield the aromatic heterocyclic compound thiazole . A thiazole based carbene ( analogous to the carbene postulated by Breslow ) has been prepared and characterised by X @-@ ray crystallography . Other non @-@ aromatic aminocarbenes with O , S and P atoms adjacent ( i.e. alpha ) to the carbene centre have been prepared , e.g. thio- and oxy @-@ iminium based carbenes have been characterised by X @-@ ray crystallography .

Since oxygen and sulfur are divalent , steric protection of the carbenic centre is limited especially when the N @-@ C @-@ X unit is part of a ring . These acyclic carbenes have diagnostic <sup>13</sup>C NMR chemical shift values between 250 ? 300 ppm for the carbenic carbon , further downfield than any other types of stable carbene . X @-@ ray structures have shown N @-@ C @-@ X bond angles of ca . 104 ° and 109 ° respectively .

=== Non @-@ amino carbenes ===