4.3 Acetylenes as Carbene Precursors

Metal carbenes are discussed as intermediates in the reaction of acetylenes with Pt(II) or Au(I/III). The reactivity observed is often similar to the one expected from a putative "mesomeric dicarbene structure".

\[
\begin{align*}
\text{R} & \quad \text{Cl}_2\text{Pt} & \quad \text{Cl}_2\text{Pt} & \quad \text{Cl}_2\text{Pt} & \quad \text{Cl}_2\text{Pt} \\
\text{R} & \quad \text{R} & \quad \text{R} & \quad \text{R} & \quad \text{R}
\end{align*}
\]

\[\text{OH} \quad \text{OH} \quad \text{OH} \quad \text{OH} \quad \text{OH}\]

\[\text{JACS 2004, 126, 8654.}\]
Similar to carbenes, vinylidene carbenes are accessible by α-elimination. These species undergo similar reactions as observed for carbenes, i.e. cyclopronanation, rearrangements, or C-H-insertions. Recall these classic reactions:
Corey-Fuchs reaction:

\[ R^1\text{C}R^2\xrightarrow{\text{CBr}_4, \text{PPh}_3} R^1\text{C}R^2\text{Br} \xrightarrow{\text{BuLi}} R^1\text{C}R^2\text{Li} \xrightarrow{} R^1\equiv R^2 \]

Bestmann reagent:

\[ \text{MeC=NP(OEt)_2} \xrightarrow{\text{K}_2\text{CO}_3, \text{MeOH}, -78 \degree\text{C}} \text{N}_2 \xrightarrow{} \text{N}_2\text{C}R \xrightarrow{} R^1\equiv R^2 \]

*Synlett 1996, 521.*
Besides undergoing sigmatropic rearrangements vinylidenes often participate in C-H insertions:

\[ \text{Gilbert, JOC 1983, 5251.} \]
NaSO$_2$Ar, CH$_2$Cl$_2$, 20 °C

**conjugate addition**

63%

Vinylidene carbene can be obtained at high temperatures
Via [1,2] H-shift at high temperature

4.5 CH-insertions

Highly valuable conversion that do not depend on "classic" functional groups. Selective C-H functionalization is the ideal transformation in organic synthesis. In the ideal case it allows to shorten reaction steps reduce side products.

Usually diazo-compounds are the most common carbenoids precursors. Used in the presence of a transition metal (most common Rh) and a ligand.
Reactivity of diazo-compounds change according to substitution:

Electrophilic Character of carbenoid

Stability toward carbenoid formation

Donor/Acceptor

Acceptor

Acceptor/Acceptor

$\text{EWG} = \text{CO}_2\text{R, COR, NO}_2, \text{PO(OR)}_2, \text{SO}_2\text{R}$

$\text{EDG} = \text{aryl, vinyl, alkynyl, heteroarylyl}$

Selectivity in intermolecular C-H insertion
Lee and coworkers recently conducted a study that sheds light on the inherent selectivity of intramolecular C-H insertions of vinylidenes. Vinylidenes were generated from ketones upon exposure to lithiated TMS-diazomethane.

(JACS 2009, 131, 8413.)
90% single isomer

74% single isomer

96% 10/1 with regio isomer
Obviously an endo-cyclic oxygen drastically activates the adjacent C-H bond. In fact it activates it better than a phenyl group.

Stereoelectronic effects seem to play an important role:
It was hypothesized that the axial C-H adjacent to the oxygen in the ring is "activated", i.e. more electron rich, due to interaction of \( \eta_{\text{pO}} \) with C-H \( \sigma^* \). In contrast the equatorial H at the same position is desactivated because of the electron withdrawing effect of O.

Further reading:


Carbenes and metal carbenoids likewise undergo C-H insertion. Note the general preference for formation of a 5-membered ring. \(\textit{Taber, JACS 1985, 196}\)

However, 6-membered rings can be formed, as seen in Du Bois’ synthesis of tetrodotoxin \(\textit{JACS 2003, 11510}\)
Asymmetric versions have been described, amongst others by Davies

*(JACS 1997, 9075)*
Nitrene insertion has also been observed. Thereby the nitrene is mostly generated by oxidation of a carbamate or sulfamate. Note that sulfamates preferentially react to give the 6-membered ring.

(Du Bois, *ACIE* 2001, 598);
(Du Bois, *JACS* 2001, 123, 6935)
(Du Bois, *JACS* 2002, 124, 12950)

presumably via:
**Intramolecular** C-H insertions proceed under retention of configuration. Normally, 5-membered rings are formed with electron rich C-H bonds being more reactive than electron poor bonds. Note that cyclopropanation usually outcompetes C-H insertion.

*(Davies, Beckwith, *Chem. Rev.* **2003, 103, 2861)*

**Intermolecular** C-H insertions are certainly extremely useful reactions. However, these reactions are challenging due to low selectivity for specific C-H bonds and cyclopropanation being generally preferred over C-H insertion.
Fine-tuning of the catalyst can be a remedy:
The mechanism of these C-H insertions is being disputed but it is believed to proceed in a concerted, asynchronous fashion, involving a 3-centered transition state.

Intermolecular C-H insertion preferentially occurs at sites that can stabilize an intermediate positive charge, \textit{i.e.} electron rich C-H bonds, \textit{i.e.} \(\alpha\) to heteroatoms, in allylic or benzylic positions. Note that cyclopropanation usually outcompetes C-H insertion but that the correct choice of catalyst can avoid cyclopropanation.

See review: (Davies, Loe, \textit{Synthesis} 2004, 2595)