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The Stereochemistry of Addition of an Alkylcarbene[1]

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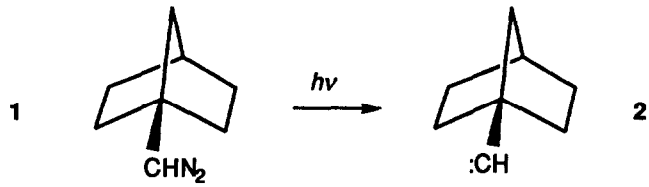
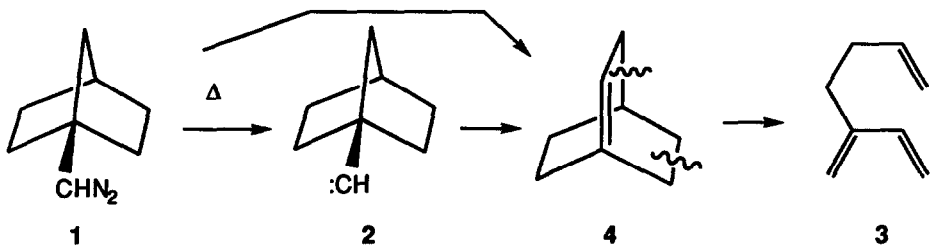
Abstract: 1-Norbornylcarbene can be intercepted through a stereospecific addition to alkenes.

Alkylcarbenes have a bad reputation. They are alleged to be difficult to study as they escape scrutiny through rapid intramolecular reactions, usually carbon-hydrogen and carbon-carbon insertions.[2] Accordingly, many of the classical experiments of carbene chemistry have not been done with these intermediates. For example, there appears to be no example of a reliable measure of the stereochemistry of addition of a simple monoalkylcarbene. There is now a body of evidence that shows that their bad press may be undeserved. Building on early work by Frey, Stevens, and Shechter,[3] Platz and his collaborators[4] and others[5] have shown that reactions of excited states of aziridines[4,5] and diazo compounds[4d] complicate what has long been assumed to be intramolecular carbene chemistry. We have used the phenylcarbene rearrangement to generate carbenes unequivocally and showed that the apparent chemistry of thermally generated carbenes also includes reactions of diazo compounds.[6] The difficulty in isolating products of intermolecular reactions of alkylcarbenes is the consequence of low efficiency in forming the carbenes, not necessarily the rapid intramolecular reactions.[4] Alkylcarbenes are likely to be much more accessible than previously thought, provided that a general, non-diazo precursor can be found. Although we have not yet solved that problem, we have paused in the midst of a study of ring expansion reactions of 1-norbornyldiazomethane (**1**) to look at the stereochemistry of addition of a monoalkylcarbene, **2**.

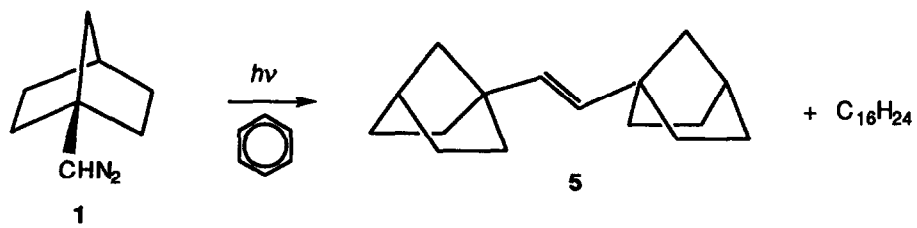
Compound **1** was made through gentle heating (90-100 °C) in a Kugelrohr apparatus of the related tosylhydrazone salt, itself formed from the known bicyclo[2.2.1]-1-carboxaldehyde.[7,8] Diazo compound **1** was obtained as an unstable orange-yellow neat liquid (IR 2043 cm^{-1}) and was immediately dissolved in solvent prior to use.



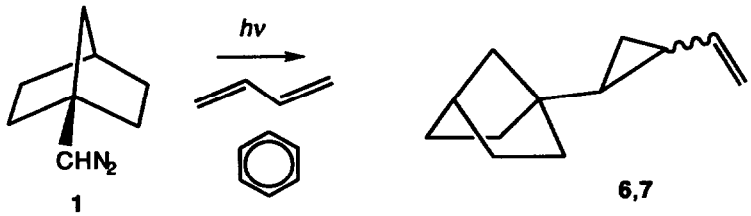
Diazo compound **1** is a useful carbene precursor, but not ideal. Platz has shown that carbon-hydrogen bond migration is far easier than carbon-carbon bond migration in diazo compound excited states.[4d] Although intramolecular insertion reactions should be minimized in the excited state of **1**, a diazo compound in which hydrogen migration in the excited state is improbable, rearrangement of carbon is certainly possible. Years ago, we used flash vacuum pyrolysis of a tosylhydrazone salt to generate what we thought was **2**. We isolated triene **3**, and attributed its formation to the reverse Diels-Alder reaction of **4**, itself formed by ring expansion of carbene **2**.[8] In fact, it is possible that **2** is not the sole, or even predominent source of **4**, as diazo compound **1** may well be involved.



Photolysis of **1** in benzene solution leads to substantial ring expansion, as the isolation of several products of the formula $C_{16}H_{24}$ proves. We have isolated small amounts of the alkene **5** (stereochemistry not yet known, but probably trans as shown) as well as several dimers not containing hydrogens attached to double bonds. These are likely the result of 2 + 2 cycloadditions of bridgehead alkene(s) and we hope to report on these in detail later.



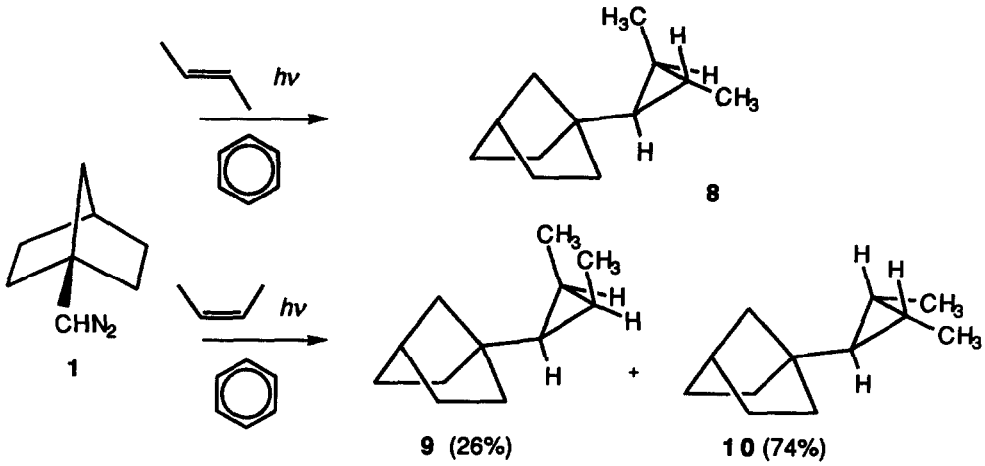
When **1** is irradiated in a solution of 1,3-butadiene in benzene (2.7 mmol/g), the dimers (~15% relative yield) are accompanied by about 85% of two cyclopropanes, **6** and **7**. In both **6** and **7** the presence of a $CH{=}CH_2$ group is unmistakable in the ^1H NMR spectrum. Moreover, the single bridgehead hydrogen appears as a broad singlet at $\delta = 2.07$ and 2.08, and two cyclopropyl hydrogens are visible as multiplets centered at $\delta = 0.5$, 0.9 and 0.4, 0.62, far upfield of the cage hydrogens in each compound.



1 **6,7**

However, the formations of **6** and **7** are not the result of carbene chemistry. When **1** is allowed to stand in the dark at 25 °C in 1,3-butadiene and the solution subsequently analyzed by GC/MS, cyclopropanes **6** and **7** are also formed. Pyrazoline formation followed by decomposition in the injector port of the gas chromatograph must be the main source of **6** and **7**.

This result shows the danger of attributing cyclopropane formation to carbenes without control reactions. Fortunately, the 2-butenes are far less prone to pyrazoline formation than is 1,3-butadiene. Analysis of solutions of **1** in *cis*- and *trans*-2-butene after 2 hours in the dark at 25 °C by GC/MS reveals only traces of compounds of the proper mass for a 1:1 adduct of **2** and the butene. By contrast, irradiation of solutions of **1** in *trans*- or *cis*-2-butene for 2 hours at 25 °C leads to large amounts of adducts **8** or **9** and **10**, respectively, along with even larger amounts of several dimers of **2**. Products of reaction with benzene were not detected, and only traces of compounds of the mass appropriate for products of carbon-hydrogen insertion into the butenes were revealed by GC/MS. The trans adduct **8** is distinguished from **9** and **10** by the presence of a pair of methyl doublets ($\delta = 1.01$, 1.08, $J = 6$ Hz in each case) in the ^1H NMR spectrum. The cis, syn compound **9** has a lone methyl doublet at $\delta = 1.04$, $J = 6$ Hz, and the cis, anti compound **10** has a single methyl doublet at $\delta = 0.98$, $J = 6$ Hz. Compounds **9** and **10** are differentiated by the relatively small coupling constant between the tertiary cyclopropyl hydrogen and the other two cyclopropyl hydrogens in the anti compound **10** ($J = 5.5$ Hz), and the relatively large J in the syn compound **9** ($J = 9.0$ Hz). This compares well with values for cyclopropane itself in which the trans and cis coupling constants are 5.6 Hz, and 9.0 Hz respectively.[9] The stereospecificity of these reactions further argues against the intervention of pyrazolines, as such compounds are known to decompose thermally to give cyclopropanes with substantial loss of the stereochemical relationships present in the starting pyrazoline.[10]



Addition of **2** is stereospecific. We are able to resolve **8**, **9**, and **10** completely, and could detect 1% of cis compound **10** in the presence of **8** and much less of **8** in the presence of **9** and **10**. Thus the reacting state of this monoalkylcarbene is singlet. Of course this does not speak to the issue of the ground state of **2**, likely to be the triplet.

In sum, we have shown that monoalkylcarbene **2** is quite easily intercepted by alkenes and that a stereospecific addition takes place from the singlet state of the carbene.

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