Effect of Substitution on the Intramolecular 1,3-Dipolar Cycloaddition of Alkene Tethered Münchnones

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J. Org. Chem. 2007, 72, 1104

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Current Literature

March 3, 2007
The Münchnone

Münchnone (1,3-oxazolium-5-olate)

- 1,3-dipolar species
- Prepared from amido acids (activated by Ac₂O, DCC or Mukaiyama’s salt)
- May react inter- or intramolecularly with dipolarophiles (alkenes or alkynes)
- Three sites to tether a dipolarophile (R¹, R², R³) for intramolecular reactions


Gribble, G. W. In Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products; Padwa, A., Pearson, W. S., Eds; John Wiley & Sons: Hoboken, NJ, 2003; pp 681-755.
1,3-Dipolar Cycloadditions


1,3-Dipolar Cycloadditions

*Indolizidine-derived myrmicarin alkaloids*

Quinolizidine münchnone intermediate allows cycloaddition to occur

Scope of Featured Article

Hemiaminal opened to form stable zwitterion in paths B and C

First example of isolable iminium zwitterions
Synthetic Utility of Novel Intermediates

Reduction leads to substituted amino alcohols

Oxidation leads to substituted pyrroles

Addition to imine by internal or external nucleophile

Methodology may be used in pyrrole, pyrrolidine (n=1) or hydroindole scaffolds (n=2)
Path A: Dipolarophiles Tethered at Nitrogen

Intramolecular 1,3-dipolar cycloaddition using aliphatic nitrogen tether
Path B: Dipolarophiles Tethered at $\alpha$-Amino Position

First reported isolation of iminium zwitterionic products
Path C: Dipolarophiles Tethered at Amido Position

Activated alkenes do not work well as dipolarophiles when tethered at amido position

Münchnone formation confirmed by trapping intermediate with DMAD to form pyrrole

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Effects of Substitution on Münchnone

Using phenyl substituent increases reactivity and thermal stability of Münchnone
Effects of Substitution on Münchnone

Substituent has little impact on reactivity
Summary/Conclusions

- Two new reaction sequences have been developed that produce novel zwitterionic intermediates

- Münchnones are both activated and stabilized by conjugated substituents

- Starting materials can be easily prepared/purchased, making these convergent reaction sequences useful in specialized synthetic applications