Enantioselective Copper-Catalyzed [3+3] Cycloaddition of Azomethine Ylides with Azomethine Imines


[3+3] Cycloaddition of Azomethine Ylides with Azomethine Imines

Significance: With the use of a [3+3] cycloaddition the authors were able to generate biologically active hexahydro-8H-pyrazolo[1,2-a][1,2,4]triazin-8-one derivatives. In a highly diastereo- and enantioselective manner, azomethine ylides were reacted with azomethine imines in the presence of copper and ferrocenyl chiral P,N-ligands.

Comment: [3+3] And [3+4] cycloadditions with azomethine ylides are not as well known as their [3+2] counterparts. Pioneering work in the use of 1,3-dipolar [3+2] cycloadditions with azomethine ylides was made by the groups of Jørgensen (Angew. Chem. Int. Ed. 2002, 41, 4236) and Zhang (J. Am. Chem. Soc. 2002, 124, 13400). In the presence of LiBH₄ the product of the [3+3] adduct rearranged to an unexpected compound. This interesting molecule was formed as a single diastereomer, but was found to be racemic.

Selected examples:

- 86% yield, 96% ee, dr > 20:1
- 89% yield, 95% ee, dr > 20:1
- 77% yield, 91% ee, dr = 2:1
- 76% yield, 90% ee, dr > 20:1

Product derivatization:

- 31% yield, racemic
- 95% ee, 85% yield