Phosphoric Acid Diesters as Efficient Catalysts for Hydroaminations of Nonactivated Alkenes and an Application to Asymmetric Hydroaminations

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Hydroamination of Nonactivated Alkenes

Significance: A catalytic amount of Brønsted acid enables high yielding intramolecular hydroaminations of electronically unactivated alkenes with basic amines. Screenings identified phosphoric acid 1 as the most active catalyst for this cycloisomerization. Substrates with ether, nitro, ester, or chloro functionalities are tolerated. By using enantiomerically pure phosphoric acid (R)-1a the authors show an unprecedented example of a metal-free asymmetric hydroamination of nonactivated alkenes, albeit with modest selectivity (er = 58.5:41.5).

Comment: This intramolecular addition of an amine to a C-C double bond depicts a direct and atom-economical access to N-heterocycles, which are ubiquitous in natural products as well as biologically active compounds. Most organocatalytic additions of N-nucleophiles to olefins require activation of the alkene functionality. The observed effectiveness of this addition might be due to the intramolecular nature of this cycloisomerization. A screening of different enantiopure phosphoric acids might result in higher enantiomeric ratios.

Selected examples:

- 93% yield
- 85% yield
- 53% yield
- R = OMe, NO₂, CO₂Me or Cl
  95–97% yield
  er = 58.5:41.5