Cooperative Catalysis: Radical Addition to Olefins and Asymmetric Protonation

**Significance:** Jiang and co-workers report the enantioselective radical conjugate addition–protonation of N-aryl glycines to α-branched vinylazaarenes using a metal-free dual catalytic system (a photosensitizer and a chiral phosphoric acid). The corresponding products are obtained in high yields with good to excellent enantioselectivities, and the methodology is applied to the synthesis of the medicinal compound pheniramine.

**Comment:** Because α-amino acids are abundant, their use as starting materials for organic synthesis is desirable. In this report, N-aryl α-glycines undergo photooxidative decarboxylation and react further with highly activated olefins in a radical pathway followed by enantioselective protonation. While many examples are shown, the presented substrate scope is still limited to pyridine- and quinoline-containing substances.

**Proposed mechanism:**

- Photoreduction of the substrate
- Protonation
- Enantioselective conjugate addition

**Selected examples:**

- 87% yield, er = 97.3
- 83% yield, er = 94.6
- 69% yield, er = 96.5:3.5
- 95% yield, er = 96:4
- 83% yield, er = 95:4.5
- 76% yield (over two steps), er = 95:4.5

**Enantioselective protonation**

**Proposed mechanism:**

1. PMP deprotection
2. Reductive amination

**R2**

- (PMP = para-methoxyphenyl)
- 83% yield, er = 95.5:4.5
- 76% yield (over two steps), er = 95:4.5

**R2**

- (R)-pheniramine (antihistamine drug)

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