**Carbonyl-Catalyzed Biomimetic Asymmetric Mannich Reaction**

Significance: The Zhao group reports the activation of primary amines by carbonyls. Using an N-quaternized pyridoxal catalyst for the direct asymmetric Mannich reaction of glycinate with aryl \( N \)-diphenylphosphinyl imines, \( \alpha,\beta \)-diamino acid esters were obtained in good yields and excellent stereoselectivities.

Comment: Based on their recently developed chiral pyridoxal and pyridoxamine catalysts for transamination reactions (J. Am. Chem. Soc. 2016, 138, 10730), the authors developed a catalyst that activates primary amines through carbonyl catalysis. In contrast to other \( \alpha \)-functionalizations of primary amines, this fascinating catalysis strategy does not require protecting-group manipulation.

**Proposed reaction mechanism:**

- Reactants: Carbonyl catalyst (1 mol%), NaHCO\(_3\), CHCl\(_3\)-H\(_2\)O (1:1), 10 °C, 4–39 h
- Products: \( \alpha,\beta \)-diamino acid esters
- Conditions: 32 examples, 47–94% yield, dr from 17:1 to >20:1, er from 97:3 to 99.5:0.5

Selected examples:

<table>
<thead>
<tr>
<th>R = Ar, HetAr</th>
<th>90% yield</th>
<th>dr &gt; 20:1</th>
<th>er = 99.5:0.5</th>
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</thead>
<tbody>
<tr>
<td>Ph(\text{N}^+\text{Cl}^-\text{N}^+\text{Ph})</td>
<td>82% yield</td>
<td>dr &gt; 20:1</td>
<td>er = 97:3</td>
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<tr>
<td>Ph(\text{N}^+\text{Ph})</td>
<td>77% yield</td>
<td>dr &gt; 20:1</td>
<td>er = 99:1</td>
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<td>Ph(\text{N}^+\text{Ph})</td>
<td>67% yield</td>
<td>dr &gt; 20:1</td>
<td>er = 99:1</td>
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N\(\text{Me}^+\text{OH}^+\text{N}^+\text{Ph})

\(\text{Ph}_2\text{P(O)N}^+\text{NH}_2\)

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