Amine-Catalyzed Direct Vinylogous Michael Addition of Dienols to Enals

Significance: Xu and co-workers report a vinylogous Michael addition of acyclic alkyl and aryl allyl ketones to enals. The reaction is catalyzed by a chiral secondary amine (A) and a chiral hydrogen bond donor (B), which in combination enable the formation of the desired enones in moderate to excellent yields and regioselectivities, and with excellent enantioselectivities. The scalability of the reaction was proven in one experiment starting with 1.46 gram of phenyl allyl ketone.

Comment: While the application of catalyst A in combination with a ‘regular’ Bronsted acid or base (e.g., benzoic acid or DABCO) already furnished small amounts of desired product with excellent enantioselectivity, it required a second, anion-binding catalyst (B) to enhance the reactivity of the proposed \( \alpha,\beta \)-unsaturated iminium ion intermediate by ion pair separation and to shield the \( \alpha \)-position of the nucleophile, effecting the desired \( \gamma \)-selectivity. The concept of supramolecular iminium ion catalysis was previously reported by the same group (Angew. Chem. Int. Ed. 2012, 51, 12339).

Selected examples:

- \( \text{PhO} - \text{Ph} - \text{O} - \text{H} \) 88% yield \( \gamma/\alpha > 20:1 \) er = 97.5:2.5
- \( \text{MeO} - \text{PhO} - \text{H} \) 77% yield \( \gamma/\alpha = 15:1 \) er = 98:2
- \( \text{NO}_2 - \text{PhO} - \text{H} \) 92% yield \( \gamma/\alpha > 20:1 \) er = 97:3
- \( \text{HexO} - \text{PhO} - \text{H} \) 80% yield \( \gamma/\alpha = 5:1 \) er = 93:7
- \( \text{PhO} - \text{Ph} - \text{O} - \text{H} \) 45% yield \( \gamma/\alpha = 4:1 \) er = 97.5:2.5

Proposed reacting ion pair complex: