PROBING THE REACTIVITY OF α,β-UNSATURATED ACYL AMMONIUM INTERMEDIATES

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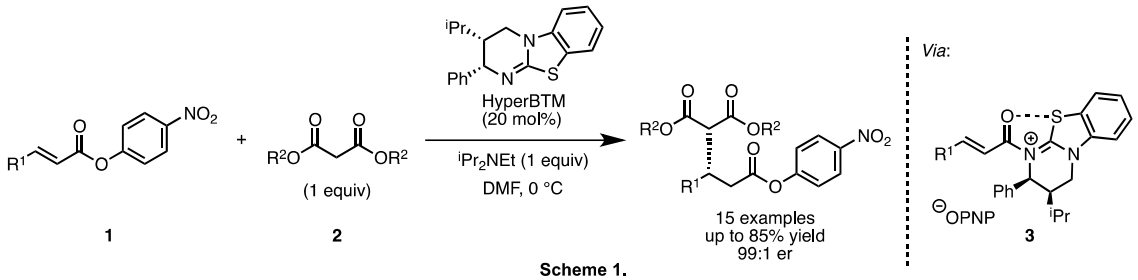
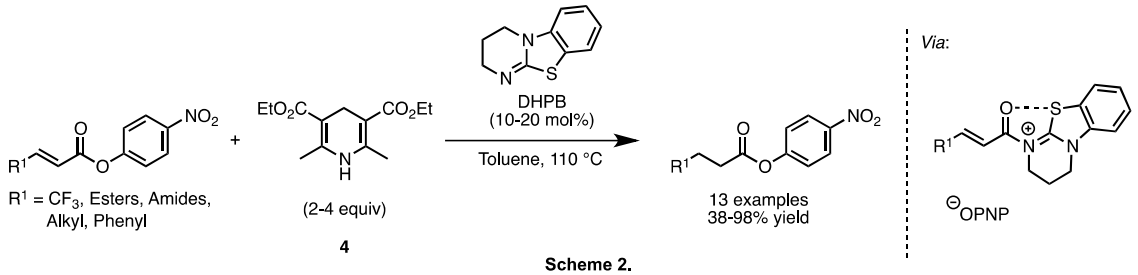
A new concept in α,β-unsaturated acyl ammonium catalysis was recently reported by our group that uses *para*-nitrophenoxide release from an α,β-unsaturated *para*-nitrophenyl ester substrate **1** to facilitate catalyst turnover.[1] In the proof of concept work we only showed the Michael addition of nitroalkanes to α,β-unsaturated *para*-nitrophenyl esters where the nitroalkane was used as the reaction solvent. Building on this precedent, a new method has been established for the enantioselective isothiourea-catalysed Michael addition of an expanded range of C-centred nucleophiles to α,β-unsaturated *para*-nitrophenyl esters, where only 1 equivalence of a malonate derivative **2** is required to give generally good yield and excellent enantioselectivity (Scheme 1). This reaction is proposed to proceed by addition of the malonate nucleophile to an α,β-unsaturated acyl ammonium intermediate **3**.[2] A variable-time normalization kinetic analysis has been applied to study the reaction kinetics for this process.



Scheme 1.

As an extension beyond the previous limitation of C-centred nucleophiles, a novel isothiourea-catalysed transfer hydrogenation of α,β-unsaturated *para*-nitrophenyl esters using a Hantzsch ester **4** as the hydride source has also been developed (Scheme 2). The synthetic utility of the process has been demonstrated on a range of α,β-unsaturated *para*-nitrophenyl esters using an achiral catalyst DHPB (13 examples, 38-98% yield). The transfer hydrogenation of β,β-disubstituted α,β-unsaturated *para*-nitrophenyl ester using the chiral catalyst HyperBTM can also lead to the hydrogenated products in moderate yield and with good enantioselectivity.



Scheme 2.

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[1] A. Matviitsuk, M. D. Greenhalgh, D. J. B. Antunez, A. M. Z. Slawin, A. D. Smith, *Angew. Chem*. Int. Ed., **2017**, 12282-12287.

[2] E. R. T. Robinson, C. Fallan, C. Simal, A. M. Z. Slawin, A. D. Smith, *Chem. Sci*., **2013**, 2193-2200.