

A METAL-LIGAND COOPERATIVE PATHWAY FOR OXA-MICHAEL ADDITIONS TO UNSATURATED NITRILES

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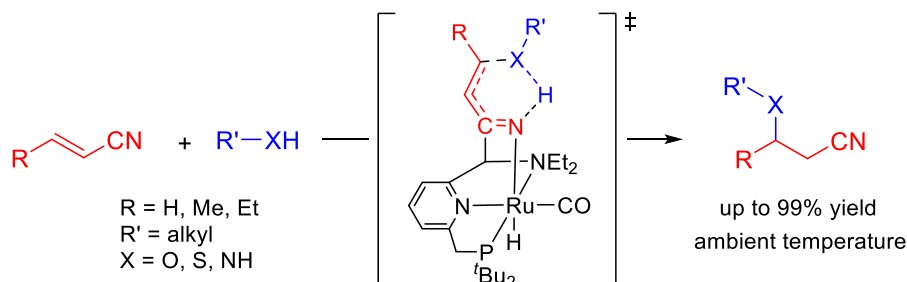
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Although conjugate addition of carbon nucleophiles to α,β -unsaturated substrates (Michael addition) is a powerful method for C-C bond formation, the analogous reaction with oxygen nucleophiles (oxa-Michael addition) to form C-O bonds is less straightforward.^[1] This is due to the low nucleophilicity of alcohols and the reversibility of the oxa-Michael addition. While catalytic methods have been developed using either strong bases (to generate a more reactive alkoxide nucleophile) or Lewis/Brønsted acids (to activate the Michael acceptor), these reactions are far from efficient, especially for challenging substrates such as β -substituted unsaturated nitriles.

Here we describe catalytic oxa-Michael additions of alcohols to butene- and pentenenitriles to give 3-alkoxyalkanenitriles in excellent yields under mild, additive-free conditions using a PNN Ru pincer complex (**1**) with a dearomatized backbone.^[2] The isolation of a catalytically competent Ru-dieneamido complex from the reaction between **1** and pentenenitrile in combination with DFT calculations supports a mechanism in which activation of the nitrile CN moiety via metal-ligand cooperativity is a key step.^[3] The nitrile-derived Ru-N moiety is sufficiently Brønsted basic to activate the alcohol and initiate conjugate addition of alkoxide to the α,β -unsaturated fragment in a concerted manner involving a 6-membered transition state (see scheme). These features allow the reaction to proceed at ambient temperature in the absence of external base. In addition, this new catalytic pathway using metal-ligand cooperativity leads to selective addition of alcohols over amines, and allows good yields to be obtained even for substrates containing base-sensitive functional groups.



1) C. F. Nising, S. Bräse, *Chem. Soc. Rev.* **2012**, 41, 988

2) C. Gunanathan, D. Milstein, *Chem. Rev.* **2014**, 114, 12024

3) S. Perdriau, D. S. Zijlstra, H. J. Heeres, J. G. de Vries, E. Otten, *Angew. Chem. Int. Ed.* **2015**, 54, 4236