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► **To cite this version:**

Alexandre Touron, Lucile Anthore-Dalio. Transfer hydroamination of O-formylated hydroxylamines derivatives. SCF 2023 - Congrès de la Société Chimique de France, Jun 2023, Nantes, France. . . cea-04237489

HAL Id: cea-04237489

<https://cea.hal.science/cea-04237489>

Submitted on 11 Oct 2023

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TRANSFER HYDROAMINATION OF O-FORMYLATED HYDROXYLAMINES DERIVATIVES

Alexandre TOURON,¹ Lucile ANTHORE-DALION¹

¹ Université Paris-Saclay, CEA, CNRS, NIMBE, 91191 Gif-sur-Yvette Cedex, France.
alexandre.touron@cea.fr, www.iramis.cea.fr

Keywords: Hydroamination; catalysis; synthetic methodology; hydroxylamines

Summary: C–N bond are present in many molecules from the pharmaceutical industry and the formation of this bond represents 35 % of all the reactions performed in this field.^[1] Usually, they are formed by *N*-alkylation, cross-couplings, or reductive amination. Another type of reaction is presenting an important interest, the hydroamination^[2] although overlooked. Indeed, despite being a powerful method to form C–N bonds, hydroamination is also limited by thermodynamic and kinetic effects such as a low difference of energy between reactants and products, or electrostatic repulsions. This reaction implies an amine^[3], and particularly an N–H bond which will be added across an unsaturated compound such as an alkene to form a C–N bond and a C–H bond with a perfect atom economy. Over the past years, *O*-acylated hydroxylamines^[4] or azanyl esters^[5] have also been used with alkenes and hydride donors to perform similar reactions.

We turned our interest toward developing a catalytic method to perform the hydroamination using *O*-formylated azanyl esters, without using hydride donor since the formate plays the role of a hydride donor. This reaction is, thus, a transfer hydroamination. Here, we use a linker, CO₂, to make the nitrogen more electrophilic and the hydrogen more nucleophilic. The N–O bond is also weaker than a C–N bond, therefore, a catalyst can easily be inserted in that bond and the loss of CO₂ allows to drive the equilibrium. This methodology allows us to perform hydroamination with CO₂ as the only stoichiometric waste and to avoid the electrostatic repulsions between the lone pair of the nitrogen and π-orbitals of the alkene.

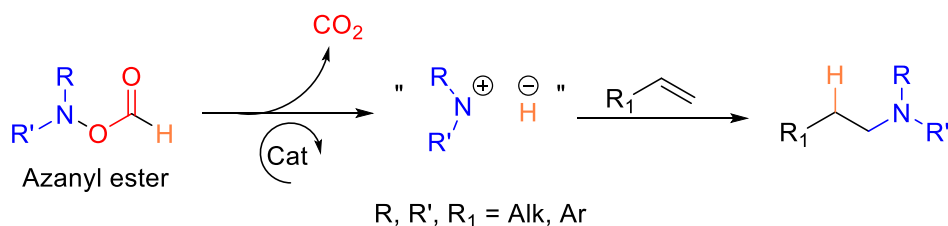


Fig. 1: Transfer hydroamination of azanyl esters

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