Electrochemically induced diastereoselective functionalization of *N*-acyloxazolidin-2-ones

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Chiral *N*-acyloxazolidin-2-ones are valuable intermediates and building blocks in asymmetric organic synthesis. In fact, they can be used for efficient diastereoselective C-C bond constructions in chiral enolate-derived reactions (such as alkylations, acylations, etc.) wherein the chiral auxiliary is both readily obtained and easily recovered after the desired bond construction has been achieved.[1]

These enolates are usually obtained by means of strong chemical bases in the presence of metallic cations, that can chelate the enolate structure, so that a diastereofacial selection can be induced.[2]

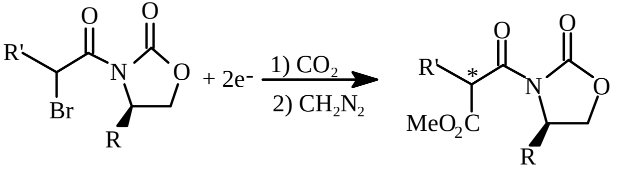
The formation of enolates is also possible by electrochemical means, reducing a proper carbon-halogen bond or using an electrogenerated base.

Electrochemistry can be a useful tool in organic synthesis, although electrochemical asymmetric synthesis is less developed than chemical, catalytic or enzimatic methods, and the development of electrochemical methodologies is currently of great interest due to the modern growing demand for efficient, selective and environmental safe procedure.

Here we wish to report our results in the field of enolate-derived reactions, *i.e.* diastereoselective carboxylation,[3] alkylation[4] and conjugate addition.[5]

The electrochemical reduction of chiral *N*-(2-bromoacyl)-oxazolidin-2-ones (Scheme 1) was carried out, under galvanostatic conditions (undivided cell, Pt cathode, Al anode), in solutions of THF-TBATFB with continuous CO_2 bubbling, at -20°C. At the end of the electrolysis (2 F/mol of brominated compound) the solution was concentrated, treated with acidic water and extracted with diethyl ether, that was treated with diazomethane to afford the desired carboxylic ester derivative in variable yields (62-90%) and diastereoselection (up to 83:17).

Scheme 1

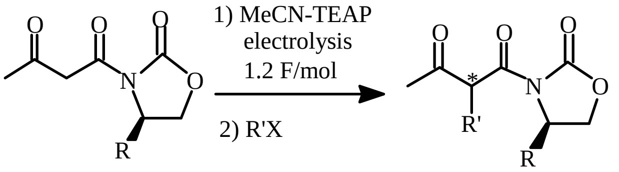


The effect of various electrochemical and physical variables (nature of the electrodes, number of Faradays per mol, solvent-supporting electrolyte system, temperature) on the yields of the carboxylate product and on the diastereoisomeric ratio will be discussed, along with the effect of the substituents R and R'.
Last, different chiral auxiliaries will be taken into account, comparing yields and d.r. with those obtained with oxazolidin-2-ones.

The electrochemical methodology has been further expoited for the deprotonation of β-dicarbonyl derivatives, containing enantiopure oxazolidinones as chiral inductors.

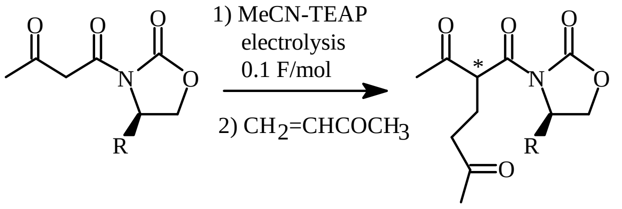
The cleavage of methylene-active C-H bond was easily performed by electrolysis in a solution of acetonitrile/ tetraethylammonium perchlorate, providing access to the corresponding enolate. The reactivity and stereoselectivity of the electrogenerated enolates have been studied both in alkylation (Scheme 2) and in conjugate addition processes (Scheme 3). In either case, with respect to the classical base- or metal-catalyzed reactions, the electrochemical methodology offered the advantage of milder condition, and short reaction times.

Scheme 2



Good to excellent yields and chemoselectivity were obtained by electrolysis under galvanostatic conditions, avoiding either metal or basic catalysts and, as a consequence, easy set-up and work-up procedures were established. Furthermore, as shown in Scheme 3, the conjugate addition process has been successfully accomplished by using only catalytic amount of electricity.

Scheme 3



Finally, regarding the stereochemical aspects, although in the absence of a chelating counterion, moderate to fairly good stereoselectivities were obtained by solely virtue of preexisting stereocenters in the enolate molecule.

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